ORAL FILM :A COMPRESNSIVE REVIEW OF FORMULATION,EVALUATION AND APPLICATION

Sakshi Y. Bodake [*1,] S.D.Bhise [1], Madhuri S.Keskar[1],R.V.Shete [2],

1.Department of Pharmaceutics, Rajgad Dnyanpeeth's college of pharmacy ,Bhor Tal:Bhor,Dist:Pune 412206.

2.Department of Pharmacology, Rajgad Dnyanpeeth's college of pharmacy ,Bhor Tal:Bhor,Dist:Pune 412206.

Corresponding Authors

Sakshi Y.Bodake

Rajgad Dnyanpeeth's college of pharmacy ,Bhor 412206

ABSTRACT:

Oral films have revolutionized the pharmaceutical landscape by offering a convenient, patient-friendly, and effective drug delivery system. This review provides an exhaustive overview of oral films, encompassing their composition, preparation methods, and evaluation protocols. The formulation aspects, including the selection of polymers, active pharmaceutical ingredients, and excipients, are thoroughly discussed. Various fabrication techniques, such as solvent casting, hot-melt extrusion, and printing technologies, are examined in detail. Furthermore, the review elaborates on the characterization protocols, including physical, mechanical, and dissolution testing, to ensure the quality and efficacy of oral films. This comprehensive review aims to provide a detailed understanding of oral films, highlighting their advantages, limitations, and potential applications in pharmaceutical drug delivery.

Keywords: oral films, formulation, fabrication, characterization, pharmaceutical drug delivery.

Introduction

Among the routes of administration, the oral route is the most accepted from the point of view of patient compliance with the treatment. Many pharmaceutical companies have directed their research activities towards reformulating existing drugs into new dosage forms. One of these relatively new dosage forms is the oral strip, a thin film made of hydrophilic polymers that dissolves rapidly on the tongue or in the oral cavity. Interestingly, the permeability of the oral mucosa is higher than that of the skin, but lower than that of the intestine.(1) The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any mucous tissue from the mouth, immediately moistened by saliva, the film hydrates quickly (2) Rapidly Dispersing Oral Film, a new drug delivery system for oral drug administration, is an ultra-thin film prepared with hydrophilic polymers that rapidly dissolves on the upper or lower part of the tongue or oral cavity. This is an ultra-thin (50-150 microns thick) postage stamp-sized film with the active agent and other excipients developed on the basis of transdermal patch technology. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wetted with saliva, the film quickly hydrates and adheres to the site of application. Then it disintegrates rapidly within seconds and dissolves to release the drug for absorption through the oral mucosa.(3)

Special features of Mouth Dissolving Film (2,4)

- Available in different sizes and shapes.
- Non-obstructive
- Excellent mucoadhesion
- Rapid dissolution
- Rapid release

Advantages of Oral Film(4,5)

- Its large surface area promotes dissolution and disintegration rapid in the oral cavity.
- Because of its flexible and less fragile nature, it is easy to transport, store and handle by the consumer.
- Ease of administration to patients who suffer mentally ill, incompetent or uncooperative.
- The accuracy of the dose administered
- Rapid absorption, faster action and bioavailability improved
- Better patient compliance.
- Improve the product life cycle.
- Good stability
- Water does not needed for administration.

Disadvantages of oral films:(6,7)

- The main disadvantage of this delivery system is that we cannot incorporate high doses into a tape or film.

- Drugs that cause irritation of the mucous membranes cannot be administered.
- Since it is fragile and must be protected from water, it requires special packaging

Types of Fast Dissolving Oral Films:[6,7]

There are three types of oral films:

1. Immediate release
2. Dissolving mucoadhesive pads
3. Sustained release mucoadhesive blisters

MATERIAL AND METHODS

Components of Oral Film[6,7]

- Active pharmaceutical ingredients
- Belt-forming polymers
- Plasticizers
- Sweeteners
- Salivary stimulants
- Flavors
- Colourants
- Stabilizing agents and Thickning agents

1. Active pharmaceutical ingredients

A typical film contains 1-30% w/w of the active pharmaceutical ingredient. For an effective formulation, it is essential to incorporate a micronized active ingredient because it improves the film structure and ensures dissolution speed and uniformity in the fast-dissolving film. Several category of drug can be used for formulation of oral film such as anti-emetic drug,Serotonin inhibitors, anti migraine drugs ,dopamine antagonist .[6]

2. Belt-forming polymers

Water-soluble polymers are used as film forms because they allow for rapid dissolution, good mouthfeel and mechanical film properties. Having desired film properties, such as hydrophilicity, flexibility, mouthfeel and digestibility, the polymers can be used alone or in combination with others.(6)

3. Plasticizers

It is an important ingredient in oral thin films.Plasticizers help improve the mechanical properties of films such as tensile strength and film elongation.

