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Mouth Dissolving Films: An Overview

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Vishal Jagtap[1]*, Sachin Dhudhe[2]

Dept. of Pharmaceutics, Maharashtra Institute of Pharmacy, Kinhi, Tal- Bramhpuri Dist. – Chandrapuri, 441206, India.

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ABSTRACT

The goal of any drug delivery is to ensure that the drug enters the body completely; However, patient compliance cannot be ignored. Rapid drug delivery systems such as oral film (MDF) provide a convenient way to deliver medication not only to people with specific swallowing difficulties, such as children and the elderly but also to the public. MDF is a new pharmaceutical form that disintegrates and dissolves in the mouth. Intraoral absorption allows rapid onset of action and helps bypass initial effects, thus reducing the dose required to produce the desired therapeutic effect. This review provides an overview of the various polymers available for MDF production and highlights the effects of polymers and plasticizers on various physical properties of MDF. The problems that arise during the formulation and production of medium-density fiberboard are also briefly mentioned.

INTRODUCTION:

The oral route is the most popular and patient-friendly route of administration. Almost all patients, including adults, children and the elderly, take most of the medication in tablet and capsule form. However, approximately 26% to 50% of patients have difficulty swallowing tablets and hard gelatin capsules [1]. These patients mostly include the elderly (those who have difficulty taking medications by mouth due to hand tremors and difficulty swallowing), the elderly (those who often fear taking medications by mouth due to weak muscles and nerves) [2], and others. Including psychiatric patients, developmentally disabled patients, uncooperative patients, diuretic or nausea patients, and travelers unable to access water [3, 4]. In addition, absorption is also poor due to the presence of many digestive enzymes in the intestinal lumen and epithelium after absorption (e.g. P-glycoprotein, etc.) and initial metabolism and subsequent elimination by hepatic enzymes. , limiting the ability of many medications to access oral health care [5]. Additionally, the tablet (as much paper as there is for this method) needs to break down in the digestive tract and then the medicine needs to dissolve. This process slightly delays the onset of the effect, which is undesirable in situations such as pain [5].

Pharmaceutical researchers around the world are studying thin films as an ideal drug delivery method. There are other options for prescriptions. Because of their simplicity, dispersible films and rapidly disintegrating films are the most commonly used materials. Compared to tablets, it increases the effectiveness of the active drug isolated in the mouth for a short time after contact with saliva. 1 Rapid destruction device is a recently discovered revolutionary drug delivery method. It provides a great way to take vitamins and supplements. These machines can crash in seconds. The drug is delivered through the film, applied to the patient's tongue or mucosal tissue, quickly moistened with saliva, rapidly degraded, and then released and absorbed by the oral mucosa.

❖ Benefits of mouth-dissolving film

- Due to its versatility, films are less brittle than orally disintegrating pills.
- Since films are more expansive, they encourage the Rima's rapid and swift breakdown and destruction.
- Choking is not a possibility.

♦ Films increase a patient's level of compliance

♦ There is no lack of water for film breakdown, which has led to improved patient satisfaction among the dysphasic population.

♦ Films break down on the patient's tongue in a matter of seconds, allowing the active medicinal component to be released quickly.

♦ The patient may watch films whenever and wherever it is most convenient for them.

♦ Molecules that survive the initial pass result have improved oral bioavailability thanks to it.

♦ Bypassing the primary pass leads to a decrease in molecule-related side effects as a result of a dosage reduction.

♦ Films have a sophisticated sense.

♦ They can manage themselves easily.

♦ Stability over a lengthy period because the medicine is stable and available indefinitely until it is eaten. It thereby combines the benefits of a liquid indeterminate amount kind with the stability and bioavailability of a solid indefinite quantity kind.

❖ **Disadvantages of mouth dissolving film**

♦ You cannot incorporate high dosages.

♦ Dose homogeneity is a difficult technological issue.

♦ Ideal characteristics of a suitable drug candidate

♦ The medication must be stable and water-soluble, even as spittle.

♦ A reduced or moderate relative molecular mass is required for the medication.

♦ The medicine should have a pleasing appearance.

