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Review Article

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A REVIEW ON ORODISPERSIBLE FILM

Rodage R.M.*[1], Sakhare V.B.[2] and Bhagat B.V.[3]

Department of Pharmaceutics Dr. Vithalrao Vikhe Patil Foundation College of Pharmacy, Vilad Ghat.

***Corresponding Author: Rodage R.M.**

Department of Pharmaceutics Dr. Vithalrao Vikhe Patil Foundation College of Pharmacy, Vilad Ghat.

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ABSTRACT

Oral fast-dissolving film is the best idea to increase consumer acceptance by rapid dissolution and self-administration without the need for water and chewing. The film is an ideal oral fast-dissolving drug delivery system. There are many techniques used to prepare oral films in the buccal cavity. A film is prepared by use of hydrophilic polymers that rapidly dissolve on the tongue or buccal cavity. Different types of buccal delivery products are proposed for some diseases like trigeminal neuralgia, diabetes, Meniere's disease, addiction etc. This novel approach of preparing the dispersible film (odf) provide benefits to pediatric, geriatric and bedridden patients. Evaluation of the prepared pdf's done by considering parameters such as film thickness folding endurance disintegration time, surface ph, weight variation, in vitro dissolution test content uniformity and FTIR. This overview provides information about advantages, disadvantages, methods polymers used, different technologies, evaluation parameters, and lastly, reference…

KEYWORDS: Buccal Film, Hydroxyl Propyl Methyl Cellulose, Oral Film, Mouth Dissolving Film, Mucoadhesion, Salivary Film, Sublingual Film.

BACKGROUND[1,2,3,4,5]

The oral route is the best route for taking drugs. It has advantages over the other route. The oral route has some disadvantages also, so new formulations are made to become preferable for patients. In oral route administration, patients have difficulty swallowing, especially geriatric and pediatric patients. Due to this reason fast dissolving drug delivery system came into existence in the late 1970s as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who have trouble swallowing traditional oral solid dosage forms. Research and development in oral drug delivery systems have done a transition of dosage forms, from simple conventional tablets or capsules to modified oral disintegrating tablets (ODT) to recent dosage forms of oral fast-dissolving films.

The main advantages of the oral fast-dissolving film are rapid dissolution and self-administration without water. The film consists of a very fine thin oral strip placed on the patient's tongue and wet by saliva; the film rapidly hydrates and gives its actions. The film is easy to handle, store, and administer. Many drugs are developed as mouth-dissolving films. They are helpful in patients like paediatrics, geriatrics, emetic patients with diarrhea, coughing and a sudden episode of allergic attacks etc.

Figure 1: Orodispersible film.

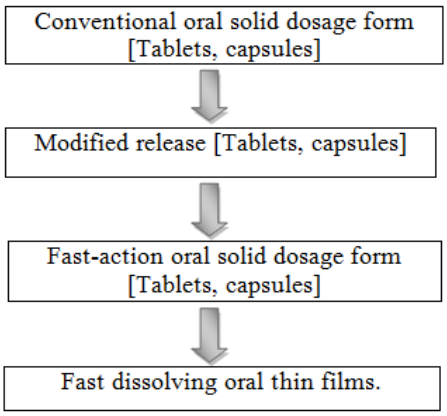

Figure 2: Development of oral solid dosage form.

Main Text

Need an objective of fast-dissolving oral films[6]

- The fast-dissolving oral film is formulated as an alternative to conventional dosage forms for pediatric and geriatric patients who have difficulty swallowing medicines like tablets and capsules and their unwanted smell.
- Pharmaceutical companies want to formulate a novel oral dosage form with higher bioavailability. Quick action and most patient compliance.
- Fast-dissolving oral films are the most advanced form of oral solid dosage form due to more flexibility and comfort.
- It maintains quick dissolving aspects that allow for gastrointestinal absorption when swallowed.
- It rapidly disintegrates and dissolves to release medication for oro mucosal absorption.

Salient features of fast-dissolving oral films[6]

- No need for water.
- Disintegration time is fast.
- Dissolution time is also fast.
- It does not leave any residue in the mouth after administration.
- No risk of choking.

Advantages of the fast-dissolving oral film[6,7,8]

- Increased oral absorption.
- Increased bioavailability.
- Overcome bad tests of drugs by adding taste-masking agents.
- Stability is improved due to better packing.
- No need for any set-up in the industry.

