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Review Article

## A Detailed Overview on Mouth Dissolving Film

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### Abstract

The present review aims to enlighten about a potential dosage form that is mouth dissolving films. Mouth dissolving film is a rapidly dissolving dosage form that dissolves in the mouth within a few seconds without the intake of water and is mainly used for pediatric and geriatric patients due to its flexibility and patient compliance. It is a potential dosage form for drugs having high metabolism and low bioavailability. Solvent casting, hot melt extrusion, solid dispersion, semisolid casting, rolling, and other processes can all be used to create mouth dissolving film, but solvent casting is the most popular due to its consistency and superior physical properties. Mouth dissolving film is evaluated for the following parameters like physical parameters and chemical parameters. The review sums up information on drug delivery by mouth dissolving films as a promising dosage form for delivering drugs to children and elderly patients, as well as information on its formulation considerations, preparation process, and evaluation criteria.

**Keywords:** Mouth dissolving film, Buccal film, Improved patient compliance, Standard composition, Method of preparation, Evaluation

## 1. Introduction

The oral course of treatment is the most popular due to its ease of administration, comfort, adaptability, patient consistency, and recognition. Many alternatives to the oral route of drug transportation have been made available for pediatric, geriatric, ill, and rebellious individuals using current creative innovations. Innovative advances have given rise to bioadhesive mucosal measuring structures such as tablets, gels, and fixes. Among the various portion structures, the use of polymeric films to deliver drugs into the buccal pit has recently demonstrated tremendous potential. Orally degrading films (ODFs) immediately hydrate by splashing saliva after degradation and disintegration, releasing the dynamic pharmacological component from the measurement structure.<sup>1</sup>

The mouth-dissolving film is a coating made using hydrophilic polymers that quickly dissolve when exposed to spit. Oral disintegrating films and tablets are two different oral medicine delivery devices. This framework developed in the latter part of the 1970s as an alternative to traditional dose structures, such as fast-disintegrating tablets and containers, for elderly and young patients who had problems swallowing those structures. The size of a typical orally degrading film is comparable to a postage stamp. The purpose of the Oral dissolving tablet presence at the commercial center was to provide patients with information on the proper organization, including warnings like "don't bite/don't swallow". Despite these restrictions, bites and gulps were frequently observed. However, orally degrading film liberated the majority from these catastrophes.<sup>2</sup>

### 1.1. Advantages of Mouth dissolving film

- i. For pediatric, elderly, and psychiatric patients who have trouble swallowing tablets and other solid dosage forms, it is simple to administer.
- ii. No water is required for swallowing.
- iii. Rapidly acting medications that are poorly water soluble that dissolve and absorb quickly.
- iv. Pregastric absorption can lead to improved clinical performance through a decrease in side effects, greater bioavailability with a smaller dosage, and.
- v. Bitter medications have the potential to be taste-masked.
- vi. Useful in situations requiring a rapid initiation of action, such as motion sickness, an unexpected allergic reaction or coughing
- vii. fit, hypertension, bronchitis, or asthma.
- viii. More affordable.
- ix. The dosing procedure is simple and precise.
- x. Reasonable transportation.

### 1.2. Special features of mouth dissolving film

- i. Should be thin and elegant.
- ii. A satisfying mouth feel is expected.
- iii. Should be available in a variety of sizes and forms.
- iv. Should disintegrate quickly in the absence of water and release medication quickly.

- v. Should be appropriate for flavor masking.
- vi. After oral administration, there should be little to no residue left in the mouth.
- vii. Be less sensitive to environmental factors like humidity and temperature.

### 1.3. Ideal requirement of mouth dissolving film

The following is an overview of the optimum conditions for ODF:

- i. To enable a reliable production and storage process as well as ease of handling and administration, mouth dissolving film should be flexible and thin but stable. The films need to be portable, non-sticky, and able to keep their level shape without rolling.
- ii. Simple administration for people who are mentally ill, disabled, or unwilling.
- iii. They need to taste good and have a pleasing texture.
- iv. No need for water exists.
- v. It should take as little time as possible for anything to decompose.
- vi. They should be mostly influenced by environmental variables like humidity and temperature.
- vii. They must be able to deliver the advantages of liquid medicine in the form of a solid formulation.
- viii. A unit MDF's size shouldn't be so big that it inhibits the patient's ability to the willingness to accept.
- ix. The MDF should have a uniform, smooth surface and be both physically and chemically stable throughout its shelf life.