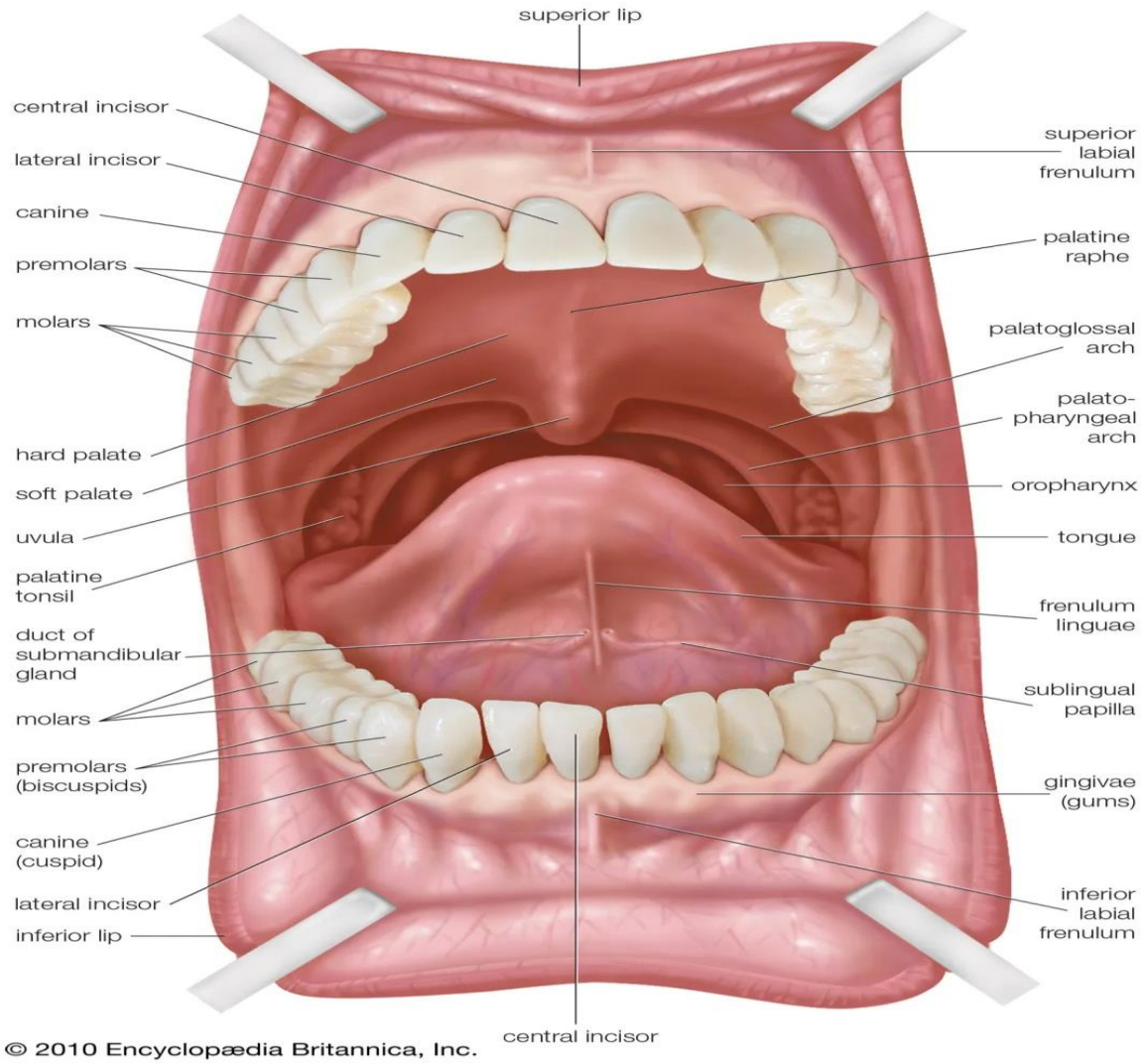
♦ The medicine should only be used in small doses, up to forty milligrams.

♦ The medication should be able to penetrate the oral tissue layer tissue.

