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Review Article

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OVERVIEW ON FAST DISSOLVING ORAL FILMS

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ABSTRACT

Fast-dissolving oral delivery systems are solid dosage forms, which disintegrate or dissolve within 1 min when placed in the mouth without drinking water or chewing. More recently, fast-dissolving films are gaining interest as an alternative to fast-dissolving tablets to definitely eliminate patient's fear of chocking and overcome patent impediments. Oral dissolving films are formulated by incorporating the drug with selected oral cavity absorption enhancers in a specially designed oral dissolving film carriers. This facilitates the rapid absorption in the oral cavity for drugs with low GIT-bioavailability and intensive first-pass effects. This it offers shortening onset time, enhancing bioavailability and reducing the probability of first pass side effect. The current review focuses on the recent development in the oral dissolving film and discusses about its technique for preparation of film as well its evaluation. Thin film drug delivery, also referred to as orally dissolving thin film, and has emerged as an advanced alternative to the traditional tablets, capsules and liquids often associated with prescription and OTC medications. Thin film enables the drug to be delivered to the blood stream either intragastrically, buccally or sublingually. The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament. ODFT offers an alternate platform for molecules that undergoes first pass metabolism. Our review article suggests that (ODFT) can be the possible way to improve patient compliance and robustness. Various pharma companies adopted advance technologies to make ODFT commercialized in large scale despite of several limitations.

Key words: Oral dissolving film, Film forming polymer, Solvent casting technique, Pediatric Patients, Geriatric Patients

INTRODUCTION

Despite of tremendous advancement in drug delivery the oral route of drug administration is the most important method of administration of drug for systemic effect. Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the parenterals and liquid orals. But the liquid orals (syrup, suspension, emulsion etc) have the problem of accurate dosing mainly and parenterals are painful drug delivery, so most patient incompliance. Each pharmaceutical company wants to formulate the novel oral dosage form which has the higher bioavailability, quick action and most patient compliance. [1]

Fast-dissolving drug-delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties swallowing traditional oral solid-dosage forms. The novel technology of oral fast-dispersing dosage forms is known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. However, the function and concept of all these dosage forms are similar. By definition, a solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in solution or suspension without the need for the administration of water, is known as an oral fast-dispersing dosage form.

Difficulty in swallowing (dysphagia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules [2]. An estimated 35% of the general population, and an additional 30.40% of elderly institutionalized patients and 18.22% of all persons in long-term care facilities, suffer from dysphagia. This disorder is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy, head and neck radiation therapy, and other neurological disorders, including cerebral palsy[3-6]. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed by surface, form and taste. The problem of swallowing tablets was more evident in geriatric and paediatric patients, as well as traveling patients who may not have ready access to water [5].

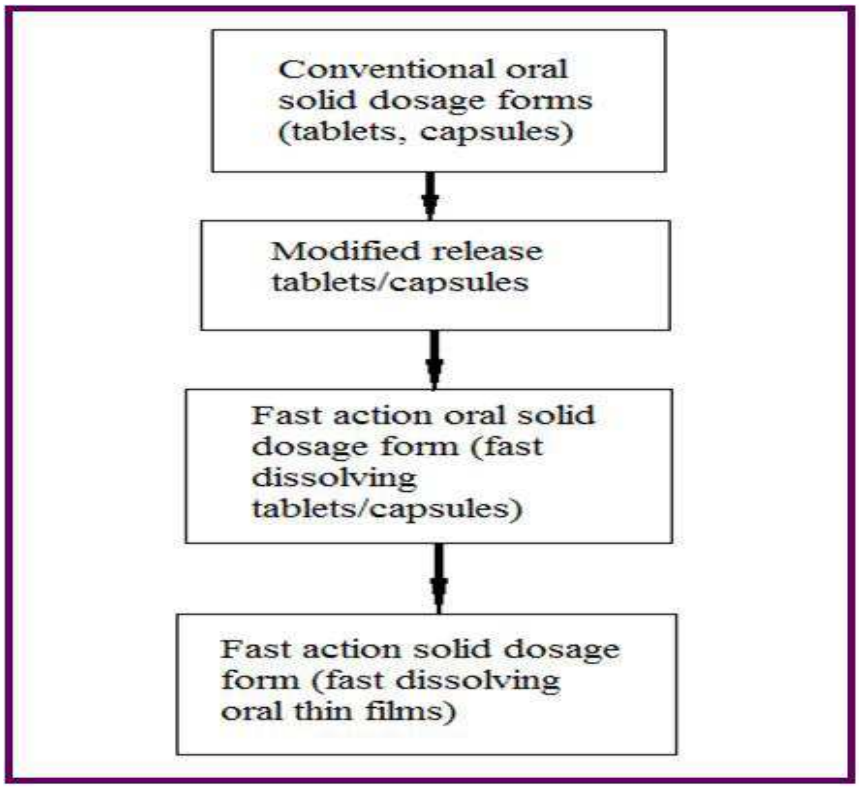
Many pharmaceutical companies have directed their research activity in reformulating existing drugs into new dosage forms. One such relatively new dosage form is the oral strip, a thin film that is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity. Developing formulations for children has been a challenging task. Amongst other factors, palatability of formulations of pediatric oral medications is one of the most significant factors influencing compliance to therapeutic regimens. [7, 8]

