AN OVERVIEW ON FAST DISINTEGRATING TABLETS


Indira College of Pharmacy, Vishnupuri, Nanded. (MS) 431601, India

ABSTRACT

Fast dissolving drug delivery systems (FDDS) were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms. Over the past three decades, fast disintegrating tablets (FDTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. FDTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. The convenience of administration and improved patient compliance are important in the design of oral drug delivery system which remains the preferred route of drug delivery inspite of various disadvantages. Such problem can be solved in the novel drug delivery system by formulating “Fast disintegrating tablets” (FDTs) which disintegrates or dissolves rapidly without water within few seconds in the mouth due to the action of superdisintegrant or maximizing pore structure in the formulation. The review describes the various formulation aspects, superdisintegrants employed and technologies developed for FDTs, along with various excipients, evaluation tests, taste masking methods, marketed formulation and drugs used in this research area.

KEYWORDS: Dysphagia, Fast Disintegrating, Disintegration Time, Lyophilization, Direct Compression, Superdisintegrant.

INTRODUCTION

The FDTs emerged with an objective to improve patient compliance. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for pediatric and geriatric patients. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elderly and dysphagic patients. This disorder of dysphagia is associated with many medical conditions including stroke, parkinson’s disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy. One study showed that 26% out of 1576 patients experienced difficulty in swallowing tablets due to their large size, followed by their surface, shape and taste. Rapid
breakdown or fast disintegrating tablet of the type of those intended to undergo disaggregation in the mouth in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. It is better known by the phase "oral disintegrating tablets".

The Center for Drug Evaluation and Research (CDER) defines FDTs as a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed under the tongue. The European Pharmacopoeia however defines a similar term, orodispersible tablets, or tablets intended to be placed in the mouth where it disperses rapidly before swallowing. FDTs are known by various names such as “fast-melting, fastdissolving, mouth melts, mouth dissolving, quick disintegrating, porous tablets, rapid melts or orodispersible tablets.” As the tablet disintegrates in mouth, this can enhance the clinical effect of drug through pregastric absorption from the mouth, pharynx and esophagus. In such cases, bioavailability of drug is significantly enhanced by avoiding first pass hepatic metabolism than those observed with conventional tablets. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction it has been shown in table 1.

Table 1: Some of promising drugs candidate for fast disintegrating tablets:

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibacterial agents</td>
<td>Ciprofloxacin, Tetracycline, Erythromycin, Rifampicin, Penicillin, Doxycyclin, Nalidixic Acid, Trimethoprim, Sulphacetamide, Sulphadiazine etc.</td>
</tr>
<tr>
<td>Anti Helminatics</td>
<td>Albendazole, Mebendazole, Thiabendazole, Livermectin, Praziquantel, Pyrantel Embonate, Dichlorophen etc.</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Acetazolamide, Clorthiazide, Amiloride, Furosemide, Spironolactone, Bumetanide, Ethacrynic Acid, etc.</td>
</tr>
<tr>
<td>Anti Diabetics</td>
<td>Glibenclamide, Glipizide, Tolbutamide, Tolazamide, Gliclazide, Chlorpropamide etc.</td>
</tr>
<tr>
<td>Anti Depressants</td>
<td>Trimipramine maleate, Nortriptyline HCl, trazodone HCl, Amoxapine, Mianserin HCl, etc.</td>
</tr>
<tr>
<td>Anti Hypertensives</td>
<td>Amlodipine, Carvedilol, Diltiazem, Felodipine, Minoxidil, Nifedipine, Prazosin HCl, Nimodipine, Terazosin HCl etc.</td>
</tr>
<tr>
<td>Category</td>
<td>Examples</td>
</tr>
<tr>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Anti Histamines</td>
<td>Acrivastine, Cetirizine, Cinnarizine, Loratadine, Fexofenadine, Triprolidine, etc.</td>
</tr>
<tr>
<td>Anti Arrhythmics</td>
<td>Disopyramide, Quinidine Sulphate, Amiodarone HCl, etc.</td>
</tr>
<tr>
<td>Analgesics/Anti-Inflammatory agents</td>
<td>Diclofenac Sodium, Ibuprofen, Ketoprofen, Mefenamic Acid, Naproxen, Oxyphenbutazone, Indomethacin, Piroxicam, Phenylbutazone, etc.</td>
</tr>
<tr>
<td>Anxiolytics, Sedatives, Hypnotics and Neuroleptics</td>
<td>Alprazolam, Diazepam, Clozapine, Amylobarbitone, Lorazepam, Haloperidol, Nitrazepam, Midazolam Phenobarbitone, Thioridazine, Oxazepam, etc.</td>
</tr>
</tbody>
</table>

