ISSN: xxxx-xxxx
Bhoyar, P.K.,&Bapna, R.S., 35-42, 2024

Journal of Innovation and Invention in Pharmacy and Sciences (JIIPS)

Official Publication of Faculty of Pharmacy, Dr. A.P.J. Abdul Kalam University, Indore

A Review on Fast Dissolving Oral Solid Formulations

Pravin K. Bhoyar*, Revathi A. Gupta, Rajendra S.Bapna, Karunakar. Shukla, Mayank. Sahu

College of Pharmacy, Dr. APJ Abdul Kalam University,Indore (M.P.)

Email ID: - pravinbhoyar007@rediffmail.com

Abstract

Fast-dissolving tablets have emerged as one of the most popular and widely recognized dosage forms, particularly for young patients due to insufficient muscle and neurological system development and in the case of senior individuals suffering from Parkinson's disease or hand tremors. Few solid dosage forms, such as capsules and tablets, are currently experiencing issues such as difficulty in swallowing (dysphagia), resulting in high rates of noncompliance and rendering the therapy ineffective. FDTs disintegrate or dissolve easily in saliva without the use of water. Fast-dissolving tablets are intended to dissolve in saliva in a matter of seconds (less than 60 seconds), and they are true fast-dissolving tablets. FDT formulations contain Super Disintegrate to improve the disintegration of tablets in the buccal cavity. FDTs have advantages such as easy transportation and manufacture, accurate dosing, strong chemical and physical stability, and are an excellent choice for elderly and pediatric patients. In the manufacturing of FDTs, several standard or patented procedures, like mass extrusion, direct compression freeze-drying or lyophilization, spray drying, cotton candy processing, sublimation, and melt granulation, have been explored. The article provides a concise overview of FDTs, including their description, benefits, uses, key characteristics, drawbacks, problems in their development, and commercially available fast-dissolving tablet formulations.

Keywords:FDTs, MDTs, Dysphagia, Super Disintegrate, Swallowing, ODTs.

INTRODUCTION

Solid dosage forms are popular because of their low cost, ease of administration, accurate dosage self-medication, pain avoidance, and most importantly patient compliance. Tablets and capsules are the most prevalent solid dosage forms. One major disadvantage of such dosage forms is dysphagia, or difficulty in swallowing, which affects people of all ages. The size, surface, as well as taste of tablets, are common causes of difficulty in swallowing. Geriatric and pediatric patients, as well as travelling patients who may not have ready access to water, are the most in need of dosage forms as it is easy to swallow.[1,5] To achieve these medical needs, pharmaceutical technologists have established a novel oral dosage form known as ODTs, which disintegrate quickly in saliva, usually within seconds, without the need of water.[2] Drug dissolution and absorption, as well as the onset of clinical effects and drug bioavailability, may be significantly faster than with regular dosage forms. ODTs deliver drugs into the mouth for absorption via the pre-gastric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric (small and large intestine) segments of the gastrointestinal tract (GIT). ODTs are also called orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets,

fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapid melts. However, the United States Pharmacopoeia (USP) approved these dosage forms as ODTs. ODTs deliver drugs into the mouth for absorption via the gastrointestinal tract's (GIT) pre-gastric (oral cavity, pharynx, and esophagus), gastric (stomach), and post-gastric (small and large intestine) segments. The European Pharmacopoeia has defined orodispersible tablets as tablets that disperse easily in the mouth within 3 minutes before swallowing. The United States Food and Drug Administration defined ODT as "a solid dosage form containing a medicinal substance or active ingredient that disintegrates rapidly, usually within seconds, when placed on the tongue." ODTs disintegration timing normally ranges from several seconds to about a minute.[3,8]

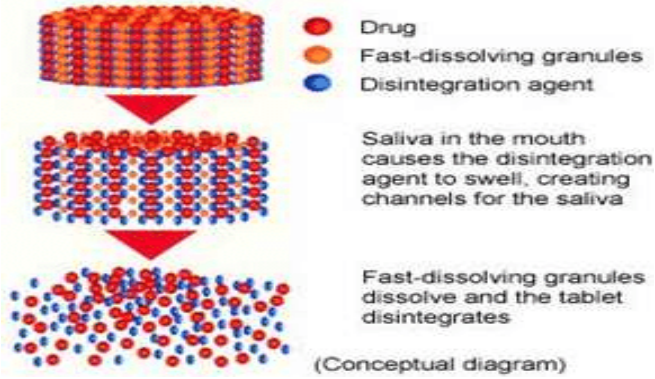

Figure1:Theoretical diagram ofFDTs.

