A REVIEW ON ORAL THIN FAST DISSOLVING FILMS RECENT TREND OF DOSAGE FORM FOR QUICK RELEASE

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ABSTRACT

The oral route is most popular route for the administration of therapeutic agents because of low cost of therapy and ease of administration lead to high levels of patient compliance. In the recent years, many of the pharmaceutical groups are focusing their research on rapid dissolving technology. The main advantage of this technology is the administration to pediatric and geriatric patient population where the difficulty of swallowing larger oral dosage forms is eliminated orally. Fast dissolving film is the type of drug delivery system which, when placed in the oral cavity, disintegrate or dissolve within few seconds without the intake of water. New taste-masking agents allow bitter ingredients to be successfully formulated. Oral thin fast dissolving films (OTFDFs) can be formulated by reduced dosage frequency with selected oral cavity absorption enhancers in a suitable oral cavity film carrier. This facilitates the rapid absorption in the oral cavity for drugs with low GIT-bioavailability and intensive first-pass effects. Thus, it offers shortening onset time, enhancing bioavailability and reducing the probability of first pass side effect. In the present review, an account of various formulation considerations, methods of preparations, different technologies, evaluation as well as packaging and application is compiled.

KEYWORDS: Oral thin fast dissolving film, pediatric and geriatric patients, rapid absorption, enhanced Bioavailability

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INTRODUCTION

FDDDS were first came into existence in 1970 as an alternative to tablets, syrups and capsules, for pediatric and geriatric patients which rapidly disintegrate and dissolve in saliva and then easily swallowed without need of water which is a major benefit over conventional dosage form. Fast dissolving drug delivery system have acquired great importance in the pharmaceutical industry due to their unique properties and advantages like availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity, noneed of water, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste and improved patient compliance especially for pediatric and geriatric. There are multiple fast-dissolving over the counter (OTC) and Prescribbed (Rx) production the market worldwide, most of which have been launched in the past 3 to 4years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolvingdrugdeliverytechnology.

**Oral strips or thin films**

Fast disintegrating oral thin films are rapidly gaining interest in the pharmaceutical industry over fast disintegrating tablets because they are friendly with patients having difficulties in swallowing or chewing solid dosage forms. A film or strip can be defined as a dosage form that employs a water-dissolving polymer (generally a hydro colloid, which may be a bio adhesive polymer), which allows the dosage form to quickly hydrate, adhere, and dissolve when placed on the tongue or in the oral cavity (i.e. buccal, palatal, gingival, lingual, or sublingual) to provide rapid local or systemic drug delivery. These oral thin films or oral strips are flexible strips similar in size, shape and thickness to a postage stamp (2x3cm) and can be packaged in multi dose containers or individually pouched.

**Overview of Oral Mucosa**

![Diagram of Oral Mucosa](image)

Drug delivery via the oral mucosa is a promising route, when one wishes to achieve a rapid onset of action or improved bioavailability for drugs with high first-pass metabolism. Thus, there is a growing interest in developing alternative dosage forms, i.e. orally fast disintegrating strip, which allow a rapidly dissolving drug to absorb directly into the systemic circulation through the oral mucosa. These kinds of dosage forms are also convenient for children, elderly patients with swallowing difficulties, and in the absence of potable liquids. However, in addition to formulation considerations, the properties of the active compound have to be appropriate in order to achieve drug delivery into systemic circulation after intra oral administration. The oral mucosa is composed of an outermost layer of stratified squamous epithelium below this lies a basement membrane, a lamina propria followed by the sub mucosa as the innermost layer.
THE CONCEPT OF ORAL DISSOLVING FILM\textsuperscript{13, 25}

1 This delivery system consists of a thin film.
2 After placing it on the top of the tongue, the film dissolves within seconds, promoting first pass metabolism as compared to tablet and other immediate release oral solid dosage forms, and may increase the bioavailability of drug.
3 FDF dissolves in the mouth like a cotton candy.

