

ORAL FAST DISSOLVING DRUG DELIVERY SYSTEM: A MODERN APPROACH FOR PATIENT COMPLIANCE

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REVIEW ARTICLE

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ABSTRACT

This review represents importance of mouth dissolving films as compared to other oral dosage forms. Fast dissolving oral drug delivery system are solid dosage form which disintegrate or dissolve within seconds when placed in the mouth without need of water or chewing. First developed fast dissolving dosage form in formulation and the rapid disintegrating properties were obtained through a special procedure or formulation modification, hence mouth dissolving film is proved to be better alternative in such cases. This fast dissolving drug delivery system is suited for the drugs which undergo high first pass metabolism and is used for improving bioavailability. Mouth dissolving film consists of thin oral strip; which release active ingredients immediately after uptake into oral cavity. In present investigation, an attempt has been made to develop oral fast dissolving film. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.

Keywords: Fast Dissolving Oral Films; Oral Strip; Film Forming Polymer; Solvent Casting Method.

INTRODUCTION

Mouth dissolving drug delivery system (MDDS):

The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy and ease of administration lead to high levels of patient compliance. Oral dosage forms are more popular than other dosage forms because of following reasons:

- Ease of administration.
- Accurate dosage.
- Self-medication.
- Pain avoidance.
- Patient compliance.

Orally administered drugs are provided to the patient in many dosage forms including solid dosage forms such as capsules, caplets, tablets and liquid dosage forms such as solution, suspension and emulsion. The most popular oral solid dosage forms are tablets and capsules. Tablets are widely accepted because of the convenience in terms of self-administration, compactness, and ease in manufacturing.

Children, geriatric patients and many other persons including disabled patient often have trouble in swallowing tablet or capsules, furthermore, dosing is an issue, as most medications are available in doses that are significantly too large for the pediatric population and cannot easily and reproducibly be divided into smaller doses (e.g. enteric-coated tablets).

Many patients find it difficult to swallow tablets and hard gelatin capsules and do not take their medicines as prescribed. Difficulty in swallowing or dysphagia is seen to affect nearly 35% of the general population. Other groups, who may experience problems in swallowing solid dosage forms, are the mentally ill, to develop mentally disabled, uncooperative patient and reduced liquid intake plans or nausea. Dysphasia's also associated with number of medical conditions including Stroke, Parkinson's disease, AIDS, head and neck radiation therapy and other neurological disorders. In some cases such as motion sickness, sudden episode of allergic attack or coughing and an unavailability of water, the swallowing of tablet or capsules may become difficult. In order to assist these patients,

several fast-dissolving drug delivery systems have been developed.

To overcome this problem, scientists have developed innovative drug delivery systems known as "melt in mouth" or "mouth dissolve (MD)" tablets. Their growing importance was underlined recently when European Pharmacopoeia (European Pharmacopoeia 2005) adopted the term "Oro-dispersible tablets" as a tablets to be placed in mouth where it disappears rapidly before swallowing and which disintegrates in less than 3 minute.

A new oral fast dissolving dosage form such as the fast dissolving film has been developed which offers the combined advantages of ease of dosing and convenience of dosing in the absence of water.

"Oral fast dissolving film is relatively a new dosage form in which thin film is prepared using hydrophilic polymers, which rapidly dissolves on tongue or buccal cavity."

Oral Fast dissolving film (FDF) is also known as mouth dissolving films (MDF), oral strips, oro dispersible films (ODF). On placing mouth dissolving films in the mouth, saliva serves to rapidly dissolve the dosage form. The saliva containing the dissolved or dispersed medicament is then swallowed and the drug is absorbed in the normal way. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach & it may produce rapid onset of action. In such cases bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. (1-3)

HISTORIC DEVELOPMENT OF THE FAST DISSOLVING ORAL FILMS DRUG DELIVERY SYSTEM:

As indicated earlier, a need exists for a fast-dissolving delivery system with the aforementioned capabilities for use within the pediatric and geriatric populations. This need has driven pharmaceutical scientists to develop a drug delivery system that will dissolve rapidly upon contact with the moist mucosal surfaces of the oral cavity and quickly release its components without mastication or water.

