A REVIEW ON FAST DISSOLVING FORMULATION TECHNOLOGIES

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ABSTRACT
Over the last few years, interest has been increased in developing innovative drug delivery systems to improve the safety, efficacy and patient compliance. Development of new chemical entity is not only expensive but also time taking process. This is why most of the pharmaceutical companies are now focusing on the development of new and improved drug delivery systems for the existing drugs. One such system is the fast dissolving tablets and films which are gaining popularity now days. These fast dissolving formulations are prepared in such a way that the total time taken by the active pharmaceutical ingredient to disintegrate is very less as compared to other formulations. This technique allows the drug to dissolve at a much faster rate thus reducing the time for the onset of action. These formulations are fast acting and can be administered without water. Therefore, they are very suitable for pediatric and geriatric patients; bed ridden patients; or patients suffering from dysphagia, Parkinson’s disease, mucositis, vomiting, migraine, fever, pain etc. Hence these are beneficial for the pediatric and geriatric patients. There are several methods employed for the manufacturing of such dosage forms such as casting, spraying, extrusion etc. the aim of the present investigation is to analyze and review rapidly disintegrating dosage forms.

KEYWORDS: Fast dissolving formulations, active pharmaceutical ingredient, pediatric, geriatric, casting, extrusion.

INTRODUCTION
Fast dissolving dosage forms have gained popularity and acceptance as new drug delivery systems due to their unique properties as they quickly disintegrate and dissolve in the mouth
and can be administered without water, making them particularly suitable for patients. Fast dissolving dosage forms include tablets, films and microspheres. Tablets are the most commonly used amongst them. Orally disintegrating drug delivery systems were originally devised by scientists at Wyeth Laboratories in the UK during the 1970s and their research lead to the outcome of Zydis, a patented formulation technology. Fast dissolving dosage forms are referred by different names like fast dissolving, porous tablet, melt-in-mouth, oro-dispersible, quick dissolving, orally disintegrating or rapidly disintegrating dosage forms.[1] The film or tablet is simply placed on patient's tongue or any oral mucosal tissue where due to instant wetting by saliva, the film rapidly hydrates and may adhere onto the site of application. It then rapidly disintegrates and dissolves to release the medicament. These formulations can be used for both local and systemic action.

**Fast Dissolving tablets**

Fast dissolving tablets (FDTs) are also known as fast disintegrating/melting tablets, Oro-dispersible tablets, rapimelts, and porous tablets. They dissolve or disintegrate within 60 seconds when placed in the mouth without drinking or chewing.[2] The active ingredients are absorbed through mucous membranes in the mouth and GIT and enter the blood stream. But due to certain disadvantages of fast dissolving tablets like: their physical solid form, sometimes difficult to carry, store and handle, leave unpleasant taste/grittiness in mouth if not formulated properly.[3] Psychological fear of swallowing, chewing or choking, low pressure molded tablets fabricated by different manufacturing methods and their expensive packaging cost. Moreover FDTs usually have insufficient mechanical strength, so careful handling is required. To protect the dosage form and to overcome such problems, a new technology was developed as fast dissolving oral films.

**Fast Dissolving Oral Films**

A fast-dissolving buccal film drug delivery system is a recent ultra thin novel formulation of postage stamp size which contains active pharmaceutical ingredients and excipients. Efficacy of API is improved as it dissolves or disintegrates in the saliva remarkably fast, within a few seconds without the need for water or chewing.[4] Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. Hydrophilic polymers are used to prepare films, which rapidly gets dissolved as soon as it comes in contact with saliva.
Salient features of fast dissolving films
These are thin and elegant films which can be made in various shapes and sizes, generally are of the size of a stamp. These strips are thin so are unobstructive and can be easily administered by pediatric and geriatric patients. They are mucoadhesive so adhere to the oral cavity for faster hydration which leads to fast disintegration of the film. Therefore, the film is quickly dissolved and releases the medicament showing quick onset of action.[5]

