

REVIEW OF FAST-DISSOLVING TABLETS - A NEW ERA IN BRAND-NEW DRUG DELIVERY SYSTEMS

ABSTRACT

Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. Oral drug delivery remains the preferred route for administration of various drugs. Recent developments in the technology have prompted scientists to develop FDTs with improved patient compliance and convenience. Upon introduction into the mouth, these tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. The popularity and usefulness of the formulation resulted in development of several FDT technologies. FDTs are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. FDTs, or orally disintegrating tablets, are highly helpful for children and old people who have trouble swallowing standard pills and capsules. This review focuses on lyophilization, moulding, sublimation, and compaction FDT methods, as well as efforts to enhancing FDT qualities, such as spray drying and the usage of disintegrants. Taste-masking technology, experimental disintegration time measurements, and dissolution are also addressed.

Keywords: Fast dissolving tablets, freeze drying, spray drying, taste masking.

INTRODUCTION

Today's basic requirement and need is the processing of drugs into a presentable form. The dosage form is a type of drug delivery device that is used to provide a medicament to a living person. Tablets, syrups, suspensions, suppositories, injections, transdermal patches, and injections are all examples of dosage forms with various drug delivery mechanisms. These conventional and advanced dose forms each had their own set of benefits and drawbacks. As a result, in the current circumstances, the pharmacist faces a major challenge in establishing an ideal medicine delivery system. To make it effective, the medicine should be delivered to the site of action at a rate and concentration that provides the most therapeutic effects with the lowest amount of symptoms. A thorough study of the physicochemical principles that govern a specific formulation of a medicine should be subjected for the development of a suitable dosage form^[1]. Oral drug delivery is commonly accepted, representing for 50-60% of total pharmaceutical formulations. Solid dosage forms are preferred because of their ease of use, exact dosing, self-medication, pain avoidance, and, most importantly, patient compliance. Tablets and capsules are the most common solid dose forms; however, for some patients, swallowing these dosage forms can be problematic. Drinking water is necessary for oral dose forms to be absorbed. When water is not available, in the case of motion sickness (kinetosis), and rapid outbreaks of coughing during the common cold, allergic condition, and bronchitis, patients frequently experience trouble swallowing conventional dosage forms such as tablet. As a result, tablets that dissolve or disintegrate quickly in the oral cavity have received a lot of attention^[2]. Swallowing challenges are common in senior patients due to fear of choking, hand tremors, dysphasia, and in teenagers due to underdeveloped muscular and neurological systems, and also in schizophrenia patients, resulting in poor patient compliance. Approximately one-third of the population (mainly paediatric and geriatric) has swallowing problems, resulting in poor oral tablet drug therapy compliance, resulting in a reduction overall therapy effectiveness. As a response, tablets that dissolve or disintegrate quickly in the oral cavity have received a lot of attention^[3]. Fast dissolving tablet (FDT) is defined by the US Food and Drug Administration (USFDA) as "a solid dosage form containing a therapeutic drug or active ingredient that disintegrates rapidly, usually within seconds when placed upon the tongue"^[3]. In the late 1970s, fast dissolving drug - delivery systems were developed as an alternative to standard dose forms for children and elderly patients. These tablets are prepared to dissolve or disintegrate quickly in the mouth, frequently within 60 seconds^[4]. To reach these medical needs, pharmaceutical technologists have created orally disintegrating (dispersible) tablets (ODTs) or Fast disintegrating (dissolving) tablets (FDTs) or mouth melting tablets

(MMTs) or mouth dissolving tablets (MDTs), controlled release tablets which dissolve rapidly in saliva, usually in a matter of seconds, without the need for water. According to recent market data, more than 50 % of patients prefer FDTs to conventional dose forms. The usage of super disintegrants such as Croscopovidone, sodium starch glycolate, and croscopovidone is used for the creation of fast dissolving tablets. Another approach is to freeze and vacuum dry the tablets to enhance their pore structure ^[4]. Direct compression is preferred over all other methods because of its convenience, efficiency, and cost-effectiveness ^[1]. Some drugs' bioavailability may be improved significantly of drug absorption in the oral cavity, as well as pregastric absorption of saliva containing distributed pharmaceuticals that travel down into the stomach. Additionally, when compared to conventional tablets, the amount of drug exposed to first pass metabolism is minimized ^[4].

