

THE PHARMA INNOVATION

Mouth Dissolving Tablets: A New Venture in Modern Formulation Technology

Arijit Gandhi *¹

1. Department of pharmaceutics, Gupta College of Technological Sciences, G.T. Road, Ashram More, Asansol-713301, Burdwan, West Bengal, India.

Mouth dissolving tablets (MDTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. 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 MDT technologies. This review describes the various formulation aspects and technologies developed for MDTs, along with various excipients, evaluation tests, marketed formulations of MDTs. There are multiple fast-dissolving OTC and Rx products on the market, most of which have been launched in the past 3 to 4 years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology. Thus, in future, it is expected that this delivery system will get much importance as that of conventional delivery systems.

Keyword: Oral Route, Fast Dissolving Drug Delivery System, Mouth Dissolving, Rapidly Disintegrating Tablet, Orodispersible Tablet.

INTRODUCTION: The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance¹.

Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is Dysphagia or difficulty in swallowing. This is seen to afflict nearly 35% of the general population². To solve the above mentioned problem, pharmaceutical technologists have put in their best efforts to develop a fast dissolving drug delivery, i.e. Mouth Dissolving Tablet that disintegrates and dissolves rapidly in the saliva, within a few seconds without the need of drinking water or chewing. A mouth dissolving tablet usually dissolves in the oral cavity within

Corresponding Author's Contact information:
Arijit Gandhi*
Department of pharmaceutics, Gupta College of Technological Sciences, G.T. Road, Ashram More, Asansol-713301, Burdwan, West Bengal, India.
E-mail: arijit.babugandhi.gandhi@gmail.com

15 secs to 3 min. Most of the MDTs include certain super disintegrants and taste masking agents³. Fast or mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult⁴. In the recent past, several new advanced technologies have been introduced for the formulation of mouth dissolving tablets with very interesting features, like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients. The technologies utilized for fabrication of MDTs include lyophilisation, moulding⁵, direct compression⁶, cotton candy process⁷, spray drying⁸, sublimation⁹, mass extrusion¹⁰, nanonization¹¹ and quick dissolve film formation¹². These techniques are based on the principles of increasing porosity and/or addition of superdisintegrants and water soluble excipients in the tablets. The formulations prepared from these techniques differ from each other on the basis of the factors like mechanical strength of final product, drug and dosage form stability, mouth feel, taste, rate of dissolution of the formulation in saliva, rate of absorption from saliva and overall drug bioavailability. Although, numerous technologies had been developed for the fabrication of these unique dosage forms in last two decades, but so far, no standardized technique has been designed or mentioned in pharmacopoeias for their evaluation except in European Pharmacopoeia (EP), which defines

orodispersible tablets as “uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed”. EP also specifies that the orodispersible tablets should disintegrate within 3 minutes when subjected to conventional disintegration test used for tablets and capsules. There are several synonyms in use of MDTs like **orodispersible, orally disintegrating tablets, quick dissolving tablet, fast melt tablets, rapid disintegrating tablets** and **freeze dried wafers**. This article presents a detailed review regarding the evaluation measures available in literature to characterize the MDTs, which have been designed keeping in view the special features of these novel drug delivery systems.

CRITERIA FOR MOUTH DISSOLVING TABLETS:^{13, 14}

- Require no water for oral administration, yet dissolve / disperse/ disintegrate in mouth in a matter of seconds.
- It should have pleasant mouth feel.
- Should have an acceptable taste masking property.
- It should have sufficient hardness to withstand rigors during manufacturing processes and post manufacturing handling.
- It should allow high drug loading.
- Should leave minimal or no residue in mouth after disintegration.
- Should exhibit low sensitivity to environmental conditions (temperature and humidity).
- Should allow the manufacture of tablet using conventional processing and packaging equipments.
- It should be cost effective.

ADVANTAGES OF MOUTH DISSOLVING TABLETS:^{13, 15}

- Ease of administration to patients who cannot swallow, such as the elderly, stroke victims and bedridden patients;

patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as paediatrics, geriatric and psychiatric patients.

- Patient's compliance for disabled bedridden patients and for travelling and busy people who do not have ready access to water.
- Good mouth feel property of Mouth dissolving drug delivery system helps to change the basic view of medication drugs.
- Convenience of administration and accurate dosing as compared to liquid formulations.
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and esophagus which may produce rapid onset of action.
- Pre-gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension.
- The risk of choking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- Beneficial in cases such as motion sickness (kinetosis), sudden episodes of allergic attack or coughing, where an ultra-rapid onset of action required.

LIMITATIONS OF MOUTH DISSOLVING TABLETS : ^{15 - 17}

- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

- Patients who concurrently take anticholinergic medications may not be the best candidates for MDTs and patients with Sjogren's syndrome or dryness of mouth due to decreased saliva production may not be the good candidates for these tablet formulations.
- MDTs are hygroscopic in nature, so must be kept in dry place.
- MDTs require special packaging for proper stabilization and safety of stable product.

THE NEED FOR DEVELOPMENT OF MDTs: ^{16, 18 - 20}

The requirement of non-invasive delivery systems persists due to patients' poor acceptance of, and compliance with, existing delivery regimes. The paediatrics and geriatric populations are the primary targets, as both the groups found it difficult to swallow conventional tablets.

The **patient related factors** for development of MDTs include the following:

- Paediatric and geriatric patients who have difficulty in swallowing or chewing solid dosage forms.
- The risk of choking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- Very elderly patients who may not be able to swallow a daily dose of antidepressant.
- An eight-year old with allergies who desires a more convenient dosage form than antihistamine syrup.
- A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H₂- blocker.
- A schizophrenic patient in an institutional setting who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.