ADVANTAGES
1. Ease of administration and improved patient compliance.
2. Helpful in more convenient dosing.
3. There is no risk of choking, as in case of tablets and capsules.
4. Enhanced stability as compared to other dosage forms.
5. Taste masking of bitter drugs can be done.
6. These films have both site specific and local action.
7. Rapid disintegration and dissolution of films leads to rapid drug release.
8. Drug enters systemic circulation with decreased first pass metabolism.
9. Dose accuracy in comparison to syrup.[6]

Criteria for selection of drug
1. It should adhere to oral cavity and should be able to permeate the oral mucosa.
2. Drug must form thin and elegant film
3. It should be able to possess fast disintegration without water
4. Drug should have good stability in water as well as in saliva.
5. Drug should be partially unionized at pH of the oral cavity for better absorption
6. Effective in low dose up to 20mg as its the maximum dose for the preparation of fast dissolving films
7. Drug with pleasant taste and low to moderate molecular weight are preferred.[7]

Table 1: Comparison between Fast Dissolving, Tablets and Films [8, 9]

<table>
<thead>
<tr>
<th>Fast Dissolving Tablets</th>
<th>Fast Dissolving Films</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is a tablet</td>
<td>It is a film</td>
</tr>
<tr>
<td>Lesser dissolution due to less surface area</td>
<td>Greater dissolution due to larger surface area</td>
</tr>
<tr>
<td>Less durable as compared with oral films</td>
<td>Better durable than oral disintegrating tablets</td>
</tr>
<tr>
<td>Less patient compliance than films</td>
<td>More patient compliance</td>
</tr>
<tr>
<td>High dose can be incorporated</td>
<td>Low dose can only be incorporated</td>
</tr>
<tr>
<td>It has a fear of choking</td>
<td>No risk of chocking</td>
</tr>
</tbody>
</table>
Preparation Techniques For Fast Dissolving Oral Strips

1. Solvent casting
This is the most preferred method to manufacture fast dissolving film. Water soluble polymers are dissolved in water to form clear viscous solution and drug is dissolved with excipients in suitable solvent separately. Both the solutions are mixed and stirred. The solution is then casted in petri plate, dried and cut in uniform dimensions.

2. Semisolid casting
Solution of water-soluble film forming polymer is prepared in this method. Resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), prepared in NH4OH or NAOH. Appropriate amount of plasticizer is then added to obtain gel mass. Prepared gel mass is casted into films using heat controlled drums. Thickness of the film should be about 0.015-0.05 inches. Ratio of the acid insoluble polymer to film forming polymer should be 1:4.[10]

3. Hot Melt Extrusion
Hot metal extrusion is commonly used to prepare granules, sustained release tablets, transdermal and transmucosal drug delivery systems. The drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. And finally the melt is shaped in to films by the dies.

BENEFITS: Fewer operation units, better content uniformity and an anhydrous process.

4. Solid Dispersion Extrusion
The term solid dispersions refer to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers. In this method immiscible components are extruded with drug and solid dispersions are prepared. Drug is dissolved in a suitable liquid solvent. Then solution is incorporated into the melt of polyethylene glycol, obtainable below 70° C. Finally the solid dispersions are shaped in to films by means of dies.[11]

5. Rolling
A solution or suspension containing the drug is rolled on a carrier. Solvent used is water or water and alcohol. The solution or suspension should have specific rheological considerations. The film is then dried on the rollers and cut into desired size.
Preparation Techniques For Fast Dissolving Tablets

1. Lyophilization
This method is generally used for drying the heat sensitive drugs. Drying is done at low temperature and water is removed by sublimation process. Freeze-drying results in the formation of glossy amorphous structure resulting in highly porous and lightweight product. Thus the resulting tablet has rapid disintegration and dissolution when placed on the tongue and dissolves instantly to release the drug. The major advantage of this technology is that it offers less disintegration time but the technique is quite expensive and special packaging procedures are required. The storage conditions should be properly maintained as these tablets are less stable to changing environment; hence special packaging procedures are required. [12]

