IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Orally Disintegrating Films : A Modern Expansion in Drug Delivery system

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Abstract

Rapidly dissolving tablets were first developed in the 1970s as an alternative to tablets, capsules and syrups for children and adult patients who had difficulty swallowing solids taken orally. The fast-disintegrating film provides an advantage over the fast-disintegrating tablet, increasing the risk of clogging and brittleness. Most ODT products are designed to dissolve in less than a minute when exposed to saliva, creating a solution that is easy to swallow. This delivery method is much better than fast-acting tablets because it can be used in patients with speech disorders and schizophrenia, and water is not needed because it can be broken down in seconds and the medicine can be released in the mouth. There are many methods to produce ODF; The most commonly used methods are casting and spraying. Companies with experience in polymer-coated formulations containing active pharmaceutical ingredients (APIs) for transdermal delivery seized the opportunity to convert this technology to the OTF format. Orally disintegrating films have potential for commercial and commercial growth as they have many advantages over orally disintegrating tablets. This review aims to focus on ODF's results, products, design process and evaluation. In addition, the commercial prospects of this new recipe are also emphasized. This approach enhances the therapeutic effect of active drugs by preventing hepatic first-pass metabolism, ensuring controlled delivery of drug molecules, facilitating and improving patient compliance. This review provides additional details on ODF components, manufacturing processes, evaluation methods, and products. Oral dissolving films (OFDFs) have recently been introduced due to their convenience and ease of use compared to other materials such as orally dissolving tablets. Technology has evolved over the last few years in the form of alcohol analyzers in the food and oral care industry and has become the latest trend and adopted by consumers, so OFDF has benefited a lot from the pharmaceutical industry.

Keywords : Novel Drug Delivery ,Innovative Dosage Form ,ODFs

INTRODUCTION : [1]

The oral administration method is the most popular method due to its ease of application, non-invasiveness, flexibility, patient compliance and acceptance. Fast-dissolving oral film (FDOF) is used as a new method because it dissolves rapidly in the oral cavity and directly reaches bacteria. Oral film technology meets all the requirements of a high capacity paper. Oral dissolving film is a new type of oral drug delivery system using transdermal patch technology. This delivery consists of a thin mouthpiece that is simply placed on the patient's tongue or oral tissue and immediately wetted with saliva, as well as a rapid video that quickly moistens and adheres to the application site. It is then rapidly broken down and dissolved, allowing the drug to be absorbed by the oral mucosa, or modified to maintain rapid solubility, allowing gastrointestinal absorption when swallowed.

Problems swallowing medications are more common in elderly and pediatric patients, as well as ambulatory patients who do not have access to water. Thus, oral contraceptives quickly emerged in the 1970s as an alternative to tablets, capsules, and syrups for children and adults who had difficulty swallowing food in the mouth. The introduction of ODT in the market is associated with advising patients on appropriate dosage by giving instructions such as "do not chew/do not swallow". However, despite these guidelines, cases involving chewing and swallowing are still reported. The oral disintegrator dosage form consists of a dissolving oral tablet and a rapid-dissolving film. Orally dissolving tablets can cause many problems such as leaving residue in the mouth and causing bad breath; Fear of choking and difficulty swallowing tablets.

Fast dissolving drug delivery system [2]

Rapid drug delivery is a new form of delivery, also known as rapid-dissolving/disintegrating films, for oral administration of drugs, which emerged in the late 1970s as an alternative to tablets, capsules, syrups. Other formulations for children and adults with dysphagia. The dosage form combines with the quality of capsule and liquid forms. FDDS is easy to administer and administer to elderly, children, mentally ill, nauseated, and uncooperative patients.

The dispensing machine has a dosage form that dissolves quickly in the mouth for a few minutes, for example without drinking water. This delivery consists of a thin mouthpiece that is placed over the patient's tongue or other oral tissues and immediately moistened with saliva. The film moistens rapidly

at the application site. It dissolves and disintegrates quickly, releasing the drug for absorption through the oral mucosa. The rapid development of oral films has become widely accepted by patients and caregivers due to their ease of distribution, portability, and accuracy. The strength of the film depends on the type and amount of polymer; The breaking time of orally dissolving films varies between 5-20 minutes. According to the Pharmacopoeia. They also have a rapid onset of action within seconds, because oral absorption of the drug occurs directly from the site of application into the body without first going through metabolism to produce the desired effect.