Technology Catalysts forecasts the market for drug products in oral thin film formulations to be valued at $500 million in 2007 and could reach $2 billion in near future according to Technology Catalysts [9]. The oral thin films place as an alternative in the market due to the consumer's preference for a fast-dissolving product over conventional tablets/capsules. The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfils all the need of patients. Eventually, film formulations having drugs will be commercially launched using the oral thin film technology [10].

In North America more than 80 oral thin film brands launched since 2003, the market remains limited when compared to Oro Dispersible Tablets. However, for future growth point of view the Oral Thin Film sector is well-positioned. In US market the OTC films of pain management and motion sickness are commercialized. More importantly, prescription Oral Thin Films have now been approved in US, EU and Japan which are the three major regions. These approved Rx films, have potential to dominate over other oral dosage forms of the same drugs. It seems that the value of the overall oral thin film market will grow significantly [11].

Many pharmaceutical dosage forms are administered in the form of pills, granules, powders and liquids. Generally, a pill is designed for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablet and capsules, are able to retain their shapes under moderate pressure. However, some patient, particularly pediatric and geriatric patients, have difficulty in swallowing or chewing solid dosage forms[12, 13]. Many pediatric and geriatric patients are unwilling to take this solid preparations due to fear of choking[7]. Although oral disintegrating tablets have an advantage of administration without choking and fast disintegration; the disintegrated materials contained in them are insoluble and remain same until swallowing. In such cases formulation of fast dissolving film will be advantageous[14, 15].

Flow Chart for the Development of Oral Solid Dosage



Hence orally dissolving tablets have come into existence. Even with these differences, most of the existing oral dissolving drug delivery systems are in the form of solid tablets and designed to dissolve/disintegrate in the patient's mouth without the need to drink or chew. However, the fear of taking solid tablets and the risk of choking for certain patient populations still exist despite their short disintegration/dissolution times. Hence mouth dissolving oral film drug delivery is a better alternative in such cases. Many drugs given orally are poor in bioavailability because of the pH of the stomach, the presence of enzymes, and extensive first-pass metabolism. Traditionally, these drugs have been administered by parenteral route, which invariably lead to poor patient compliance. This made the pharmaceutical industries to look for alternative routes of drug delivery system. Intraoral fast-dissolving drug delivery system where in the dosage form (film) will be placed on the surface of the tongue or in the oral/buccal cavity, where drug release rapidly for local and systemic absorption.

Oral Thin Films (OTF)[16]: Oral films, also called oral wafers in the related literature, are a group of flat films which are administered into the oral cavity. Although oral film systems, the third class, have been in existence for a number of years, they have recently become the new area of interest in fast-dissolve pharmaceutical drug delivery. Dissolvable oral thin films (OTFs) or oral strip (OS) 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. Companies with experience in the formulation of polymer coatings containing active pharmaceutical ingredients (APIs) for transdermal drug delivery capitalized on the opportunity to transition this technology to OTF formats. Today, OTFs are a proven and accepted technology for the systemic delivery of active pharmaceutical ingredients (APIs) for over-the-counter (OTC) medications and are in the early- to mid development stages for prescription drugs.