**ADVANTAGES OF FAST DISINTEGRATING TABLETS:2:**

- Does not require water for oral administration.
- Insensitive to environmental conditions such as humidity and temperature.
- Have a pleasant mouth feel.
- FDT passes all the advantages of solid dosage forms like good stability, easy manufacturing, unit and accurate dosing, easy handling etc.
- Provides rapid drug therapy intervention.
- There is no risk of physical obstruction due to dosage form.
- The possibility of an improved bioavailability due to rapid absorption and faster onset of action.
- Ease of administration to patients who are unable or refuses to swallow a tablet, such as pediatric, geriatric and psychiatric and disabled patients.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.
- Allows high capacity of drug loading.
✓ FDTs helps avoids hepatic metabolism by allowing pregastric drug absorption thus reducing the dose of drug required.
✓ Adaptable to existing processing and packaging machinery.
✓ Cost effective.
✓ Mark potential faster onset of action than conventional oral dosage forms.

LIMITATION OF FAST DISINTEGRATING TABLETS:
✓ 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.
✓ Drugs with relatively large doses are difficult to formulate into FDTs.
✓ Patients who concurrently take anti-cholinergic medications may not be the best candidates for FDTs.

DRUG SELECTION CRITERIA:\(^3\):
✓ The ideal characteristics of a drug for FDT include:
✓ Ability to permeate oral mucosa.
✓ At least partially non-ionized at the oral cavity.
✓ Have the ability to diffuse and partition into the epithelium of the upper GI (log P>1 or log P>2).
✓ Small to moderate molecular weight.
✓ Low dose drugs preferably less than 50 mg.
✓ Short half-life and frequent dosing drugs are unsuitable for FDT.
✓ Drug should have good stability in saliva and water.
✓ Very bitter or unacceptable taste and odor drugs are unsuitable for FDT.

MATERIALS AND METHODS:
✓ Freeze drying/Lyophilization
✓ Moulding
✓ Mass extrusion
✓ Sublimation
✓ Spray drying
✓ Cotton candy process
✓ Nanonization
✓ Direct compression
Freeze drying / lyophilization:

It is one of the first generation techniques for preparing FDT, in which sublimation of water takes place from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allow removal of water by sublimation.

Freeze drying process normally consists of three steps:

- Material is frozen to bring it below the eutectic point.
- Primary drying to reduce the moisture around 4% w/w of dry product.
- Secondary drying to reduce the bound moisture up to required final volume.

Due to lyophilization, bulking agent and sometimes drug acquire glossy amorphous structure and thus dissolution is enhanced. The tablets prepared by freeze drying or lyophilisation are very porous in nature and disintegrate or dissolve rapidly when it comes in contact with saliva.

Molding:

Tablets produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. There are two types of molding process:

1. Solvent method: Solvent method involves moistening the powder blend with a hydroalcoholic solvent followed by compression at low pressure in molded plates to form a wetted mass. Air drying is done to remove the solvent. Such tablets are less compact than compressed tablets and possess a powder structure that hastens dissolution.

2. Heat method: In the heat molding process a suspension is prepared that contains a drug, agar and sugar (mannitol or lactose). This suspension is poured in the blister packaging wells, and then agar is solidified at the room temperature to form a jelly and dried at 30°C under vacuum. The main concern about these molded tablets is their mechanical strength, which can be achieved by using binding agents.