The **effectiveness factors** are:

- Increased bioavailability and faster onset of action are a major claim of these formulations. Because the tablets disintegrate inside the mouth, drugs may be absorbed in the buccal, pharyngeal, and gastric regions.
- The pre-gastric drug absorption avoids the first-pass metabolism and drug dose can be reduced if a significant amount of the drug is lost through the hepatic metabolism.
- Safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism.

The **Manufacturing and marketing factors** involving:

- Developing new drug delivery technologies and utilizing them in product development is critical for pharmaceutical industries to survive, regardless of their size.
- As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form.
- A new dosage form allows a manufacturer to extend market exclusivity, unique product differentiation etc.
- Marketers build a better brand and company image when they offer a unique easier-to-take form that satisfies the need of an underserved patient population.

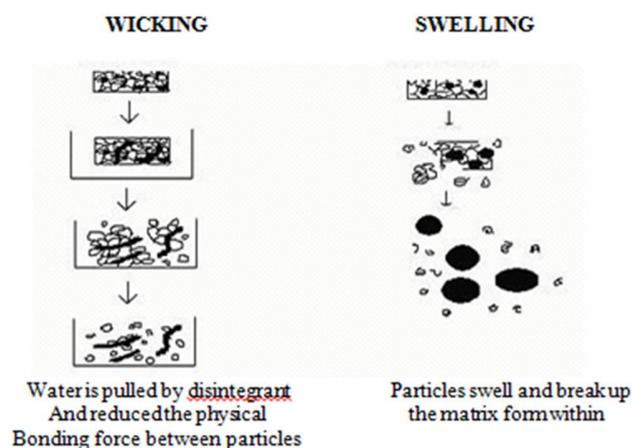
MECHANISM OF SUPERDISINTEGRATION : 21

There are four major mechanisms for tablets disintegration as follows:

1. Swelling: The most widely accepted general mechanism of action for tablet disintegration is

swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity.

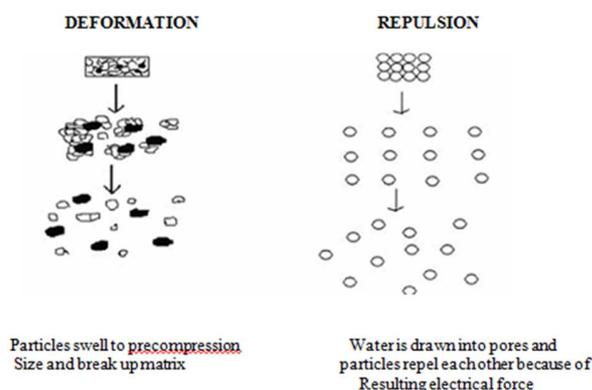
2. Porosity and capillary action (Wicking): Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.



3. Due to disintegrating particle/particle repulsive forces: Another mechanism of disintegrant attempts to explain the swelling of tablet made with nonswellable disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that no swelling particle also causes disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

4. Due to deformation: During tablet compression, disintegrated particles get deformed

and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet.



TECHNIQUES FOR PREPARING MOUTH DISSOLVING TABLETS:

Some of the new advanced technologies which are commonly being used in last few decades are summarized as:-

1. Freeze drying/Lyophilization
2. Molding
3. Direct Compression
4. Cotton Candy Process
5. Spray drying
6. Sublimation
7. Mass Extrusion
8. Melt granulation
9. Nanonization
10. Fast Dissolving Films
11. Phase Transition Process
12. Three-dimensional Printing (3DP)

1. Lyophilization or Freeze-Drying:

A process in which water is sublimated from the product after freezing is called freeze drying. Freeze dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution

characteristics of the formulation. A typical procedure involved in the manufacturing of MDT using this technique is mentioned here. 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. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze-drying. After freeze-drying the aluminium foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability^{22, 23}.

2. Tablet Molding :

Molding process is of two type's i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution. The heat molding process 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 30⁰C under vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to 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. Compared to the lyophilization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture²¹.

3. Direct Compression:

Direct compression represents the simplest and most cost effective tablet manufacturing technique. MDT can be prepared by using this technique because of the availability of improved excipients especially super-disintegrate and sugar based excipients.

(a) Super-disintegrants:

The rate of disintegration gets affected by the addition of superdisintegrants and hence the dissolution. Other ingredients like water-soluble excipients and effervescent agents also increase the disintegration.

(b) Sugar based excipients:

The sugar based excipients which are commonly used are especially bulking agents (like dextrose, fructose, lactilol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol) which display high aqueous solubility and sweetness, and hence impart taste masking property and provide pleasing mouth feel. Mizumito et al classified sugar-based excipients into two types on the basis of molding and dissolution rate: Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate. Type 2 saccharides (maltose and maltitol) exhibit high mouldability but low dissolution rate.²¹

4. Cotton Candy Process:

Another technology for manufacturing fast dissolving tablets is the cotton candy process, also known as candy floss process, which involves centrifugation to produce a floss-like crystalline structure. In this technology, the matrix is formed from saccharides or polysaccharides processed into an amorphous floss through a shear foam process. The matrix is cured and milled to make flowable, compactible, and highly soluble filler. Because of the formation of the formation of porous three-dimensional structures with the active ingredients encased in the pores, the resulting surface area is high. Therefore, dispersion and dissolution occur quickly when the product is placed in the mouth. This technology is patented as FlashDose® by Fuisz Technology (Chantilly, Virginia, U.S.A.)²⁴.

5. Sprays-Drying:

Allen et al., have used spray-drying for the production of MDTs. The formulations contained hydrolyzed and non hydrolyzed gelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose as a disintegrant. By adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The porous powder was obtained by spray drying the above suspension which was compressed into tablets. Tablets manufactured by this method shows disintegration time < 20 sec in an aqueous medium²⁵.