IdealpropertiesofODTs

- The medication is administered easily to patients who cannot swallow, including the elderly, stroke victims, bedridden patients, renal failure patients, and those who refuse to swallow.
- Drugs that can diffuse into the upper GIT epithelial (log P > 2)
- Rapid drug dissolution and absorption, resulting in a rapid onset of action.
- Mostly drugs are absorbed from the mouth, pharynx, and oesophagus as saliva passes into the stomach, increasing their bioavailability.
- Pre-gastric absorption enhances bioavailability and reduces dosage, thereby improving clinical performance by reducing unwanted effects.
- The dosage form can be swallowed without the need for water, making it convenient for patients traveling without immediate access to water.
- Good mouth feels property can alter the perception of medication as a bitter pill, especially in pediatric patients.

Advantagesoffastdissolvingtablets

- Administration to patients who cannot swallow, such as elderly, stroke victims, bedridden, renal failure patients, and pediatrics, geriatric, and psychiatric patients. [6,8]
- The study focuses on patient compliance in disabled patients, bedridden patients, and busy individuals who lack access to water.
- The mouth feel property of medication can alter the perception of it as a "bitter pill," especially for pediatric patients, offering convenience and accurate dosing.
- Pre-gastric absorption can enhance bioavailability, reduce dose, and improve clinical performance by minimizing side effects.
- Liquid medication in solid form offers rapid absorption from the pre-gastric area, including the mouth, pharynx, and esophagus, resulting in a quicker onset of action.

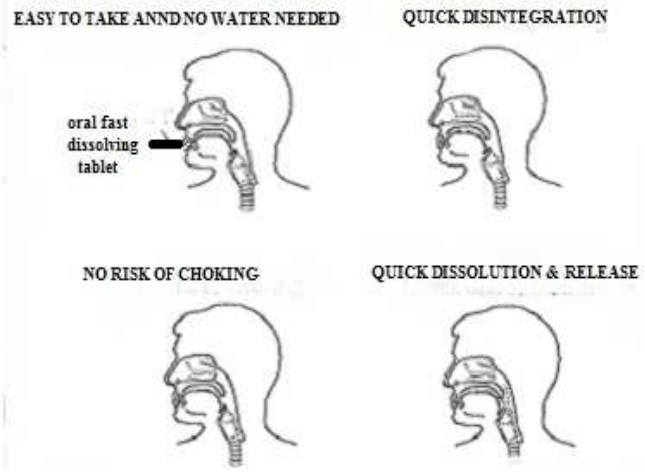

Figure 2:AdvantagesofFDTs.

LimitationsofFDTs

- One of the major drawbacks of FDTs is their low mechanical durability.

- FDT, a porous and softly molded material, can be compressed into tablets with low compression, resulting in friability and brittleness, making them difficult to handle. [5,7]
- Certain FDTs are hygroscopic and cannot maintain their physical integrity under normal humidity conditions, necessitating the use of specialized packages.
- Since these tablets quickly dissolve and disintegrate, this increases bioavailability, especially in the case of hydrophobic and insoluble drugs. Longer-lasting stability due to the drug's continued presence in solid dosage form until consumption. As a result, it combines the advantages of liquid dosage forms for bioavailability and solid dosage forms for stability.[2,5,7]

CHALLENGES TO DEVELOP FDTs

Palatability

Since most medications have an unpleasant taste, FDTs typically contain the medication in this disguised form. After being administered, FDTs break down or dissolve in the patient's mouth, releasing the active ingredients that contact the taste buds. Consequently, taste-masking of the medications is essential for ensuring patient compliance.[9]

Mechanicalstrength

FDTs can be made of a very porous, soft-molded matrix or compressed into tablets with a very low force, which makes the tablets brittle, difficult to handle, and frequently involves specialized peel-off blister packaging that could increase the cost. There are only two technologiesWow Tab and Durasolvthat can make tablets strong and durable enough to be packaged in multi-dose bottles.[6,7]

Hygroscopicity

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal temperature and humidity conditions.[3,11] They require humidity protection, which necessitates specialized product packaging.[12]

Amountofdrug[3,4]

The amount of medication that can be included in each unit dose limits the application of technologies used for FDTs. For insoluble drugs and soluble drugs, the level of drug dose in lyophilized dosage forms must be less than 400 mg and 60 mg, respectively. This parameter is especially difficult to formulate when creating fast-dissolving oral films or wafers.