### 1.4. Limitation of Mouth dissolving film

- i. Due to the narrow surface area of the buccal cavity, only little doses of drug can be delivered.
- ii. Stability issues such brittleness and moisture absorption during storage.
- iii. It is impossible to deliver medications that are unstable at buccal pH.
- iv. The administration of drugs that irritate the mucosa is prohibited.

## 2. Standard composition of mouth dissolving film

- 1) Drug (Active pharmaceutical component)
- 2) film forming agent
- 3) Plasticizer
- 4) Saliva stimulating agent
- 5) Sweetening agent
- 6) Flavoring agent
- 7) Surfactant
- 8) Colour, Filler

### 2.1. Active pharmaceutical component

Any class of pharmaceutically active drugs that can be delivered orally or through the buccal mucosa considered as active pharmacological substance. such as expectorants, antianginals, antitussives, antihistaminic, antiepileptic, antianalgesic and antiulcer drugs.<sup>3</sup>

### Ideal drug candidate for drug delivery:

- i. Low dose, less than 40mg, is required.
- ii. Low molecular weight drugs are preferable.
- iii. It should have a pleasant flavor.
- iv. It should be reasonably stable in both saliva and water.
- v. It need to be capable of penetrating the mucosal tissue of oral cavity.

### 2.2. Film forming agent

Water-soluble polymers are employed as film formers because they give the films a quick disintegration, a pleasant mouth feel, and mechanical qualities. Polymers can be employed individually or in mixture with others to create films with the necessary hydrophilicity, flexibility, mouth feel, and solubility. The rate of polymer disintegration reduces as the molecular weight of polymer film bases increases.<sup>4</sup>

### Ideal properties of polymer:

- i. Polymers that are plain, nontoxic, and inexpressive should be used.
- ii. It should have no flavor. It should be free of drainable toxins.
- iii. It should be affordable and simple to obtain.
- iv. It shouldn't be a major hindrance during the deterioration interaction.
- v. It must possess exceptional wetting and spreading qualities. It must be sufficiently flexible, shear, and able to strip.
- vi. It should not induce additional oral disease and have a long time frame of realistic usability.

### 2.3. Plasticizer

It serves as a key component in oral thin films. The plasticizers aid in enhancing the mechanical characteristics of the film, such as its tensile strength and elongation. Additionally, it makes the film less brittle. It might increase the strength and flow of polymer. The choice of plasticizers must be made carefully. It should interact well with the polymers, the drug, and the other excipients. The wrong selection could result in the film peeling, splitting, and cracking. Dimethyl, dibutyl, diethyl phthalate, tributyl, triethyl, actyl citrate, triacetin, propylene glycol, polyethylene glycol, and glycerol are some examples of plasticizers that are frequently employed.<sup>5</sup>

### 2.4. Saliva stimulating agent

Saliva stimulating drugs are used to boost saliva production in to accelerate the breakdown and dissolution of the oral film insight the mouth. It has a range of 2-6% that can be used alone or in mixture. Citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid are often used saliva-stimulating substances. Citric acid is the most popular of them.<sup>6</sup>

### 2.5. Sweetening agent

Sweeteners are typically used to cover up the bitter taste of some drugs. One can use natural and artificial sweeteners alone or together. Types of sweetener includes natural sweeteners, such as corn syrup solids, xylose, ribose, glucose, mannose, galactose, fructose, dextrose, and sucrose and artificial sweeteners aspartame, cyclamate, and saccharin. Acesulfame K, sucralose, alitame, and neotame.<sup>7</sup>

## 2.6. Flavoring agent

Both natural and artificial flavors, including methyl salicylate, eucalyptol, thymol, artificial vanilla, cinnamon, various fruit flavors, mints like peppermint and menthol, and essential oils, may be used singly or in combination.<sup>2</sup>

