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RECENT ADVANCES IN DEVELOPMENT OF ORAL FILM

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Abstract

Oral films are an innovative drug delivery system that offers several advantages over traditional drug delivery methods, such as enhanced patient compliance, improved bioavailability, and rapid drug absorption through the oral mucosa. This review article summarizes recent advancements in the development of oral films, including their formulation, manufacturing techniques, classification, and potential applications. The formulation of oral films is a crucial factor that determines their success, and a variety of film-forming polymers and excipients are commonly used to optimize the drug loading, stability, and release profile. Solvent casting and hot-melt extrusion are two prevalent techniques used for producing oral films, while advancements in nanotechnology and 3D printing technology offer the possibility of personalized and smart oral films. Oral films come in different classifications and subcategories, such as flash delivery, mucoadhesive sustained release wafers, and mucoadhesive melt-away wafers, each providing unique drug delivery characteristics and potential applications. The potential applications of oral films in various fields, including the pharmaceutical industry, dentistry, veterinary medicine, and sports medicine, are also discussed. These advancements in the development of oral films offer new possibilities for improving drug efficacy, patient outcomes, and revolutionizing the field of drug delivery.

Keywords: Oral films, drug delivery system, formulation, film-forming polymers, excipients, solvent casting, hot-melt extrusion, personalized oral films, smart oral films

INTRODUCTION

Oral films, also known as buccal films or sublingual films, are a new drug delivery system that has attracted attention from researchers and pharmaceutical companies. Oral films are thin, flexible sheets that can be placed in the mouth and dissolve quickly to deliver medication. The benefits of oral films over other drug delivery systems include ease of use, improved drug bioavailability, reduced side effects, and increased patient compliance. This review article will discuss recent advances in the development of oral films and their potential applications in the field of drug delivery. Synonyms- Rapid Film, fast dissolving film, oral disintegrating film (ODF) , Oral thin film (OTF) , and Rapid dissolving film (RDF)[3,4]

Oral films have gained increasing attention as an alternative drug delivery system due to their ease of use, patient compliance, improved bioavailability, and reduced side effects. The ability to bypass the hepatic first-pass effect and the potential for rapid drug absorption through the buccal or sublingual mucosa make oral films an attractive option for the delivery of both small and large molecules. The oral film formulation is a crucial factor for the success of this drug delivery system, and recent advances in the development of oral films have focused on improving the formulation, manufacturing techniques, drug delivery mechanism, and potential applications. This review article aims to provide an overview of recent advances in the development of oral films as a drug delivery system and their potential applications. The article covers the formulation of oral films, manufacturing techniques, drug delivery mechanism, applications, and future perspectives.

Classification of Oral films

1. Oral Fast Dissolving Film
2. Buccal Slow-Release Film
3. Transdermal Film[1]

1. Oral Fast Dissolving Film[8]

This type of oral film dissolves rapidly in the mouth, within seconds to a minute, and delivers the drug through the oral mucosa. It is particularly useful for drugs that are poorly soluble, have low bioavailability, or are difficult to swallow. The oral fast dissolving film can also enhance patient compliance by providing a more convenient and discreet drug delivery method. [1]

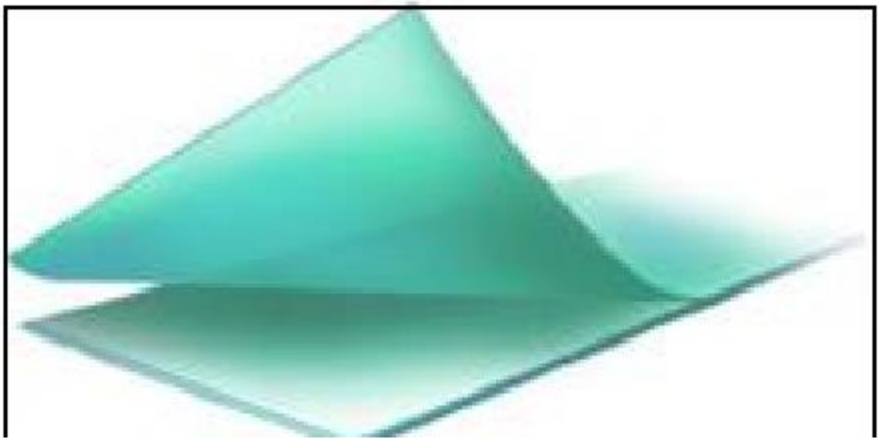

Fig 1 : Fast Dissolving Film

Advantages:

- Improved patient compliance due to the ease of administration and convenience.
- Faster onset of action compared to traditional oral dosage forms.
- Enhanced drug bioavailability and efficacy due to the direct delivery of the drug through the oral mucosa.
- Suitable for patients who have difficulty swallowing or require rapid drug delivery.[3]

Disadvantages:

- Limited drug loading capacity due to the thin film thickness.
- Formulation challenges due to the need to balance the film's mechanical properties and drug release rate.
- Stability issues, including sensitivity to moisture and temperature, which can impact drug efficacy.[1]

Classification of oral fast dissolving film

Oral films come in three distinct subcategories:

a. Flash delivery
b. Mucoadhesive sustained release wafers
c. Mucoadhesive melt-away wafers[24]

a. Flash Delivery

Flash delivery oral films are designed to rapidly dissolve or disintegrate in the mouth, allowing for fast and efficient drug delivery through the oral mucosa. These films are typically used for drugs with a short half-life, low bioavailability, or that require rapid onset of action. Flash delivery films can also improve patient compliance by providing a convenient and discreet drug delivery method.

b. Mucoadhesive Sustained Release Wafers

Mucoadhesive sustained release wafers are designed to adhere to the buccal or sublingual mucosa and release the drug over an extended period of time. These films are typically used for drugs that have a short half-life, require sustained drug delivery, or are not well absorbed through the gastrointestinal tract. Mucoadhesive sustained release wafers can also avoid the hepatic first-pass effect and improve drug bioavailability.

c. Mucoadhesive Melt-Away Wafers

Mucoadhesive melt-away wafers are designed to adhere to the buccal or sublingual mucosa and rapidly dissolve or melt in the mouth, allowing for fast and efficient drug delivery through the oral mucosa. These films are typically used for drugs that have a short half-life, low bioavailability, or require rapid onset of action. Mucoadhesive melt-away wafers can also improve patient compliance by providing a convenient and discreet drug delivery method.[28]

2. Buccal Slow-Release Film

This type of oral film releases the drug slowly and continuously over an extended period of time, typically hours to days, and delivers the drug through the buccal mucosa. It is particularly useful for drugs that have a short half-life or require sustained drug delivery. The buccal slow-release film can also avoid the hepatic first-pass effect, which can increase drug bioavailability.[22]

Advantages

- Prolonged drug release, which can improve drug efficacy and reduce the frequency of administration.
- Avoids the hepatic first-pass effect, which can increase drug bioavailability.
- Suitable for drugs with a short half-life or that require sustained drug delivery.
- Can provide a non-invasive and discreet drug delivery method.[22]

Disadvantages

- Limited drug loading capacity due to the thin film thickness.
- Formulation challenges due to the need to balance the film's mechanical properties and drug release rate.
- The potential for irritation or allergic reactions in the buccal mucosa.[18]

3. Transdermal Film:

This type of oral film delivers the drug through the skin and is typically used for drugs that require systemic delivery or have a high first-pass effect. Transdermal films can also provide a non-invasive and convenient drug delivery method, particularly for patients who have difficulty swallowing or require long-term drug therapy.

Advantages:

- Direct delivery of the drug to the systemic circulation, bypassing the gastrointestinal tract and avoiding the hepatic first-pass effect.
- Prolonged drug release, which can improve drug efficacy and reduce the frequency of administration.
- Non-invasive and discreet drug delivery method.
- Can provide a steady-state drug concentration in the bloodstream.

Disadvantages:

- Limited drug loading capacity due to the thin film thickness.
- Formulation challenges due to the need to balance the film's mechanical properties and drug release rate.
- The potential for skin irritation or allergic reactions.
- Restricted to lipophilic drugs that can penetrate the skin.

Formulation aspects of Oral Films

Oral films are a promising drug delivery system that has gained increasing attention due to their ease of use, patient compliance, and improved bioavailability. The formulation of oral films is a critical factor that affects the success of this drug delivery system. The oral film formulation must be designed to balance the mechanical properties of the film with the desired drug release rate and drug stability. This section will provide an overview of the factors that influence the oral film formulation, the materials used, and the techniques employed to produce high-quality oral films.

