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REVIEW ARTICLE

Review on Mouth Dissolving Film Technology

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ABSTRACT

Oral drug delivery is the most widely utilized route of administration. Major drawbacks related to solid oral delivery systems are lower bioavailability, longer onset of time. Also geriatric, pediatric and dysphasic patients have difficulty in swallowing or chewing solid dosage forms. They are unwilling to take solid preparations due to fear of chocking. Even with fast dissolving tablets there is fear of choking due to its tablet type appearance. Fast dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility and comfort. It improve the efficacy of APIs by dissolving within minute in oral cavity after the contact with less saliva as compared to fast dissolving tablets, without chewing and no need of water for administration. In US market the OTC films of pain management and motion sickness are commercialized. More importantly, prescription OTFs have now been approved in US, EU and Japan which are the three major regions. 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.

KEYWORDS

Mouth Dissolving Film, Film Forming Polymer, Solvent Casting Technique, Disintegration Time, Dissolution Test

INTRODUCTION

Among the delivery routes, Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients, ease of ingestion, pain avoidance and versatility (to accommodate various types of drug candidate)[1,2]. About 60% of all dosage forms available are the oral solid dosage form. Also solid oral delivery systems do not require sterile conditions and are, therefore, less expensive to manufacture, but oral drug delivery systems still need some advancements to be made because of their few drawbacks such as low bioavailability, long onset time. Also in case of geriatric, pediatric and dysphasic patients, they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. This 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 of the patients show incompliance.

Research and development in the oral drug delivery segment has led to transition of simple conventional tablet /capsules to modified release tablet / capsules to mouth dissolving tablets to mouth dissolving films, which have higher bioavailability, quick action and most patient compliance. Fast dissolving drug delivery systems were first developed in the late 1970's

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as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who experience difficulties in swallowing oral solid-dosage forms. The novel technology of oral fast dissolving dosage form is known as fast dispersing, rapid dissolve, rapid melt and fast disintegrating dosage form. Even with mouth dissolving tablets there is a fear of choking due to its tablet type appearance[3].

Mouth dissolving films are the most advanced form of oral solid dosage form due to more flexibility and comfort. It is thin film typically the size of postage stamp that dissolves or disintegrates quickly in the oral cavity after contact with saliva without chewing resulting in solution or suspension. There is no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4-1000 times greater than that of skin[4].

In North America more than 80 oral thin film brands launched since 2003, the market remains limited when compared to ODT's. However, for future growth point of view the OTF sector is well-positioned. In US market the OTC films of pain management and motion sickness are commercialized. More, importantly, prescription OTF's 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[5].

Special Features of Mouth Dissolving Film[6]

1. Thin elegant film.
2. Available in various sizes and shapes.
3. Unobstructive.
4. Excellent mucoadhesion.
5. Fast disintegration and rapid release.

Advantages

1. Larger surface area promotes rapid disintegration and dissolution in the oral cavity.
2. Mouth dissolving films are flexible and thus less fragile as compared to ODT's. Hence, there is ease of transportation and during consumer handling and storage.
3. Precision in the administered dose.
4. Improved patient compliance.
5. Ease of swallowing and no need of water have led to better acceptability amongst the dysphagic patients[7].
6. Dosage form can be consumed at any place and anytime as per convenience of the individual.
7. Good mouth feel.
8. No risk of choking.
9. 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[8].
10. Enhanced oral bioavailability of molecules that undergo first pass effect.
11. OTF's are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of second for the rapid release of one or more API's[9].
12. Bypassing the first pass effects leads to reduction in the dose which can lead to reduction in side effects associated with the molecule. Rapid onset of action.

Disadvantages

1. High dose cannot be incorporated into film.
2. Expensive packaging of mouth dissolving films[10].
3. These films are moisture sensitive

Limitations

1. Drugs with larger doses are difficult to formulate into MDF eg. Rifampin (600mg), Ethambutol (1000mg) etc. 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 strip has a loading of 62.5 mg of simethicone per strip[11].

