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FORMULATION AND EVALUATION OF FAST DISSOLVINGORAL FILMS BY USING HONEY

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ABSTRACT

The market has lately seen the introduction of oral fast dissolving films (OFDFs), which offer greaterconvenience and usability than traditional dosage forms like orally disintegrating tablets. The pharmaceutical industry is becoming more interested in OFDFs as a result of this technology's evolution over the past few years from the confection and dental care markets to a novel and widely accepted form by consumers in the shape of breath strips. When an oral fast-dissolving film is inserted in the oral cavity, it dissolves or disintegrates in a matter of seconds without requiring the ingestion of water. OFDFs are very similar to postage stamp intheir thickness, size, and shape.These films have been utilized for local action and have the ability to administer the drug systemically through the intragastric, sublingual, or buccal routes. This kind of technology provides a practical method of administering medication to the general public as well as to specialized populations like children, the elderly, bedridden patients, and mentally ill people. An explanation of the several formulation factors, the preparation process, and quality control of the OFDFs are given in this review.

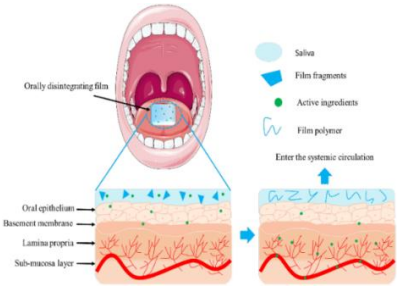
Key words: Oral strips, Fast dissolving films, Tensile strength, Fast disintegration

INTRODUCTION

Oral administration is the most widely used method because of its simplicity, ability to avoid pain, adaptability (to accept many types of drug candidates), and, most importantly, patient compliance. Since solid oral delivery systems don't need to be manufactured in sterile conditions, their manufacturing costs are also lower. Many cutting-edge methods for oral delivery are currently available to enhance patient compliance and address the physicochemical and pharmacokinetic aspects of drugs. Other recent advancements include tablet production, electrostatic drug deposition and coating, and computerized three-dimensional printing (3DP).As an alternative to tablets, capsules, and syrups, fast dissolving drug delivery systems were developed in the late 1970s when typical oral solid dose forms proved difficult for young and elderly patients to swallow. The words "rapid dissolve," "rapid dissolve," "rapid melt," and "quick disintegrate" all allude to the latest advancements in dosage form dispersion technology. All of these dosage formulations, however, work on a similar premise.By definition, an oral fast-dispersing dosage form is a solid that quickly dissolves or breaks down in the oral cavity to produce a suspension or solution without the need for water to be administered. All ages are affected by dysphagia, or trouble swallowing, although the elderly are most likely to have it. Taking regular pills and capsules may also cause it. Dysphagia is associated with a number of diseases, including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck thyroid therapy, and other neurological conditions like cerebral palsy. The most commonly voiced concern was tablet size, which was followed by form, surface, and flavor. Elderly and pediatric patients, as well as those who were traveling and might not have had easy access to water, found it more difficult to swallow tablets.

The availability of a broad range of biocompatible polymers and differences in production processes have made it possible to construct a variety of OTFs. Because of this, OTFs are gaining popularity as a unique drug carrier dosage form in pharmaceutical technology. Polymeric OTFs that can be applied topically, topically, sublingually, topically, or transdermally have been the subject of extensive research and development. In recent years, the use of OTFs for the administration of medication through the buccal or sublingual mucosa has grown in popularity. The basic building block of thin films is composed of different ratios of polymers, which can also be utilized to alter the material's mechanical strength, related properties, mucoadhesive properties, and rate of drug release.

The pharmaceutical industry is developing thin-film technology and is currently submitting patent applications for these formulations because of the attractive characteristics of OTFs.



Orally disintegrating film

Special features of fast dissolving films

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

Ideal characteristics of the fastdissolving drug delivery system

1. Easeofadministration forpatients whoarementallyill disabledand requirenowater.
2. Overcomesunacceptable tasteofthedrugs.
3. Canbedesignedtoleaveminimalornoresidueinthemouthafteradministrationand alsoprovide apleasantmouth feel.
4. Ability to provide advantages of liquid medication in the form of solidpreparation.
5. Costeffective.