Table 1: Formulation of Oral Film[5]

Ingredients	Concentration
API	5 to 30 % weight/weight
Hydrophilic polymer	45 % weight/weight
Plasticizer	0 to 20 %weight/weight
Salivary stimulants	2 to 6 % weight/weight
Surfactant	q. s.
Sweetening agent	3 to 6 % weight/weight
Flavors, colors	q. s.

Factors Influencing Oral Film Formulation:

The formulation of oral films is influenced by several factors, including the physicochemical properties of the drug, the desired release rate, the patient's needs, and the materials used. The formulation must be designed to optimize the drug loading, stability, and release profile of the oral film.

Materials Used in Oral Film Formulation:

The materials used in oral film formulation can be divided into two categories: film-forming polymers and excipients. Film-forming polymers provide the structural integrity of the oral film, while excipients are used to modify the drug release rate, enhance the drug solubility, and improve the film's mechanical properties.

Film-Forming Polymers:

Film-forming polymers used in oral film formulation must have the appropriate mechanical properties, such as flexibility, tensile strength, and adhesion, to ensure the stability and effectiveness of the oral film. The commonly used film-forming polymers in oral film formulation include:

Hydroxypropyl methylcellulose (HPMC): HPMC is a commonly used film-forming polymer that provides good mechanical properties and film integrity. It is a water-soluble polymer that is highly compatible with many drugs.

Polyvinyl alcohol (PVA): PVA is a water-soluble polymer that provides excellent film-forming properties and adhesion. It can be used alone or in combination with other film-forming polymers.

Pullulan: Pullulan is a water-soluble polysaccharide that provides good film-forming properties and film integrity. It is biocompatible and has low toxicity, making it suitable for oral drug delivery.

Eudragit: Eudragit is a family of acrylic copolymers that are insoluble in water but can be dissolved in acidic pH. They provide good film-forming properties and drug release control.

Excipients:

Excipients are used in oral film formulation to modify the drug release rate, improve the drug solubility, and enhance the mechanical properties of the oral film. The commonly used excipients in oral film formulation include:

Plasticizers: Plasticizers are added to the oral film formulation to improve the flexibility and tensile strength of the film. Commonly used plasticizers include glycerin, propylene glycol, and polyethylene glycol.

Surfactants: Surfactants are used to improve the wettability and surface tension of the oral film, which can enhance drug delivery. Commonly used surfactants include Tween 80 and sodium lauryl sulfate.

pH modifiers: pH modifiers are used to adjust the pH of the oral film to enhance drug solubility and release. Commonly used pH modifiers include citric acid and sodium bicarbonate.

Flavoring agents: Flavoring agents are added to the oral film formulation to improve the taste and palatability of the film. Commonly used flavoring agents include menthol and fruit flavors.

Techniques Used to Produce Oral Films:

The techniques used to produce oral films can be divided into two categories: solvent casting and hot-melt extrusion. Solvent casting is the most commonly used technique for oral film production, while hot-melt extrusion is a more recent development in oral film manufacturing.

Solvent Casting:

Solvent casting is a simple and cost-effective technique for producing oral films. In this technique, the film-forming polymers and excipients are dissolved in a suitable solvent, such

as water or ethanol, to form a homogeneous solution. The drug is then added to the solution, and the mixture is cast onto a flat surface, such as a glass plate or a Teflon-coated surface. The solvent is evaporated, leaving behind a thin film that contains the drug.

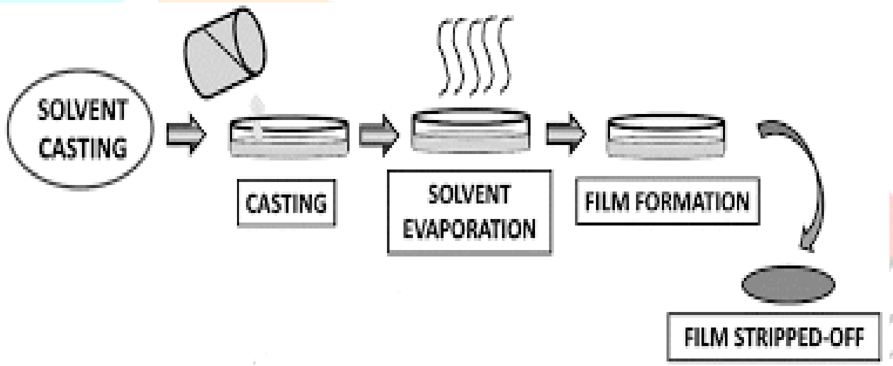

Fig 2 : Solvent Casting Technology

The advantages of solvent casting include:

- Simple and cost-effective technique.
- Suitable for a wide range of drugs and polymers.
- High drug loading capacity.
- The disadvantages of solvent casting include:
- Limited control over the thickness and uniformity of the film.
- High risk of solvent residue, which can impact the stability and efficacy of the oral film.

Hot-Melt Extrusion:

Hot-melt extrusion is a more advanced technique for producing oral films. In this technique, the film-forming polymers and excipients are mixed with the drug in a twin-screw extruder at high temperatures. The mixture is then extruded through a die to form a continuous film that is cooled and cut into the desired shape.

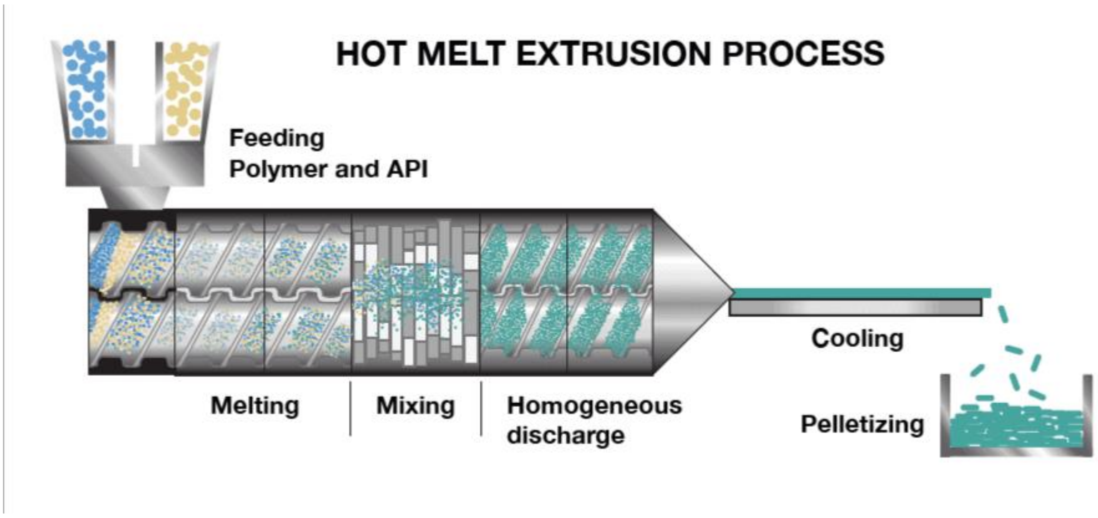

Fig 3 : Hot Melt Extrusion

The advantages of hot-melt extrusion include:

- Precise control over the film thickness and uniformity.
- Reduced risk of solvent residue.
- Suitable for temperature-sensitive drugs.

The disadvantages of hot-melt extrusion include:

- High capital investment and operating costs.
- Limited drug loading capacity compared to solvent casting.
- Strategies to Enhance Oral Film Performance:
- Several strategies have been developed to enhance the performance of oral films. These strategies include:

Nanoparticles:

Nanoparticles can be incorporated into the oral film formulation to enhance drug solubility and stability. The nanoparticles can also provide sustained drug release and improve drug bioavailability.

Mucoadhesive Polymers:

Mucoadhesive polymers can be added to the oral film formulation to enhance adhesion to the oral mucosa and prolong drug delivery. Commonly used mucoadhesive polymers include chitosan, poly(acrylic acid), and polyethylene glycol.

Multilayer Films:

Multilayer films can be used to control the drug release rate and provide targeted drug delivery. The different layers can be designed to release the drug at different rates or in different locations within the oral cavity.