Disadvantages of the fast-dissolving oral film[3,7,8]

- Drugs that irritate mucosa cannot be administered by oral route.
- Some drugs are unstable at buccal pH and cannot be administered.
- The packaging of the film is expensive.
- Dose uniformity is more problematic because it requires clever and experienced people.
- Drugs are bitter, so taste agents are needed.

Development of oral films[9,10]

Table 1: Composition of orodispersible film.

Sr. No	Ingredient	Amount (W/W)
1.	Water soluble polymer	45%
2.	Plasticizer	0 to 20 %
3.	Active pharmaceutical ingredient	5 to 30%
4.	Saliva stimulating agent	2 to 6%
5.	Surfactant	q.s.
6.	Flavours, Colours, Fillers	q.s.
7.	Sweeting agent	3 to 6%

1. Strip-forming polymers

The polymers used in this are non-toxic and non-irritant. It should have good wetting and spreadability property. The polymer should be readily available and should be affordable. The film obtained should be tough enough to prevent any damage during handling and transportation.

2. Plasticizer

Plasticizers are used in the preparation of fast-dissolving films. It improves the flexibility of the film. Plasticizers are compatible with polymers and enhance the polymer's strength. Examples of plasticizers are propylene glycol [PG], polyethylene glycol, and glycerol. Phthalate derivatives like dimethyl, diethyl and dibutyl phthalate. Citrate derivatives like tributyl, triethyl, acetyl citrate and castor oil. Plasticizers are volatile.

3. Flavourants

Flavourants play an essential role in the preparation of the oral film. They are two types: **a] Natural Flavourants and b] Artificial Flavourants.** Examples of natural Flavourants are various fruit flavours and mints like peppermint and menthol. Essential oils like thymol eucalyptol and methyl salicylate etc.....…

4. Sweeteners

Sweeteners play an essential role in making the oral thin film because a sweet taste in the formulation is essential in the case of the pediatric population. They are of two types **a] natural b] Artificial** Examples of natural sweeteners are: xylose, ribose, glucose mannose, galactose, fructose, dextrose, sucrose, and maltose. Examples of artificial sweeteners are aspartame, xylitol, acesulfame-k, and sucralose.

5. Saliva stimulating agent

The aim of using a saliva-stimulating agent is to increase the saliva production rate, which helps in the faster disintegration of fast-dissolving films. Acids are used as salivary stimulants Examples of salivary stimulants are citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid. Citric acid is most used as a saliva stimulant in preparing the oral film.

6. Stabilizing and thickening agents

Stabilizing and thickening agents are used to improve the viscosity and consistency of strip preparation. Examples of stabilizing and thickening agents are xanthan gum, carrageenan, and locust bean gum.

7. Active pharmaceutical ingredients

In preparation of oral fast-dissolving films, the size of dosage forms has limitations. High-dose molecules are difficult to be incorporated into the os. Generally, 5% w/w to 30 % w/w of active pharmaceutical ingredients are included os.

Table 2: Classification of oral films.

Property/ Subtype	Flash release wafer	Mucoadhesive melt-away wafer	Mucoadhesive sustained release wafer
Thickness(mm)	20-70	50-500	50-250
Area(cm2)	2-8	2-7	2-4
Structure	Single layer System	Single or multilayer	Multilayer system
Drug phase	Solid solution	Solid solution or suspended solution	Suspension and solid solution
Excipient	Soluble hydrophilic polymer	Soluble hydrophilic polymer	Low or non-soluble polymer
Dissolution	60 sec	Few min	Max 8-10 hr
Site of action	Systemic or oral	Systemic or oral	Systemic or oral
Application	Tongue	Buccal region	Gingival (other regions in the oral cavity)

Methods of preparations[4,6,13,28]