Advantages of fast Dissolving Tablets:

Fast dissolving tablets are taken by the pre-gastric area, such as the throat and oesophagus, resulting in a rapid commencement of action ^[5, 6]. This could result in higher bioavailability of active pharmacological drugs by dose reduction and clinical effectiveness with a reduced risk of side effects ^[7]. Patients' acceptance of medicines with an unpleasant taste may be enhanced by fast-dissolving tablets formulated with good taste-masking agents, particularly in paediatric patients. Another advantage is that it allows to resist blocking an oral route by using a conventional dosage form ^[8, 9].

Disadvantages of fast Dissolving Tablets:

- The major disadvantages of FDTs is related to the mechanical strength of tablets.
- FDT are very porous and soft molded metrics or compressed in a tablet with low compression, which makes tablet friable and brittle which difficult to handle.
- Bad tastes drugs are difficult to formulate as FDT; special precaution should have to be taken before formulate such kind of drug.
- Several FDT are hygroscopic cannot maintain physical integrity under normal condition from humidity which requires specialized package.
- Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- Rate of absorption from the saliva solution and overall bioavailability.
- Drug and dosage form stability.

Ideal Properties of Drug for Development of fast Dissolving Tablets:

In the development of MDTs various factors keeps for selecting the drug candidate.

- Drugs that can diffuse into the upper GIT epithelial layer ($\log P > 2$).
- Drugs with a short half-life and frequent dosing.
- Drugs that cause dangerous metabolites during first pass of metabolism.
- MDTs are not suitable for medicines with a long or controlled release.
- Drugs that are extremely bitter or have a bad taste are inappropriate for MDTs ^[10].

Potential Drug Candidates for fast Dissolving Tablets:

- Non-steroidal Anti-Inflammatory Drugs: Ketoprofen, Piroxicam, Paracetamol, Rofecoxib, Nimesulide, Ibuprofen.
- Anti-ulcer Drugs: Famotidine, Lansoprazole.
- Antidepressants Drugs: Mirtazapine, Fluoxetine.
- Antiparkinsonian Drugs: Selegiline.
- Antimigraine Drugs: Sumatriptan, Rizatriptan benzoate, Zolmitriptan.

- Anti-histaminic Drugs: Loratadine, Diphenhydramine, Meclizine.
- Antiemetic Drugs: Ramosetron HCl, Ondansetron, Baclofen ^[11, 12, 13].

Salient features of fast dissolving tablets or fast dissolving drug delivery system ^[14, 15, 16]

- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, a patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric and psychiatric patients.
- No need of water to swallow the dosage form, which is a highly convenient feature for patients who are travelling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce the quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, the bioavailability of the drug is increased.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage;

Improve clinical performance through a reduction of unwanted effects.

- Good mouth feels property helps to change the perception of medication as a bitter pill particularly in the pediatric patient.
- The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets. Stability for a longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines the advantage of the solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- Adaptable and amenable to existing processing and packaging machineries.
- Allow high drug loading, Cost effective.

Superdisintegrants ^[17, 18, 19]

The need for the faster dissolving formulation grows with each passing day. As a result, the pharmacist must develop disintegrants, such as super disintegrants, that are effective at low concentrations, have higher disintegration efficiency, and are more effective unusual case. These super disintegrants work via swelling, which causes the tablet to explode or the faster absorption of water, resulting in a large rise in the volume of granules, promoting disintegration.

Mechanism of Superdisintegrants^[37,38,39,40,41]

Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by various mechanisms. The mechanism by which the tablets are broken into small pieces and then produces a homogeneous suspension is based on:

1. Swelling
2. Porosity and capillary action(Wicking)
3. Heat of wetting
4. Chemical reaction (Acid-Base reaction)
5. Particle repulsive forces
6. Deformation recovery
7. Enzymatic reaction

Swelling: Although water penetration is a necessary first step for disintegration, swelling is probably the most widely accepted mechanism of action for tablet disintegrants. Particles of disintegrants swell on coming in contact with suitable medium and a swelling force develops which leads to break-up of the matrix. 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.

Porosity and capillary action (Wicking): Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. Tablet porosity provides pathways for the penetration of fluid into tablets. 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.