## 2.7. Surfactant

As a solubilizing, wetting, or dispersion agent, surfactants are employed. Surfactant is used to breakdown the film quickly and release the active ingredient. Surfactant can increase the solubility of poorly soluble drugs in rapidly dissolving oral films. Polaxamer 407, sodium lauryl sulphate, benzalkonium chloride, benzthonium chloride, tweens, and spans are a few examples.<sup>1</sup>

## 2.8. Coloring agent

When some of the ingredients or drugs in the formulation are present in insoluble or suspension form, titanium dioxide or FD&C approved coloring additives are added (not exceeding concentration levels of 1%w/w).<sup>7</sup>

## 3. Method of preparation of mouth dissolving film

The methods for manufacturing oral thin films include:

- 1) Solvent casting method
- 2) Semisolid casting method
- 3) Hot melt extrusion method
- 4) Solid dispersion extrusion method
- 5) Rolling method

### 3.1. Solvent casting method

Polymers that are water soluble are dissolved to create a homogeneous solution. Drugs and other water-soluble ingredients are given a little amount of water to dissolve in. Continuous stirring is used to combine the two solutions. Applying a vacuum removes air bubbles that have become entrapped. The produced solution is cast onto Petri dish and then divided into bits.<sup>8</sup>

### 3.2. Semisolid casting method

When acid-insoluble polymers are required for the film preparation, this approach is preferred. Gel mass is cast in to the films or ribbons using the semisolid casting technique, which uses heat-controlled drums. Gel mass is created by mixing a film-forming solution with an acid-insoluble polymer solution in sodium hydroxide or ammonium hydroxide. The polymers cellulose acetate phthalate and cellulose acetate butyrate are insoluble in acids. The proportion of 1:4 acid-insoluble polymer to film-forming polymer should be taken.<sup>9</sup>

### 3.3. Hot-melt extrusion technique

In the hot melt extrusion procedure, the drug and carriers are first combined in solid form. After that, dry granular material is poured to the extruder.

Processing of the granules inside the extruder barrel for about 3–4 minutes, the speed of screw is set at 15 rpm. The recommended processing temperatures are 650C, 800C, 1150C, and 1000C for zones one through three (zone-4). The extrudate was subsequently compressed insight cylindrical calendar to produce a film.<sup>8</sup>

## 3.4. Solid dispersion method

In this approach, more than one drug candidate are dispersed in an non reactive carrier in a conventional dosage form while amorphous hydrophilic polymers are present. To create a solution, Active pharmaceutical ingredient is dissolved in a appropriate solvent. A solution is incorporated to the melt of an appropriate polymer (PEG) beneath 70° C without extracting the liquid solvent. Finally, solid dispersion is formed into films using dies.<sup>9</sup>

## 3.5. Rolling method

The rolling approach involves preparing a drug solution or suspension with a film-forming polymer before putting it through the roller. Specific rheological considerations should be made for the suspension. The majority of the solvent is composed of water and an alcohol-water mixture. After the film has dried on the rollers, it is cut into the desired shapes and sizes.<sup>10</sup>

## 4. Evaluation Parameters

The films are evaluated after they have been created using one of the above mentioned manufacturing processes. To preserve inter- and intra-batch homogeneity amongst films, evaluation is a vital and necessary stage. Numerous criteria are investigated and classified into categories based on their physical and chemical characteristics.<sup>11</sup>

### 4.1. Physical Parameters

Physical parameters are essential since they are applied to the final dosage form, providing information about the consistency between batches and helping to maintain the final formulation's visual appeal. Technical rules from other industries, such as the plastic industry, can be used as templates because the USP only specifies a tensile strength test for surgical sutures and patches. Tensile testing in accordance with the DIN EN ISO 527-1 and 527-3 regulations or the ASTM International Test Method for Thin Plastic Sheeting (D 882-02)<sup>15</sup> can be used.<sup>10</sup>

#### 4.1.1. Mechanical Parameters

##### 4.1.1.1. Tensile strength

The greatest stress that can be given to a film specimen before it breaks is known as the tensile strength, and it may be calculated using the applied load at rupture as the mean of three measurements and the cross-sectional area of the fractured film using the equation below.