2. Most bitter drugs should be avoided or taste masking is required.
3. Proteinaceous drugs should be avoided. If used then co-administration of enzyme inhibitors such as aprotonin, bestatin, puromicin and bile salts required for the inhibition of proteolytic enzymes present in saliva.

Figure 1: Mouth Dissolving Film

Classification of Fast Dissolving Technology

For ease of description, Fast dissolving technologies can be divided into three broad groups

1 Lyophilized systems

2 Compressed tablets- based systems

3 Mouth dissolving films

The Lyophilized Systems

The technology around these systems involves taking a suspension or solution of a drug with other structural excipients, through the use of a mould or blister pack, forming tablet shape units. The units or tablets are then frozen and lyophilized in the pack or mold. The resulting units have very high porosity, which allows rapid water or saliva penetration and very rapid disintegration.

Compressed Tablet – Based Systems

This system is produced using standard tablet technology by direct compression of excipients. Depending on the method of manufacture, the tablet technology has different levels of hardness and friability. The speed of disintegration for fast dissolve tablet compared with a standard tablet is achieved by formulating it using water soluble excipients or super disintegrants or effervescent components to allow rapid penetration of water into the core of tablet[12].

Mouth Dissolving Films

Mouth dissolving films, also called oral wafers in the literature are a group of flat films which are administered into the oral cavity. Dissolvable mouth dissolving films or oral strip evolve the past few years from the confection and oral care markets in the forms breath strips and became a novel and widely accepted forms by consumers for delivering vitamins and personal care products. Today MDT are proven and accepted technology for systemic delivery of APIs for over the counter medications and are in the early to mid-development stages for prescription drugs. This is largely due to success of consumer breath freshener products such as Listerine pocket pack in the US consumer markets.

Such systems use variety of hydrophilic polymers to produce 50- 200 mm film. This film can reportedly incorporate soluble, insoluble or taste mask drug substances. The film is manufactured as large shit and then cut into individual dosage unit for packaging in the range of pharmaceutically acceptable formats[13].

Application of Oral Films 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.

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Topical Applications

The use of dissolvable films may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications.

Gastro Retentive Dosage Systems

Dissolvable films are being considered in dosage forms for which water-soluble and poorly soluble molecules of various molecular weights are contained in a film format[14]. Dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially be used to treat gastrointestinal disorders.

Diagnostic Devices

Dissolvable films may be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic device[15].

Physico-Mechanical Properties of Films

Tensile Strength, Elastic Modulus, Elongation at Break

The tensile testing gives an indication of the film strength and elasticity of the film, reflected by the parameters, strain, tensile strength (TS), elastic modulus (EM) and elongation at break (E/B). Strain is the geometrical measure of deformation representing the relative displacement between particles in a material body, when stress induced by either external force or temperature change. A high strain value indicates that the film is strong and elastic. Tensile strength is the stress at which a material breaks or permanently deforms. Tensile strength is an intensive property and, consequently, does not depend on the size of the test specimen. However, it is dependent on the preparation of the specimen and the temperature of the test environment and material. An elastic modulus also referred as young's modulus, is the mathematical description of a material's tendency to be deformed elastically when a force is applied to it. The elongation-to-break (also called ultimate elongation) is the strain on a material when it breaks and it gives an indication of toughness and stretch-ability prior to breakage. These parameters dictate the end-use handling properties and mechanical performance of the films.

A soft and weak polymer is characterized by a low TS, EM and E/B; a hard and brittle polymer is defined by a moderate TS, high EM and low E/B; a soft and tough polymer is characterized by a moderate TS, low EM and high E/B; whereas a hard and tough polymer is characterized by a high TS, EM and E/B[16]. Hence, it is suggested that a film should have a moderately high TS, E/B and Strain but a low EM[17].

Glass Transition Temperature (Tg)

The Glass transition temperature, Tg, is the temperature at which brittle polymer becomes soft or plastic. Cohesive strength and inter-chain attraction, and, thus glass transition temperature (Tg) of the polymer are related to the presence, concentration, location and relative polarities of functional groups along the polymer chain, rigidity of the polymer backbone, bulkiness of side groups and also molecular weight of the polymer. Polymer with low Tg form films that are flexible, with a low elastic modulus and exceptionally high percent elongation[18]. Films formed with polymer having very high values of Tg are stiff, with a high elastic modulus and a very low percent elongation. Above parameters dictate the selection of polymers to obtain desired MDF. Therefore it is important to consider all the above parameters of the polymer.