The administration of ODFs has numerous advantages and some of them are as follows:

(3)

1. Ease of Administration: ODFs dissolve quickly in the mouth without the need for water, making them convenient for individuals with difficulty swallowing or those on the go.

2. Rapid Onset of Action: The film's rapid disintegration allows for faster absorption of the active ingredients, leading to a quicker onset of therapeutic effects.

3. Improved Patient Compliance: ODFs are often more palatable than traditional dosage forms, potentially enhancing patient adherence to prescribed regimens.

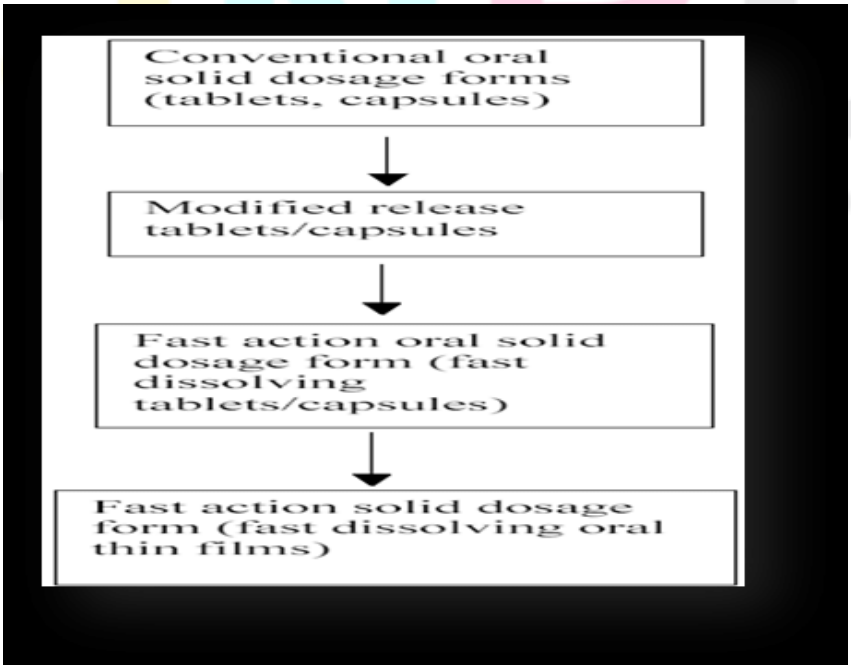
4. Accurate Dosing: The films are typically pre-dosed, minimizing the risk of dosing errors associated with traditional oral forms like tablets or capsules.

5. Reduced Gastrointestinal Irritation: Bypassing the digestive system can reduce the likelihood of gastrointestinal irritation, making ODFs a preferable option for certain medications.

6. Enhanced Stability: ODFs can enhance the stability of sensitive drugs, protecting them from environmental factors like moisture and light.

7. Pediatric and Geriatric Suitability: ODFs can be particularly beneficial for pediatric and geriatric populations where swallowing difficulties are common.

8. Discreet Administration: ODFs offer a discreet way to take medication in public settings, as they dissolve rapidly and leave no residue.



DISADVANTAGE (2) (3)

1. Film packing requires the use of specialized equipment.
2. Difficult to pack.
3. A high dose cannot be incorporated in an oral film.
4. Oral film that are moisture sensitive
5. Eating and drinking can be prohibited.
6. High doses cannot be incorporated.
7. Excessive bitter drugs are not feasible.
8. Dose uniformity is a technical challenge.
9. They require special packaging for the products stability and safety.
10. Drugs which irritate the oral mucosa cannot be administered by this route.

The Ideal Characteristics of Drug To Be Selected. (4)

1. The drug should have pleasant taste. The drug should have small molecular size and low molecular weight.
2. The drug should have good solubility and stability in water as well as in saliva.
3. It should be partially unionized at the pH of oral cavity.
4. The drug should exhibit low sensitivity to environmental conditions.
5. It should have the ability to permeate oral mucosal tissue.
6. The therapeutic dose of the drug should not be greater than 40mg.