Spray drying:

Spray drying is a process, in which fine powders can be produced. Spray dryers are invariably used in the pharmaceutical industry to produce highly porous powders.

Allen et al. have used spray drying for the production of FDT’s. The formulations contained hydrolysed and nonhydrolysed 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 (eg: citric acid) or an alkali (eg: sodium bicarbonate) disintegration and dissolution were further
enhanced. Tablets manufactured by this method show disintegration time < 20 sec in an aqueous medium.

**Sublimation**:  
This process involves addition of some inert volatile substances like urea, urethane, camphor etc to other excipients and compression of blend into tablet. Removal of volatile material by sublimation creates pores in the tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Fast dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.

**Fig 1: Steps involved in sublimation process**

**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 and cutting into even segments up to heated blade to form tablets.

**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 in to
of the FDT’s. This technique is mainly advantageous for poor water soluble drugs and also for wide range of doses (up to 200 mg of drug per unit).

**Cotton candy process**: This process is so named as it utilizes an inimitable spinning mechanism to produce floss like crystalline structure, which mimics cotton candy. This technique involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have better flow properties and compressibility. This matrix is milled and blended with active ingredients as well as excipients and subsequently compressed to FDTs. This process can accommodate high doses of drug and offers improved mechanical strength. However, high process temperature limits the use of this process.

**Direct compression**: Direct compression represents the simplest and most effective tablet manufacturing technique. FDT can be prepared by using this technique because of the availability of improved excipients especially superdisintegrants and sugar based excipients.

(a) **Superdisintegrants**: In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases. Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorbs water and swells due to capillary action and are considered as effective disintegrants in the preparation of fast dissolving tablets. Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug. The major drawback of effervescent excipients is their hygroscopicity. Hence their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product.

(b) **Sugar based excipients**: This is another approach to manufacture FDT by direct compression. The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, maltitol, sorbitol, starch hydrolysate, polydextrose and xylitol which display high aqueous solubility and sweetness and hence impart taste masking property and a pleasing mouth feel.

**EXCIPIENTS USED FOR FORMULATING FDTs**: 
Excipients:

Super disintegrants:
Crosspovidone, Microcrystalline cellulose, sodium starch glycollate, sodium carboxy methyl cellulose, pregelatinized starch, calcium carboxy methyl cellulose, and modified corn starch. Sodium starch glycollate has good flowability than croscarmellose sodium. Cross povidone is fibrous in 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, citrus oils, fruit essences.

Sweetners: Aspartame and 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.

Lubircants:
Stearic acid, Magnesium stearate, Zinc state, Calcium stearate, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide.

Mechanism of Superdisintegrants:\(^5\):
There are four major mechanisms for tablet disintegration as follows

1. Swelling:
Perhaps 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. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration again slows down.

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.

WICKING SWELLING
Water is pulled by disintegrant Particles swell and break up and reduced the physical the matrix form within bonding force between particle

DEFORMATION REPULSION
Particles swell to precompression Water is drawn into pores and particles repel each size and break up matrix other because of resulting electrical force.

3. Due to disintegrating particle/particle repulsive forces
Another mechanism of disintegration attempts to explain the swelling of tablet made with ‘nonswellable’ disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on
the observation that nonswelling particle also cause 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. This may be a mechanism of starch and has only recently used in studies.

Table 2: Superdisintegrants used in FDTs:

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Example</th>
<th>Mechanism of action</th>
<th>Special comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosscarmellose® Ac-Di-Sol®</td>
<td>Crosslinked cellulose</td>
<td>Swells 4-8 folds in &lt; 10 seconds. - Swelling and wicking both</td>
<td>Swells in two dimensions. - Direct compression or granulation - Starch free</td>
</tr>
<tr>
<td>Nymce ZSX®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primellose®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solutab®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vivasol®L-HPC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crosspovidone</td>
<td>Crosslinked PVP</td>
<td>Swells very little and returns to original size after compression but act by capillary action</td>
<td>- Water insoluble and spongy in nature so get porous tablet</td>
</tr>
<tr>
<td>Crosspovidon M®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kollidon®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyplasdone®</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
TASTE Masking METHODS:
The drugs are mostly bitter in nature. Skillful taste masking is needed to hide the bitter taste in FDTs formulations. This can be achieved by using combination of right flavor and right sweeteners. The taste masking in FDTs has more influences on dissolution method development, specifications, and testing. Following methods are used in taste masking.

