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MOUTH DISSOLVING FILMS : A REVIEW

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ABSTRACT

The purpose of current review is to enlighten the present and future prospective on Mouth dissolving film drug delivery system. Now a days, we observe padietric and geriatric patients facing the problem of dysphasia due to administration of monolithic solid dosage form, which are also seen in the case of fast dissolving tablets. 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. These films have potential to deliver a drug systematically through intragastric, sublingual or buccal route of administration and also has been used for local action. The present review provides an account of various formulation considerations, method of preparation, and quality control of mouth dissolving films.

KEYWORDS: Mouth dissolving films, Solvent casting method, Fast dissolving drug delivery, First pass metabolism, Buccal route.

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INTRODUCTION

Fast Drug Delivery Systems are rapidly gaining interest in the pharmaceutical industry. These systems either dissolve or disintegrate generally within a minute without needing water or chewing. These systems offer superior clinical profiles with potentional oro mucosal absorption thus increasing the drug bioavailability with respect to oral administration. Recently thin films have been proposed which rapidly dissolves or disintegrates into buccal cavity. Mouth dissolving films are novel dosage forms that disintegrates or dissolves in the oral cavity. These are ultra thin postage stamp size with an active agent or pharmaceutical excipients. These dosage forms are placed on the tongue or any mucosal tissue. When wet with saliva, the films rapidly hydrates and adheres on to the site of application. It rapidly dissolves or disintegrates to release the medicine for mucosal absorption or with modification, allows for oral GIT absorption with quick dissolving properties. An important benefit of these dosage forms is accurate dosing as compared to liquid dosage form, no water is needed and there is no fear of choking as compared to tablets and capsules. Fast-dissolving oral delivery systems are solid dosage forms, which disintegrate or dissolve within 1 minute when placed in the mouth without drinking of water or chewing. After disintegrating in the mouth, enhanced the clinical effect of drug through pre-gastric absorption from mouth pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form[1]. More recently, Fast-dissolving buccal film drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. They are usually used for pharmaceutical and nutraceutical products. It is the newest frontier in drug delivery technology that provides a very convenient means of taking medications and supplements. Fast dissolving films are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething[1,2].

Fast dissolving film is prepared using hydrophilic polymers that rapidly dissolve/disintegrate in the mouth within few seconds without water and eliminates the fear of chocking as an alternative to fast dissolving tablets.

Special features of Mouth dissolving films[3,4]

- Thin elegant film
- Available in various size and shape
- Unobstructive
- Excellent mucoadhesion
- Fast disintegration
- Rapid release

Advantages

- Oral dissolving films can be administered without water, anywhere, any time.
- Due to the presence of larger surface area, films provides rapid disintegrating and dissolution in the oral cavity.
- Oral dissolving films are flexible and portable in nature so they provide ease in transportation, during consumer handling and storage.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated[5].
- Beneficial in cases such as motion sickness, acute pain, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability[6].
- As compared liquid formulations, precision in the administered dose is ensured from each strip of the film.
- 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.

- 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.
- Provide new business opportunity like product differentiation, product promotion, patent extension.

Disadvantages

- High doses cannot be incorporated .
- Dose uniformity is a technical challenge.
- Hygroscopic in nature.
- Require special packaging for products stability and safety.

Ideal characterstics of suitable drug candidate

- The drug should have pleasant taste.
- The drug to be incorporated have low dose upto 40 mg.
- The drug with smaller and moderate molecular weight are preferable.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

Table 1
General Composition of MDF

Sr.No.	Ingredients	Concentration (%)
1.	Active pharmaceutical ingredient	1-25
2.	Hydrophilic polymer	40-50
3.	Plasticizer	0-20
4.	Colors, Flavors, Fillers	0-40

Active Pharmaceutical Ingredient[7-12]

A typical composition of the film contains 1-25% w/w of the drug. Variety of APIs can be delivered through fast dissolving films. Small dose molecules are the best candidates to be incorporated in Oral fast dissolving film. 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 Oral fast dissolving films. A no. of molecules can be incorporated, they may include Cough/ cold remedies (antitussives, expectorants), antianxiety drugs, cardiovascular agents, erectile dysfunction drugs, antihistaminincs, GIT disorders, nausea, pain and CNS (antiparkinson disease). Examples of some drugs that can be incorporated in Mouth dissolving films are listed in Table 2.