This is largely as a result of the success of the consumer breath freshener products such as Listerine Pocket Paks in the US consumer market. Such systems use a variety of hydrophilic polymers to produce a 50-200 mm film of material. This film can reportedly incorporate soluble, insoluble or taste-masked drug substances. The film is manufactured as a large sheet and then cut into individual dosage units for packaging in a range of pharmaceutically acceptable formats[17].

Classification of Oral Films:

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

Types of wafers and their properties

Sub type	Flash release wafer	Mucoadhesive melt- away wafer	Mucoadhesive sustained release wafer
Area (cm^2)	2-8	2-7	2-4
Thickness (µm)	20-7	50-500	50-250
Structure	Film: single layer	Single or multilayer System	Multi layer system
Excipients	Soluble, highly hydrophilic polymers	Soluble, hydrophilic Polymers	Low/Non-soluble Polymers
Drug phase	Solid solution	Solid solution or suspended drug particles	Suspension and/or solid Solution
Application	Tongue(upper palate)	Gingival or buccal Region	Gingival, (other region in the oral cavity)
Dissolution	Maximum 60 seconds	Disintegration in a few minutes, forming gel	Maximum 8-10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

The concept of oral dissolves film

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.

Advantages of Oral Film

This dosage form enjoys some distinct advantages over other oral formulations such as
1. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.
2. The disadvantage of most Oro Dispersible Tablet is that they are fragile and brittle which warrants special package for protection during storage and transportation. Since the films are flexible they are not as fragile as most of the Oro Dispersible Tablets. Hence, there is ease of transportation and during consumer handling and storage.
3. As compared to drops or syrup formulations, precision in the administered dose is ensured from each of the strips.
4. Pharmaceutical companies and consumers alike have embraced Oral Thin Films as a practical and accepted alternative to traditional OTC medicine forms such as liquids, tablets, and capsules. Oral Thin Films offer fast, accurate dosing in a safe, efficacious format that is convenient and portable, without the need for water or measuring devices [18].
5. The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect [19].
6. Since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in side effects associated with the molecule.

7 Patients suffering from dysphagia, repeated emesis, motion sickness, and mental disorders prefer this dosage form as they are unable to swallow large quantity of water.
8. Oral Thin Films are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of seconds for the rapid release of one or more APIs.
9. The formulation of dissolvable films is customarily facilitated through aqueous polymer matrices that span a wide molecular weight (MW) range, thereby providing flexibility to achieve certain physical properties.

Special features	Advantages
Thin elegant film	Convenient dosing
Various sizes and shapes	No water needed
Un obstructive	No risk of choking
Fast disintegration	Taste masking
Quick dissolving	Enhanced stability
Rapid release	Improved patient compliance

Disadvantage of Oral Film

The disadvantage of Oral Film is that high dose cannot be incorporated into the strip. However, research has proven that the concentration level of active can be improved up to 50% per dose weight. Novartis Consumer Health's Gas-X® thin film has a loading of 62.5 mg of simethicone per strip [20].

Application of Oral Strip in Drug Delivery:

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of OTFs 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 oral thin films (OTFs) 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.

Formulation considerations

Formulation of Oral Film involves the intricate application of aesthetic and performance characteristics such as taste masking, fast dissolving, physical appearance, mouth-feel etc. The excipients used in formulation of Oral Film are given below as per their categories. From the regulatory perspectives, all excipients used in the formulation of Oral Film should be Generally Regarded as Safe (i.e. GRAS-listed) and should be approved for use in oral pharmaceutical dosage forms.
A typical composition contains the following [21]

- Drug ----- 05% to30%w/w
- Water soluble polymer ----- 45%w/w
- Plasticizers ----- 0-20%w/w
- Surfactants ----- q.s.
- Sweetening agent ----- 3 to 6 %w/w
- Saliva stimulating agent ----- 2 to 6%w/w
- Fillers, colors, flavors etc. ----- q.s.