Aqueoussolubility

Water-soluble drugs present various formulation challenges because they form eutectic mixtures, resulting in freezing-point depression and the formation of a glassy solid that may collapse upon drying due to loss of supporting structure during the sublimation process.[3, 5, 11] Such collapse can sometimes be avoided by using various matrix-forming excipients, such as mannitol, which can induce crystallinity and thus impart rigidity to the amorphous composite.[12]

Sizeoftablet

A tablet's size affects how quickly it should be administered. According to reports, a tablet should be 7-8 mm in size to be easily swallowed, while a tablet larger than 8 mm should be easy to handle. As a result, it is challenging to formulate tablets that are both easy to handle and easy to swallow.[2,3]

Mouth feel

In the oral cavity, FDTs do not break down into larger particles. The different particles that are produced after the FDTs break down should be as tiny as possible. The mouthfeel is improved by the addition of various flavors and cooling agents like menthol.[13,17]

TECHNIQUES FOR PREPARING FAST DISSOLVING TABLETSCONVENTIONAL TECHNOLOGIES

VariousconventionalmanufacturingtechniquesforFDTs

Freeze-dryingorlyophilization

It is a pharmaceutical procedure that enables the drying of biologicals and drugs that are sensitive to heat by applying a vacuum to remove water through

sublimation. Drugs are dissolved or dispersed in an aqueous solution of a carrier, transferred to preformed blister packs, and then frozen out using nitrogen flushing before being finished in the refrigerator. The high porosity and specific surface area of lyophilization techniques, as well as their rapid dissolution in the mouth and high drug bioavailability, are their identifying characteristics. The main disadvantages of this system are its high cost, labor-intensive process, and fragility, which renders conventional packaging inappropriate for use with this dosage form and causes stability problems under pressure.[16,8]

Mouldingmethod

Tablets are designed with hydrophilic ingredients to achieve maximum drug dissolution. A mass of powder is wetted with a hydroalcoholic solvent and compressed into a dosage form. The solvent system is then allowed to evaporate. The taste of drug particles is developed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, and polyethylene glycol, which contains an active ingredient, into lactose-based tablet triturate. The moulding method is very porous because the solvents are removed by drying, leaving a porous mass that promotes rapid dissolution.[12,13]

Meltgranulation

The meltable binder used in melt granulation technique is typically a lipid or wax, which melts at a relatively low temperature. This allows for the formation of solid bridges between the particles, resulting in improved flow properties and increased drug release. Additionally, melt granulation can also be advantageous for heat-sensitive drugs that may degrade during traditional wet granulation processes. [17,18]

Mass-extrusion

This mixture of ingredients is softened by adding polyethene glycol, a water-soluble ingredient, and using methanol as the solvent after it has been extruded into thin cylinders. which is then further divided using a heated blade to create tiny tablets. This method's characteristics include the ability to disguise bitter-tasting medications by converting them into small granules, which improve oral bioavailability.[18]

Sublimation

This method allows for the incorporation of various inert solid ingredients, such as urea, camphor, ammonium carbonate, ammonium bicarbonate, and hexamethylene-tetramine, which volatilize rapidly. These ingredients are mixed with other components and compressed to form a porous mass. By reducing pressure and applying a slight temperature, the volatile material evolves, resulting in a porous form.[11]

Directcompression

Direct compression is a highly efficient method for tablet production, as it eliminates the need for any pre-processing steps. However, it is crucial that the mixture being compressed possesses excellent flow properties to ensure optimal results. This technique not only simplifies the manufacturing process but also proves to be cost-effective in comparison to other methods. [14,15]

MILLING ➡SIEVING ➡MIXING➡MPRESSION

Spray-drying

By using sodium starch glycolate or crosscarmellose sodium as a disintegrating agent, hydrolyzed and nonhydrolyzed gelatins as binding agents, mannitol as a bulking agent, citric acid as an acid or alkali to enhance dissolution, and sodium bicarbonate as a disintegrating agent, ingredients are combined in this way. When the dosage form comes into contact with the aqueous medium using the spray-drying method, the dosage form dissolves quickly (within 20 seconds).[19]