There are three different subtypes
1. Flash release
2. Mucoadhesive melt-away wafer
3. Mucoadhesive sustained-release wafers

**Table 1**

*Properties of oral films*

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Flash Release wafer</th>
<th>Mucoadhesive melt away wafer</th>
<th>Mucoadhesive sustained release wafer</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Area (cm(^2))</strong></td>
<td>2-8</td>
<td>2-7</td>
<td>2-4</td>
</tr>
<tr>
<td><strong>Thickness (µm)</strong></td>
<td>20-7</td>
<td>50-500</td>
<td>50-250</td>
</tr>
<tr>
<td><strong>Structure</strong></td>
<td>Film: single layer</td>
<td>Single or multilayer System</td>
<td>Multi-layer system</td>
</tr>
<tr>
<td><strong>Excipients</strong></td>
<td>Soluble, hydrophilic polymers</td>
<td>Soluble, hydrophilic Polymers</td>
<td>Low/Non-soluble Polymers</td>
</tr>
<tr>
<td><strong>Drug phase</strong></td>
<td>Solid solution</td>
<td>Solid solution or Suspended drug particles</td>
<td>Suspension and/or Solid Solution</td>
</tr>
<tr>
<td><strong>Application</strong></td>
<td>Tongue(upper palate)</td>
<td>Gingival or buccal Region</td>
<td>Gingival,(other Region in the oral cavity)</td>
</tr>
<tr>
<td><strong>Dissolution</strong></td>
<td>Maximum60sec</td>
<td>Disintegration in a few min forming a gel</td>
<td>Maximum8-10 hours</td>
</tr>
<tr>
<td><strong>Site of action</strong></td>
<td>Systemic or local</td>
<td>Systemic or local</td>
<td>Systemic or local</td>
</tr>
</tbody>
</table>
**BIOPHARMACEUTICAL CONSIDERATION OF FDOFS**

Before designing a new dosage form, the bio pharmaceutical factors need to be considered. Fast disintegrating oral films quickly disintegrate, facilitating the absorption of drug from the mouth, pharynx and oesophagus through the oral mucosa (Kaushik et al., 2004). Factors like age, nature of the oral cavity, and blood flow to oral cavity should be considered. Distribution of drug depends on tissue permeability, perfusion rate binding of drug to tissue, druginteraction etc.\(^{15}\)

**ADVANTAGES OF FDF\(^3, 5, 18\)**

- Improved oral absorption
- Faster onset of action
- Minimized first-pass effect
- Improved bioavailability
- Oral mucosa highly vascularised.
- Consume at anyplace at anytime....
- No tablet or capsule to swallow or chew
- No water needed
- Improved safety and efficacy
- Improved compliance
- Accurate dosing
- precision in admn dose
- Contain sugars and other GRAS excipients.

**DISADVANTAGES OF FDF**

- High doses cannot be incorporated.
- Drugs which are unstable at buccal pH cannot be administered.
- Drugs which irritate the mucosa cannot be administered by this route.
- Taste masking- Most drugs have bitter taste, and need taste masking.
- Special packaging- OTFDFs are fragile and must be protected from water so it needs special packaging\(^{14, 22}\)

**MECHANISMOF FAST DISSOLUTION IN MOUTH**

The name “fast dissolving” indicates that these dosage forms dissolves quickly and disintegrates into smaller particles by saliva and swallowed into the stomach. The time to reach from mouth to the stomach is estimated to be between 5 and 10 minutes. Hence, fast dissolving drug delivery system has the advantage of liquid dosage form i.e. convenient drug administration. The fast passage of dissolved dosage form to the stomach provides a better opportunity for the medication to be absorbed through the membrane of the buccal cavity, pharynx and oesophagus for improved bioavailability and quick onsetofdrugaction\(^{16, 20}\)

**FORMULATION DEVELOPMENT**

Oral film includes various ingredients for its formulation which includes polymers, active pharmaceutical ingredient, film stabilizing agents, sweeteners, flavours, colours, saliva stimulating agents, preservatives, surfactants etc Drug (Active pharmaceutical ingredient)\(^{38, 39, 40, 41, 42}\) Different type's of API can be successfully incorporated in the oral strip technology. Micronized API can improve the texture of the film and also dissolution and uniformity of the oral fast dissolving film. Different molecule can be incorporated into the delivery system. Taste of bitter drug need to be masked for that cyclodextrins or resins can be used; they prevent the direct contact of API with the saliva. It include cough/cold
remedies (antitussive, expectorants), anxiety drugs, CVS agent, sore throat, erectile dysfunction drugs, antihistamines, antiasthamatics, GI disorders, nausea, pain and CNS (antiparkinson’s disease).

Ideal properties of drug for the development of oral film formulation:

- The drug should have low dose.
- The drug have extensive high first pass metabolism.
- It should be non-bitter.
- It should have quick on set of action.
- The drug should have high solubility and high permeability (BCS class I).