2. Tablet moulding
Tablets formed by molding process are highly porous in structure, resulting in high rate of disintegration and dissolution. This process includes moistening, dissolving, or dispersing the drugs with a solvent then molding the moist mixture into tablets. The powder mixture may be sieved prior to the preparation in order to increase the dissolution. The powder blend is moistened with a hydro-alcoholic solvent and is moulded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution. They disintegrate very quickly because these are made from water soluble excipients. In comparison to lyophilization process, tablets produced by moulding technique are easier to adapt to the industrial scale. Moulded tablets are cheaper and have poor mechanical strength. [13]

3. Direct compression
Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied for the formulation of FDT because of the availability of improved tablettting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugar based excipients. A type of disintegrant and its proportion are of prime importance. There are number of factors which affect disintegration like particle size distribution, contact angle, pore size distribution, tablet hardness, water absorption capacity and type and proportion of disintegrants.
4. Cotton – candy process

In this process Shearform technology is used in the preparation of a matrix known as FLOSS, made from the combination of the recipients either alone or with the drugs. The fibrous nature of the floss is similar to the cotton-candy fibers. The floss is commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F. Other polysaccharides such as polymaltodextrins and polydextrose can be transformed into fibers at 30-40% lower temperature range.[14]

5. Spray drying

Spray drying is a transformation of feed from a fluid state into a dried particulate form by spraying the feed into a hot drying medium. This technique is based on particulate support-matrix, which is prepared by spray drying the solvent. This matrix then becomes the carrier for the active ingredients. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating agent and an acidic material (e.g. citric acid) and / or alkali material (e.g. Sodium bicarbonate) to enhance disintegration and dissolution.

Finally, the formulation is spray-dried in a spray drier. Spray drying process is widely used to provide products with high porosity in fine powder because the processing solvent can be easily dried. Fast dissolving tablets prepared through this method are disintegrated in less than 20 seconds.[15]

6. Sublimation

By this technique, the active drug, volatilizing substance and other ingredients are compressed to form a tablet. After the compression of the tablets, the volatile ingredients are evaporated and the remnant is highly porous tablet which can be easily disintegrated and rapidly soluble in saliva. Volatile substances that may be used include camphor, hexamethylene tetramine, ammonium bicarbonate, urea, ammonium carbonate etc. Mannitol and camphor were used as a tablet matrix material and subliming the material respectively. Sublimation of camphor was done in vacuum at 80 C for 30 minutes to develop pores in the tablets that yields highly porous tablets with satisfactory mechanical strength and a high dissolution rate. [16]
7. **Taste masking**

Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques. Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers. Cefuroxime axetil is microencapsulated in various types of acrylic polymers (e.g., Eudragit E, Eudragit L-55 and Eudragit RL) by solvent evaporation and solvent extraction techniques. These polymer micro spheres showed efficient taste masking and complete dissolution in a short period. Fine granules of drug and disintegrant (e.g. low substituted hydroxypropyl cellulose) when coated with a water insoluble polymer (e.g. ethyl cellulose) masked the bitter taste of sparfloxacin. The addition of low substituted hydroxypropyl cellulose as disintegrant to the drug in cores resulted in increased dissolution rate and bioavailability of sparfloxacin compared to its conventional tablets.\[17\]

8. **Mass extrusion**

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste.\[18\]

9. **Melt granulation**

It is a process in 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 FDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate©, PEG – 6 – stearate).

10. **Nanonization**

A recently developed Nano melt technology involves reduction in the particle size of drug to nano size by milling the drug using a proprietary wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into fast dissolving tablets. This technique is especially advantageous for poor water soluble drugs. Other advantages of this technology include fast
disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging, due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).[19]

PATENTED TECHNOLOGIES

1. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes. This is applied to flavour-release products such as mouth fresheners, confectionery and vitamin products. SOLULEAVES™ technology can be used to deliver active ingredients to oral cavity efficiently and in a pleasant and easily portable form.