Tensile strength of film in N/mm<sup>2</sup> =

breaking strength (Newton) /cross-sectional area of the sample (mm<sup>2</sup>).<sup>4</sup>

##### 4.1.1.2. Dryness / Tack test

Tack is the strength with which the film attaches to any piece of paper that is put into contact with the strip, whereas dryness is the quality to measure the solvent or water content present in the film. It has been determined that there are eight distinct stages in the drying process for films: set-to-touch, dust-free, tack-free, dry-to-touch, dryhard, dry-through, dry-to-recoat, and dry print free. These characteristics can currently be measured using many different equipment. This can be accomplished at lab scale by pressing the thumb against the film.

##### 4.1.1.3. Young's modulus

The stiffness of a film is measured by its elastic or Young's modulus. The techniques used to calculate tensile strength could also be applied in this situation. It is shown as the

following when the applied stress to strain ratio in the elastic deformation zone is used:

Young's Modulus = Slope x 100/Film Thickness x Cross Head Speed

A tough and brittle film exhibits a high Young's modulus and tensile strength with little elongation.

#### 4.1.1.4. Percentage elongation

A type of deformation is elongation. Anything under stress simply changes shape, and a texture analyzer used to measure this change. In other words, a sample deforms, lengthens, or elongates when it is subjected to tensile stress. The following formulae used to determine it by measuring the increase in length of the film following tensile measurement:

$$(L-L_0) \times 100 / (L-L_0) = \text{Percent Elongation}$$

$L_0$  was the initial length, and  $L$  was the finished length.

#### 4.1.1.5. Tear resistance

Plastic film or sheeting's tear resistance is a complicated function of its ultimate rupture resistance. The force needed to start tearing is essentially measured using a very modest loading rate of 51 mm (2 in.) /min. The tear resistance value is expressed in Newton's (or pounds-force) and represents the maximum stress or force (which is typically obtained close to the outset of tearing) needed to tear the specimen.

#### 4.1.1.6. Folding endurance

Film's flexibility is a crucial physical quality required for easy application on the administration site. The strength of the film can be quantitatively measured in terms of folding endurance by simply folding the mouth dissolving film at a 180° angle of the surface at the same layer until it fractures or by folding it three hundred times without breaking. The folding endurance value is calculated as the folding number of the film can endure without breaking.

#### 4.1.2. Other Physical parameter

##### 4.1.2.1. Appearance

Any produced film can be examined to determine whether it looks transparent or opaque. Surface qualities are often determined through visual inspection, however tools like microscopes can also be utilized.

##### 4.1.2.2. Thickness

Micrometer screw gauges used to measure the produced film's thickness at various key spots. Film thickness should be measured five times, starting from the centre and moving outward from all four corners, before calculating the mean thickness. It is crucial to confirm uniformity in the film thickness because it has a direct impact on the strip's dosage accuracy.

##### 4.1.2.3. Weight variation

Each film should be weighed individually, then the average weights should be determined. The particular weight of the film is then reduced by the weight of the films as a whole. A significant weight fluctuation suggests that the procedure used was ineffective and suggests that the medication content was likely not uniform.

##### 4.1.2.4. Contact angle

At 37°C, contact angle can be determined with a goniometry (AB Lorentz and wetter, Germany). You can accomplish this by taking a dry film and dabbing a drop of distilled water on its surface. Digital cameras can capture images of water droplets within 10 seconds of their deposition. On both sides of the

descent, the contact angle can be measured, and an average is taken.

#### 4.1.2.5. Transparency

Simple UV spectrophotometers used to determine the films' transparency. Place the film inside the spectrophotometer cell after cutting it into a rectangular shape. Find the film's transparency at 600 nm. The following formula used to calculate the film's transparency:

$$\text{Transparency} = (\log T_{600})/b = -\epsilon C.$$

$T_{600}$  stands for transmittance at 600 nm,  $b$  for film thickness (mm) and  $C$  for concentration.