6. Sublimation:

In this method a subliming material like camphor, is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva²⁶. Granules containing nimusulide, camphor, crospovidone, and lactose were prepared by wet granulation technique. Camphor was sublimed from the dried granules by vacuum exposure²⁷. Conventional methods like dry granulation, wet granulation and direct compression with highly soluble excipients, super disintegrants and/or effervescent systems can also be used.

7. Mass Extrusion:

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat

granules of bitter tasting drugs and thereby masking their bitter taste¹⁸.

8. Melt Granulation:

Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. Because there is no drying step, the process is less time consuming and uses less energy than wet granulation. It is a useful technique to enhance the dissolution rate of poorly water soluble drugs, such as griseofulvin. This approach to prepare MDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate©, PEG-6-stearate). So it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solubilizes rapidly leaving no residues²⁸.

9. Nanonization:

A recently developed Nanomelt technology involves reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit)²⁹.

10. Fast Dissolving Films:

It is a newer developing front that provides a very convenient means of taking medications and supplements. In this technique, water soluble film forming polymer (pullulan, CMC, HPMC, HEC, HPC, PVP, PVA etc.), drug and other taste masking ingredients are dissolved in non-aqueous solvent to prepare non-aqueous solution, which on evaporation of solvent forms a film. Resin adsorbate or coated micro particles of the drug can be incorporated into the film if the drug is bitter. This film when placed in mouth melts or dissolves rapidly and releases the drug in solution or suspension form. This system forms the thin

films of size less than 2x2 inches which dissolves within 5 sec with instant drug delivery and flavored taste.

11. Phase Transition Process:

Kuno et. al., investigated processes for the disintegration of MDTs by phase transition of sugar alcohols using erythritol (m. pt. 122°C), xylitol (m.pt. 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 heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol³⁰.

12. Three-dimensional Printing (3DP):

Three-dimensional printing (3DP) is a rapid prototyping (RP) technology. Prototyping involves constructing specific layers that uses powder processing and liquid binding materials. A novel fast dissolving drug delivery device (DDD) with loose powders in it was fabricated using the three dimensional printing (3DP) process. Based on computer-aided design models, the DDD containing the drug acetaminophen were prepared automatically by 3DP system³¹. It was found that rapidly disintegrating oral tablets with proper hardness can be prepared using TAG. The rapid disintegration of the TAG tablets seemed due to the rapid water penetration into the tablet resulting from the large pore size and large overall pore volume³².

PATENTED TECHNOLOGIES:

Some of the important patented technologies for preparation of MDTs and the list of patented technologies and their products are given in Table 1 and 2 respectively.

Table 1: Some of the important patented technologies for preparation of MDTs: ^{18-19, 33-37}

S.No	Technique	Novelty	Advantages	Disadvantages
1.	Zydis	First to market, Freeze Dried	Quick dissolution, Self-preserving and increased bioavailability	Expensive process, poor stability at higher temperature and humidity
2.	Orasolv	Unique taste-masking, lightly compressed	Taste-masking is twofold, quick dissolution	Low mechanical strength
3.	Durasolv	Compressed dosage form, Proprietary taste masking	Higher mechanical strength than Orasolv, Good rigidity	Inappropriate with larger dose
4.	Flashdose	Unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy	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
5.	Flashtab	Compressed dosage form containing drug as microcrystal	Only conventional tableting Technology	-----
6.	Wowtab	Combination of low mouldability and high mouldability saccharides. SMOOTHMELT action gives superior mouth feel	Adequate dissolution rate and hardness	No significant change in bioavailability
7.	Oraquick	Uses patented taste masking technology	Faster and efficient production	-----
8.	Ziplet	Incorporation of water insoluble inorganic excipients for excellent physical performance	Good mechanical strength, satisfactory properties can be obtained at high dose (450 mg) and high weight (850 mg)	As soluble component dissolves, rate of water diffusion in to tablet is decreased because of formation of viscous concentrated solution

Table 2: List of patented technologies and their products: ^{19, 28, 38-40}

S.No	Technology	Process Involved	Patent Owner	Drugs Used (Brand Name)	Drug Release
1.	Zydis	Lyophilization	R.P. Scherer Inc.	Loratidine (Claritin Reditab and Dimetapp quick dissolve)	Dissolves in 2-10 sec.
2.	Quicksolv	Lyophilization	Jansen Pharmaceuticals	Cisapride monohydrate (Propulsid Quicksolv)	-----
3.	Flashtab	Lyophilization	Ethypharm	Ibuprofen (Nurofen Flashtab)	Dissolves within 1 min.

4.	Lyoc	Multiparticulate Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyoc)	-----
5.	Orasolv	Compressed tablets	Cima Labs Inc.	Paracetamol (Temptra Quicklets), Zolmitriptan (Zolmig Rapimelt)	Disintegrates in 5-45 sec.
6.	Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulphate (NuLev),	Disintegrates in 5-45 sec.
7.	Rapitab	Compressed tablets	Schwarz Pharma	-----	-----
8.	Wowtab	Multiparticulate Compressed tablets	Yamanouchi PharmaTechnologies, Inc.	Famotidine (Gaster D)	Disintegrates in 5-45 sec.
9.	Fast Melt	Molding	Elan Corp.	-----	-----
10.	Ziplets	Molding	Eurand	Ibuprofen (Cibalgina Due Fast)	-----
11.	Flashdose	Cotton-candy process	Fuisz Technology Ltd.	Tramadol Hcl (Relivia Flash dose)	Dissolves within 1 min.
12.	Oraquick	Micromask	KV Pharm. Co, Inc.	Hyoscyamine sulphate ODT	-----
13.	Advatab	Taste masking Microcaps and diffuscap CR Technology	Eurand International	Advatab Cetirizine, Advatab Paracetamol	Disintegrates in less than 30 sec.
14.	Fuisz	Sugar based matrix known as floss	Fuisz pharmaceutical Ltd.	Diphenhydramine & Pseudoephedrine	-----

EXCIEPIENTS USED TO PREPARE MDTs: 17, 41

Superdisintegrants: Crospovidone, Microcrystalline cellulose, sodium starch glycollate, sodium carboxy methyl cellulose, pre-gelatinized starch, calcium carboxy methyl cellulose, and modified corn starch. Sodium starch glycollate has good Flowability than crosscarmellose sodium. Cross povidone is fibrous nature and highly compactable.