Table 2
List of Drug molecules that can be incorporated in MDF

Drug	Dose (mg)	Therapeutic Class
Chlorpheniramine maleate	4	Antiallergic
Loperamide	2	Antidiarroheal
Triplolidine hydrochloride	2.5	Antihistaminic
Famotidine	10	Antacid
Azatidine maleate	1.0	Antihistaminic
Sumatriptan succinate	35	Antimigraine
Ketoprofen	12.5	Analgesic
Nicotine	2	Smoking Cessation
Loratidine	10	Antihistaminic
Cetrizine	5-10	Antihistaminic
Omeprazole	10-20	Proton pump inhibitor

Film Forming Polymers[13-14]

A variety of polymers are available for preparation of mouth dissolving films. The polymers can be used alone or in combination to improve hydrophilicity, flexibility, mouth feel and solubility characteristics of mouth dissolving films. The stiffness of the film depends on the type of polymer and the amount of polymer in the formulation. The various polymers which can be used for making mouth dissolving films must be water soluble with low molecular weight and excellent film forming capacity, since the primary use of all thin film oral dosage forms relies on their disintegration in the saliva of the oral cavity. The polymer employed should be non-toxic, non-irritant with good wetting and spreadability property. The polymer should not be very expensive and should be readily available. Water soluble polymer that may be used include natural gums such as xanthan, guar, acacia, tragacanth other available polymers include cellulose or cellulose derivatives, hydroxypropylmethyl cellulose with different grades like HPMC E15, HPMC E5, HPMC K4M, HPMC K100, hydroxyethylcellulose, hydroxypropylcelluose, carboxymethylcellulose, polyvinylpyrrolidone, polyvinyl alcohol, pullulan, gelatin. Modified starches are also used for preparation. The physicochemical characteristic of the polymer or polymers selected for film formulation play a vital role in determining the resultant disintegration time of the cast thin film oral dosage form.

Plasticizer[15-17]

Plasticizer is a vital ingredient of the fast dissolving films. Plasticizer helps to improve the flexibility of the strip and reduces the brittleness of the films. It significantly improves the film forming properties by reducing the glass transition temperature of the polymer. The chemical structure and concentration of plasticizers play an important role in alleviating the glass transition temperature of the polymers. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of the film. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such astributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients. Typically the plasticizers are used in the concentration of 0–20 percent; w/w of dry polymer weight. However, inappropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug.

Sweetening agents[18]

Sweeteners have become the important part of pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Sweeteners can be used either alone or in combination. Both natural as well as artificial sweeteners are used in the formulation of these mouth dissolving film. The classical source of sweetener is sucrose, dextrose, fructose, glucose, liquid glucose and isomaltose. 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, and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation. Polyhydric alcohols are less carcinogenic and do not have bitter after taste which is a vital aspect in formulating oral 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.

Saliva stimulating agents[19]

The purpose of saliva stimulating agent is to increase the rate of production of saliva that would aid in the faster disintegration. These agents are used alone or in combination. Examples : Citric acid, Tartaric acid, Ascorbic acid, Malic acid

Flavoring agents[20]

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 flower. 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.

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 an insoluble or suspension form.

METHOD OF PREPARATION OF MOUTH DISSOLVING FILMS[21-2]

One or a combination of the following processes can be used to manufacture the Mouth dissolving film:

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

1. Solvent casting method

Fast dissolving films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in a suitable solvent then both the solutions are mixed and stirred and finally casted into the Petri plate and dried.

Water soluble ingredients are dissolved in water

⇩

API and other agents are dissolved in suitable solvent to form a clear viscous solution

⇩

Both the solutions are mixed

⇩

Degassed under vacuum

⇩

Resulting solution is cast as a film

⇩

Film is dried in drying oven and collected

2. Hot melt extrusion

Hot melt extrusion method has various benefits; those are fewer operation units, minimum product wastage, better content uniformity, an anhydrous process, absence of organic solvents.

In hot melt extrusion method-

Drug is mixed with carriers in solid form.

⇩

The extruder having heaters melts the mixture

⇩

Finally the melt is shaped in films by the dies

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