2. WAFERTAB™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. WAFERTAB™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release, or for use by patients who have difficulty swallowing.[10]

3. FOAMBURST™ is a special variant of the SOLULEAVES™ technology which got a new patent granted in 2004 is a capsule form made up of foamed film. An inert gas is passed into the film during production resulting in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. To produce specific taste-burst characteristics, the voids in the film may be gas filled, empty or filled with other materials.[20] FOAMBURST™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

4. X GEL™ film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. It is non animal- derived, approved on religious grounds and is suitable for vegetarians; the film is GMO free and continuous production processing provides an economic and competitive manufacturing
platform. These films can be taste masked, coloured and layered whilst also having the capability to incorporate active pharmaceutical ingredients. The XGEL™ film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water.\(^\text{[21]}\)

**Table No. 2: Examples of commercially available fast dissolving tablets**

<table>
<thead>
<tr>
<th>Product</th>
<th>Active Drug</th>
<th>Application</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Felden FM</td>
<td>Piroxicam</td>
<td>Relieves pain and Inflammation</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Torrox MT</td>
<td>Rofecoxib</td>
<td>Non-steroidal anti-inflammatory drug</td>
<td>Torrent Pharma</td>
</tr>
<tr>
<td>Nimulid MD</td>
<td>Nimesulide</td>
<td>Analgesic and antipyretic</td>
<td>Panacea</td>
</tr>
<tr>
<td>Vomidon MD</td>
<td>Domperidone</td>
<td>Safe gastrokineletic, use in nausea and vomiting</td>
<td>Olcare Lab</td>
</tr>
<tr>
<td>Kozicold</td>
<td>Nimesulide</td>
<td>Decongestion and antihistaminic</td>
<td>Kaizen Drugs</td>
</tr>
<tr>
<td>Zofer MD</td>
<td>Ondansetron</td>
<td>In nausea and vomiting</td>
<td>Sun Pharma</td>
</tr>
<tr>
<td>Mosid MT</td>
<td>Mosapride</td>
<td>Gastroprokinetic agent helps in hurnburn, nausea and vomiting</td>
<td>Torrent Pharma</td>
</tr>
<tr>
<td>Valus</td>
<td>Valdecoxib</td>
<td>Analgesic and antipyretic</td>
<td>Galen Mark</td>
</tr>
<tr>
<td>Ondem MD</td>
<td>Ondansetron</td>
<td>Antiemetic, helps in nausea and vomiting</td>
<td>Alkem Pharma</td>
</tr>
<tr>
<td>Olanex Instab</td>
<td>Olanzapine</td>
<td>Antipsychotic drug</td>
<td>Ranbaxy Labs Ltd</td>
</tr>
<tr>
<td>Rofixx MD</td>
<td>Rofecoxib</td>
<td>Anti-inflammatory drug</td>
<td>Cipla Ltd.</td>
</tr>
<tr>
<td>Romilast</td>
<td>Montelukast</td>
<td>In asthma and allergy</td>
<td>Ranbaxy Labs Ltd</td>
</tr>
<tr>
<td>Zontacet MD</td>
<td>Cetrizine</td>
<td>As anti-inflammatory in dermatological disorders</td>
<td>Zosta Pharma India</td>
</tr>
<tr>
<td>Lonazep MD</td>
<td>Olnazepine</td>
<td>Antiepileptic drug</td>
<td>Sun Pharma</td>
</tr>
<tr>
<td>Pepcid RPD</td>
<td>Famotidine</td>
<td>In heart burns and duodenal ulcers</td>
<td>Merck Pharma</td>
</tr>
</tbody>
</table>

1. **DuraSolv** This technology provides quick-dissolving tablets along with robust nature. These tablets consist of water-soluble excipients and are manufactured using direct compression techniques. However, DuraSolv utilizes no directly compressible diluents in fine particle form. Diluents used have a high surface area, which increases dissolution rate. The incorporation of a high proportion of such diluents causes the tablet to “melt” or dissolve rather than disintegrate. Wicking agents assist the entry of water into the body of the tablet whereas swelling disintegrants are avoided.