Flavours: Peppermint flavour, cooling flavor, flavor oils and flavoring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, eucalyptos oil thyme oil, oil of bitter almonds. Flavoring agnets include, vanilla, citus oils, fruit essences.

Sweeteners: Aspartame, Sugars derivatives.

Fillers: Directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulfate, pregelatinized starch, magnesium trisilicate, aluminium hydroxide.

Surface active agents: Sodiumdoecylsulfate, sodiumlaurylsulfate, polyoxyethylene sorbitan fatty acid esters (Tweens), sorbitan fatty acid esters (Spans), polyoxyethylene stearates.

Binder: Polyvinylpyrrolidone(PVP), Polyvinylalcohol(PVA), Hydroxypropyl methylcellulose(HPMC).

Colour: Sunset yellow, Amaranth etc.

Lubricants: Stearic acid, Magnesium stearate, Zinc stearate, calcium stearate, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide.

PRECOMPRESSION PARAMETERS:

Prior to compression into tablets, the blend was evaluated for properties such as:

1. Angle of Repose (θ): The frictional forces in case of loose powder are measured by the angle of repose. It is defined as the maximum angle possible between the surface of a pile of powder and the horizontal plane. It is determined by funnel method. Angle of Repose was calculated using the formula:

$$\begin{aligned} \tan \theta &= 2h/d \\ \text{Or, } \tan \theta &= h/r \\ \text{Or, } \theta &= \tan^{-1}(h/r) \end{aligned}$$

Where, θ = Angle of repose, H = height of the pile (cms), r = radius of heap (plane surface occupied by the powder)^{42, 43}. Table 3 shows the angle of repose and their flow characteristics.

Table 3: Angle of repose as an indication of powder flow properties

S.No.	Angle of Repose($^{\circ}$)	Type of Flow
1.	<20	Excellent
2.	20-30	Good
3.	30-40	Passable
4.	>40	Very Poor

2. Bulk Density (D_b): It is the ratio of total mass of powder (M) to the bulk volume (V_b). Apparent bulk density was determined by pouring pre-sieved drug excipient blend into a graduated cylinder and measuring the volume and weight "as it is". Bulk density (expressed in gm/ml) was calculated according to formula mentioned below:

$$D_b = M / V_b$$

Where, M = Mass of the Powder V_b = Bulk volume of the powder^{44, 45}.

3. Tapped Density (D_t): It is the ratio of total mass of powder to the tapped volume of powder. It was determined by placing a graduated cylinder, containing a known mass of drug-excipient blend, on mechanical tapping apparatus. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10 cm at 2 seconds interval. The tapping was continued until no further change in volume was noted. Tapped density (expressed in gm/ml) was calculated according to formula mentioned below:

$$D_t = M / V_t$$

Where, M = Mass of the Powder V_t = Tapped volume of the powder^{44, 46}.

4. Carr's Index (Carr's Consolidation Index):

It indicates the powder flow properties. It is expressed in percentage and is given by formula: % compressibility (I) = [Tapped density – Bulk density/ Tapped density] x 100⁴³. Table 4 shows the relationship between % compressibility and Flowability.

Table 4: Relationship between % compressibility and Flowability

S. No.	% Compressibility	Flowability
1.	5-12	Excellent
2.	12-16	Good
3.	18-21	Fair passable
4.	23-35	Poor
5.	33-38	Very Poor
6.	<40	Very Very Poor

5. Hausner Ratio: It is an indirect index of ease of powder flow. It is calculated by the following formula: Hausner ratio = Tapped density/ Bulk density. Lower Hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25)⁴³.

6. Porosity: The porosity ϵ of powder is defined as the ratio of void volume to the bulk volume of

the packaging. The porosity of the powder is given by:

$$\epsilon = V_b - V_p / V_p = 1 - V_p / V_b$$

Porosity is frequently expressed in percentage and is given as: $\% \epsilon = (1 - V_p / V_b) \times 100$ ⁴⁷.

EVALUATION OF FAST DISSOLVING TABLETS:

Tablets from all the formulation were subjected to following quality control test.

1. General Appearance: The general appearance of a tablet, its visual identity and overall elegance is essential for consumer acceptance. It indicates tablet size, shape, colour, presence or absence of an odour, surface texture, physical flaws, consistency and legibility of any identification markings⁴⁸.

2. Size and shape: The size and shape of the tablet can be dimensionally described, monitored and controlled⁴⁸.

3. Tablet Thickness: Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer⁴⁹. Thickness of the tablet is measured by using vernier callipers. It is expressed in mm⁵⁰.

4. Uniformity of weight: I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity^{49, 51}. Table 5 shows the average weight of the tablets and their % deviation.

Table 5: Average weight of the tablets and their % deviation

S. No.	Average Weight of Tablets (mg)	Maximum percentage difference Allowed
1.	130 or less	±10
2.	130-324	±7.5
3.	More than 324	±5

6. Tablet hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation was determined using Monsanto Hardness tester or Pfizer hardness tester. It is expressed in Kg/cm²^{43, 49}.