Thin-film and strip intraoral dosage forms have been developed by several companies including LTS (Lohmann Therapie-System) AG, Zengen Inc., and Lavipharm Laboratories (Quick-Dis™ and Slow-Dis™ technology), Pfizer's Warner-Lambert consumer healthcare division (Listerine® PocketPaks™). Chloraseptic® Relief Strips™ were the first oral thin-film product to incorporate a drug and were introduced in the United States in September 2003 by Prestige Brands International for relief of sore throat.

As one possible solution to the problem of swallowing conventional solid dosage forms, a few major pharmaceutical companies have developed fast-dissolving intraoral tablets. The major drawback of these conventional fast dispersing and/or dissolving tablets is their physical solid form. The fear of swallowing, chewing, or choking on such solid shaped articles is still a concern in certain populations. In addition, the fragility/friability of wafer-like, porous, and low-pressure molded tablets fabricated by various manufacturing processes, which require special and expensive packaging to protect the dosage forms. The oral fast dissolving films are thin films for oral mucosal delivery that overcomes the shortfalls of conventional fast-dissolving intraoral tablets. The film alleviates the danger/fear of choking, easy to handle and administer, maintains a simple and convenient packaging, alleviates unpleasant taste, and is straightforward to manufacture. (4).

Special features of Mouth dissolving films (5,6)

1. Thin elegant film
2. Available in various size and shape
3. Unobstructive
4. Excellent mucoadhesion
5. Fast disintegration
6. Rapid release

Criteria for fast dissolving film (7):

Fast dissolving film should:

1. Have a pleasant mouth feel

2. Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
3. Compatible with taste masking
4. Leave minimum or no residue in the mouth after oral administration.
5. Exhibit low sensitivity to environmental conditions such as temperature and humidity.

Advantages of fast dissolving film (7):

1. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.
2. Administered without water, anywhere, any time.
3. Suitability for geriatric and pediatric patients, who experience difficulties in swallowing and for the other groups that may experience problems using conventional oral dosage form, due to being mentally ill, the developmentally disabled and the patients who are uncooperative, or are on reduced liquid intake plans or are nauseated.
4. Advantageous in patient which is suffering from motion sickness, cold, sudden episodes of allergic attack coughing, bronchitis or asthma where an ultra rapid onset of action is required.
5. The disadvantage of most orally dispersible tablet(ODT) 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 orally disintegrating Tablets (ODTs). Hence, there is ease of transportation and during consumer handling and storage
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. Oral fast dissolving systems may provide drug manufacturers with significant opportunities in lifecycle management, market expansion, and product differentiation.

Disadvantages of Film Dissolving Film (7):

Drugs which are unstable at buccal pH cannot be administered

1. Drugs which irritate the mucosa cannot be administered by this route
2. Drug with small dose requirement can only be administered
3. Taste masking- Most drugs have bitter taste, and need taste masking
4. Special packaging- must be protected from water so it needs special packaging

Criteria for selection of drug candidate for Fast Dissolving Oral Film's:

1. The drug should have pleasant taste
2. The drug should preferably have a dose up to 40 mg
3. The drug should have small or moderate molecular weight
4. The drug should have good stability and solubility in water and in saliva
5. It should be partially unionized at the pH of oral cavity
6. It should have the ability to permeate oral mucosal tissue

Challenges for preparing Fast Dissolving Oral Film:

1. Palatability
2. Mechanical strength
3. Hygroscopicity
4. Amount of drug
5. Aqueous solubility's
6. Cost-effectiveness

Structure and function of oral mucosa (8):

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 which have high first-pass metabolism. Thus, fast dissolving films allows the film to dissolve in mouth so drug gets directly absorb into the systemic circulation through the oral mucosa. 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 submucosa as the innermost layer.