Phasetransitionprocess

This method is used for the disintegration of FDTs by phase transition of sugar alcohols using erythritol (melting point 122 °C), xylitol (93–95 °C), trehalose (97 °C), and mannitol (166 °C). Tablets were produced by compressing a powder containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. Before the heating process, the tablets did not have sufficient hardness because of low compatibility. The tablet hardness increased

after heating due to the increase in interparticle bonds or the bonding surface area in tablets induced by the phase transition of lower melting point sugar alcohol.[18,25]

Spray-DryingProcess [18,22]

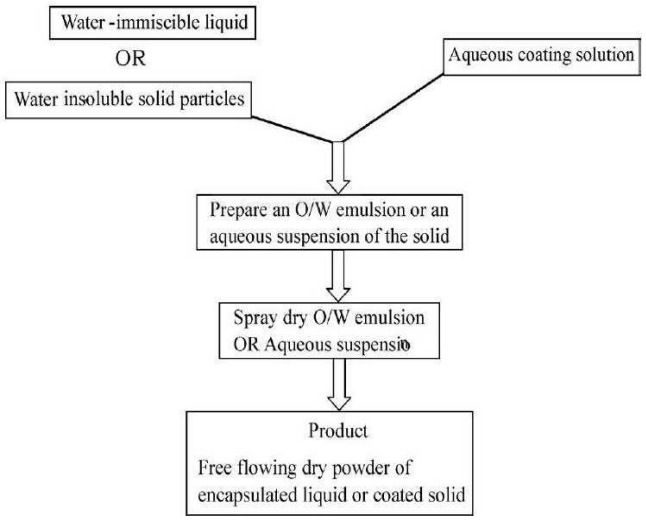

Figure3:Flowchartforcoatingliquid andsolidparticlesusing Spray-DryingProcess

Nanoionization

A recently developed nanomelt technology involves milling the drug using a proprietary wet-milling technique to reduce the particle size of the drug to nano size. Surface adsorption on selected stabilizers stabilizes the drug nanocrystals against agglomeration, which is then incorporated into MDTs. This method is especially useful for drugs that are poorly soluble in water. Other benefits of this technology include fast disintegration/dissolution of nanoparticles, which leads to increased absorption and thus higher bioavailability and dose reduction, a cost-effective manufacturing process, traditional packaging due to exceptional durability, and a wide range of doses (up to 200 mg drug per unit). [18,20-21]

Oraldisintegratingorfastdissolvingthinfilms

It is a new frontier in immediate release tablet that provides a very convenient means of taking medications and supplements. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxymethylcellulose, hydroxypropyl methyl cellulose, hydroxyl ethyl cellulose, hydroxyl propyl cellulose, 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 the case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film. This film, when placed in the 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 2×2 inches, dissolution in 5 sec, instant drug delivery and flavoured aftertaste.[18, 21,24]

PATENTEDTECHNOLOGIESFORFASTDISSOLVINGTABLETS

The technology can be used for almost any drug including marketplace and extension of patent in terms of the innovator. The clinical studies showed that FDTs can improve patient compliance, provide rapid onset of action, and increase bioavailability. Considering the many benefits of FDTs, it is only a matter of time until a majority of oral formulations are prepared in FDTs forms. Patented technologies of FDTs are tabulated in Table 1.

Table: 1Patented technology of FDTs

Patented technology	Organization
Zydis® [36]	R.P. Scherer, Inc.
Orasolv® [37]	Cima Labs, Inc.
Durasolv® [38]	Cima Labs, Inc.
Orodis® [39]	Physica Pharma Ltd.
Melt Ease® [40]	Eurand Pharmaceuticals Ltd.
Quick Dis® [41]	Lavipharm Laboratories Inc.
Wow Tab® [42]	Yamanouchi Pharma Technologies
Flashdose® [43]	Fuisz Technologies, Ltd
Flash Tab® [44]	Ethypharm, Ltd.
Oraquick® [45]	KV Pharmaceuticals, Ltd.
Nanomelt™ [46]	Elan Ltd.
AdvaTab® 47	Eurand Pharmaceuticals Ltd.
Pharmaburst® [48]	SPI Pharma Ltd.
Frosta® [49]	Akina Ltd.
Sheaform® [50]	Fuisz Technologies Ltd.
Ceform® [51]	Fuisz Technologies Ltd.
Lyoc® [52]	Pharmalyoc, Inc.