1. Casting and drying

A] Solvent casting

B] Semisolid casting

2. Freeze-dried wafer

3. Extrusion

A] Hot melt extrusion

B] Solid dispersion extrusion

C] Rolling method

A] Solvent casting method

- First, prepare the casting solution.
- Then deaeration of the solution is done.
- Transformation of the solution is done.
- Transformation of the accurate volume of solution into a mold. After this, the casting of the dried solution takes place.
- Cutting the final dosage form takes place to contain the desired amount of the drug.
- Packing oral fast-dissolving films are prepared by dissolving strip-forming agents and plasticizers in distilled water. After this, the solution is continuously stirred for up to four hours by a magnetic stirrer and kept for one hour to remove all entrapped air bubbles. In separate containers sweetening agents, saliva-stimulating agents, flavor and drugs are dissolved with constant stirring for 45 min. After stirring, both solutions are mixed with going another by a magnetic stirrer. Keep the solution stable for 1 hour to settle down the foam. The resulting formulation is cast on a suitable platform and is dried to form a film. The film is dried or dried under the oven after this film is carefully removed.

B] Semisolid Casting method: In this method, at first, a solution of water-soluble film-forming polymer is prepared. Prepared solution of insoluble acid polymer for, e.g. - (cellulose acetate phthalate, cellulose acetate butyrate) designed by ammonium, sodium hydroxide. After this correct amount of plasticizers is added to get a gel mass. After this, a gel mass is cast into films using heat-controlled drums. The thickness of the film is about 0.015-0.05 inches.

2] Freeze-dried wafer

It is a technique called lyophilization, a dehydration technique based on the sublimation of water in a product. This transitions from a solid to a gaseous state or from ice to vapourwithout going to a liquid form.

3] Extrusion

a) Hot melt Extrusion: It is a process of continuously applying heat and pressure to melt a polymer and forcing it through an orifice. In this hot melt, the extrusion drug is mixed with the carrier/ vehicle in the solid form. Extruders have the facility of the heater; it is used to melt the reliable form carrier and drug, then this melt product is placed in dies and cut into a different shape. This process does not need or use any solvent system. The hot melt extrusion process involves lower temperature, absence of organic solvents, continuous operation possibility, minimum project wastage, reasonable control of operating parameters, and the possibility to scale up. Extrusion equipment is classified into three main categories ram, radical screen and roll and screw extruders. Screw extruders are essential in the pharmaceutical industry due to it helps to convert feed material to the finished form like rod tube and film. Rotating screws force feed materials are softened by frictional heat developed by the barrel wall. The feed reaches of the screw in a viscous state that can be forced through an orifice and molded into a desired shape.

B] Solid dispersion extrusion: A solid dispersion is defined as a formulation of poorly soluble compounds as solid dispersions might lead to particle size reduction, improved wetting, reduced agglomeration changes in the physical state of the drug and possibly dispersion on a molecular level by the physical form of solid dispersion. Solid dispersion extrusion refers to the dispersion of one or more active ingredients in an inert carrier in a stable state in the presence of amorphous hydrophilic polymers. In this method, the drug is dissolved in a liquid solvent. The solution is incorporated into the melt of

polyethylene glycol, and lastly, solid dispersion is shaped into films by the use of dies.

C] Rolling method: A solution or suspension containing a drug is rolled on a carrier. The Solvent is mainly water or a mixture of water and alcohol, and the film is dried on the rollers and out into desired shapes and sizes.

Evaluation parameters of fast dissolving films[15-24]

1] Organoleptic Evaluation

Unique controlled human taste panels are used for the evaluation of the product. In-vitro taste assessment apparatus and methodologies are suitable for high-throughout taste screening of oral films.

2] Mechanical properties

a) Thickness

It is essential, which is related to the dose accuracy of the film. Thickness can be measured by a micrometer screw gauge or calibrated digital vernier calipers, or dial gauge tester at different 5 locations of the film. It should be between a range of 5 to 500 micrometers.

b) Tack test

It is the tenacity with which the strip adheres to an accessory or a piece of paper that has been passed into contact with the strip. There are eight stages of the film drying process; instruments are also available for this study.

c) Tensile strength

It is maximum stress applied to a point at which the strip specimen break.