**Polymer:** A variety of polymers are available for preparation of FDF. As the strip forming polymer (which forms the platform for the FDF) is the most essential and major component of the FDF at least 45% w/w of polymer should generally be present based on the total weight of dry film but typically 60 to 65% w/w of polymer is preferred to obtain desired properties. The polymers can be used alone or in combination to obtain the desired strip properties. The film obtained should be tough enough so that there won’t be any damage while handling or during transportation. The robustness of the strip depends on the type of polymer and the amount in the formulation.

### Table 2
**Various natural polymers used for preparation of fast dissolving oral films.**

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Sodium Alginate</th>
<th>Pullulan Gum</th>
<th>Gelatin</th>
<th>Pectin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Film forming ability</strong></td>
<td>have film forming capacity</td>
<td>forms flexible film in 5-25% solution</td>
<td>Very good film forming capacity</td>
<td>It have film forming capacity</td>
</tr>
<tr>
<td><strong>Melting point</strong></td>
<td>&gt;300°C (572°F)</td>
<td>107°C</td>
<td>-</td>
<td>152°C</td>
</tr>
<tr>
<td><strong>Solubility</strong></td>
<td>Slowly soluble in water and form colloidal solution</td>
<td>Soluble in hot &amp; cold water</td>
<td>Soluble in Glycerin, acid, alkali &amp; Hot water</td>
<td>Soluble in water, insoluble in methanol (95%) &amp; other organic solvents</td>
</tr>
<tr>
<td><strong>Applications</strong></td>
<td>Stabilizing &amp; Suspending agent; tablet &amp; capsule disintegrant; tablet binder; viscosity increasing agent</td>
<td>Used in food industry to provide bulk &amp; texture, for coating of immediate releasing tablets &amp; preparation of capsule shell.</td>
<td>Used in implantable delivery system, microcapsulation of drugs, used topically in wound dressing.</td>
<td>Used as adsorbant, emulsifying agent, stabilizing agent, bulk forming agent.</td>
</tr>
</tbody>
</table>

**IDEAL PROPERTIES OF THE FILM FORMING POLYMERS**

- It should have good wetting and spread ability property
- The polymer should exhibit sufficient peel, shear and tensile strengths
- It should not aid in cause secondary infections in the oral mucosa/dental region
- The polymers employed should have good shelf life, should have a good mouth feel property

It would be ideal to have a polymer that would have local enzyme inhibition action along with penetration enhancing property.
Table 3
Various synthetic polymers used for preparation of fast dissolving oral films.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>Hydroxy propyl methyl cellulose</th>
<th>Sodium carboxy methyl cellulose</th>
<th>Polyvinyl alcohol</th>
<th>Starch and Modified starch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Film forming ability</td>
<td>It has a film forming ability in 2-20% w/w concentration</td>
<td>Good film forming property</td>
<td>Good film forming property</td>
<td>Modified starches have a property to form quick dissolving films</td>
</tr>
<tr>
<td>Melting point</td>
<td>Browns at 190-200°C Glass transition temperature is 170-180°C</td>
<td>Browns at approximately 227°C &amp; chars at approximately 252°C</td>
<td>228°C for fully hydrolyzed grades, 180-190°C for partially hydrolyzed grades.</td>
<td>It decomposes at 250°C</td>
</tr>
<tr>
<td>Solubility</td>
<td>Soluble in cold water, forming viscous colloidal solution, insoluble in chloroform, ethanol</td>
<td>Practically insoluble in acetone, ethanol (95%), ether &amp; toluene</td>
<td>Soluble in water, Slightly soluble in ethanol (95%), insoluble in organic solvents.</td>
<td>Soluble in water and ethanol, it swells in water by above 5-10% at 37°C</td>
</tr>
<tr>
<td>Applications</td>
<td>Used as a tablet binder, film coating agent, film forming agent, suspending &amp; stabilizing agent in gels &amp; ointments, adhesive in plastic bandage and as a wetting agent in contact lenses.</td>
<td>Coating, stabilizing &amp; suspending agent, disintegrant, tablet binder, viscosity increasing agent, water absorbing agent.</td>
<td>Coating agent, lubricant, stabilizing agent, viscosity increasing agent</td>
<td>Starch is used as a binder, diluents &amp; disintegrates, used in the treatment of dehydration.</td>
</tr>
</tbody>
</table>

Maltodextrin
Maltodextrin is an oligosaccharide that is used as a food additive. It is produced from starch by partial hydrolysis and is usually found as a white hygroscopic spray-dried powder. Freely soluble in water, slightly soluble in anhydrous alcohol. The maltodextrin is non-toxic, edible and is in powdered form. Thermal to dextrin is the film former, the polyethylene glycol 400 and the glycerin are the plasticizers. Good stableness against recrystallization.