Film Forming Polymers

A variety of polymers are available for preparation of Oral Film. 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 [22]. On the other hand, fast dissolving strip dosage form should have the property to disintegrate in seconds when placed in mouth and deliver the drug to the oral cavity instantaneously. Lists of polymers which are used in oral strip are given in Table 1. As the film forming polymer (which forms the platform for the Oral Film) is

the most essential and major component of the Oral Film, at least 45%w/w of polymer should generally be present based on the total weight of dry Oral Film [23]. Of the various polymers available, pullulan, gelatin and hypromellose are most commonly used for preparation of Oral Film.

Table -1: List of polymers used in oral film formulation

Pullulan	Modified starches
Gelatin	hydroxyl ethyl cellulose
Hydroxyl propyl methyl cellulose (hypromellose)	Xanthan gum
Polyvinyl pyrrolidone(PVP)	locust bean gum
sodium carboxymethyl cellulose	guar gum
Polyvinyl alcohol	Carrageenan
Polyethylene oxide	Low viscosity grade HPC

Plasticizers

Plasticizer is a vital ingredient of the OS formulation. It helps to improve the flexibility of the strip and reduces the brittleness of the strip. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of strip. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer [24, 25]. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, Citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients. However inappropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip [26-28]. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug [24]. Plasticizer employed should impart the permanent flexibility to the strip and it depends on the volatile nature plasticizer and the type of interaction with the polymer. It should be noted that the properties of plasticizer are important to decrease the glass transition temperature of polymer in the range of 40.60 ºC for non aqueous solvent system and below 75 ºC for aqueous systems [28, 31]. Plasticizer should be compatible with drug as well as other excipients used for preparation of strip [30]. Cellulosic hydrophilic polymers were easily plasticized with hydroxyl containing plasticizers like PEG, propylene glycol, glycerol and polyols. In contrast, less hydrophilic cellulosic polymers were plasticized with esters of citric acid and phthalic acid [31]. Glycerol acts as a better plasticizer for polyvinyl alcohol while diethylene glycol can be used for both Hypromellose as well as polyvinyl alcohol films [24].

Active pharmaceutical ingredient:

The oral fast dissolving film technologies have the prospective for delivery of variety of API. But as the size of the dosage form is limited, High dose molecule is difficult to be incorporated into the films. Only 5mg to 30mg of API can be incorporated into the film. Insoluble API is dispersed uniformly in the film. API s can also be added as milled, micronized and also in the form of nanocrystals or particles depending upon the ultimate release profile. Several APIs that can be potentially used for oral film technology are with bitter taste which makes the formulation unpleasant, especially for pediatric formulations. This leads to the very significance unit operation –taste masking, before incorporating the API in the oral dissolving film. Various methods can be used to improve the palatability of the formulation.

Simplest method

It occupied the mixing and blending of bitter tasting API with pleasurable taste which is termed as obscuration technique.

Barrier method

This method can be used to mask the bitter taste which includes complexation, polymeric coating and micro particle and coated particle. [32]

Sweetening agents: Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Suitable sweeteners include: (a) water soluble natural sweetener:

xylose, ribose, glucose, sucrose, maltose, stevioside, etc, (b) Water soluble artificial sweeteners: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc, (c) Dipeptide based sweetener: aspartame (d) protein based sweeteners: thaumatin I and II. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, isomalt and maltitol can be used in combination as they additionally provide good mouth-feel and cooling sensation. [33,34]. Generally sweeteners are used in the concentration of 3 to 6 %w/w either alone or in combination [33].

Saliva stimulating agent: The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them. These agents are used alone or in combination between 2 to 6%w/w of weight of the strip. [34]

Surfactants: Surfactants act as solubilizing or wetting or dispersing agent in formulation so that the film is getting dissolved within seconds and release active agent quickly. Some of the commonly used are sodium lauryl sulfate, benzalkonium chloride, tweens etc. One of the most important surfactant is polaxamer 407 that is used as solubilizing, wetting and dispersing agent [35].

Flavoring agents: It was observed that age plays a significant role in the taste fondness. Flavoring agents can be selected from synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. Peppermint oil, cinnamon oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence type. The amount of flavor needed to mask the taste depends on the flavor type and its strength.