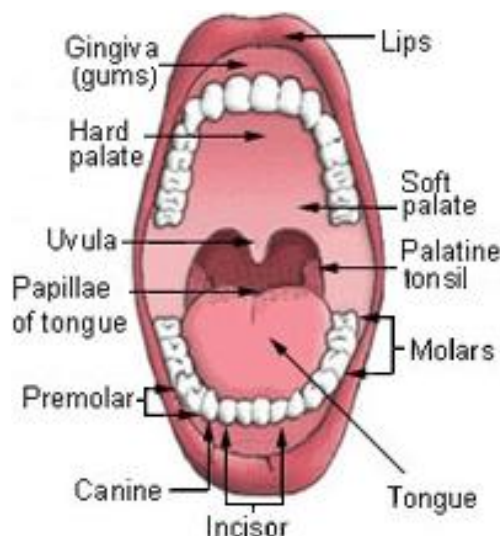


Figure 1: Oral cavity

A stratified, squamous epithelium lines the oral cavity. Three different types of oral mucosa can be identified, i.e., masticatory, lining, and specialized mucosa (Fig. 2). The masticatory mucosa covers the gingiva and hard palate. It comprises a keratinized epithelium strongly attached to underlying tissues by a collagenous connective tissue and as such is able to withstand the abrasion and shearing forces of the masticatory process. The lining mucosa covers all other areas except the dorsal surface of the tongue and is covered by a non-keratinized and hence more permeable epithelium. This mucosa is capable of elastic deformation and hence stretches to accommodate speech and mastication requirements. The epithelium in humans varies in thickness according to the region, e.g. Floor of the mouth 190 μm , hard palate 310 μm , buccal 580 μm . A loose, elastic connective tissue attaches the lining mucosa to underlying structures. The specialized mucosa of the dorsum of the tongue is characteristic of both the masticatory and lining mucosa in that it consists of epithelium partly keratinized and partly non-keratinized. This epithelium is bound to the muscle of the tongue. The regional differences in morphology result in different permeability characteristics that have considerable influence on the design and sitting of drug delivery systems. The differentiation process that gives rise to the regional

differences occurs as the keratinocytes migrate from the buccal layers to the epithelial surface. Within the basal layer the keratinocytes are cuboidal or columnar with a surrounding plasma membrane and containing the usual intracellular organelles. A constant population of epithelial cells is maintained by the division of the basal keratinocytes at a rate equating to the desquamation of surface cells. Aging and disease can result in a loss of this balance, which can lead to a thickening (hyper-trophia) or thinning (atrophia) of the epithelium.

NATURE OF THE LIPID BARRIERS:

Phospholipids, cholesterol and glycosyl ceramides predominate with the phospholipid fraction composed of sphingomyelin and phosphatidylcholine, ethanolamine, serine, and inositol. Triglycerides and cholesterol esters are also present with traces of fatty acids and ceramide. This lipid cocktail may well give rise to fluid lamellae.

Blood Flow:

The blood flow through a tissue is important for achieving good drug absorption. The external carotid artery is the main source of blood supply to the oral tissues. It branches into the maxillary, supplying the hard palate and cheeks, the lingual, supplying the tongue, sublingual, and gingival areas and the facial

artery, supplying blood to the soft palate and

lips.

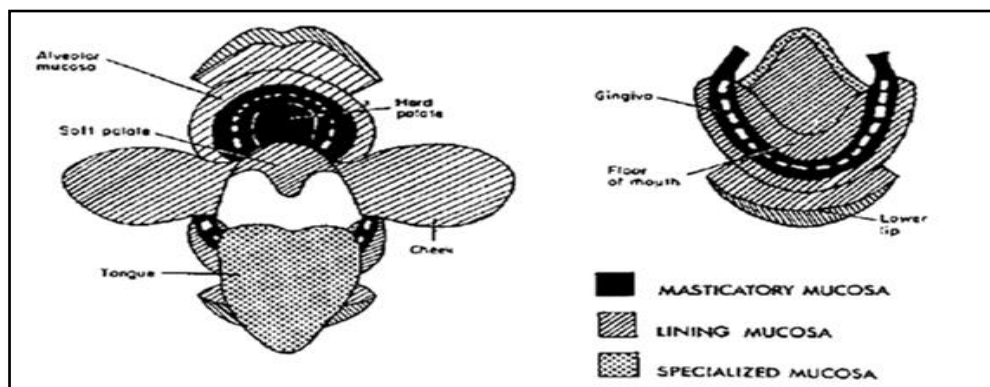


Figure 2: Distribution of masticatory, linings and specialized mucosa within the oral cavity

Blood from the capillary beds is collected by three principal veins that flow into the internal jugular vein. Even during disease, blood flow through human oral mucosa is believed to be sufficiently fast as not to be rate limiting in drug absorption.