2. **WOWTAB tablets** It refers to “Without Water Tablet” (WOWTAB) technology developed by Yamanouchi Pharmaceutical Co. ltd., Japan. WOWTAB tablet possesses...
sufficient hardness to maintain physical and mechanical integrity of the dosage form prior
to contact with saliva. When placed in the oral cavity it rapidly becomes soft by absorbing
saliva and disintegrates or dissolves within 15 to 20 seconds. The disintegration or
dissolution is quicker when pressure is applied between the upper jaw and tongue or a
licking movement is provided to the tablets. Conventional granulators, standard tablet
compression machines are used for manufacturing.

3. ZYDIS tablets R.P. Scherer Corp. has developed and commercialized various quick
dissolving products based on Zydis technology. The Zydis dosage form is a freeze-dried
tablet made from excipients, which does not require water to aid swallowing. When
placed on the tongue, the tablet disintegrates, instantaneously releasing the drug in the
mouth. The drug is physically entrapped or dissolved within the matrix of the fast-
dissolving carrier material which is composed of glassy amorphous excipients that impart
strength and hardness during handling of the tablet. Polymers such as gelatin, dextran,
alginates, and saccharides such as mannitol or sorbitol are the examples of excipients
used in Zydis fast dissolving tablets. The porous structure, poor crystallinity, and freeze-
dried matrix are necessary attributes to achieve fast- dissolving tablets.[1]

### TABLE: 3 Examples of commercially available Fast Dissolving Oral Films

<table>
<thead>
<tr>
<th>Product</th>
<th>Active Drug</th>
<th>Application</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triaminic</td>
<td>Diphenhydramine HCl</td>
<td>Thin Strip for Long acting cough</td>
<td>Novartis</td>
</tr>
<tr>
<td>Theraflu</td>
<td>Dextromethorphan HBr</td>
<td>For Long acting cough</td>
<td>Novartis</td>
</tr>
<tr>
<td>Gas-X</td>
<td>Simethicone</td>
<td>Gas-X Thin Strip Anti Gas</td>
<td>Novartis</td>
</tr>
<tr>
<td>Sudafed PE</td>
<td>Phenylephrine HCl</td>
<td>Decongestant oral strips</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Klonopin wafers</td>
<td>Clonazepam</td>
<td>Antianxiety</td>
<td>Solvay pharmaceuticals</td>
</tr>
<tr>
<td>Benadryl</td>
<td>Diphenhydramine HCl</td>
<td>Antiallergic</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Chloraseptic</td>
<td>Benzocaine: Menthol</td>
<td>Chloraseptic Relief Strips</td>
<td>Prestige</td>
</tr>
<tr>
<td>Suppress</td>
<td>Menthol</td>
<td>Suppress Herbal Cough relief Strips</td>
<td>InnoZen</td>
</tr>
<tr>
<td>Orazel</td>
<td>Menthol/Pectin</td>
<td>Cough and cold relief strips</td>
<td>Del</td>
</tr>
<tr>
<td>Listerine</td>
<td>Cool mint</td>
<td>Antiseptic mouthwash</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Little Colds</td>
<td>Pectin</td>
<td>Sore throat strips</td>
<td>Prestige brands</td>
</tr>
<tr>
<td>Eclipse</td>
<td>Sugarfree mints</td>
<td>Chewing gum, Breath mint</td>
<td>Wrigley’s</td>
</tr>
<tr>
<td>Donepezil</td>
<td>Donepezil HCL</td>
<td>In Alzheimer's disease</td>
<td>Labtec GmbH</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>Ondensteron</td>
<td>Antiemetic, helps in nausea and vomiting</td>
<td>Labtec GmbH</td>
</tr>
</tbody>
</table>
CONCLUSION
Fast dissolving drug delivery technologies are the novel approach in oral health care systems. They can also be used where quick action is required and it provides more patient compliance to pediatric and geriatric patients. They possess many advantages over conventional dosage form and can also be used in cases of dysphagia, Parkinson’s disease, mucositis, motion sickness or vomiting.

REFERENCES