7. Friability: Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator was employed for finding the friability of the tablets. 20 tablets from each formulation were weighed and placed in Roche friabilator that rotated at 25 rpm for 4 minutes. The tablets were dedusted and weighed again. The percentage of weight loss was calculated again. The percentage of weight loss was calculated using the formula:

$$\% \text{ Friability} = [(W1 - W2)100] / W1$$

Where, W1= Weight of tablet before test (Initial Weight) W2 = Weight of tablet after test (Final Weight).

Thus, it is necessary that this parameter should be evaluated and the results are within bound limits (0.1-0.9%)⁵².

8. Wetting Time: Five circular tissue papers were placed in a Petri dish of 10-cm diameter. 10

ml of water containing 0.5% eosin, a water-soluble dye, was added to the Petri dish. The dye solution was used to identify complete wetting of the tablet surface. A tablet was carefully placed on the surface of the tissue paper in the Petri dish at 25°C. The time required for water to reach the upper surface of the tablets and to completely wet them was noted as the wetting time. These measurements were carried out in a replicate of six. Wetting time was recorded using a stopwatch⁵³.

9. Moisture uptake studies: Moisture uptake studies for FDTs should be conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37°C for 24 h. The tablets were then weighed and exposed to 75% relative humidity, at room temperature for 2 weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccator for 3 days. One tablet as control (without superdisintegrants) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded^{54, 55}.

10. Water Absorption Ratio: A small piece of tissue paper folded twice was placed in a small petri dish containing 6ml of water. A tablet was put on the paper and the time required for complete wetting was measured. The wetted tablet was then reweighed. Water absorption ratio, R was determined by using following formula given:

$$R = 100 \times \frac{W_a - W_b}{W_b}$$

W_b is the weight of tablet before water absorption

W_a is the weight of tablet after water absorption⁵⁶.

11. In-vivo Disintegration test: The test was carried out on 6 tablets using the apparatus specified in I.P 1996 distilled water at 37°C±2°C was used as a disintegration media and the time in seconds is taken for complete disintegration of

the tablet with no particulate matter remaining in the apparatus was measured in seconds⁵⁷.

12. In-vitro dispersion time: In-vitro dispersion time was measured by dropping a tablet in a beaker containing 50 ml of sorenson's buffer pH 6.8. Three tablets from each formulation was randomly selected and in-vitro dispersion time was performed^{46, 48}.

13. Dissolution test: The development of dissolution method for MDT is comparable to approach taken for conventional tablets and is practically identical when MDT does not utilize taste masking. Commonly the drugs may have dissolution conditions as in USP monograph. Other media such as 0.1NHCl, pH 4.5 and pH 6.8 buffers should be used for evaluation of MDT. Experience has indicated that USP 2 paddle apparatus is most suitable and common choice for dissolution test of MDT tablets, where a paddle speed of 50 rpm is commonly used. The USP 1 (basket) apparatus may have certain applications for MDT but used less frequently due to specific physical properties of tablets. Specifically tablet fragments or disintegration tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible results in dissolution profile⁵⁸.

14. Stability Study (Temperature Dependent): The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies. (i) 40 ± 1 °C (ii) 50 ± 1°C (iii) 37 ±1 ° C and RH 75% ± 5% The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegration, Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25°C^{41, 59}.

SUITABLE CANDIDATE FOR MDTs: 16, 20, 47, 60

Anxiolytic, Sedatives, Hypnotics and Neuroleptics: Alprazolam, Amyiobarbitone, Barbitone, Bentazepam, Bromazepam, Bromperidol, Brotizolam, Butobarbitone, Carbromal, Chlordiazepoxide, Chlormethiazole.

Anti-diabetics: Glipizide, Tolazamide, Tolbutamide Acetohexamide, Chlorpropamide, Glibenclamide, Gliclazide.

Analgesics and Anti-inflammatory Agents: Aloxiprin, Auranofin, Azapropazone, Benorylate, Diflunisal, Etodolac, Fenbufen, Fenoprofen Calcium.

Anthelmintics: Albendazole, Bephenium Hydroxynaphthoate, Cambendazole, Dichlorophen, Ivermectin, Mebendazole, Oxarnniquine, Oxfendazole, Praziquantel, Pyrantel Embonate, Thiabendazole.

Anti-neoplastic Agents and Immunosuppressants: Aminoglutethimide, Amsacrine, Azathioprine, Busulphan, Chlorambucil, Cyclosporin, Dacarbazine, Estramustine, Etoposide.

Anti-Arrhythmic Agents: Amiodarone, Disopyramide, Flecainide Acetate, Quinidine Sulphate.

Anti-bacterial Agents: Benethamine Penicillin, Cinoxacin, Ciprofloxacin HCl, Clarithromycin, Cloxacillin, Doxycycline, Erythromycin, Ethionamide, Imipenem, nalidixic acid, Nitrofurantoin, Rifampicin.

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

Anti-depressants: Amoxapine, Ciclazindol, Maprotiline HCl, Mianserin HCl, Trazodone HCl, Trimipramine Maleate.

Anti-fungal Agents: Amphotericin, Butoconazole nitrate, Clotrimazole, Econazole nitrate, Fluconazole.

Anti Protozoal Agents: Benznidazole, Clioquinol, Decoquinol, Diodohydroxyquinoline, Diloxanide Furoate, Dinitolmide, Furzolidone, Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.

Anti-malarials: Amodiaquine, Chloroquine, Chlorproguanil HCl, Halofantrine HCl, Mefloquine HCl, Proguanil HCl, Pyrimethamine.

Anti-Epileptics: Beclamide, Carbamazepine, Clonazepam, Ethotoin, Methoin, Methsuximide, Methylphenobarbitone, Oxcarbazepine.

Anti-gout Agents: Allopurinol, Probenecid, Sulphinpyrazone.