Heat of wetting: When disintegrants with exothermic properties get wetted, localized stress is created due to capillary air expansion, which aids in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

Chemical reaction (Acid-Base reaction): The tablet is quickly broken apart by internal liberation of CO₂ in water due to interaction between tartaric acid and citric acid (acids) with alkali metal carbonates or bicarbonates (bases) in presence of water. The tablet disintegrates due to generation of pressure within the tablet. Due to liberation in CO₂ gas, the dissolution of active pharmaceutical ingredients in water as well as taste masking effect is enhanced. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during preparation of the tablets. The effervescent blend is either added immediately prior to compression or can be added in two separate fraction of formulation.

Particle Repulsive Forces: This is another mechanism of disintegration that attempts to explain the swelling of tablet made with non-swelling disintegrants. According to Guyot-Hermann's particle-particle repulsion theory, water penetrates into tablet through hydrophilic pores and a continuous starch network is created that can convey water from one particle to the next, imparting a significant hydrostatic pressure. The water then penetrates between starch grains because of its affinity for starch surfaces, thereby breaking hydrogen bonds and other forces holding the tablet together. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

Deformation Recovery: Deformation recovery theory implies that the shape of disintegrant particles is distorted during compression and the particles return to their pre-compression shape upon wetting, thereby this increase in size of the deformed particles causing the tablet to break apart. Such a phenomenon may be an important aspect of the mechanism of action of disintegrants such as Crospovidone and starch that exhibit little or no swelling. Fig. 3 illustrates the repulsion and deformation mechanism in tablet disintegration.

Enzymatic Reaction: Enzymes present in the body also act as disintegrants. These enzymes deact the binding action of binder and helps in disintegration. Due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration. Some examples of disintegrating enzymes are presented in table 1 along with the binders against which these are active.

Factors to be considered for selection of super disintegrants^[20, 21, 22]

Disintegration

To produce rapid disintegration in the mouth, the disintegrant must swiftly wick saliva into the tablet to generate the volume expansion and hydrostatic pressure required.

Compatibility

To make strong tablets that eliminate the requirement for specialised packaging while increasing production speed, FDT with appropriate hardness and less friability at a given compression force is required..

Mouth feel

A rough feeling in the mouth might be caused by large particles .Small particles are so recommended. When the tablet comes into touch with water and produces a gel-like consistency, it provides a sticky taste that many consumers dislike.

Flow

Super disintegrants are typically utilized in tablet formulations at a rate of 2-5 wt% of the total weight of the tablet. The disintegrant level can be much higher with FDT formulation ^[21].

Bulking materials^[22, 23]

In the production of fast-dissolving tablets, bulking ingredients are critical. They serve as a diluent, filler, and cost reducer, among other things. Bulking agents improve the texture of the tablets, which improves disintegration in the mouth, as well as adding volume and lowering the active concentration in the formulation. For increased aqueous solubility and sensory perception, bulking agents for this dosage form should be sugar-based, such as mannitol, polydextrose, lactose derivatives such as directly compressible lactose (DCL), and starch hydrolysate. Mannitol, in particular, has a high aqueous solubility and good sensory perception, as its negative heat of solution gives a cooling effect. Bulking agents are used in amounts ranging from 10% to 90% by weight of the final product.

The descending order of brittleness of excipients is ranked as microcrystalline cellulose>alpha lactose monohydrate>spray-dried lactose>anhydrous beta lactose>anhydrous alpha lactose>> dicalcium phosphate dihydrate.

Bulking agents (such as dextrose, fructose, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose, and xylitol) are extensively used sugar-based excipients that have a high water solubility and sweetness and so give taste masking and a pleasant tongue feel.

Sugar based excipients can be of types on the basis of molding and dissolution rate:

Type 1 saccharides: (lactose and mannitol) which exhibit low moldability but high dissolution rate.

Type 2 saccharides: (maltose and maltitol) which exhibit high moldability but low dissolution rate.