The formula for tensile strength:

$$Tensile\ strength = \frac{Load\ at\ failure \times 100}{Film\ thickness \times Film\ width}$$

d) Percentage Elongation

When stress is applied, a film stretches, and this is referred to as a strain. Strain is a deformation of a strip divided by the original dimension of the sample, and it increases as the plasticizer's content increases.

$$\%\ elongation = \frac{Increase\ in\ the\ length\ of\ strips}{Initial\ size\ of\ strip} \times 100$$

e) Tear resistance

Tear resistance is a complex function of its ultimate resistance to rupture. A meager rate is adjusted to measure the force required to tear the specimen, recorded as the tear resistance value in newtons [pounds force].

f) Young's modulus

Young's modulus is the measure of the strip's stiffness, representing the ratio of applied stress over the strain in the elastic deformation region.

$$Youngs\ modulus = \frac{Force\ at\ corresponding\ strain}{cross\ sessional\ area} \times \frac{1}{Corresponding\ strain}$$

g) Folding Endurance test

It can be determined by repeated folding of film at the same place till the film breaks. The number of times the film folded without breaking is a compound called folding endurance value.

3] Swelling properties

A film swelling study is conducted using a simulated saliva solution. Each film sample is weighed and placed in a pre-weighed stainless steel wire mesh. The typical disintegration time for strips is 5 to 30s.

4] Transparency

Using a simple UV spectrophotometer can determine the transparency of the film. First, cut the film samples into rectangles and place them on the inner side of the spectrophotometer cell. Determine the transmittance of films at 600nm.

5] Contact angle

At room temperature, by using goniometry, contact angle measurements are performed. A drop of double distilled water was placed on the surface of the dry film. After this, the image of the water droplet was recorded by use of a digital camera.

6] Content uniformity

Content uniformity is determined by estimating the API content in the individual strip. The limit of content uniformity is 85-115 %.

7] Disintegration time

The disintegration time limit of the 30s or less for orally disintegrating tablets described in CDER guidance can be applied to fast-dissolving oral strips. Although no official advice is available for oral fast disintegration film strips, this may be used as a qualitative guideline for quality control tests or at the development stage. The typical disintegration time for strips is 5-30s.

8] In –vitro dissolution test

A standard basket or paddle apparatus described in any pharmacopoeia is used for dissolution tests. The dissolution medium selection will take place per the sink conditions and the API's most significant dose. Dissolution taste can often be complex due to the tendency of strips to float on the dissolution medium where the paddle system is used.

Applications of fast-dissolving oral films[25]

1] Topical applications

They are used as antimicrobial ingredients for wound care and other applications.

2] Diagnostic devices

Dissolvable films are created with a sensitive reagent to allow controlled release when exposed to biological fluid or to create an isolation barrier for separating multiple reagents to enable a time reaction in a diagnostic device.

3] Vaccines

Fast-dissolving films can be delivered in the form of vaccines, which is stable at room temperature; due to this, it is quickly dissolved in the mouth and saliva. Rotavirus vaccines prepared in the united states are room temperature stable fast, dissolving buccal film delivery system for vaccines.

- Taste masking of bitter taste
- Oral films are applicable to enhance the bioavailability of the poorly bioavailable drug.

Storage and packaging of the film[26,27]

Different types of storage and packaging options are available for fast-dissolving films. The stages of packaging provide product flexibility to drug manufacturers. Single packaging is mandatory for cinema. An aluminium pouch is the most commonly used packaging format. The rapid card is a term developed especially for quick films. The quick card has the same size as a credit card and holds three raid films on each side. Every dose can be taken out individually. Criteria must be considered during packaging barcode labeling, the content in instructions or use, child-resistant seals and senior-friendly packaging. The material selected for packaging must have the following characteristics. They must be FDA-approved. They must not impart to product taste and odours.

CONCLUSION

Fast-dissolving films have advantages over conventional dosage forms. Fast-dissolving films are considered the essential drug delivery system due to rapid disintegration and improved dissolution. They ensure safety, efficacy as well as patient compliance. ODFs do not require water to intake, and ODFs are stable and have improved absorption and bioavailability. This dosage form is applicable in various emergency conditions like allergic reactions, asthmatic attacks, and hypertension, where the immediate onset of action is required. So this technology is growing fast, challenging most pharmaceutical companies to develop oral films for a wide range of active pharmaceutical ingredients.

List of Abbreviations

1. ODF: Orodispersible Film
2. FTIR: Fourier Transformation Infra-Red
3. ODT: Oral Disintegrating Tablet
4. PG: Propylene Glycol
5. OS: oculus sinister (by mouth)
6. CDER: Center for Drug Evaluation and Research
7. API: Active Pharmaceutical Ingredients
8. FDA: Food And Drug Administration.

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