Patented Approaches For Oral Film[2]

SOLULEAVES™ TECHNOLOGY

WAFERTAB™ TECHNOLOGY

FOAMBURST™ TECHNOLOGY

X GEL™ TECHNOLOGY

MICAP

Fast dissolving oral film by three dimensional printing[9]

Three Types Of 3D Printing

1. Inkjet 3D Printing
2. Fused Deposition Modelling
3. Three Dimensional based extrusion printing.

Applications of Oral Films[28]

Oral films have several potential applications in various fields, including the pharmaceutical industry, dentistry, veterinary medicine, and sports medicine. Here are some of the potential applications for oral films:

Pharmaceutical Industry:

Oral films offer several advantages over traditional drug delivery systems in the pharmaceutical industry, including improved patient compliance, enhanced bioavailability, and rapid drug absorption through the oral mucosa. Oral films could be used for a wide range of drugs, including those that have poor solubility or low bioavailability, and those that require rapid drug delivery or sustained release. Oral films also offer the potential for personalized drug delivery, where the films can be tailored to the specific needs of each patient.

Dentistry:

Oral films could be used in dentistry for the delivery of local anesthetics, anti-inflammatory agents, and other drugs that are commonly used in dental procedures. Oral films could also be used for the treatment of oral infections, such as gingivitis or periodontitis, and for the delivery of fluoride or other agents for the prevention of dental caries.

Veterinary Medicine:

Oral films could be used in veterinary medicine for the delivery of drugs to animals, especially those that have difficulty swallowing pills or tablets. Oral films could be used for the treatment of various diseases in animals, including pain management, anxiety, and inflammation. Oral films could also be used for the delivery of vaccines to animals.

Sports Medicine:

Oral films could be used in sports medicine for the delivery of drugs to athletes for the prevention or treatment of injuries. Oral films could be used for the delivery of anti-inflammatory agents, pain relievers, and muscle relaxants to athletes. Oral films could also be used for the delivery of nutritional supplements to athletes.

Evaluation of fast dissolving oral film

- General appearance- by visual appearance
- Weight of films- analytical balance
- Organoleptic evaluation- color, odor
- Thickness-by using vernier calipers or micrometer screw gauge
- Mechanical properties- tensile strength ,Young's modulus,
- Folding Endurance- Film folded until it breaks, the amount of fold at breaking point .
- In vitro disintegration time- Disintegration apparatus or petri dish is used
- P^H Value-one oral film has been dissolved in 10-cc of distilled water
- Stability studies-done for find out how temperature and humidity affects drug stability
- Assay-by using standard pharmacopeia
- Dissolution test-by using paddle or basket apparatus

Fast Dissolving Oral Film Packaging-

1. Plastic bags or foil paper container
2. Aluminum and single pouch container
3. Multiple blister card unit

Conclusion:

In conclusion, oral films are a promising drug delivery system that offers several advantages over traditional drug delivery systems, including improved patient compliance, enhanced bioavailability, and rapid drug absorption through the oral mucosa. Recent advances in the development of oral films have focused on improving their formulation, manufacturing techniques, drug delivery mechanism, and potential applications. The formulation of oral films is a critical factor that affects the success of this drug delivery system. The oral film formulation must be designed to balance the mechanical properties of the film with the desired drug release rate and drug stability. The materials used and techniques employed to produce high-quality oral films continue to evolve, and new strategies are being developed to enhance the performance of oral films. Overall, oral films are a promising drug delivery system that has the potential to revolutionize the field of drug delivery. Recent advances in the development of oral films offer several advantages over traditional drug delivery systems, and further research is needed to fully realize their potential and improve patient outcomes.

Future prospective

The future prospects of oral films are exciting, and ongoing research is expected to continue to refine and optimize this drug delivery system. The development of personalized oral films is an area of particular interest, with the potential to tailor drug delivery to individual patient needs. Personalized oral films could be designed to release drugs at specific rates or locations within the oral cavity, potentially improving patient outcomes. The use of nanotechnology in oral film formulation is another area of active research. Nanoparticles can be incorporated into the oral film formulation to enhance drug solubility and stability, and provide sustained drug release. The development of smart oral films that can respond to environmental stimuli, such as pH or temperature changes, is another area of interest. Smart oral films could potentially be used for targeted drug delivery or controlled drug release. Finally, the development of sustainable oral film formulations is an important area of future research. The use of biodegradable polymers and eco-friendly manufacturing techniques can reduce the environmental impact of oral films and improve their sustainability.

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