Table3. Workdone onfastdissolvingdrugdeliverysystemorFDTs.[26]

S.No.	Author	Drug	Method	Inference
1	Durgabh	Valsartan	Vaccum	Improved

	avani et al.(2016)		drying technique	disintegration time.
2	Karia et al. (2015)	Olmesartan medoxomil	Co-processed excipients technique	Better in vitro drug release.
3	Subbaiah et al.(2015)	Amoxicillin Trihydrate	Direct compression	Improved disintegration time and in vitro drug release
4	Munde et al.(2015)	Lansoprazole	Direct compression	Improved in vitro drug release
5	Metkari et al.(2014)	Carbamazepine	Direct comp. using solid dispersion	Good Dissolution Profile with short disintegration time.
6	Babu et al. (2014)	Carbamazepine	Direct compression	In vitro drug release increased.
7	Arunachalam et. al (2013)	Levofloxacin	Direct compression	Improved disintegration time.
8	Valera et. al (2013	Amoxicillin Trihydrate clavunate	Dry granulation	Improved in vitro drug release
9	Rawat et. al (2013)	Pioglitazone hydrochloride	Direct compression	Improved patient compliance.
10	Saroha et. al (2013)	Amoxicillin Trihydrate	Direct compression	Better disintegration rate
11	Bhati et. al (2013)	Metoclopramide hydrochloride	Direct compression	Improved patient compliance in pediatric and geriatric.
12	Layer et al. (2013)	Risperidone	Solvent evaporation method	Enhanced dissolution and increase bioavailability.
13	Rao et al. (2012)	Fosinopril	Sublimation method	Increase rate of dissolution and bioavailability

CONCLUSION:

Fast dissolving tablets are innovative dosage forms and specially designed to overcome those problems that have be seen in conventional solid dosage form i.e. difficulty in swallowing of the tablet in geriatric and pediatric patients. FDTs are designed to dissolve or disintegrate quickly in saliva generally, within less than 60 seconds (range of 5-60 seconds). Fast dissolving tablets have better patient compliance and acceptance may improve biopharmaceutical properties, bioavailability, improved efficacy, convenience, and better safety as compared with conventional oral dosage forms. The popularity of FDTs has increased over the last decade. FDTs need to be formulated for psychotic patients, bedridden, geriatric, pediatric patients, for those patients who may not have access to water, patients who are busy in traveling. FDTs formulations formulated by some of these conventional and patent technologies and FDTs have sufficient mechanical strength, quick disintegration/dissolution in the buccal cavity without water. The newer technologies utilized for the formulation of the FDTs, provides more effective dosage forms with more advantages and minimal disadvantages.

ACKNOWLEDGMENTS:

The author would like to thank Dr. Revathi A Gupta, Dr. Karunakar Shukla, Dr. R.S Bapna and Mr. Mayank Sahu for their kind support during preparation of this review article.

REFERENCES:

1. Hannan PA, Khan JA, Khan A, Safiullah S. Oral dispersible system: a new approach in drug delivery syste. Indian Journal of Pharmaceutical Sciences. 2016; 78(2):17. Doi.org: 10.4103/0250-474x.180244.
2. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. International Journal of Pharm Science Revue Research 2010;2(3):87-96. Doi.org:researchgate.net/publication/266355723.
3. Pagar R, Ahirrao S, Yallatikar T, Wagh M. Review on orodispersible tablets. International J Research Dev Pharm L Science. 2014;3(2):949-958.
4. Mishra US, Prajapati SK, Bhardwaj P. A review on formulation and evaluation for mouth dissolving tablet. World Journal of Pharm Science. 2014;8(2):778-810. Doi.org: 10.20959/wjpr201816-13214.
5. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: a review. Journal of Pharm Chem Biol Science.

2014;2(2):5-26.
Doi.org:10.22159/ijcpr.2017v9i2.17382.

6. Sharma S. New generation of the tablet: fast dissolving tablet. Latest Rev Pharmainfo Net. 2008;1(2): 6-7.
Doi.org:10.22159lrpfr.2017v9i2.17382.

7. Kumari S, Visht S, Sharma PK, Yadav RK. Fast dissolving drug delivery system: a review article. Journal of Pharmaceutical Research. 2010; 3(3):1444-9.
Doi.org:10.22159/ijcpr.2017v9i2.17382.

8. Mohanachandran PS, Sindhumol PG, Kiran TS. Superdisintegrants: an overview. International Journal of Pharma Science Revue Research. 2011; 6(2):105-9.
Doi.org: 10.20959/ijpsr20227-24317.