Chitosan
Chitosan (β-(1, 4)-2-amino-2-deoxy-D-glucopyranose), which is mainly made from crust ocean shells, is the second most abundant natural and non-toxic polymer in nature after cellulose. However, a major drawback of chitosan is its poor solubility in neutral solutions. Chitosan products are highly viscous, resembling natural gums.

Gum Carrageenan
Carrageenans are polymers with a linear chain of partially sulphated galactans, which present as film-forming material, different red sea weeds (Rhodophyceae) produce different carrageenans. Carrageenan film formation includes gelation mechanism during moderate drying, leading to a three-dimensional network formed by polysaccharide double helices and to a solid film after solvent evaporation. Recently, carrageenan films were also found opaque than those made of starch.

Poly Vinyl Pyrrolidone
Poly vinyl Pyrrolidone (PVP), also commonly called Polyvidone or Povidone, this polymer made from the monomer N-vinylpyrrolidone. PVP is soluble in water and other polar solvents. When dry it is a light flaky powder, which readily absorbs up to 40% of its weight in atmospheric water. In solution, it has excellent wetting properties and readily forms films. This makes it good as a coating or an additive to coatings. PVP is a branched polymer, meaning
its structure is more complicated than linear polymer, though it too lies in a two-dimensional plane.

**Hydroxy Propyl Cellulose**

Hydroxy propyl cellulose as partially substituted poly (hydroxypropyl) ether of cellulose. Hydroxy propyl cellulose (HPC) is non-ionic water soluble thermoplastic polymer. (HPC) has excellent surface properties and forms highly flexible films. Films formed with polymer shaving very high glass transition temperature values are stiff. Because of relatively high glass transition temperatures (compared to other film forming polymers) of HPC, the formed films were shown to exhibit brittle fracture and were found to best if, with a high elastic modulus and a very low per cent elongation (less than 5%). Typically slow dissolving, the films have good carrying capacity and reasonable clarity. HPC has a good film forming property. It imparts low surface and interfacial tension to its solution and thus can be used for the preparation of flexible films alone or in combination with Hypromellose\(^{48,49}\).

**Kollicoat**

Kollicoat a polyvinyl alcohol–polyethylene glycol graft copolymer is pharmaceutical excipient that was especially developed as a coating polymer for instant release formulations. The polyvinyl alcohol moiety has good film-forming properties and the polyethylene glycol part acts as an internal plasticizer. The molecule is hydrophilic and thus readily soluble in water. Film forming agent ideal for instant release formulations as well as drug delivery like drug layering and binding it is robust yet flexible the result is highly reliable, cost effective process and gives excellent appearance. Effective sealing against moisture, fast release of active ingredients from the film, it is Safe and easy to handle, re-disperse without lump organic solvent and lump, easily dispersible in water, highly flexible film through integrated plasticizer, high pigment loading capacity, easy to formulate and process\(^{50}\).

**Table 4**

*Overview of different ingredients employed in formulating of fast dissolving films.*

<table>
<thead>
<tr>
<th>Plasticizers</th>
<th>Sweetening Agent</th>
<th>Saliva Stimulating</th>
<th>Surfactant</th>
<th>Flavouring Agent</th>
<th>Colouring Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycerol</td>
<td>Sorbitol</td>
<td>Citric Acid</td>
<td>Polaxamer</td>
<td>Pipermint</td>
<td>Titanium</td>
</tr>
<tr>
<td>Propylene Glycol</td>
<td>Sucrose</td>
<td>Malic Acid</td>
<td>Sodium</td>
<td>Cinnamon</td>
<td>Sunset</td>
</tr>
<tr>
<td>PEG 400,200,600</td>
<td>Cyclamate</td>
<td>Lactic Acid</td>
<td>Tweens</td>
<td>Menthol</td>
<td></td>
</tr>
<tr>
<td>Dibutyl Phthalate</td>
<td>Aspartame</td>
<td>Ascorbic Acid</td>
<td>Spans</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triacetin</td>
<td>Neotame</td>
<td></td>
<td></td>
<td>Lemon Oil</td>
<td></td>
</tr>
<tr>
<td>Citrate Ether</td>
<td>Mannitol</td>
<td></td>
<td></td>
<td>Chloroform</td>
<td>Water</td>
</tr>
<tr>
<td>Castor Oil</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
METHOD OF PREPARATION OF FDF\textsuperscript{14, 17,35,36,11}