Composition of Mouth Dissolving Film[19, 20]

Formulation of mouth dissolving film involves the intricate application of aesthetic and performance characteristics such as taste masking, fast dissolving, physical appearance, mouth feel etc. Mouth dissolving film is thin film with an area of 1-20 cm^2 (depends on dose and drug loading) containing drug. Drug can be

loaded up to single dose of 30 mg. Formulation considerations (plasticizers etc.) have been reported as important factors affecting mechanical properties of the films. The excipients used in formulation of the mouth dissolving film are given below as per their categories. From the regulatory aspect, all excipients used in the formulation of mouth dissolving film should be Generally Regarded as Safe (i.e. GRAS- listed) and should be approved for the use in oral pharmaceutical dosage form.

Typical composition of Mouth Dissolving Film is

1. Active pharmaceutical agent 5-30%
2. Film forming polymer 0-40%
3. Plasticizer 0-20%
4. Surfactant q.s.
5. Sweetening agent 3-6%
6. Saliva stimulating agent 2-6%
7. Colors, Flavours, etc. q.s

Active Pharmaceutical Agent

The mouth dissolving film technology has the potential for delivery of variety of APIs. A number of molecules can be incorporated into this delivery system. They may include cough/ cold remedies (antitussives, expectorants), antianxiety drugs, cardiovascular drugs, sore throat, erectile dysfunction, antihistaminics, antiasthamatic, gastrointestinal disorders, nausea, pain and CNS (e.g. Antiparkinson's disease). Other applications comprise caffeine strips, snoring aid, multivitamins, sleeping aid etc. However since the size of the dosage form has limitation, high dose molecules are difficult to be incorporated in MDF. Generally 5 to 30% w/w of active pharmaceutical agent can be incorporated in the MDF[21]. It is always useful to have micronized API which will improve the texture of the film and also for better dissolution and uniformity in the MDF[22]. Many API's which are potential candidate for MDF technology have bitter taste. This makes the formulation unpalatable especially for pediatric preparations. Thus before incorporating the API in the MDF, the taste needs to be masked. Various methods can be used to improve the palatability of the formulation. Certain pathologies require instantaneous release of the medicament for prompt relief. For instance, in case of migraine a rapid clinical effect is desired by the individual. Regiospecific delivery of the medicament would be required in the cases of sore throat, cough, allergy and other local oral manifestations. Water soluble API's are present in the dissolved state in the MDF or in the solid solution form, the water insoluble drugs are dispersed uniformly in the strip. The distribution of water insoluble molecules in water miscible polymer becomes important from the large scale point of view.

Film Forming Polymer

A variety of polymers are available for preparation of MDF. The polymers can be used alone or in combination to obtain the desired film 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 film depends upon type of polymer and its amount in the formulation[23]. On the other hand, mouth dissolving film dosage form should have the property to disintegrate in seconds when placed in mouth and deliver the drug to the oral cavity instantaneously.

Generally water soluble polymers are used as film formers. The use of film forming polymers in dissolvable films has attracted considerable attention in medical and nutraceutical application. The water soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the film. The disintegration rate of polymers is decreased by increasing the molecular weight of polymer film bases. Some of the water soluble polymers used as film former are HPMC E3, E5 and E15 and K3, Methyl cellulose, A-3, A-6 and A-15, Pullulan, carboxymethyl cellulose cekol 30, polyvinylpyrollidone PVP K-90, Pectin, gelatin, sodium Alginate, Hydroxypropyl cellulose, Polyvinyl alcohol, Maltodextrin and Eudragit RD108,9,10,11,12, Eudragit RL100.

Polymerized rosin is a novel film forming polymer[24, 25].