Coloring agents: Pigments such as titanium dioxide or FD & C approved coloring agents are incorporated (not exceeding concentration levels of 1 percent; w/w) in OS when some of the formulation ingredients or drugs are present in insoluble or suspension form. [36]

Manufacturing Methods

The methods for manufacturing oral films are

- Solvent casting
- Semisolid casting
- Hot melt extrusion
- Solid dispersion extrusion
- Rolling

SOLVENT CASTING METHOD

In this method, water soluble polymer is completely dissolved in to form uniform clear viscous solution other ingredients including API are dissolved in a small portion of aqueous solvent by using a high shear processor. This viscous solution is degassed under the vacuum to remove the air bubbles. This bubble free solution is poured into a glass mold and kept in oven at 40 º-50 º C [37-38].

Advantages:

1. Better uniformity of thickness and better clarity than extrusion.
2. Film has fine gloss and freedom from defects such as die lines.
3. Film has more flexibility and better physical properties. The preferred finished film thickness is typically 12-100µm, although various thicknesses are possible to meet API loading and dissolution needs.

Disadvantages:

1. The polymer must be soluble in a volatile solvent or water.
2. A stable solution with a reasonable minimum solid content and viscosity should be formed.

3. Formation of a homogeneous film and release from the casting support must be possible.

Semisolid Casting Method:

In this method, first of all a solution of water soluble film forming polymer is prepared. Then resulting solution is added to a solution of acid insoluble polymer. Then approximate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted into the films or ribbon by using heat controlled drums. The thickness of film is about 0.015- 0.05 inches. The ratio of the acid insoluble polymers to film forming polymer should be 1:4. [39]

Hot Melt Extrusion:

In present method the mass is prepared first under the control of temperature and steering speed. Afterwards, the film is coated and dried in a drying tunnel; once again the temperature, air circulation and line speed are controlled. Then follows a slitting and in the last step the films are punched, pouched and sealed. Ex. F. Cilurzo *etal*.[40] formulated Piroxicam film with Maltodextrin plasticized by glycerin by using Hotmelt extrusion method.

Advantages:

1. Improved bioavailability of poorly soluble compounds.
2. During Processing solvents and water are not required.
3. Cost-effective process with reduced production time and reduced number of unit operations.
4. Homogeneous distribution of fine particle occurs.
5. Sustained, modified and targeted release capability.
6. Superior stability at varying pH and moisture levels.
7. Better content uniformity was obtained among granules of different size ranges.

Disadvantages:

1. Thermal degradation due to use of high temperature.
2. Flow properties of the polymer are essential to processing.
3. Limited number of available polymers.
4. Require high power input.
5. All excipients must be devoid of water or any other volatile solvent.
6. Lower-melting-point binder risks situations where melting or softening of the binder occurs during handling and storage of the agglomerates.
7. Higher-melting-point binders require high melting temperatures and can contribute to volatility problems especially for heat-labile materials.[41]

Solid Dispersion Extrusion:

In solid dispersion extrusion method immiscible components is extrude with drugs and then solid dispersions are prepared. Finally the solid dispersions are shaped into films by means of dies [42].

Rolling Method:

In this method, suspension or solution containing drug is rolled on a carrier. The solution or suspension should have a specific rheological consideration. Solvent is mainly used water as well as a mixture of water and alcohol. Film is dried on the rollers and cut into desired shapes and sizes [18].

Evaluation

Film thickness: A thickness of the film should be calculated by using micrometer screw gauge. Film should be measured at five positions i.e. central and the four corners and the mean thickness are calculated. This test should be performed on six films of each formulation maximum variation in the thickness of the films should be less than 5% and mean ±S.D calculated. [43]

Dryness test/tack tests: About eight stages of film drying process have been identified and they are set-to-touch, dust-free, tack-free (surface dry), Dry-to touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat and dry print-free. Although these tests are primarily used for paint films most of the studies can be adapted intricately to

evaluate pharmaceutical OS as well [44]. Tack is the tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with the strip. Instruments are also available for this study.