SOLVENT CASTING METHOD

- Preparation of the casting solution,
- De aeration of the solution,
- Transfer of the appropriate volume of solution into a mold,
- Drying the casting solution,
- Cutting the final dosage form to contain the desired amount of drug and then packaging.

SEMISOLID CASTING METHOD
- Water soluble polymers are dissolved in water
- Solution added to solution of acid in soluble polymer (CAP, CAB) which was prepared in NaOH.
- Plasticizer is added to obtain gel mass.
- The prepared gel mass is cast into films.
- Thickness: 0.015-0.05inch

HOT MELT EXTRUSION METHOD
In the extrusion process the API and other ingredients are mixed in dry state, subjected to heating process and then extruded out in molten state.
- In this process, solvents are completely eliminated. The strips are further cooled and cut to the desired size.
- The high temperature used in this process may degrade thermolabile APIs
Table 5
Comparisons of solvent casting method and hot melt extrusion method

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>API selected</th>
<th>Solvent required</th>
<th>Process</th>
<th>Equipment required</th>
<th>Scale up</th>
<th>Chance of air entrapment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOLVENT CASTING</td>
<td>Thermolabile</td>
<td>Yes</td>
<td>Hydrous</td>
<td>Rollers, Coaters</td>
<td>May create problems</td>
<td>High chance</td>
</tr>
<tr>
<td></td>
<td>Thermostable</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HOT MELT EXTRUSION</td>
<td>Thermostable</td>
<td>No</td>
<td>Anhydrous</td>
<td>Hot melt extruder</td>
<td>May not be difficult</td>
<td>Low chance</td>
</tr>
</tbody>
</table>

**ROLLING METHOD**
- A solution or suspension containing the drug is rolled on a carrier.
- Solvent: water or water and alcohol
- The film is dried on the rollers and cut into desired size

**Different Technologies used in film formulation**

**XGel:** XGel™ film provides unique product benefits for healthcare and pharmaceutical products: It is non-animal derived, approved on religious grounds, and is suitable for vegetarians; the film is genetically modified organism (GMO) free and continuous production processing provides an economic and competitive manufacturing platform. XGel™ film can be taste masked, coloured, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients.

**Soluleaves:** This technology is applied to flavor-release products such as mouth fresheners and vitamin products. For pharmaceutical uses, this method of administration is especially useful for pediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. Soluleaves™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 min.

**Wafertab:** Wafertab™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible film strip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The Wafertab™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a pre manufactured XGel™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. 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.

**Foamburst:** It is a special variant of the Soluleaves™ technology where an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. Foamburst™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

**Micap:** Micapplic signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water soluble films. The developments will be aimed at providing new delivery mechanisms for the $1.4 billion global market for smoking cessation products (SCPs).

**EVALUATION PARAMETERS**

**In Vitro Evaluation**

**Drug-Excipients interaction studies:** Fourier Transform Infra-Red Spectrum (FTIR), Differential scanning colorimeter (DSC), thin layer chromatography and X-ray Diffraction (XRD) can be used to assess possible drug excipients interaction.

**Thickness:** Thickness test can be carried out using electronic micrometer. The thickness
of the film sample should be measured at five locations (centre and four corners), and the mean thickness is calculated. Typical thickness for film is 130±3µm

**Folding endurance**\textsuperscript{24}: The number of times the film could be folded at the same place without breaking gives the value of folding endurance. Typical folding endurance for film is between 100-150.

**Swelling index**: The degree of swelling is calculated using the formula: \[ SI = \frac{wt - w_0}{w_0} \]

Where SI = swelling index, wt = weight of the film at time “t”, and w\(_0\) = weight of the film at t=0

**Uniformity of drug content**\textsuperscript{20, 30}: This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of simulated saliva of pH 6.8 for 30 min with continuous shaking. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%.

**Tensile strength**\textsuperscript{23}: It is the property of the film that requires a load to cause load deformation failure of film.