Advantages

- These quickly dissolving films provide several of benefits, including
- Films dissolve and disintegrate quickly in the oral cavity because of their enormous surface area.
- Dosing convenience.
- Quick dissolution or disintegration followed by a prompt effect, which is preferable in certain situations, like pain.
- Oral dissolving films can be used anytime, anyplace, and without the need for water.
- Suitable for patients who are elderly or young and have trouble swallowing; this includes people who are mentally ill, developmentally disabled, uncooperative, or on reduced liquid intake regimens.
- No choking hazard

Disadvantages

- Drugs that are unstable at buccal pH cannot be given.
- This route cannot be used to give medications that irritate the mucosa.
- Only medications with a little dosage requirement may be given.
- Flavor masking: Since most medications have an unpleasant flavor, taste masking is necessary.
- Special packaging: Because OFDFs are delicate and need to be kept dry, they require particular packaging.
- Dose uniformity presents a technological difficulty.
- Expensive oral film packaging

FAST DISSOLVING ORAL FILMS

Oral films are a more modern technology utilized in the manufacturing of oral disintegrating dosage forms. These are flexible, thin films that come in square, rectangular, and disk shapes, and they are composed of water-soluble, digestible polymers. The stripes could be flexible or stiff, translucent or opaque. They are designed to dissolve swiftly on your tongue without the need for water. The

surface area of fast dissolving films (FDFs) is large, specifically for disintegration. The films reduce the chance of choking, are easy to handle and administer, and retain a standard, simple packing that is simple to create, which helps them overcome the shortcomings of oral fast-disintegrating tablets. Two of the key disadvantages of these dosage forms are their limited options for flavor masking and their low drug loading capacity.

A thin film of any geometry with an area of 1–20 cm2 and a thickness of 1–10 mm is referred to as a fast dissolving film. A maximum of 15 mg of medication can be added at one time. Saliva dissolves immediately because of a special matrix made of polymers that are soluble in water. Low tack is usually present in this matrix to facilitate handling and application. Conversely, the purpose of the system's wet tack and mucoadhesiveness is to keep the film in place at the application site when it's wet. To facilitate die cutting, packing, and rewinding, among other production procedures, films are selected based on their strength and adaptability.

Table 1: comparison between oral disintegrating tablets and oral fast-dissolving films.

Oral dissolving films	Oral disintegrating tablet
Itisafilm.	It is a tablet.
Large surface area allows for more dissolution.	Reduced surface area, which results in less disintegration
Increased adherence from patients.	Less long-lasting than oral films
Better durability than oral disintegrating tablets.	Less adherence from patients than with films
Only low doses can be used.	One can incorporate a high dose.
No chance of choking.	It is afraid it will choke.

FORMULATIONCONSIDERATION

- Active pharmaceutical ingredient
- Film forming polymer
- Plasticizers
- Sweeteningagents
- Salivastimulatingagents
- Flavoringagents
- Coloringagents

Active pharmaceutical ingredient

Drugs make up one to two third of the weight percent in a typical film mix. A variety of APIs can be delivered via fast-solving films. The best options to include in OFDFs are the tiny dosage compounds. Up to 10% w/w of dry film weight in multivitamins that disintegrated in less than 60 seconds was added to the films. Since micronized API can enhance the smoothness of the film and encourage better dissolving and uniformity in the OFDF, it is often beneficial. Many bitter-tasting APIs are promising candidates for OFDF technology. This makes the formulation unpleasant, particularly in situations involving young children. Thus, before adding the API to the OFDF, the flavor needs to be covered.The formulation can be made more palatable in a number of ways.

Film forming polymer

Since the primary purpose of all thin film oral dosage forms is to dissolve in saliva within the oral cavity, the final film that is utilized must be water soluble. To make a water soluble thin-film formulation, you need excipients or polymers with a low molecular weight and strong film-forming capacity that dissolve in water. It must be devoid of irritants, toxicants, and leachable pollutants. It should have good wetting and spreading qualities. It ought to be inexpensive and readily available. Microcrystalline cellulose was also used to shorten the drug's breakdown period and hasten its dissolution from the films. Examples of polymers are

- Xanthumgum
- Acacia
- Polyethyleneoxide
- Sodiumcarboxymethylcellulose
- Hydroxylpropylmethylcellulose
- Polyvinylalcohol

Plasticizer

Plasticizer helps to increase the flexibility of the strip and lessens the brittleness of the films. The plasticizer of choice will be determined by how well it reacts with both the polymer and the type of solvent used in the casting film. Examples of plasticizers are