Plasticizer

Plasticizer is a vital ingredient of the MDF formulation. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of film. It helps to improve the flexibility of the film and reduces the brittleness of the film. Plasticizer significantly improves the film properties by reducing the glass transition temperature of the polymer in the range of 40-60˚C for non-aqueous solvent system and below 75˚C for aqueous system[26, 27]. Typically the plasticizers are used in the concentration of 0-20% w/w of dry polymer weight. Mechanical property is plasticizers concentration dependent only.

The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer[28,29]. 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 film.

It is also reported that the use of certain plasticizers may also affect absorption rate of the drug. The plasticizer employed should impart the permanent flexibility to the film and it depends upon volatile nature plasticizer and the type of interaction with the polymer. Cellulosic hydrophilic polymers were easily plasticized with hydroxyl containing plasticizers like PEG, propylene glycol, glycerols, polyols. In contrast, less hydrophilic cellulosic polymers were plasticized with easters of citric acid and phthalic acid[30]. Glycerol acts as a better plasticizer for polyvinyl alcohol while diethylene glycol can be used for both hypromellose as well as polyvinyl alcohol films[28].

1. Surfactant

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 surfactants are sodium lauryl sulphate, benzalkonium chloride, tweens etc. One of the most important surfactant is poloxamer 407 that is used as solubilizing, wetting or dispersing agent[31].

Sweetening Agent[32]

The sweet taste in formulation is more important in case of pediatric formulation. There are two types of sweeteners.

a) Natural Sweeteners

Sweeteners have become the important component for those nutraceuticals products as well as pharmaceutical products whose dissolution occurs in the oral cavity. The classical source of sweetener is sucrose, dextrose, isomaltose, glucose and liquid glucose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol and isomalt can be used in combination as they additionally provide good mouth feel and cooling effect. Polyhydric alcohols are less carcinogenic and do not have after taste which is a vital aspect in formulating oral preparations.

b) Artificial Sweeteners

The artificial sweeteners have gained more popularity in food and pharmaceutical preparations. They are preferred over natural sugars because lower concentration is required and multiple uses don't result in dental caries in individuals. The artificial sweeteners can be classified in I generation and II generation sweeteners which are given below in table. Acesulfame-K and sucralose have more than 200 and 600 times sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Rebiana which is herbal sweetener, derived from plant stevia rebaudiana (South American plant) has more than 200-300 time sweetness[33].

Table 1: Types of Sweetener

Sr no	First Generation	Second generation
1	Saccharin	Acesulfame-k
2	Cyclamate	Sucralose
3	Aspartame	Alimate
4		Neotame

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 mouth dissolving film formulations. Generally acids which are used in 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 film[34].

Flavoring Agent

Perception for the flavors changes from individual to individual depending upon the ethnicity and liking. It was observed that age plays a significant role in the taste fondness. The geriatric population likes mint or orange flavors while younger generation likes flavors like fruit punch, raspberry etc. The selection of flavor is also dependent on the type of drug to be incorporated in the formulation. The acceptance of the oral disintegrating or dissolving formulation by an individual by and large depends on the initial flavor quality which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min[35].

Synthetic flavor oils: peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg

Fruity flavors: vanilla, cocoa, coffee, chocolate and citrus

Fruity essence type: Apple, raspberry, cherry, pineapple

The amount of flavor needed to mask the taste depends on the flavor type and its strength. Preferably up to 10% w/w flavors are added in the MDF formulation.

Coloring Agents

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

Cooling Agents

Cooling agents like monomethyl succinate can be added to improve the flavor strength and to enhance the mouth-feel effect of the product. Other cooling agents like WS3, WS23 and Utracoll II can also be used in conjunction with flavors[37].

Stabilizing and Thickening Agents

The stabilizing and thickening agents are employed to improve the viscosity and consistency of dispersion or solution of the film preparation solution or suspension before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivatives can be used in the concentration up to 5% w/w as thickening agents and stabilizing agents.

Manufacturing Methods[38, 39]:

There are five methods for manufacturing purpose i.e.

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Solid dispersion extrusion
5. Rolling

But the most commonly used industrial methods are solvent-casting method and Hot melt extrusion.