Tensile strength (N/mm\(^2\)) = breaking force (N)/cross-sectional area of sample (mm\(^2\))

Typical tensile strength for film is 1.80±0.20 MPa

**Percent elongation**\textsuperscript{28}: The percent elongation is measured when the film snaps as sufficient force applied so as to exceed the elastic limit.

\[ \text{Elongation at break} \% = \frac{\text{increase in length at breaking point (mm)}}{\text{original length (mm)}} \times 100\% \]

Typical Percent elongation value for film is 322.4±63.3%

**Disintegration test**\textsuperscript{30}: Disintegrating time is defined as the time (seconds) at which a film breaks when brought in contact with water or saliva. Pharmacopeial disintegrating test apparatus may be used for this study. Typical disintegration time for film is 5-30s.

(1) Slide frame method\textsuperscript{31}: One drop of distilled water was dropped by a Pipette onto the oral films. Therefore the films were clamped into slide frames and were placed planar on a Petri dish. The time until the film dissolved and caused a hole within the film was measured.

(2) Petri dish methods\textsuperscript{31}: 2mL of distilled water was placed in a Petri dish and one film was added on the surface of the water and the time measured until the oral film was dissolved completely.

**Dissolution test**\textsuperscript{30}: Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API.

**Morphology Studies**\textsuperscript{13, 30}: Scanning electron microscopy (SEM) study refers the differences between upper and lower side of the films. It also helps in determination of the distribution of API. Near-infrared chemical imaging (NIR-CI) study helps in determining the difference between drug distributions in drug loaded films and recrystallization.

**Tear resistance**\textsuperscript{30}: Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. The maximum stress or force required to tear the specimen is recorded as the tear resistance value in Newton (or pounds-force).

**Young’s modulus**\textsuperscript{20, 30}: Young’s modulus or elastic modulus is the measure of stiffness of strip. It is represented as

\[
\text{Young's modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{Cross-head speed}}
\]

Hard and brittle strips demonstrate a high tensile strength and Young’s modulus with small elongation. Typical Young’s modulus value for film is 0.30±0.07 MPa

**Stability studies**\textsuperscript{19}: Stability study is conducted at accelerated condition of 65% relative humidity and 35°C temperature in the humidity chamber for the three months. After 3 months films are evaluated for the drug content, disintegration time and physical appearance.
**Organoleptic Evaluation**: This is essential step in case of most oral formulation due to more residence time in the oral cavity. The product should possess the desired features of sweetness and flavor which is acceptable to a large mass of population. Experiments using electronic tongue measurements have also been reported to distinguish between the sweetness levels in taste-masking formulation.

**InVivoEvaluation**

**Animal and Human safety studies**: Local or mucosal irritation studies performed on animals and humans were conducted to demonstrate the safety of the Quick-Dis™ drug delivery system. An animal safety study was conducted using the hamster cheek pouch model. In the hamster cheek pouch study, the film was given to the animal twice a day for 4.5 consecutive days (9 doses in total). A clinical acute or mucosal irritation test for Quick-Dis™ was conducted on healthy human volunteers to ensure and demonstrate the clinical safety of the fast-dissolving system.

**Packaging of fast dissolving film**

In the pharmaceutical industry it is vital that the package selected adequately preserve the integrity of the product. Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast dissolving dosage forms. A variety of packaging options are available for fast dissolving films. Single packaging is mandatory for films, which are pharmaceutical products; an aluminum pouch is the most commonly used packaging format. APR-Labtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for the Rapid films. The rapid card has same size as a credit card and holds three raid films on each side. Every dose can be taken out individually. The material selected must have the following characteristics:
- They must be FDA approved.
- They must meet applicable tamper-resistant requirement.
- They must be non-toxic.
- They must not be reactive with the product.
- They must not impart to the product tastes or odours.

**Application of fast dissolving film**

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of FDFs could become a preferential delivery method for therapies in which rapid absorption is desired, including those used to manage pain, allergies, sleep difficulties, and central nervous system disorders. Dissolvable FDFs evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products.
CONCLUSION

Pharmaceutical industries have recognized the potential for delivering medicinal products through OTF and have launched several products for the OTC market using this technology. Recently RDFs have gained popularity as dosage forms for the mouth fresheners. Gaining importance as they are ideal dosage form for use in young children, as well as geriatric patients. Also, many industries have pipelines of molecules of shifting their existing tablets preparation to oral strips.

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