They also reduce film brittleness. They can improve flow and enhance the strength of the polymer. Therefore, choosing the right plasticizer is very important. The film was prepared with PEG 400 as the plasticizer did not look good and/or was a bit sticky to the touch. This may be due to the formation of a wet layer on the surface of the film, which can affect its appearance and handling.Therefore, PG was found to be a better plasticizer than PEG 400 for film preparation.[8]

4.Sweeteners

Sweeteners have become an important part of pharmaceutical products that are intended to be dissolved or dissolved in the oral cavity. Commonly used sweeteners include dextrose, sucrose, fructose, glucose, isomaltose, polyhydric alcohols (sorbitol, mannitol), etc. Artificial sweeteners such as saccharin, cyclamate, aspartame (first generation) and acesulfame K, sucralose, alitame, neotame (second generation) can also be used. Typically, sweeteners are used to mask the bitter taste of certain medications. Natural and artificial sweeteners can be used alone or in combination.[9]

5.Salivary stimulants

Salivary stimulants tend to speed up the dissolution of formulas by increasing saliva absorption. Salivary stimulants are usually found in food grade acids.Salivary relaxants include citric acid, malic acid, lactic acid, with citric acid being the most common and the most widely used of all. These can be used separately or together. The purpose of using saliva stimulants is to increase the rate at which saliva is produced.Salivary stimulants are used individually or in combination in amounts ranging from 2% to 6% of the bar weight.[10]

6.Flavors

The type of substance to be added influences the choice of flavor. The initial taste is perceived in the first seconds after the absorption of the dosed product. Flavors should be used separately or in a mixture. The perception of odors varies from one individual to another, depending on ethnicity and tastes. For example, the geriatric population likes mint or orange flavors, while the younger generation likes fruit flavors, raspberries, etc[10].

7.colourants

FD and C approved colors are used (not exceeding 1 percent concentration levels; w/w) in the production of fast-dissolving oral films. For example, titanium dioxide.[11]

8. Stabilizing agents and Thickning agents

Stabilizing and thickening agents are used to improve the viscosity and consistency of the dispersion or solution of the tape preparation.

Natural gums, carrageenan and cellulose derivatives can be used in concentrations up to 5% w/ w as stabilizing and thickening agents .[12]

Methods of prepration of oral film [13]

1. Solvent casting method
2. Semisolid casting method
3. Rolling Method

4. Solid dispersion extrusion

1.SOLVENT CASTING METHOD [13]

Water soluble poymers dissolved in water

Drug and other excipients dissolved in suitable solvents

Both solutions are mixed and stirred to form homogeneous solution

Homogeneous solution is casted into petri plate and then dried to form oral film.

Advantages

1. High thickness uniformity and more clarity of extrusion.
2. The films have a nice gloss and have no defects such as matrix lines.
3. The films have more flexibility and better physical properties

Disadvantages:

1. The polymer must be soluble in a volatile solvent or in water.
2. A stable solution with a reasonable minimum solids content and viscosity must be formed**.**

3. SEMISOLID CASTING METHOD [14]

The polymer was added part by part onto Distilled water on a magnetic stirrer

mixing was continued until it was completely dissolved at room temperature.

saliva stimulant, sweetener, plasticizer , flavor added to the polymer solution.

3.Rolling Method [15]

Prepare pre-mix with film forming polymer,Solvents and other additives except a drug

Add pre mix to master batch feed tank.

Fed it via a 1 st metering pump and control valve to either or both of the 1 st and 2 nd mixer

Add required amount of drug to the desired mixer.Blend the drug with master batch pre mix to give a uniform matrix.

Then a specific amount of uniform matrix is then fed to the pan through 2 nd metering pumps

The film is formed.

4. SOLID DISPERSION EXTRUSION [16]

Drug is dissolved in sutiable solvent and form mixture.

Melting of polymer should be done.

Mixture is added in melted polymer

Solid dispersion is formed cutting of solid dispersion into fil

EVALUATION OF ORAL FILM [17]

Weight Variation
Thickness
Folding endurance
Tensile strength
Percent elongation
PH value
Drug content
Disintegration time
In Vitro Dissolution study
In Vitro Disintegration study

1. Weight Variation

The weight change test is determined by measuring the weight of each 2 cm x 2 cm surface film. A digital analytical balance was used for weight measurement. The weight of three films was measured and the average was taken.[17]

2. Thickness

The thickness of the tape was measured with a digital caliper at various locations. This is essential to verify film thickness uniformity as this is directly related to the accuracy of the in-band dosage.[17]

3. Folding endurance

Folding endurance is assessed by subjecting the film to repeated folding at the same location until it ruptures. The folding endurance value is calculated as the number of folds the film withstands before breaking.(17)

4. Percent elongation

When a strip sample is subjected to stress, it undergoes stretching, which is quantified **as** strain. Strain is calculated by dividing the deformation of the strip by its original dimensions**.** Notably, the elongation of the strip tends to increase with a higher concentration of plasticizers**.**
The formula for calculating percentage elongation is:

Percentage Elongation = (Increase in Length / Original Length) × 100

Mathematically, it can be represented as:

% Elongation = ((L - L0) / L0) × 100

Where:

- L = Final length of the strip after stretching
- L0 = Original length of the strip before stretching

This formula calculates the percentage increase in length of the strip after applying stress, which is a measure of its elasticity and flexibility.(17)

5. PH Value

To determine the pH value of an oral film, a simple method involves dissolving a single film in 10ml of distilled water, followed by measurement of the pH of the resulting solution. Ideally, the pH value of the film should be consistent and uniform throughout .(17)

6.Tensile strength

The tensile strength of the film was assessed in the laboratory using a custom device. A small fil m sample (2 RAW 2cm²) was carefully cut and attached to the assembly. The weight required to tear the film was recorded and at the same time the extension of the film was measured with a po inter attached to the assembly. Three time measurements were performed for each batch to ensur e accuracy. Mechanical properties, particularly tensile strength and stretch ratio, were rapidly cal culated from these measurements of soluble films
Tensile Strength (TS) = Breaking Force (BF) / (Width (W) x Thickness (T))

Mathematically, it can be represented as:

TS = BF / (W x T)

Where:

- TS = Tensile Strength (in units of force per unit area, such as N/mm² or MPa)
- BF = Breaking Force (in units of force, such as Newtons or grams-force)
- W = Width of the film (in units of length, such as mm or inches)
- T = Thickness of the film (in units of length, such as mm or inches [17]

7..Drug content

To determine the drug content of Bisoprolol Fumarate oral films, a sample equivalent to a 2.5 mg dose was dissolved in 50 ml of pH 6.8 buffer solution. The mixture was then sonicated for 10 minutes to ensure complete dissolution, followed by filtration through a Whatman filter paper (No. 41) to remove any insoluble excipients. A 1 ml aliquot of the filtrate was subsequently diluted to 100 ml with pH 6.8 buffer. The absorbance of the resulting solution was measured at 225 nm using a UV spectrophotometer, and the drug content was calculated accordingly**.** **[17]**

8. Disintegration time

Although the CDER guidance for orally disintegrating tablets can serve as a reference for oral films, a standardized protocol for Fast Dissolving Oral Films (FDOF) is currently unavailable. As a result, the disintegration time for FDOF can be assessed using a modified approach. In this study, disintegration time was measured by placing an individual film in a 50 ml beaker containing 25 ml of distilled water. The time required for the film to disintegrate was recorded, providing a qualitative assessment of its disintegration properties. **[17]**

9.In Vitro dissolution study

A dissolution study of the film was conducted using a modified type 5 dissolution apparatus (Electrolab, Mumbai) at a controlled temperature of 37°C ± 0.5°C. Simulated saliva (pH 6.8) was used as the dissolution medium, with a total volume of 300 ml. The paddle agitation speed was set at 50 rpm. At specified time intervals, a 5 ml sample was withdrawn and replaced with an equal volume of fresh medium. The collected samples were filtered through Whatman filter paper and subsequently analyzed at a wavelength of 247 nm using a UV spectrophotometer.([18])

10 .In vitro disintegration study

The disintegration test was conducted to evaluate the ability of the film to disintegrate in a phosphate buffer solution (pH 6.8). A single film was placed in a beaker containing 10 ml of the buffer solution. Gentle agitation was applied at 10-second intervals. The disintegration time was recorded as the moment when the film began to break apart or disintegrate. [18]

CONCLUSION

Oral disintegrating films (ODFs) have gained popularity over the last decade due to their potential to address limitations associated with traditional dosage forms. Conventional dosage forms often suffer from issues related to administration, bioavailability, solubility, and palatability, leading to poor patient compliance. In contrast, ODFs made from natural, synthetic, and semi-synthetic polymers offer a promising solution to enhance compliance.

Various techniques are available for developing oral thin films that enable instant drug delivery. These techniques can also be adapted to design films for ocular, rectal, vaginal, and transdermal drug delivery. As a result, novel films can serve as alternatives to conventional dosage forms, overcoming their associated limitations.Although film formulation and manufacturing present some challenges, these issues can be addressed through formulation optimization. The future of film technology appears promising for delivering drugs via various routes, offering a potential solution to the limitations of conventional technologies [19].

Oral films, including mucoadhesive and orodispersible films, have emerged as versatile platforms for effective drug delivery, particularly for proteins and peptides. The inherent advantages of oral films, such as rapid drug absorption, enhanced bioavailability, user-friendly nature, and evasion of the first-pass effect in both the gastrointestinal tract and liver, contribute to their popularity.Advancements in fabrication techniques and formulation strategies leveraging natural and synthetic polymers have significantly enhanced the practical applications of oral films, rendering them a promising tool in drug delivery systems.

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