Incorporation of Sweeteners and Flavors:
Mannitol and aspartame are most widely used excipients in formulating FDTs. (Chang et al., 2000.) Different flavors are also used in FDT formulations to mask the bitter taste and give pleasant mouth feel. Most commonly used flavors are mint, orange, strawberry, pineapple, peppermint flavors.

Adjustment of pH values:
Many drugs are less soluble at pH different from the pH of the mouth, which are around 5.9. Drugs can be insufficiently solubilized to be available to taste if the equilibrium concentration is below the taste threshold.

Effervescent Technique:
Effervescent tablet rapidly disintegrates and carbon dioxide is produced by contact with saliva or aqueous fluid. So the bitter taste of the drugs can be masked by this method.

Spray Drying Technique:
It involves simple wet granulation method or roller compaction of other excipients. Spray drying can also employed to shroud the drug.

Coating of Drug Particles with Inert Agents: Coating is an extremely useful technique for number of applications in the pharmaceutical field. By coordinating the right type of coating material it is possible to completely mask the taste of a bitter drug, while at the same time, not adversely affecting the intended drug release profile. Any nontoxic polymer that is insoluble at pH 7.4 and soluble at acidic pH would be an acceptable alternative for taste masking.

Taste Masking by Formation of Inclusion Complexes:
The complexing agent is capable of masking the bitter taste of the drug by decreasing the amount of drug particles exposed to taste buds thereby reducing the perception of bitter taste. Vander Waals forces are mainly involved in inclusion complexes. –cycloextrin is most widely used complexing agent for inclusion type complexes. It is sweet, nontoxic, cyclic oligosaccharide obtained from starch. Cyclodextrin help to solubilize many drugs.

Ion Exchange Resin:
When the drug resinates comes into contact with the gastrointestinal fluids, such as the acid of the stomach. The drug is released from resinate directly into solution and then absorbed in the usual way. The resin passes through the GI tract without being absorbed. Examples of drugs where this technique has been successfully demonstrated include ranitidine, risperidone and paroxetine.

**Molecular Complexes of Drug with other Chemicals:**

Molecular complex formation can decrease the intensity of bitterness of drug. Higuchi and Pitman reported that caffeine forms complexes with organic acids that are less soluble than xanthane and as such can be used to decrease the bitter taste of caffeine.

**Microencapsulation:**

Microencapsulation as a process has been defined by Bakan as a means of applying relatively thin coating to small particles of solid, droplets of liquid and dispersion. This process can be used for masking of bitter tasting drugs microencapsulating drug particles with various coating agents.

**Mass Extrusion Method (Dispersion coating):**

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.

**Solid Dispersion System:**

Solid dispersion is also called as co precipitates for those preparations obtained by solvent method such as co precipitates of sulphathiazole and povidone. Solid dispersions using insoluble matrices or bland matrices may be used to mask the bitter taste of drugs. Also using them as absorbents on various carriers may increase the stability of certain drugs.

**PATENTED TECHNOLOGIES FOR FDTs**

**Zydis Technology:**

Zydis formulation is a unique freeze dried technique in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When Zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many material designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed
drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freezedrying process or long-term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

**Durasolv Technology:**

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amount of active ingredients.

**Orasolv Technology:**

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable.

**Flash Dose Technology:**

Flash dose technology has been patented by Fuisz. Nurofen Meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

**Wow tab Technology:**

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means “Without Water”. In this process, combination of low mouldability saccharides an high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (e.g. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (e.g. Maltose, oligosaccharides) and compressed into tablets.