- Glycerol
- Propyleneglycol
- Polyethyleneglycol

- Dimethylphthalate
- Dibutylphthalate
- Triacetin
- Castoroil

Sweetening agents

These days, sweeteners are an essential part of formulations that are supposed to dissolve or degrade in the mouth. Sweeteners are commonly used in concentrations between 3 and 6% w/w. These easily dissolved films are created with sweeteners, both natural and artificial. Because polyhydric alcohols have a fantastic tongue feel and a cooling effect, they can be mixed, such as isomalt, sorbitol, and mannitol. However, it should be noted that people with diabetes or on diets should limit their intake of natural sugars in these kinds of recipes. As a result, artificial sweeteners are now more frequently used in food and medicine preparations.
The initial phase of synthetic sweeteners includes

- Saccharin
- Cyclamate
- Aspartame

Saliva stimulating agents

In order to promote a faster breakdown of the formulations for the rapid dissolving stripes, salivary flow is increased by the use of salivary stimulating chemicals. Generally speaking, salivary stimulants come from acids that are utilized to prepare meals.Between 2 and 6% w/w of the stripes are combined with these substances.

- Citricacid
- Lactic acid
- Ascorbic acid
- Tartaric acid

Flavouring agents

Up to 10% w/w of tastes are present in the OFDF formulations. The flavor quality that is detected in the initial seconds after ingestion and the aftertaste that lingers for at least ten minutes are the primary factors that define an individual's acceptability of an oral disintegrating or dissolving formulation. Vanilla, cocoa, coffee, chocolate, and citrus are examples of fruity flavor; apple, pineapple, raspberry, and cherry are examples of fruity flavors.

Colouring agents

Orally fast dissolving films are made using FD&C-approved colouring chemicals, with concentration levels not to exceed 1% w/w. such as titanium dioxide.

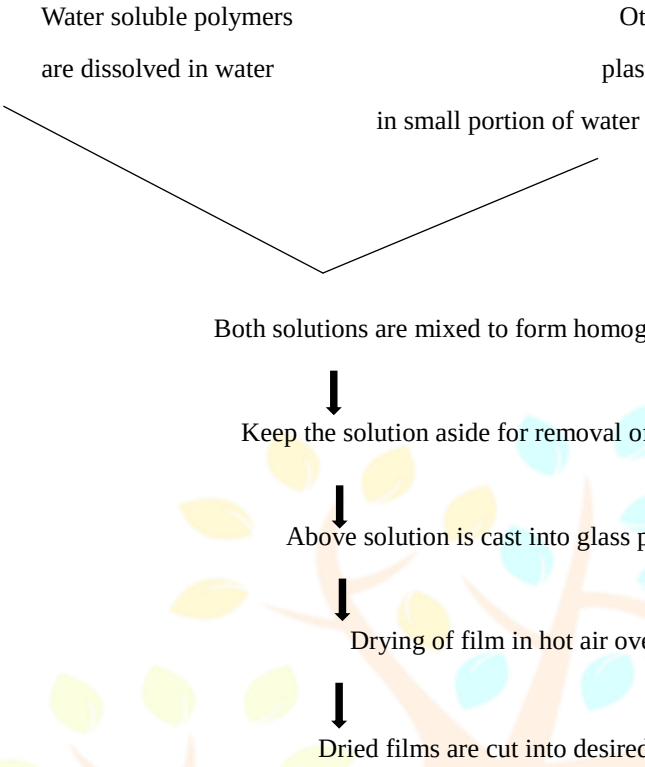
Method of preparation

One or more of the following methods can be used to make oral dissolving films.

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

1.Solvent casting method

In the solvent casting process, water-soluble materials are dissolved in water with the medicine. After dissolving the excipients in the suitable solvent and combining and swirling the two solutions, the mixture is put into a petri dish and left to dry.



2.Semisolid casting method

For the semisolid casting technique, a water-soluble film-forming polymer solution is initially prepared. The resulting solution is combined with an acid-insoluble polymer solution (such as cellulose acetate butyrate or phthalate) prepared with sodium or ammonium hydroxide. After that, the appropriate quantity of plasticizer is added to produce a gel mass. Ultimately, the gel bulk is cast into the films or ribbons using heat-controlled drums. The film is between 0.15 and 0.5 inches thick. The ratio of film-forming polymer to acid insoluble polymer must be 1:14. The two mixtures are mixed to produce a homogenous, viscous solution that is vacuum-degassed. An aeration drying oven is used to coat the untreated casting film with a bubble-free solution.

3.Hotmelt extrusion

First, solid carriers and medication are mixed using the hot melt extrusion technique. The extruder, which has heaters, subsequently melts the mixture. In the end, the melt is formed by the dies. There are certain benefits to hot melt extrusion.

1. Fewer operation units.
2. Better content uniformity.
3. An anhydrous process.

4.Solid dispersion method

Drug-immiscible ingredients are extruded using this method, and solid dispersions are then created. In the end, the solid dispersions are formed into films using dies.