Saliva and Mucus:

Saliva is essentially a protective fluid for the tissues of the oral cavity. The major components of the mucous secretions are the soluble mucins that can associate to form oligomeric mucins. These structures provide both visco-elastic and lubricating properties. Salivary mucins have a number of host-defense functions including the establishment of a permeability barrier overlying the epithelia, lubrication of surface tissues and modulation of the colonization of oral microorganisms. Approximately 750 ml of saliva is produced daily in an adult with 60% from the submandibular glands, 30% from the parotids, 5% from the sublingual glands, and around 6% from the minor salivary glands found beneath the epithelium in most regions of the oral mucosa. Saliva is composed of 99% water and is complex fluid containing organic and inorganic material, which is high in glycosylated protein of low viscosity and mucus secretions, which have a higher carbohydrate-to-protein ratio and little to no enzymatic activity. The parotids produce almost entirely serous secretions, the submandibular largely mucous secretions, while the sublingual glands produce a mixed serous/mucous secretion. Up to 70% of the

total saliva mucin content arises from the minor salivary glands. Saliva contains a variety of esterases (mainly carboxylesterases) that may hydrolyze susceptible drug ester groups. The mode of administration of tablets for the oral transmucosal delivery of drugs and their disintegration rate were shown to influence saliva secretion and, because of the link between esterase activity and saliva flow rate, saliva esterase activity. The pH of saliva ranges from 5.8 to 7.4 with the principal buffering function ascribed to the bicarbonate system and to a lesser extent phosphate and protein buffers. Control of saliva pH in localized areas may be considered to optimize the transcellular absorption of ionisable drugs, i.e., by promoting the presence of the un-ionized species. Salivary film thickness has been estimated to be between 0.07 and 0.10 mm and the mucins within this film may permit the attachment of delivery systems such as patches by the employment of mucoadhesive polymers. Interfacial mixing of the polymer with the mucin allows the establishment of secondary bonds and hence retention of the dosage forms at the delivery site. The extent to which such adhesion stimulates further flow of mucus from the occluded minor salivary glands is unclear. The mucus film may act as a further barrier to the absorption of drugs.

THE ABSORPTION BARRIER:

For some drugs a considerable barrier contribution arises as a result of presystemic metabolism. For drugs not subject to such metabolism, the principal barrier is provided by

the oral mucosa. The mucus film may act as a barrier, although unless the drugs bind specifically with the mucins or are large molecules (>1 kDa), the diffusion through the mucus is not a rate-determining step. For keratinized epithelium, the major diffusional barrier is encountered in the upper keratinized layer, which results in lower permeability coefficients compared with non-keratinized tissue. However, for large hydrophilic species such as horseradish peroxidase or lanthanum, only minor differences have been reported for permeability coefficients between keratinized and non-keratinized tissues. Permeability rates of solutes will depend on their molecular characteristics, e.g., size, lipophilicity and extent of ionization. There are two principal routes of penetration transcellular and paracellular (intercellular). A compound may access both these routes, although one is generally preferred according to the physicochemical properties of the compound. The paracellular route is the principal route for hydrophilic compounds whereas for lipophilic molecules the transcellular route predominates.

Dosage forms under oral film drug delivery system:

Open Matrix Type – Wafers and Tablets: Lyophilized wafers are based on processes involving lyophilization or freeze drying that result in fragile porous wafer like tablets. A lyophilized polymeric wafer system is formulated for the provision of rapid drug release in the oromucosal region. Lyophilization produced a porous sponge like matrix which allowed saliva to be rapidly imbibed into the hydrophilic structure. This surge of saliva results in rapid disintegration of the wafer. (9)

Orally disintegrating tablets: The center for Drug Evaluation and Research states an ODT to be “a solid dosage form containing medicinal substance, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue”. (8) The basic approach used in development of ODT is the use of superdisintegrants like cross-linked carboxymethyl cellulose (croscarmellose), sodium starch glycolate, polyvinyl pyrrolidone

which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing the drug in saliva.(9) Quick disintegrating intraoral tablets have also been created by using lipid waxy binders that melt at body temperature. (10) Another approach used in developing mouth dissolving tablets is maximizing pore structure of the tablets.(11)

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 handy with patients having difficulties in swallowing or chewing solid dosage forms. (12) A film or strip can be defined as a dosage form that employs a water-dissolving polymer (generally a hydrocolloid, which may be a bioadhesive 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 (2x3 cm) and can be packaged in multidose containers or individually pouched. (13)

Oral film drug delivery technology and development:

SOLULEAVES™ technology is used to produce a range of oral delivery films that can incorporate active ingredients, colors and flavors. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. This method of administration is especially useful for pediatric or geriatric patients who may have difficulty swallowing traditional tablets or capsules The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas and delivering nutritional products. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes. (14,15)