**Flash tab Technology:**

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like coacervation, microencapsulation and extrusion spheronisation. All the processing utilized conventional tableting technology.

**EVALUATION OF FAST DISINTEGRATING TABLETS:**

FDTs formulations have to be evaluated for the following evaluation test.

**General Appearance:**
The general appearance of a tablet, its visual identity and overall elegance is essential for consumer acceptance. It includes tablets size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and eligibility of any identifying marking.

**Size and Shape**

The size and shape of the tablet can be dimensionally described, monitored and controlled.

**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 micrometer.

**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.

**Table No. 03**:

<table>
<thead>
<tr>
<th>Average weight of tablets</th>
<th>Maximum percentage difference allowed</th>
</tr>
</thead>
<tbody>
<tr>
<td>130 or less</td>
<td>10</td>
</tr>
<tr>
<td>130-324</td>
<td>7.5</td>
</tr>
<tr>
<td>More than 324</td>
<td>5</td>
</tr>
</tbody>
</table>

**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.

**Friability**:

It is a measure of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabilator. Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At
the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as; %Friability = loss in weight / Initial weight x 100

**In Vivo Disintegration test**: 
The test was carried out on 6 tablets using the apparatus specified in Pharmacopoeias using various disintegration media and the time in seconds taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured.

**Wetting time**: 
The method reported by Yunixia et al., was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson’s buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined.

**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 were randomly selected and in vitro dispersion time was performed.

**Stability testing of drug (temperature dependent stability studies)**: 
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;

- 40 ± 1°C
- 50 ± 1°C
- 37 ±1°C
- 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 used for plotting graph according Arrhenius equation and to determine the shelf life at 250°C.

**In vitro dissolution test**: 
The development of dissolution methods for FDTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent FDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for FDT much
in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

**Table No. 4: List of Commercially Available Fast Dissintegrating Tablets**

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Active Drug</th>
<th>Manufacturer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxalt MLT</td>
<td>Rizatriptan</td>
<td>Merck and Co., NJ, USA</td>
</tr>
<tr>
<td>Zofran ODT</td>
<td>Ondansetron</td>
<td>Glaxo Welcome, Middlesex, UK</td>
</tr>
<tr>
<td>Nimulid MDT</td>
<td>Nimesulide</td>
<td>Panacea Biotech, New-Delhi, India</td>
</tr>
<tr>
<td>Olanex</td>
<td>Instab Olanzapine</td>
<td>Ranbaxy Labs Ltd., New-Delhi, India</td>
</tr>
<tr>
<td>Torrox MT</td>
<td>Rofecoxib</td>
<td>Torrent Pharmaceuticals, Ahmedabad, India</td>
</tr>
</tbody>
</table>

**CONCLUSION**

FDTs offer numerous significant advantages over conventional dosage forms because of improved efficacy, bioavailability, rapid onset of action, better patient compliance, and acceptance. Pediatric and geriatric patients are primary concerns, as both the groups find these dosage forms convenient to administer as compared to the conventional dosage forms. FDTs can be prepared in several ways and product performance depends upon the drug suitability and excipients selection in the delivery system. Due to the availability of various formulation techniques, good patient compliance and huge potential, several products have already been commercialized. Furthermore, market size and popularity of these dosage forms will surely expand in future. It is also emphasized that newer with continued development of new pharmaceutical scientific and technological innovations should be undertaken for the emergence of promising and versatile dosage form with novel performance and characteristics for FDTs in days to come.
REFERENCES

1. Gavaskar B, Kumar SV and Nagarju M. Present investigation and future prospects of orodispersible tablet: A Review. Inter Journ Pharm Sciences and Research. 8(1);2010:14-20

2. Agarval VA, Rajurkar RM and Ingale RG. Fast Disintegrating Tablet as new Drug Delivery system: A Review. Pharmacophore.2(1);2011:1-8


For Correspondence
Sawant Samarth Mali
Email: malisawant54@gmail.com