Anti-Hypertensive Agents: Amlodipine, Carvedilol, Benidipine, Darodipine, Diazoxide, Felodipine, Nicardipine, Nifedipine, Nimodipine, Phenoxybenzamine, Prazosin, Reserpine, Terazosin.

Anti-migraine Agents: Dihydroergotamine Mesylate, Ergotamine Tartrate, Methysergide Maleate, Pizotifen Maleate, Sumatriptan Succinate.

Anti-parkinsonian Agents: Bromocriptine Mesylate, Lysuride Maleate.

Table 6: List of Marketed Mouth Dissolving Tablets: ⁶¹⁻⁶²

S. No.	Trade Name	Active Drug	Manufacturer
1.	Felden fast melt	Piroxicam	Pfiser Inc., NY, USA
2.	Claritin redi Tab	Loratidine	Schering plough Corp., USA
3.	Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
4.	Zyprexia	Olanzapine	Eli Lilly, Indianapolis, USA
5.	Pepcid RPD	Famotidine	Merck and Co., NJ, USA
6.	Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
7.	Zoming-ZMT	Zolmitriptan	AstraZeneca, Wilmington, USA
8.	Zeplar TM	Selegiline	Amarin Corp., London, UK
9.	Temptra Quiclets	Acetaminophen	Bristol Myers Squibb, NY, USA
10.	Febrectol	Paracetamol	Prographarm, Chateaufort, France
11.	Nimulid MDT	Nimesulide	Panacea Biotech, New Delhi, India
12.	Torrox MT	Rofecoxib	Torrent Pharmaceuticals, India
13.	Olanex instab	Olanzapine	Ranbaxy Lab. Ltd. New-Delhi, India
14.	Romilast	Montelukast	Ranbaxy Lab. Ltd. New-Delhi, India
15.	Benadryl Fastmelt	Diphenhydramine and pseudoephedrine	Warner Lambert, NY, USA
16.	Propulsid Quicksolv	Cisapride monohydrate	Janssen Pharmaceuticals
17.	Risperdal MTab	Risperidone	Janssen Pharmaceuticals
18.	Spasfon Lyoc)	Phloroglucinol Hydrate	Farmalyoc
19.	Nurofen FlashTab)	Ibuprofen	Ethypharm
20.	Temptra Quicklets	Paracetamol	Cima Labs, Inc.
21.	Zolmig Repimelt	Zolmitriptan	Cima Labs, Inc.
22.	(NuLev	Hyoscyamine Sulfate	Cima Labs, Inc.
23.	Gaster D)	Famotidine	Yamanouchi Pharma Tech. Inc.
24.	Cibalgina DueFast	Ibuprofen	Eurand International
25.	Relivia Flash dose	Tramadol HCl	Fuisz Technology, Ltd.
26.	Hyoscyamine Sulfate ODT	Hyoscyamine Sulfate	KV Pharm. Co., Inc.
27.	Abilify Discmelt	Aripiprazole	Otsuka America/Bristol-Myers Squibb

28.	Allegra ODT	Fexofenadine	Sanofi Aventis
29.	Aricept ODT	Donepezil	Eisai Co.
30.	Clarinet RediTabs	Desloratadine	Schering-Plough
31.	Alavert	Loratadine	Wyeth
32.	Clonazepam ODT	Clonazepam	Par Pharmaceutical
33.	FazaClo	Clozapine	AzurPharma
34.	Jr. Tylenol Meltaways	Acetaminophen	McNeil Consumer Healthcare
35.	Klonopin Wafers	Clonazepam	Roche
36.	Loratadine Redidose	Loratadine	Ranbaxy
37.	Mirtazapine ODT	Mirtazapine	Teva Pharmaceuticals
38.	Niravam	Alprazolam	Schwarz Pharma
39.	Ondansetron ODT	Ondansetron	Teva Pharmaceuticals
40.	Orapred ODT	Prednisolone	Sciele Pharma

FUTURE PERSPECTIVE:

Although there are a large number of commercial products on the market, there are still many aspects to improve in the MDT formulations. MDT technologies are now a day's very advanced, but formulation of hydrophobic drugs is still a challenge, especially when the amount of drug is high. A new technology is being developed to incorporate higher doses of hydrophobic drugs without affecting the fast disintegrating property. In future scientists also involve in the development of MDTs with controlled release properties. If one MDT can deliver drugs with short half-lives for 12–24 hours, it would be a quantum improvement in the MDT technology. The added convenience and compliance of such formulations would be enormous. In future, new technologies will be invented in order to development of effective taste-masking properties. The use of coating in case of poorly tasting drugs is commonly used, but it increases the total volume of the final formulation. So, with continued innovations, one

can expect the emergence of more novel technologies for MDTs in the days to come. A number of companies are having their own brands of fast dissolving tablets. The use of modern technologies and the advantages of fast dissolving tablets will increase its popularity in the near future and it is expected that, a day may come where these fast dissolving tablets due to their remarkable advantages may replace a large percentages of the conventional products.

CONCLUSIONS:

The popularity of MDTs has increased tremendously over the last decade. The key to MDT formulations is fast disintegration, dissolution, or melting in the mouth, and this can be achieved by producing the porous structure of the tablet matrix or adding superdisintegrant and/or effervescent excipients. The clinical studies show MDTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability. However, common people are not much aware of this delivery system. Therefore, pharmacists are responsible to

spread the knowledge regarding this system. This dosage form should be handled carefully since they do not have sufficient mechanical strength. The packaging of MDTs are also very important. Patients who suffer from dryness of mouth should not be prescribed with MDTs, because, minimum volume of saliva is necessary for it to disintegrate/dissolution. This dosage form is very much suitable for paediatric patients who having no primary teeth and for geriatric patients who have lost their teeth permanently. Extensive works had been carried out till date in order to evaluate the MDTs and among them many are proved to have significant discriminatory power. Thus, in near future, it is expected that this delivery system will get much importance as that of conventional delivery systems.