Tensile strength: Tensile strength is the maximum stress applied to a point at which the strip specimen breaks [45]. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

Percent elongation: When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases. [46]

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip X 100}}{\text{Initial length of strip}}$$

Tear resistance: Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. Basically very low rate of loading 51 mm(2 in.)/min is employed and is designed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newtons (or pounds-force) [47].

Young's modulus: Young's modulus or elastic modulus is the measure of stiffness of strip. It is represented as the ratio of applied stress over strain in the region of elastic deformation as follows:

$$\text{Young's modulus} = \frac{\text{Slope X 100}}{\text{Strip thickness X Cross-head speed}}$$

Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation.

Folding endurance: Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value [48].

Surface pH: The surface pH of the oral dissolving film is calculated in order to investigate the risk of any side effects *invivo*. Since acidic or alkaline pH may cause irritation to the oral mucosa, it is determined to maintain the surface pH as close to neutral as possible [49]. A combined pH electrode is used for this purpose. The oral film is slightly wet with the help of water. The pH is measured by bringing the electrode in contact with the surface of the oral film. This study is performed in six films of each formulation and mean±S.D calculated [32].

Disintegration time testing: The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips [50]. Although, no official guidance is available for oral fast disintegrating films/strips, this may be used as a qualitative guideline for quality control test or at development stage. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for strips is 5-30s [51]. A small amount of medium is used, so natural conditions could be simulated. Due to the use of the Small amount of medium the dissolved drug substance could not be measured by spectral analysis.

1. Slide frame method: 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: 2 ml 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. [52]

Dissolution test: 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 [15]. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.

Stability studies: Stability study is conducted at accelerated condition of 65% relative humidity and 35 ºC temperature in the humidity chamber for the three months. After 3 months films are evaluated for the drug content, disintegration time and physical appearance [53].

Assay/drug content and content uniformity:

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85–115 percent.

Organoleptic evaluation:

For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. *Invitro* methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are being used for this purpose. These *invitro* taste assessment apparatus and methodologies are well suited for high-throughput taste screening of oral pharmaceutical formulations [54].

List of some marketed Products available as FDF. [55, 56, 57]

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Brand name	Manufacturer/ Distributor	API (strength)	Uses
Klonopin Wafers	Solvay Pharmaceuticals	Clonazepam (in five strengths: 0.125mg, 0.25mg, 0.5mg, 1mg and 2mg.)	Treatment of anxiety
Listerine Cool Mint Pocket Paks	Pfizer, Inc	Cool mint	Mouth Fresheners
Sudafed PE	Wolters Kluwer Health, Inc.	Phenylephrine	Relieving Congestion
Suppress®.	InnoZen®, Inc	Menthol (2.5 mg)	Cough Suppressants
Triaminic	Novartis	Diphenhydramine HCL (12.5 mg)	Anti allergic
Theraflu	Novartis	Dextromethorphan HBR(15 mg)	Cough Suppressant
Orajel	Del	Menthol/pectin (2mg/30mg)	Mouth ulcer
Gas-X	Novartis	Simethicone (62.5mg)	Anti Flatuating
Chloraseptic	Prestige	Benzocaine/menthol (3mg/3 mg)	Sore throat
Benadryl	Pfizer	Diphenyhdramine HCl (12.5mg or 25mg)	Anti allergic

CONCLUSION

Recently RDFs have gained popularity as dosage forms for the mouth freshners. Meanwhile pharmaceutical industries have recognized their potential for delivering medicinal products ad has launched several products for the OTC market using this technology. The fast dissolving thin film are hardly described and investigated in literature, but seem to be an ideal dosage form for use in young children, especially in geriatric and pediatric patients. They combine the greater stability of a solid dosage form and the good applicability of a liquid. Due to lack of standard

methodology for preparation and analysis products existence in the market is limited. Fast dissolving oral films have several advantages over the conventional dosage forms. So they are of great importance during the emergency cases such as allergic reactions and asthamatics attacks whenever immediate onset of action is desired. The oral dissolving films are getting importance in pharmaceutical field. They offer many advantage over other dosage forms as well as they offer easy production and evaluation technique. This review is an effort to combine the knowledge available on oral dissolving films. A lot of research work is going on and will be started in near future on oral dissolving film.

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