- At Rima's concentration of hydrogen ions, it should be somewhat unionised.
- It should be perishable and non-nephrotoxic.
- It should be capable of loading drugs sufficiently.
- It should be less sensitive to external factors like humidity and temperature.2

Characteristics of Oral Mucosa

outer layer of squamous epithelial tissue forms the oral mucosa. Beneath it lies the basement membrane, lamina propria and connective tissue (deepest layer). Epithelial tissue increases from the mitotically active basal cell layer through various intermediate layers to the superficial layers, where cells are from the surface of the epithelial tissue. This is similar to the stratified squamous epithelium found elsewhere in the body. The turnover time of buccal epithelial tissue is 5-6 days, which represents the entire buccal membrane. The length of the oral membrane is 500-800 m, but the membrane thickness of the hard palate, soft palate, floor of the mouth, ventral tongue and gingiva is approximately 100-200 m. Depending on its location in the rim, the composition of the epithelial tissue also changes. The gingiva and upper mucosa are keratinized, similar to the stratum corneum, and contain intermediate lipids called ceramides and ceramides that participate in barrier function. However, the membranes of the palate, viscera, and cheek area are not keratinized, are not sufficiently hydrated, and contain only small amounts of ceramides. They also contain traces of neutral but polar lipids, especially glucosylceramide and steroid alkoxides. Nonkeratinized epithelium is more leaky than keratinized epithelium.



Mechanism of absorption through oral mucosa

There are two penetration methods for passive transport of drugs in the oral mucosa: transcellular (goes through the cell) and paracellular (goes around the cell periphery). Drugs can be used in two ways, but often one way is preferred over the other depending on the chemical research of the drug. Since the environment and protoplasm have a hydrophilic structure, lipophilic substances have less solubility in this environment. However, the lipophilic portion of the cell membrane will make it difficult for hydrophilic solutes to pass through the limited distribution. Thus, cell membranes play an important role in the transport of hydrophilic substances, and living tissues play an important role in the permeability of lipophilic substances. Because the oral epithelium is stratified, a combination of these two methods can be used for drug penetration. But the path with the fewest barriers to entry usually wins. 3

Classification of quick-drying machines

Quick drying can be divided into 3 main groups:

• Drying.

▪ Compressed tablet-based system.

▪ Thin Film strips.

Lyophilization Systems

This method is the most efficient method in terms of sales price, volume and product, approved worldwide. The drug is suspended or dissolved with additives of different structures and can be converted into tablets using equipment or packaging. The units or tablets are then freeze-dried and frozen into packs or molds. The device follows a high demand, which is responsible for the rapid breakdown and rapid penetration of water or saliva. These systems can retain more depending on whether the material is soluble or insoluble; Firstly, it has lower capacity than systems based on some active ingredients. tablets. These devices can combine various taste-masking ingredients and dissolve faster than capsules.

Formulation consideration

• A pharmacological active component.

• Polymer that forms films.

• Plasticizers.

• Agent for disintegrating.

• A soluble substance.

• Sweetening substance.

• A stimulant for saliva.

• Flavouring substance.

• A colorant.

Active pharmaceutical ingredients

A typical film composition has 1-25% weight/weight of the medication. Quick dissolving films can be used to deliver a range of pharmaceutical substances. The easiest choices to be included in a mouth-dissolving film are small dosage compounds. For mouth-dissolving films, different classes of medications such as neuroleptics, vessel agents, analgesics, anti allergic, anti epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and medications used for dysfunction, antialzheimers, and expectorants are suitable.5,6 List of the pharmaceutical molecules that will be included in the mouth film.48

Table: Pharmaceutical ingredients incorporated in mouth film

Drug	Dose	Therapeutic category
Loratadine	10 mg	Anti histaminic
Chlorpheniramine maleate	4 mg	Anti allergic
Famotidine	10 mg	Antacid
Azatadine maleate	1 mg	Anti histaminic
Sumatriptan succinate	35-70 mg	Anti migraine
Ketoprofen	12.5mg	Analgesic
Ondansetron	2.5 mg	Antiemetic
Nicotine	2 mg	Smoking cessation
Acrivastine	8 mg	Anti histaminic