REFERENCE:

1. Sastry SV, Nyshadham JR, Fix JA. Recent technological advances in oral drug delivery. A review. *Pharm Sci Technol Today* 2000; 3:138–145.
2. Kaur T, Bhawandeep G, Sandeep K, Gupta G D. Mouth dissolving tablets: a novel approach to drug delivery. *Int J Curr Pharm Res.* 2011; 3:1-7.
3. Habib W, Khankari RK, Hontz J. Fast-dissolve drug delivery systems. *Crit Rev Ther Drug Carrier Sys* 2000; 17:61–72.
4. Lindgren S, Janzon L. Dysphagia: prevalence of swallowing complaints and clinical finding. *Med Clin North Am* 1993; 77:3–5.
5. Hanawa T. New oral dosage form for elderly patients: preparation and characterization of silk fibroin gel. *Chem Pharm Bull* 1995; 43: 284–288.
6. Gisel EG. Oral motor skills following sensorimotor intervention the moderately eating impaired child with cerebralpalsy. *Dysphagia* 1994; 9: 180–192.
7. Virely P, Yarwood R. Zydis - a novel, fast dissolving dosage form. *Manuf Chem* 1990; 61: 36–37.
8. Pebley WS, Jager NE, Thompson SJ. Rapidly disintegrating tablet. US Patent 5, 298, 261; 1994.
9. Watanabe Y. New compressed tablet rapidly disintegrating in the mouth using crystalline cellulose and a Disintegrant. *Biol Pharm Bull* 1995; 18: 1308–1310.
10. Myers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product there from. PCT Patent WO 95/34293-A1;1995.
11. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. US Patent 5,587,180; 1996 .
12. Koizumi KI, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method for preparing high porosity rapidly saliva soluble compressed tablets using mannitol with Camphor, a subliming material. *Int J Pharm.* 1997; 152: 127–131
13. Dutta S, De P. Formulation of fast disintegrating tablets. *Int J Drug Formulation & Res* 2011; 2: 45-51.
14. Deshmukh KR, Patel V, Verma S, Pandey AK, Dewangan P. A review on mouth dissolving tablet techniques. *Int J Res in Ayurveda & Pharmacy* 2011; 2: 66-74.
15. Dinesh V, Sharma I, Sharma V. A comprehensive review on fast dissolving tablet technology. *J Applied Pharma Sci* 2011; 1: 50-58.
16. Reddy Brahma DR, Reddy VY, Lalitha CT. Rapimelts: A review. *J Pharma and Biomedical Sci* 2011; 6: 1-8.
17. Kumari S, Visht S, Sharma PK. Fast dissolving drug delivery system: Review article. *J Pharma Res* 2010; 3: 1444-1449.
18. Ghadge SJ, Keskar SR, Dube RK. Oral disintegrating tablets: An Overview. *Int J Universal Pharmacy and Life Sci* 2011; 1: 35-50.
19. Patel GJ, Patel RJ, Patel PK, Bharadia PD, Pandya VM, Modi DA. An overview on future trends in oral formulation technologies: Orally disintegrating tablet. *J Pharma and Cosmetology* 2011; 1: 42-55.
20. Sharma R, Rajput M, Prakash P, Sharma S. Fast dissolving drug delivery system- A Review. *Int Res J Pharm* 2011; 2 : 21-29.
21. Bhowmik D, Chiranjib B, Krishnakanth , Pankaj, Chandira RM. Fast Dissolving Tablet: An Overview. *J Chemical Pharma Res* 2009; 1: 163-177.
22. Sreenivas SA, Dandagi PM, Gadad AP, Godbole AM, Hiremath SP, Mastiholimath VS et al. Orodispersible tablets: New-fangled drug delivery system – A Review. *Indian J Pharma Edu Res* 2005; 39: 177-181.