WAFERTAB™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a premanufactured 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, or for use by patients who have difficulty in swallowing. (16)

FOAMBURST™ 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 flavours.(7)

XGEL™ film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. 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 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. The XGEL™ film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water. XGEL™ film is comprised of a range of different water-soluble polymers, specifically optimised for the

intended use. All of the XGEL ingredients are well known and generally regarded as safe. (GRAS) (17)

RAPID FILM™: Applied Pharma Research (APR), a leading Swiss R&D company focusing on innovative drug delivery. In conjunction with Labtec GmbH, APR has developed a novel OTF technology called Rapid Film™. Dr. Paulo Galfetti, Head of Licensing & Business Development states that Rapid Film offers unique potential to deliver a variety of drugs, particularly when a fast onset of action is required. Galfetti advises that this technology can be used with poorly soluble drugs. Classes of drugs that can benefit from delivery via the Rapid Film system include hypnotics, anxiolytics, antiemetics, NSAIDs and pain killers, 5HT1 agonists for migraine treatment, antiallergics, antacids, vitamins, minerals, asthma and treatments for the oral cavity. (18,19)

FORMULATION CONSIDERATION (20):

Table No. 1: Typical composition of a fast dissolving oral film:

Sr. No	Ingredient	Concentration (%)
1	Drug	1-25
2	Polymer	40-50
3	Plasticizer	20-35
4	Sweetener	2-10
5	Flavor and coloring agent	2-5

Active Pharmaceutical agent:

A typical composition contains 5 to 30 % w/w of the drug. Small dose molecules are the best to be incorporated in oral mouth dissolving films. Multivitamins up to 10 % w/w of dry film weight was incorporated in the films with dissolution time of less than 60 seconds; Suitable drug candidate for FDF should possess.

1. Drug should have low dose.
2. No bitter taste.
3. Good stability in water and pH of saliva
4. Permeable through buccal mucosa

Various categories of drug such as cardiovascular, antiemetic, analgesics, antiallergic, antiepileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction, antialzheimers, expectorants, antitussive can be formulated as film. (21-30).

Film forming polymer:

The oral film must disintegrate in the saliva of the oral cavity. So, the final film must necessarily be water soluble, for the preparation of FDF the various polymers can be used in the film up to 40% w/w of the film content. The polymers are responsible for the strength of the film. The film should be tough to prevent damage during handling and transportation. The polymers can be used as single or in combination as per requirement. The name of the polymers is as follows Hypromellose (HPMC), Hydroxy Propyl cellulose, Starch and modified starch, Pullulan, Pectin, Gelatin, Carboxy methyl cellulose, PVP + Cross linked PVP, Alginates, Poly vinyl Alcohol, Maltodextrin, Polyox. (31-35)

Plasticizer

The role of Plasticizer is beneficial for preparation of FDF. Plasticizer helps to improve the flexibility of the film and reduces the brittleness of the film. The plasticizer should be compatible with polymer and solvent the flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer.

Propylene glycol (PG), Poly ethylene Glycol (PEG), Glycerol, 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. Plasticizer may lead to film cracking, splitting and peeling of the film. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug. (36,37)

Flavouring agents:

Preferably up to 10% w/w flavours are added in the fast dissolving film formulations. The acceptance of the oral disintegrating or dissolving formulation has been consumed and the after taste of the formulation which lasts for at least about 10 min. The selection of flavour is dependent on the type of drug to be incorporated in the formulation. It was observed that age plays a significant role in the taste fondness. Flavouring agents can be selected from synthetic flavour oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavours can be used alone or in the combination. Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg are examples of flavour oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavours. Apple, raspberry, cherry, pineapple are few examples of fruit essence types. (38-40)

Sweetening agents:

Sweeteners are the important part of the formulations intended to be disintegrated or dissolved in the oral cavity. Generally sweeteners are used in the concentration of 3 to 6 % w/w either alone or in combination. Both natural sweeteners as well as artificial sweeteners are used in the formulation of these fast dissolving films. Polyhydric alcohols such as sorbitol, mannitol, and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation. However, it should be noted that the use of natural sugars in such preparations need to be restricted in people who are on diet or in the case of diabetic patients. Due to this reason, the artificial sweeteners have gained more popularity in food and pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame-K and sucralose have more than 200 and 600 time sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. (41)

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. e.g. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. These agents are used alone or in combination between 2 to 6%w/w of weight of the strip. (42)

METHODS OF PREPARATION OF FAST DISSOLVING FILM (43-45):

The following processes can be used to manufacture the oral fast dissolving films.