The film-forming component, which accounts for 20–75% (w/w) of the mouth-dissolving film's total dry weight, determines the physical and mechanical qualities of the mouth-dissolving film. Therefore, one of the most important and challenging factors for the formulation's effective development is the choice of chemical. The polymers utilized should have the right mechanical characteristics, quick disintegration, smart mouth feel, and smart hydrophilicity. Along with being intelligently soluble, the molecule must also possess further mechanical, chemical, and porous qualities. A movie has to have a high mechanical strength with room for elongation and physical property qualities to maintain its integrity against the internal and external stresses created during storage and in especially once exposed to environmental conditions.4,5

Ideal properties of the film-forming polymers

1. It should have astute wetting and spreading capabilities.

2. There shouldn't be any leachable contaminants in it.

3. It shouldn't cost a much.

4. It should have a respectable amount of time.

5. It should have a sophisticated mouth feel.

6. The substance must be strong and have ample peeling capacity. An inventory of the polymers used in twin films.4,5

Plasticizer Plasticizers are employed to lower the glass transition temperature and enhance polymer flow. It aids in enhancing the strip's suppleness and lowering its brittleness. It also affects how quickly the medicine is absorbed. The proper usage of plasticizers can have several impacts, including cracking, blooming, pilling, and spitting of the strip. Several polymers that are plasticized with other polymers include,

1. With the help of hydroxyl-containing plasticizers including glycerol, polyols, propylene glycol, and PEG, cellulose hydrophilic polymers were easily plasticized.

2. Citric acid and phthalic acid esters were used to plasticize less hydrophilic cellulose polymers.

3. The table below includes examples of several medications that include various plasticizers.

Saliva stimulating Agent This substance will promote saliva production, which might hasten the breakdown of the oral thin film. Water-soluble vitamins, malic, tartaric, citric, and lactic acids are a few examples. Between 2 and 6 w/w of the strip, one of these agents will be utilized alone or in combination.7 Flavouring agent The type of medicine that will be included in the formulation will influence the flavour choice. The kind and strength of the flavour will determine how many flavors are required to complete the assignment. Any flavour that has received US FDA approval will often be used to cover up the formulation's bitter flavour. Examples include essential oils, menthol, strong mints like pepper, sweet, spear, wintergreen, cinnamon, and clove, as well as sour fruits like lemon and orange and

sweet confectionery flavours like vanillin and chocolate.2,8 Sweetening Agent: Sweeteners are typically used to cover up the bitter flavour of binding drugs. Both natural and artificial sweeteners may be used separately or in combination.9

Surfactant Surfactants are employed in formulations as solubilizing or wetting agent to break down films quickly and release active ingredients. Examples include Tweens, Benzalkonium chloride, and Sodium Lauryl Sulphate. Manufacturing methods There are several methods for producing rapid disposing film, which is categorised as follows: 8 1. Solvent casting 2. Semisolid casting 3. Hot melt extrusion 4. Solid dispersion extrusion 5. Rolling A. Method of preparation of film: Solvent casting method Excipients are dissolved in water for the solvent casting procedure before water-soluble polymers are added, followed by the medicine and stirring to create a homogenous solution. The fluid is then dried after being cast into the Petri dish.11 Advantages: 1. 1. More flexibility. 2. 2. Better physical properties. 3. 3.Finished film thickness is 12-100um. 4. 4. Great clarity then extrusion. 5. 5.great uniformity of thickness. Disadvantage: polymer must be soluble in a volatile solvent or water viscosity should be formed.[2]

Semi-Solid Casting

This method is preferred when acid-insoluble polymers are needed for film production. In the semisolid casting process, a thermally controlled roller is used to cast the gel material into a film or ribbon. The gel product is sodium hydroxide or ammonium hydroxide obtained by mixing the film with an acid-insoluble polymer liquid. Cellulose acetate phthalate and cellulose acetate butyrate polymers are insoluble in acids and can be used to make films. The ratio of acid-insoluble polymer to film-forming polymer should be 1:1.12. Hot Melt Extrusion

During the hot melt extrusion process, the solution and carrier are first combined in the form. Then dry granular material is fed into the extruder. The screw speed needs to be set to 15 rpm to keep the pellets in the extruder drum for approximately 3 - 4 minutes. The operating temperature of zones 1, 2, 3 and 4 should be 800°C, 1150°C, 1000°C and 650°C respectively. A film is produced by pressing the extrudate (T = 650°C) against a cylindrical calendar. Hot melt extrusion has several advantages 28, 29. Less processing- better ingredient integrity - waterless process.