#### 4.1.2.6. Moisture content

The brittleness and friability of films are impacted by the moisture content. In short, the product's ingredients control how much moisture is present in a given film. Generally, moisture content testing equipment, the Karl Fisher titration method, or the weighing method used to determine how much moisture is contained in the film. Usually, a pre-weighed film of a certain size is heated to between 100 and 120 °C until it reaches a consistent weight, and the difference in weight indicates the amount or level of moisture contained in the film.

% Moisture content = [(Starting mass - Final mass) 100/Initial weight] used to compute moisture content.

The optimal moisture content for a film is 5% or less.<sup>6</sup>

### 4.2. Chemical Parameters

#### 4.2.1. Surface pH test

Agar gel with a 1.5% weight / volume ratio and pH paper with a pH range of 1 to 11 used to measure the surface pH of a film. It is noted and reported that pH paper's colour changes.

#### 4.2.2. Disintegration time

The film's dissolution and disintegration properties can be determined from the disintegration time. A stainless steel wire mesh is filled with 25 ml of pH 6.8 simulated salivary fluid, and the necessary size of film (2 x 2 cm<sup>2</sup>) is placed inside of it. In-vitro disintegration time is the amount of time it takes for film to break and dissolve.

#### 4.2.3. Test for *in vitro* dissolution

The paddle or basket apparatus mentioned in the pharmacopoeias used to conduct dissolution testing. The sink conditions and API dose will primarily be taken into consideration while choosing the dissolving medium. The tendency of the strip to float onto the dissolving media when the paddle equipment is used frequently makes the dissolution test challenging.

#### 4.2.4. Thermal analysis

A differential scanning calorimeter used to record thermo grams of the samples, which gives information about the status of the drug molecules within the film. Any re-crystallization, phase change, or molecular interaction of the drug molecule enclosed inside the film is immediately represented by a shift in the endothermic or exothermic peak or a widening of peak area. This can be determined by heating the sample in an aluminum pan at a predetermined heating rate (about 10°C/min) from ambient temperature to an increased temperature (about 500 °C).

#### 4.2.5. Crystallinity

By performing X-ray crystallographic investigations with an X-ray diffractometer, it is simple to detect if the drug molecule inside the film is crystalline or amorphous. Films can be

inserted in the sample holder, and an X-ray source used to acquire XRD transmission diffractograms over a start-to-end diffraction angle, scan range, and scan speed.

#### 4.2.6. Assay / Uniformity of content

Standard assay technique specified for the specific drug candidate in the standard pharmacopoeias are used to determine uniformity of content. The consistency of the material is evaluated through determining the API content in every separate film. The maximum content uniformity is between 85 and 115%.

#### 4.3. In vivo test

Measurements of the contact angle and thermo-mechanical analyses of the film swelling tendency have both been used to simulate in vivo disintegration. With the assistance of a tasting panel and live volunteers, in vivo testing primarily entails tasting the films and measuring there in vivo disintegration time. The taste of the movies is also evaluated using an electronic tongue tester.

#### 4.4. Additional tests

Analyses of the polymer solution's viscosity, the homogeneity of the content, and the detection of residual solvents are additional techniques for characterizing and monitoring the quality of orally dissolving film. By using scanning electron microscopy, X-ray diffraction, and near-infrared chemical imaging, Garsuch and Breitreutz discovered caffeine recrystallization in Mouth dissolving films changing between the upper and lower surface. Raman and near-infrared spectroscopy are suitable technologies to identify and measure APIs in the films.

Crystalline and glass transition temperature are studied using differential scanning calorimetry, thermo-mechanical analysis, and X-ray diffraction. Isothermal calorimetry was used by Gaisford to monitor the crystallization of drug from Oral film. By using dynamic vapor sorption or by weight, researchers examine hygroscopic and residual water content. Further research about standard guidelines should be done on microbiological studies and stability tests.<sup>11</sup>

## 5. Conclusions

This review shows that mouth dissolving films are promising dosage form as they have more patient compliance and rapid onset of action. Moreover they are potential candidate for oral route as they can deliver drug locally as well as systematically. MDF are used for pediatric and geriatric population or for patient those who have difficulty in swallowing. Due to these advantages MDF used to treat patient efficiently.

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