23. Bhatu P, Mundada AS. The technologies used for developing orally disintegrating tablets: A review. *Acta Pharm* 2011; 61: 117–139 .
24. Augsburger Larry L, Hoag Stephen W. Orally disintegrating tablets and related tablet formulations. *Pharmaceutical dosage forms: Tablets*. Informa Healthcare 2008; 2: 293-311.
25. Gupta A, Mittal A, Jha KK. Fast Dissolving Tablet-A Review. *The Pharma Innovation* 2012; 1: 1-7.
26. Koizumi K, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method of preparing high-porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material. *International Journal of Pharmaceutics* 1997; 152: 127-31.
27. Gohel M, Patel M, Amin A, Agrawal R, Dave R, Bariya N. Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique. *AAPS PharmSciTech* 2004; 5: 10-15.
28. Gavaskar B, Kumar SV, Sharan G, Nagaraju M, Rao YM. Present investigations and future prospects of oral disintegrating tablets: A review. *Int J Pharma Sci and Res* 2010; 1: 14-28.
29. Shukla D, Chakraborty S, Singh S, Mishra B. Mouth Dissolving Tablets I: An Overview of Formulation Technology. *Sci Pharm*. 2009; 77: 309–26.
30. Kuno Y, Kojima M, Ando S, Nakagami H. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. *J Control Release* 2005; 105: 16-22.
31. Yu DG, Shen XX, Han J, Zhu LM, Branford-White C, Li XY et al. Oral Fast-Dissolving DDD Fabricated Using 3DP, Bioinformatics and Biomedical Engineering. *The 2nd International Conference* 2008; 1602–1605.
32. 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: 2132-2136.
33. Modi A, Tayade P. Enhancement of dissolution profile by solid dispersion (kneading) technique. *AAPS Pharm. Sci. Tech.* 2006; 7: 68.
34. Reig AR, Plazas F, Galvan CJ, Heras NJ, Artes FM, Gabarron HE. Acceptance survey of a fast dissolving tablet pharmaceutical formulation in allergic patients, Satisfaction and expectancies. *Allergol Immunopathol. (Madr.)* 2006; 34 : 107-112.
35. Ahmed IS, Nafadi MM, Fatahalla FA. Formulation of a fast-dissolving ketoprofen tablet using freeze-drying in blisters technique. *Drug Dev Ind Pharm* 2006; 32: 437-442.
36. Cirri M, Valleri M, Mura P, Maestrelli F, Ballerini R. Development of fast-dissolving tablets of flurbiprofen-cyclodextrin complexes. *Drug Dev Ind Pharm* 2005; 31: 697-707.
37. Takagi H, Kajiyama A, Yanagisawa M. Rapidly disintegrable pharmaceutical composition. U.S. Patent 6,899,899; 2005.
38. Siddiqui MN, Garg G, Sharma P. Fast dissolving tablets: Preparation, characterization and evaluation: An Overview. *Int J Pharma Sci Review and Res* 2010; 4: 87-96.
39. Nagar P, Singh K, Chauhan I, Verma M, Yasir M, Khan A et al. Orally disintegrating tablets: Formulation, preparation techniques and evaluation. *J Applied Pharma Sci* 2011; 1: 35-45.
40. Gajare GG, Bakliwal SR, Rane BR, Gujrathi NA, Pawar SP. Mouth dissolving tablets: A review. *Int J Pharma Res & Deve* 2011; 3 : 280 – 296.
41. Arunachalam A, Karthikeyan M, kumar A, Konam K, Prasad P, Sethuraman S et al. Fast dissolving drug delivery system: A review. *J Global Trends in Pharma Sci* 2010; 1: 92-110.
42. Chawla M, Srinivasan G. Evaluation of galen IQ polymer in tramadol hydrochloride orally disintegrating tablet. *Int J Drug Delivery* 2011; 3: 439-455.
43. Bhowmik D, Jayakar B, Kumar SK. Design and characterisation of fast dissolving tablet of telmisartan. *Int J Pharma Recent Res* 2009; 1: 31-40.
44. Kumar R, Patil S, Patil SR, Paschapur MS. Formulation, evaluation of mouth dissolving tablets of fenofibrate using sublimation technique. *Int J Chem Tech Res* 2009; 1: 840-850.
45. Subrahmanyam CVS. *Textbook of Physical Pharmaceutics*. 2nd edn, Vallabh Prakashan, Delhi, 2000, 215.
46. Bikshapathi D, Kandikonda S, Uppuluru AK, Gade S, Bhupathi S. Fast dissolving tablets: An update. *Int Res J Pharmacy* 2011; 2: 45-53.

47. Patwa S, Narang N, Singla M, Singla RK. An overview on fast dissolving tablet. *Webmed Central Pharma Sci* 2011; 2: 1-16.
48. Roshan RR, Chirra P, Venkataramudu T. Fast dissolving tablets: A novel approach to drug delivery—A Review. *Int J Preclinical and Pharma Res* 2012; 3: 23-32.
49. Ratnaparkhi MP, Mohanta GP, Dr. Upadhyay L. Review on: Fast dissolving tablet. *J Pharmacy Res* 2009; 2: 5-12.
50. Sivakranth.M, Althaf Abdul S, Rajasekhar S. Formulation and evaluation of oral fast dissolving tablets of sildenafil citrate. *Int J Pharm and Pharma Sci* 2011; 3: 112-121.
51. Lachman Leon, Liberman Herbert A, Kanig Joseph L. *The Theory and Practice of Industrial Pharmacy*. 3rd edn., Varghese publishing house, 1987, 296-303.
52. Panigrahi R, Behera SA review on fast dissolving tablets. *Webmed Central quality and patient safety* 2010; 1: 1-15.
53. Basu B, Bagadiya A, Makwana S, Vora V, Batt D, Dharamsi A. Formulation and evaluation of fast dissolving tablets of cinnarizine using superdisintegrant blends and subliming material. *J Advanced Pharma Tech & Res* 2011; 2: 266-273.
54. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. *Asian J Pharma* 2008; 2: 2-11.
55. Parashar B, Chauhan A, Prashar D, Chandel A, Kumar H, Purohit R. Formulation and evaluation aspects of tablets—An overview. *Am J PharmTech Res* 2012; 2: 68-80.
56. Panigrahi R, Behera S, Panda C. A review on fast dissolving tablets. *Webmed Central Pharma Sci* 2010; 1: 1-15.
57. Swamivelmanickam M, Manavalan R, Valliappan K. Mouth dissolving tablets: An overview. *Int J Pharma Sci and Res* 2010; 1: 43-55.
58. Velmurugan S, Vinushitha Sundar. Oral disintegrating tablets: An overview. *Int J Chemical and Pharma Sci* 2010; 1: 1-12.
59. Sehgal P, Gupta RG, Singh UK, Chaturvedi A, Gulati A, Sharma M. Fast Dissolving Tablets: A New Venture in Drug Delivery. *Am. J. PharmTech Res*. 2012; 2: 253-279.
60. Puttalingaiah L, Kunchu K, Tamizh MT. Fast disintegrating tablets: An overview of formulation, technology and evaluation. *Res J Pharma, Biological and Chemical Sci* 2011; 2: 589-601.
61. Sammour OA, Hammad MA, Megrab NA. Formulation and Optimization of Mouth Dissolve Tablets Containing Rofecoxib Solid Dispersion. *AAPS PharmSciTech*. 2006; 7: 162-169
62. Fini A, Bergamante V, Ceschel GC, Ronchi C. Fast dispersible/slow releasing ibuprofen tablets. *European Journal of Pharmaceutics and Biopharmaceutics* 2008; 69: 335–341.