TECHNIQUES IN PREPARATION OF FDTs

The various methods have been attempts for formulation of FDTs;

Freeze drying

Lyophilization is the process of removing water by sublimation while drying at a low temperature. The drug is encapsulated in a water-soluble matrix that is then freeze-dried to create a porous structure. When lyophilized tablets are inserted in the oral cavity, saliva quickly penetrates pores and disintegrates the tablets in less than 5 seconds. Heat-sensitive medications, also known as thermo-labile compounds, benefit from lyophilization.^[24]

Molding:

Molded tablets are made utilising water-soluble components in this manner, allowing the tablets to dissolve entirely and quickly. The powder mixture is wet with a hydroalcoholic solvent before being moulded into tablets at a lower pressure than traditional tablet compression. After that, the solvent is removed by air drying. Compressed tablets are much more compact than moulded tablets. These prostheses have a porous construction, which aids in dissolution^[25].

Tablet Molding

There are two types of moulding processes: solvent and heat. Solvent-produced tablets are less compact than compressed tablets and have a porous structure that speeds up dissolving. The mechanical strength of moulded tablets is an issue that needs to be addressed. Binding agents, which improve the tablets' mechanical strength, must be included^[26]. The masked drug particles are made by spray congealing a molten mixture of hydrogenated polyethylene glycol, cottonseed oil, lecithin, and sodium carbonate an active component into a lactose based tablet triturate form, which solves the problem of taste masking. When compared to the lyophilisation approach, the moulding technique produces tablets that are straightforward to scale up for industrial manufacturers^[27].

Direct Compression:

The most cost-effective and straightforward method of tablet production is direct compression. This technology can now be used for the manufacturing of Fast Dissolving Tablets^[28] due to the availability of better excipients, particularly super disintegrants and sugar-based excipients.

Spray drying

Spray drying can result in tiny, porous particles that dissolve quickly. This method uses a particulate support matrix, which is made by spray drying an aqueous composition comprising the support matrix and other ingredients into a highly porous and fine powder. The active components were then added, and the mixture was crushed into tablets. Hydrolyzed and non-hydrolyzed gelatins are used as supporting agents, mannitol is used as a bulking agent, sodium starch glycolate or cross carmellose sodium is used as a disintegrating agent, and an acidic and/or alkali material (e.g. sodium bicarbonate) is used to enhance disintegration and dissolution. When immersed in an aqueous media, a tablet compacted from spray dried powder disintegrated in 20 seconds.^[29, 30]

Mass Extrusion

In this method, a mixture of active drug and other ingredients is softened with a solvent mixture of water soluble polyethylene glycol and methanol, and then the softened mass is extruded through an extruder or syringe to produce a cylinder of product, which is then cut into even segments using heated blades to produce tablets. The dried cylinder can be used to coat bitter tasting medication granules, reducing their unpleasant taste^[31, 32].

Evaluation of fast dissolving tablets

1. Thickness

The thickness of a tablet is an important property that is measured in millimetres. A micrometre screw gauge was used to measure the thickness and diameter of the tablets^[33].

2. Weight variation test

For this test, 20 tablets are chosen at random from the lot and individually weighted to check for weight variation^[34].

3. Hardness

The amount of force required to break a tablet in a diametric compression test is referred to as hardness (crushing strength). The Monsanto Hardness Tester is used to determine hardness.

4. Friability

The Roche friabilator is used to measure friability using a total of 20 tablets. Twenty tablets are weighed and rotated at a speed of 25 revolutions per minute for four minutes (100) rotations^[34]. After the particles were removed from the tablets, the percentage of weight reduction was calculated.

$$(\%) = \frac{W_1 - W_2}{W_1} \times 100$$

5. Measurement of Tablet Porosity

Porosity of tablet can be determined by using mercury penetration porosimeter³³

6. Water absorption ratio

A tablet is placed on the paper and the time required for complete wetting is determined.^[35]

7. In-vitro disintegration time

This test was carried out on six tablets by placing one tablet into each tube (3 inches long and with a 10 mesh screen) of the apparatus using distilled water (as a disintegration medium) at a frequency of 28-32 cycles per minute and 37 degrees Celsius, and recording the time in seconds when no lumps remained in the apparatus^[36].

8. In-vitro dissolution study

The USP type-II apparatus is used to conduct the dissolution study. At 50 rpm and 37.5°C, the dissolution test is done using 900ml of the dissolving media. To maintain sink condition, 10ml of aliquots were periodically extracted and the sample volume was replaced with an equivalent volume of new dissolving medium^[36]. The samples are spectrophotometrically examined at the desired wave length.