9. Deshmukh VN. Mouth dissolving drug delivery system: A review. International Journal of Pharma Tech Research. 2012; 4(2):412-21.
Doi.org: 10.35629/ijptr.7781-0605905921.

10. Kumaresan C. Orally disintegrating tablet-mouth dissolving, sweet taste and target release profile. Pharm Rev 2008;6:1.
Doi.org: 10.35629/pr7781-06012364474.

11. Parkash V, Maan S, Deepika, Yadav SK, Hemlata, Jogpal V. Fast disintegrating tablets: opportunity in drug delivery system. Journal Advance Pharma Technology Research. 2011; 2(1):223-35.
Doi.org:10.4103/2231-4040.90877.

12. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A. Orally disintegrating tablets: formulation, preparation techniques and evaluation. Journal Appl Pharm Science. 2011; 4(1):35-45.
Doi.org:10.22159ljaps.2017v9i2.17382.

13. Velmurugan S, Vinushitha S. Oral disintegrating tablets: an overview. International Journal of Chem Pharm Science. 2010 ;1(4):1-12.
Doi.org: 10.35629/ijcps.8881-0605536921.

14. Patel TS, Sengupta M. Fast dissolving tablet technology. World Journal of Pharm Science 2013;2(1):485-508.
Doi.org: 10.20959/wjpr201816-13214.

15. Khan AB, Tripuraneni A. Fast dissolving tablets–a novel approach in drug delivery. Journal of Pharmaceutical Science. 2014; 1(4):7-16.
Doi.org:10.5530/RJPS.2014.1.3

16. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. Journal Chem Pharm Res. 2009; 1(3):163-77.
Doi.org:10.22159/ijcpr.2017v9i2.17382.

17. Chowdary YA, Soumya M, Madhubabu M, Aparna K, Himabindu P. A review on fast dissolving drug delivery systems-A pioneering drug delivery technology. Bulletin of environment, pharmacology and life sciences. 2012;1(2):8-20.
Doi.org:10.22159/bepls.2017v9i2.17382.

18. Abdulraheman ZS, Patel MR, Patel KR. A review on immediate release tablet. International Journal Univers Pharm Bio Science. 2014; 3(2):93-113.
Doi.org: 10.22159/ijcpr.2018v10i2.25876.

19. Sri KV, Raj GB, Ravishanker D, Kumar CA. Preparation and evaluation of montelukast oral dispersible tablets by direct compression method. International Res Journal of Pharmacy. 2012 ;7(2):315-8.
Doi.org: 10.4103/2008-7802.193097.

20. Shukla D, Chakraborty S, Singh S, Mishra B. An overview of formulation of mouth dissolving tablets. Science Pharma. 2009 ;7(4):309-26. Doi.org/10.3797/scipharm.0811-09-01.

21. Menat AK, Patel MS, Patel MR, Patel NM. Fast dissolving tablets a novel approach to drug delivery. Asian Journal of Pharm Science and Research. 2012; 2(3):13-21.
Doi.org:10.22159/ajops.2017v9i2.17382.

22. Keshari R, Bharkatiya M, Rathore KS, Shyama S, Kumar, Sirvi G, somani N. Fast disolving tablet drug delivery system-an overview. International Journal of current Pharma research. 2015; 5(2):577-89.
Doi.org:10.22159/ijcpr.2017v9i2.17382.

23. Gupta DK, Bajpai M, Chatterjee DP. Fast mouth is dissolving disintegrating tablet and patient counselling points for FDDTS- a review. Int J Res Dev Pharm L Sci 2014;3:949-58. Doi: 10.20959/wjpr201816-13214.

24. Mohan SC, Margret CR. Recent advances in orodispersible tablets: a review. International Journal Drug Discovery Herbal Research. 2011; 2(4):78-83. Doi.org/10.3457/ijddsr.0811-09-01.

25. Kuchekar BS, Badha AC, Mahajan HS. Mouth dissolving tablets: a novel drug delivery system. Pharmatimes. 2003; 3(5):7-9. Doi.org: 10.35629/7781-0605905921.

26. Asija R, Asija S, Gupta A, Hemlata A. A review on fast dissolving drug delivery system. International Journal Research Pharm Science. 2014; 4(2):7-12. Doi.org:10.22159/ijap.2018v10i6.28134.