Solvent-Casting Method

The OTF is preferably formulated using the solvent casting method, whereby the water-soluble ingredients are dissolved to form a clear viscous solution. The API and other agents are dissolved in smaller amounts of the solution and combined with the bulk. This mixture is then added to the aqueous viscous solution. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size.

Eg: levocetirizine.2HCl oral film with pullulan polymer was formulated by using solvent casting method. The optimized films of levocetirizine dihydrochloride were obtained[40].

Advantages

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

Disadvantages

- The polymer must be soluble in a volatile solvent or water.
- A stable solution with a reasonable minimum solid Rolling Method: In this method a solution or content and viscosity should be formed.
- Formation of a homogeneous film and release from the casting support must be possible.

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.

Eg. Piroxicam film was formulated with Maltodextrin plasticized by glycerin by using Hot melt extrusion method[41].

Advantages

- Without use of any solvent or water.
- Fewer processing steps.
- Compressibility properties of the API may not be of importance.
- Better alternative for poorly soluble drugs.
- More uniform dispersion because of intense mixing and agitation.
- Less energy compared with high shear methods.

Disadvantages

- Thermal degradation due to use of high temperature.
- Flow properties of the polymer are essential to processing.
- Limited number of available polymers.
- All excipients must be devoid of water or any other volatile solvent.

Semisolid Casting

In this method solution of water soluble film forming polymer are mixed to solution of acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate, cellulose acetate butyrate).After sonication it is coated on non-treated casting film. On drying the thickness of the film is about 0.381-1.27 cm. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

Solid Dispersion Extrusion

Solid dispersions are prepared by immiscible components and drug. Finally the solid dispersions are shaped in to films by means of dies. Suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol.

Rolling Method

In this method solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and gives desired shape and size[42].

Evaluation

Thickness

As the thickness of film is directly concern with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital Vernier Calipers at different strategic locations.

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 OFDF. The details of evaluation of these parameters can be checked elsewhere and are beyond the scope of this review. 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[43].

Tensile Strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below: [43]

Tensile strength = Load at breakage

Strip thickness × 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[43].

% Elongation = Increase in length ×100

Original length

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:

Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation [43].

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[44, 45].

Organoleptic Evaluation

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

Surface pH of Film

Surface pH of the films was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the color of pH paper was observed and reported[44, 45].

Swelling Property

Film swelling studies is conducted using simulated saliva solution. Each film sample is weighed and placed in a pre-weighed stainless steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weight of the

film was determined at preset time interval until a constant weight was observed [44, 45].

The degree of swelling was calculated using parameters

$$\alpha = wt - wo/wo$$

wt is weight of film at time t, and wo is weight of film at time zero.

Assay/ 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.

Disintegration Time

Disintegration of orally fast dissolving films requires USP disintegration apparatus. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Disintegration time will vary depending on the formulation but typically the disintegration range from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films strips[43].

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. 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.

CONCLUSION

MDFs are convenient and reliable dosage forms that can circumvent problems associated with solid dosage forms. The commercial launch of MDFs was primarily in OTC, but now their use has been extended to prescription drugs. MDF are preferred to MDT which requires expensive manufacturing, special packaging due to their fragile nature. Selection of polymers and plasticizers greatly affects physicomechanical properties of MDF. Parameters such as, glass transition temperature, and molecular weight of polymers has a significant influence on mechanical properties of MDF. Thus, with a proper polymer-plasticizer combination, desired MDF can be formed and can be used as reliable delivery systems for most of the therapeutic agents.

Table 2: Marketed Products Mouth Dissolving Film

Product	Manufacturer	API	Strength (mg)
Triaminic	Novartis	Dextromethorphan HBr	7.5
Triaminic	Novartis	Diphenhydramine HCl	12.5
Theraflu	Novartis	Dextromethorphan HBr	15
Gas-X	Novartis	Simethicone	62.5
Sudafed	Pfizer	Phenylephrine HCL	10
Benadryl	Pfizer	Diphenhydramine HCL	12.5
Chloraseptic	Prestige	Benzocaine Menthol	3/3
Suppress	Innozen	Menthol	2.5
Orajel	Del	Menthol/Pectin	2/30
Listerine	Pfizer	Cool mint	-

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