9. Stability studies

Tablets are subjected to stability testing to determine whether they are a stable product and to ensure that the formulations remain intact during their shelf life. The created formulation should be packed in a unique way: first, it should be wrapped with butter paper, then aluminium foil should be wrapped over it, and last, it should be put in an aluminium bag and heat sealed. The formulation should be stored at 45°C and 75% relative humidity. Formulas should be kept in the refrigerator for three months. Triplicate samples should be taken at three sampling intervals during the stability research, namely 0, 1, and 3 months, and tablets should be examined for physical changes and drug content^[36].

Conclusion:

Due to the porous structure of the tablet matrix or the addition of superdisintegrants and/or effervescent excipients, FDTs are new dosage forms specially intended to dissolve in saliva without the use of water. When compared to normal tablets, fast dissolving tablets have superior patient compliance, especially in elderly and paediatric populations, and offer improved biopharmaceutical characteristics, efficacy, and safety. The invention of a fast-dissolving tablet also opens up the possibility of market expansion. Another reason for the creation of rapid dissolving products is pharmaceutical marketing. As a result of patient demand and the availability of numerous technologies, Fast dissolving tablets have grown in popularity, extending the patent life of a drug. Improved manufacturing procedures for rapid dissolving tablets are needed to make them mechanically strong, allow for easy handling and packing, and produce them in a method similar to the old tablets.

References:

1. Hannan PA, Khan JA, Khan A, Safiullah S. Oral dispersible system: a new approach in drug delivery system. *Indian J Pharm Sci* 2016; 78:2-7.
2. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablet: an overview. *J Chem Pharm Res* 2009; 1:163-77.
3. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. *Int J Pharm Sci Rev Res* 2010; 2:87-96.
4. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: a review. *J Pharm Chem Biol Sci* 2014; 2:5-26.
5. Aggarwal P, Nautiyal U and Mali RR: A review on fast dissolving tablet. *International Journal of Recent Advances in Science and Technology* 2015; 2: 20-8.
6. Masih A, Kumar A, Singh S and Tiwari AK: Fast dissolving tablets: A review. *Int J Curr Pharm Res* 2017; 9: 8-18.
7. Konar S and Mukhopadhyay A: Fast dissolving drug delivery system A novel approach. *International Journal of Pharmacy & Bio-Sciences* 2014; 14: 1.
8. Sharma S: New generation of the tablet: fast dissolving tablet. *Latest Rev Pharm info Net* 2008; 6.
9. Kumari S, Visht S, Sharma PK and Yadav RK: Fast dissolving Drug delivery system: Review Article *Journal of Pharmacy Research* 2010; 3: 1444-49.
10. Siddiqui MN, Garg G and Sharma PK: Fast dissolving tablets: Preparation, characterization and evaluation: An overview. *Int J of Phar Sci Rev and Res* 2010; 4: 87-96.
11. Fu Y, Yang S, Jeong SH, Kimura S and Park K: Orally fast disintegrating tablets: Developments, technologies, taste-masking and clinical studies. *Critical Reviews™ in Therapeutic Drug Carrier Systems* 2004; 21: 433-76.
12. Dollo G, Chevanne F, Le Corre P, Chemtob C and Le Verge R: Bioavailability of phloroglucinol in man. *Journal de pharmacie de Belgique* 1999; 54: 75-82.
13. Gafitanu E, Dumistracel I and Antochi S: Formulations and bioavailability of propyphenazone in lyophilized tablets. *Revista medico-chirurgicala a Societatii de Medici si Naturalisti din Iasi* 1991; 95: 127-28.
14. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: preparation, characterization and evaluation: an overview. *Int J Pharm Sci Rev Res* 2010; 2:87-96.
15. 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.