Solvent Casting Method:

The oral fast dissolving films are prepared by dissolving strip forming agents, plasticizer and saliva stimulating agent in the distilled water, then solution is continuously stirred on magnetic stirrer and kept for 1 hour to remove all the air bubbles entrapped. Meanwhile, in the separate container remaining water soluble excipients i.e. sweetening agent, disintegrating agent, saliva stimulating agent, flavor and drug are dissolved with constant stirring. When the stirring is over both the solutions are mixed together with stirring for another 1 h on magnetic stirrer. Then keep the solution stationary for 1 hr to let the foams settle down. The resulting formulation is casted on a suitable platform and is dried to form a film. The film is preferably air-dried or dried under oven then the film is carefully removed.

Hot-Melt Extrusion Method:

Drug and polymers are blended into a sigma blade mixer for 10 min, and then plasticizer is slowly added. The mixture is granulated in the presence of an anti-sticking agent. Granules are stored overnight at room temperature and then sieved through a 250 μm sieve in order to remove the excess of powder and standardize the particle size. The dried granular material is fed into the extruder. The screw speed is set at 15 rpm in order to process the granules inside

the barrel of the extruder for approximately 3–4 min. The processing temperatures are set at 80⁰ C (zone 1), 115⁰ C (zone 2), 100⁰ C (zone 3) and 65⁰ C (zone 4). The extrudate (T = 65⁰ C) is then pressed into a cylindrical calendar in order to obtain a film with a thickness of about 200 μm . At the end of the preparation processes, the films are cut according to the size required for testing, individually sealed in airtight packets and stored at 25⁰C until use. (46,47)

Semisolid Casting:

In semisolid casting method, firstly a solution of water soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4. (48)

Rolling Method:

In rolling method, a 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 cut in to desired shapes and sizes.(49)

Storage and Packaging:

The converting and packaging stage also provides product flexibility to drug manufacturers. The rolled film can be die-cut into any shape or size or slit into narrower rolls as required for the application. For branding purposes and to meet industry regulations, converters may choose to print information directly onto the film unit doses before packaging. Criteria that may be taken into consideration include the need for unit dose packaging, barcode labeling, and the content in instructions for use, child-resistant seals, and senior-friendly packaging.

Table 2: Patented packaging systems(U.S. Patent July 22, 2003.)

Packaging	Company
Rapid Card	Labtec
Core-Peel®	Amcor Flexibles

Table 3: Marketed products available as fast dissolving oral films

Brand Name	Manufacturer	Drug	Strength (mg)
Klonopin wafers	Solvay Pharmaceuticals	Clonazepam	0.125/ 0.25/ 1/2
Listrine Cool Mint Pocket Perks	Pfizer, Inc.	Cool mint	-
Sudafed PE	Wolters Kluwer Health, Inc.	Phenylephrine	-
Suppress®	InnoZen®, Inc.	Menthol	2.5
Triaminic	Novartis	Diphenhydramine HCl	12.5
Therflu	Novartis	Dextromethorphan HBr	15
Gas – X	Novartis	Simethicone	62.5
Chloraseptic	Prestige	Benzocaine/ Menthol	3 / 3
Benadryl	Pfizer	Diphenhydramine HCl	12.5 / 25

CONCLUSION

Fast dissolving drug delivery systems have better patient compliance and may offer improved biopharmaceutical properties, improved efficacy and better safety compared with conventional oral dosage forms. The future potential for fast dissolving dosage forms is promising because of the availability of new technologies combined with strong market acceptance and patient demand. Future possibilities for improvements in fast dissolving drug delivery system are bright, but the technology is still relatively new and the research is still going on. More products need to be commercialized to use this technology properly. The present report concludes that fast dissolving oral film is most acceptable and accurate oral dosage form which by pass the hepatic system and show more therapeutic response. Fast dissolving films have several advantages over conventional dosage forms and fast dissolving tablets. The pharmaceutical companies prefer this dosage form due to both patient compliance (especially pediatric and

geriatric) as well as industrial acceptability. Oral films can replace the over-the-counter (OTC) drugs, generic and branded product from market due to lower cost and consumer's preference. This technology is a good tool for product life cycle management for increasing the patent life of existing products.

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CONFLICT OF INTEREST

Author declares that there are no conflict of interest.

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