5.Rolling method

The rolling method involves rolling a suspension or solution containing drugs on a carrier. Mixtures of alcohol and water are the main solvents. The film is cut into the necessary sizes after curing on the rollers.

Evaluations

- Thickness
- Folding endurance
- Invitro disintegration
- Tensile strength

- Surface morphology
- Percentage elongation
- Young's modulus
- Drug assay

1.Thickness

A micrometer screw gauge was used to measure the film's thickness. To guarantee consistency, the film's thickness is measured five times. The film should have a thickness of no more than 5%.

2.Folding endurance

To evaluate folding endurance, a film is sliced and quickly folded in the same location until it breaks. The number of times the film could be folded in the same way without breaking is what determines the folding endurance value.

3.Invitro disintegration

The time (in seconds) at which a film dissolves when it comes into contact with saliva or water is known as the disintegrating time.

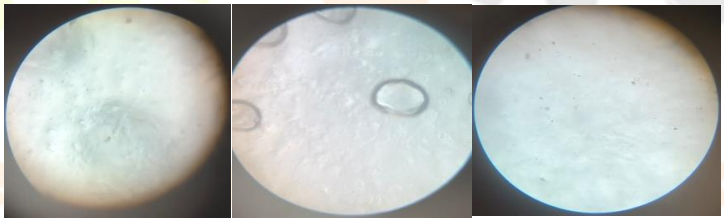
4.Tensile strength

Tensile strength is the maximum stress applied to the strip specimen at the breaking point. It is computed using the formula.

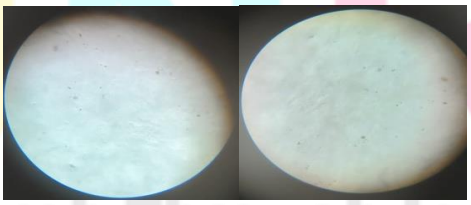
$$\textbf{Tensilestrength}=\frac{\textbf{Load at failure}\times 100}{\textbf{Strip thickness}\times\textbf{strip width}}$$

5.Surface morphology

The surface morphology of the ODF is analyzed using the environment-scanning-electron microscopy technique. The film's homogeneity and the absence of flaws and striations imply that the ODF is of the highest caliber.



F1 F2 F3



F4 F5

6.Percentage elongation

Strain is the term for the stress that causes a film sample to expand. Strain is essentially the distortion of the film divided by the starting dimension of the sample. As the amount of plasticizer increases, the film is seen to lengthen. It was computed by

$$\textbf{Percentage elongation} = \frac{\textbf{Increase in the length of strip}\times 100}{\textbf{Initial length of strip}}$$

7.Young's modulus

The elastic modulus, often known as Young's modulus, is a measurement of the film's stiffness. In the zone of elastic deformation, it is expressed as the ratio of applied stress divided by strain.

Young's modulus = (slope/strip thickness × cross head speed) × 100

Table 2: Evaluation parameters of fast dissolving oral films

Formulations	Thickness (mm)	Folding endurance	Tensile strength (g/cm²)	% elongation (%)	Invitro disintegration Time (sec)	Young's modulus
F1	0.55	12	56.45	7	36	3.24
F2	0.58	9	48.41	8	34	1.20
F3	0.52	11	52.33	8	27	2.64
F4	0.53	11	53.68	10	35	3.98
F5	0.51	9	54.25	9	31	1.14

8.Drug assay

A 2 cm square of thin film was dissolved in 50 ml of pH 6.8 phosphate buffer while being stirred during the test. This solution was filtered through Whatmann filter paper, and the filtrate was then diluted in a volumetric flask to 100 ml using the same buffer. A UV spectrophotometer was used to evaluate this solution.

Table 7. Drug Assay

Formulations	Assay
F1	98.34
F2	97.25
F3	97.85
F4	98.14
F5	99.18

Conclusion

From aboveit can be seen that rapidly dissolving oral films have demonstrated their effectiveness as a novel medication delivery method for patients with swallowing difficulties as well as for all other demographic groups. Fast-acting oral films have shown to be helpful in situations requiring a quick start to treatment, such as epilepsy, heart failure, and asthma attacks. When fast-dissolving oral films are patented, oral thin films are a useful tool for extending the life of an existing product. Therefore, the majority of pharmaceutical companies are finding it difficult to manufacture oral films for a wide range of active pharmaceutical components due to the rapid growth of this technology. Numerous studies are being conducted and will soon be initiated.

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