16. Mishra US, Prajapati SK, Bhardwaj P. A review on formulation and evaluation for mouth dissolving tablet. *World J Pharm Pharm Sci* 2014; 8:1778-810.
17. Sharma S. New generation of the tablet: fast dissolving tablet. *Latest Rev Pharmainfo Net*; 2008. p. 6.
18. Kumari S, Visht S, Sharma PK, Yadav RK. Fast dissolving drug delivery system: a review article. *J Pharm Res* 2010; 3:1444-9.
19. Kumaresan C. Orally disintegrating tablet-mouth dissolving, sweet taste and target release profile. *Pharm Rev* 2008; 6:1.
20. Nautiyal U, Singh S, Singh R, Gopal, Kakar S. Fast dissolving tablets as a novel boon: a review. *J Pharm Chem Biol Sci* 2014; 2:5-26.
21. Deshmukh VN. Mouth dissolving drug delivery system: a review. *Int J Pharm Tech Res* 2012; 4:412-21.
22. Khan AB, Tripuraneni A. Fast dissolving tablets—a novel approach in drug delivery. *Rguhs J Pharm Sci* 2014; 1:7-16.
23. Patel TS, Sengupta M. Fast dissolving tablet technology. *World J Pharm Sci* 2013; 2:485-508.
24. Habib W, Khankari RK, Hontz J. Fast-dissolve drug delivery systems. *Crit Rev Ther Drug Carrier Sys* 2000; 17:61-72.
25. Van Scoik KG. Solid Pharmaceutical dosage in tablet triturates form and method of producing the same. *US Patent* 5,082, 667.
26. Sharma, R., Rajput, M., Prakash, P., Sharma, S., Fast dissolving drug delivery system: A Review, *Int Res J Pharm*, 2011; 2(11):21-29.
27. Rai, R.R., Chirra,P., Thanda, V., Fast dissolving tablets: A novel approach to drug delivery—A Review,*Int J Preclinical and Pharma Res*,2012; 3(1):23-32.
28. Ito, A., Sugihara, M., Development of Oral Dosage forms for elderly patients: Use of agar as Base of rapidly disintegrating oral tablets,*Chem Pharm.Bull*,1996; 44(11):2132-2136.
29. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. *US Patent* 5,587,180; 1996.
30. Allen LV, Wang B, Davis LD. Rapidly dissolving tablet. *US Patent* 5,807,576; 1998.
31. Wagh M. A, Kothawade P. D, Salunkhe K.S, Chavan N.V, Daga V.R. Techniques used in orally disintegrating drug delivery system. *Inter. J. Drug Delivery* 2010; 2:98-107.
32. Hirani J.J, Rathod D.A, Vadalia K.R. Orally Disintegrating Tablets: A Review. *Trop J Pharm Res.* 2009; 8 (2):161-172.
33. Panigrahi R, Saiprasanna MS. A review on rapidly disintegrating tablet.*Web MedControl.* 2010; 2-8.
34. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablet: A novel drug delivery system. *Pharma Times*2003; 35; 7-9.<https://doi.org/10.4103/0250-474X.73930>

35. Kumari S, Visht S, Sharma PK, Yadav RK. Fast dissolving drug delivery system: A review article. *J Pharm Res* 2010; 3(6): 1444-1449.
36. Kalia A, Khurana S, Bedi N. Formulation and evaluation of mouth dissolving tablets of Oxcarbazepine. *J Pharm Pharma Sci* 2009; 1:12-23.
37. Konapure AS, Chaudhari PS, Oswal RJ, Kshirsagar SS, Antre RV and Chorage TV: Mouth dissolving tablets-an innovative technology. *International Journal of Applied Biology and Pharmaceutical Technology* 2011; 2(1): 496-503.
38. Pahwa R, Piplani M, Sharma PC, Kaushik D and Nanda S: Orally disintegrating tablets – friendly to pediatrics and geriatrics. *Archives of Applied Science Research* 2010; 2(2): 35-48.
39. Bhowmik D, Chiranjib B, Yadav J, Chandira RM and Kumar S: Emerging trends of disintegrants used in formulation of solid dosage form. *Scholars Research Library Der Pharmacia Lettre* 2010; 2(1): 495-504.
40. Mohanachandran PS, Sindhumol PG and Kiran TS: Superdisintegrants: an overview. *Journal of Pharmaceutical Sciences Review and Research* 2011; 6(1): 105-109.
41. Uddhav S Bagul. (2006). Current status of tablet disintegrants: a review. Retrieved March 5, 2011 from Pharmainfo.net. <http://www.pharmainfo.net/reviews/current-status-tablet-disintegrants-a-review>.