Solid dispersion extrusion In this process, immiscible ingredients are coextruded with the solution, followed by. by preparing explosives. Finally, the mold is used to convert the crushed material into film. 12

Advantages:

1. Cost-effective processes that shorten production time and reduce the number of jobs.
2. Increase the bioavailability of poorly soluble compounds.
3. Ability to support, update and publish directly.
4. It is stable at different pH and moisture levels.
5. Rolling method

In the rolling process, the prepared drug solution or suspension containing the film-forming polymer is placed in the cylinder. For solutions or suspensions, special rheological factors must be taken into account. Water and alcohol-water mixtures make up most of the solvent. After the film is dried in rolls, it is cut into the desired shape and size. 12 Use of oral drugs to deliver drugs aimed at rapid absorption for the treatment of pain, allergies, sleep problems and central nervous system problems Oral mucosal distribution Use of buccal, sublingual, and mucosal routes using OTF will become the preferred distribution strategy. Originally developed in the form of breathing patches for use in the confectionery and oral health industries, dissolvable mouth films have become a popular new method for vitamin delivery and personal care over the past few years. Items.28

EVALUATION PARAMETERS

Weight variation test

Each formulation batch is subjected to a random examination of films. Each film strip's weight was measured using a digital analytical balance, and both the weight variation and the mean deviation of the films were computed and recorded.1

Thickness

The thickness was measured using tools including dial gauges, Vernier calipers, screw gauges, and microscopes. To determine the average thickness of the film, thickness is measured at several locations. As long as the sample is equal to the dose of the medicine that

was consumed, the thickness may be determined using a Vernier calliper. After ensuring that the pointer was adjusted to zero and lifting the anvil of the thickness gauge, the film was inserted, held against the anvil, and the reading on the dial was recorded. A three-reading average was computed. It is crucial to confirm the uniformity of the film's thickness since it has a direct impact on the accuracy of the dosage in the strip.18

Folding endurance: The folding endurance value is calculated as the number of folds the film can withstand without breaking. The number of folds necessary to produce cracks—300 in certain cases—gives the value of folding endurance. The folding is done at the same location repeatedly.1,11

Tensile strength

Tensile strength is the amount of tension needed to rip the film. It is determined as follows by dividing the load at rupture by the cross-sectional area of the film.22 To achieve the best results, use a physically flawless film. The film was pulled at a rate of 5 to 10 mm/min while being held 10 mm apart between two clamps. Three times the entire experiment is conducted.2,13

Drug Uniformity

For a given API all selected analytical methods listed in the standard pharmacopoeia are used to check whether chemical homogeneity exists in each film made. Measure content consistency by measuring the API content of each strip.85-115% is maximum content integrity. For loperamide, dissolve each film in a 50 ml volumetric flask filled with methanol. Mann's filter paper No. Further filtering was done using 1. 41. Add 1 ml of filtrate to a 25 ml volumetric flask containing 6 ml of phosphate buffer. This solution was tested in a UV spectrophotometer at 223 nm using a phosphate buffer solution at pH 6.8 as blank. Medical homogeneity All analytical systems Indicated for specific API Tested using standard pharmacopeia.

CONCLUSION:

Current research shows that one of the decisions in drug research is the use of rapid oral films. They require better patient compliance and greater acceptance than traditional models without causing harm. The main purpose of developing oral tablets is to solve the problem of

taking oral tablets in children, adults, and mentally ill patients. Oral dissolving films are now widely used to treat diseases such as pain, acidity, allergies and heart disease. Emphasize their importance. The main advantage of the indeterminate dose type is that it does not need water for administration, meeting the target group's need for easy administration and also improving the response by preventing visceral metabolism.

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