Mechanism of film formation (5)

The film-forming system is applied directly to the skin and forms a thin and transparent film in place after the solvent evaporates. After application of the formulation to the skin, the composition of the film-forming system underwent significant changes due to the loss of volatile components of the carrier, which led to the formation of a comfortable residual film on the skin. During this process, the drug concentration increases, reaching the saturation level and potentially oversaturation of the skin. Supersaturation improves the flow of the drug through the skin by ensuring that the thermodynamic effect of the formulation does not affect the skin barrier, thus reducing side effects or irritation. The concept of supersaturation can be explained by a modification of Fick's law of diffusion. Fick's law of diffusion is given by

Eq.:

Where

J = rate of drug permeation per unit area of skin per unit time (flux)

D = diffusion coefficient of drug Cv= concentration of drug

h = thickness of barrier to diffusion

From this equation, it is clear that the rate of drug permeation across the skin is proportional to the concentration of the drug. However this is true when the entire drug is dissolved in the vehicle. Equation describes the modified form of Fick’s law of diffusion:

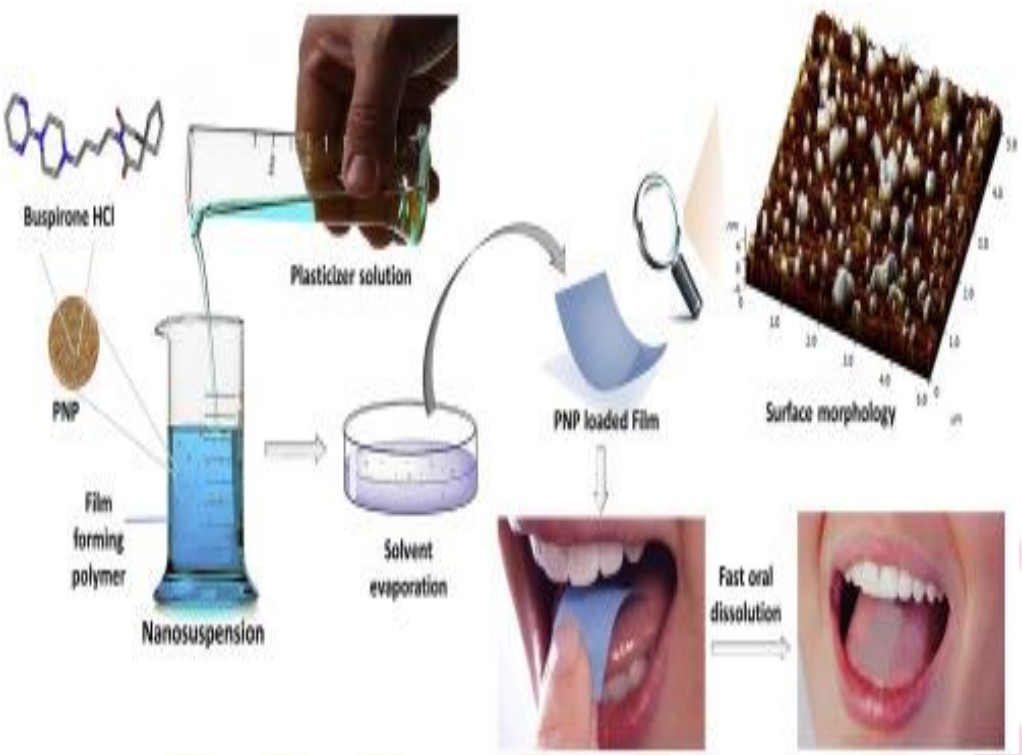
$J = \alpha D/\gamma h$

Where a=thermodynamic activity of drug within formulation

γ=thermodynamic activity of drug within membrane

According to this equation, the flux of the drug is directly proportional to the thermodynamic c activity of the system, which is related to saturation. However

increasing the super saturation increases thermodynamic instability.



FFS forms a supersaturated layer immediately after passing through the human epidermal patch (EVRA®) in vitro. It overcomes the problem of instability in film production and skin production. Therefore, its improved formulation shows more permeability than commercial patches. Compared to other transdermal dosage forms, the formulation provides twice the penetration of drug through the skin without enhancers. The distribution of the film solution of ethinyl estradiol is higher than in the commercial field. Tested with estradiol supplements. Permeation of ethinyl estradiol from the formulation provides approximately seven times more ethinyl estradiol in the film-forming solution compared to commercial patches prepared with or without the enhancer. Therefore, these systems have proven to be very useful in improving drug access to commercial products.

Formulation of Fast Dissolving Films [2]

Fast dissolving Oral films include various ingredients for its formulation

> Active pharmaceutical ingredient

> Film forming polymers

> Plasticizer

>Superdistegrants

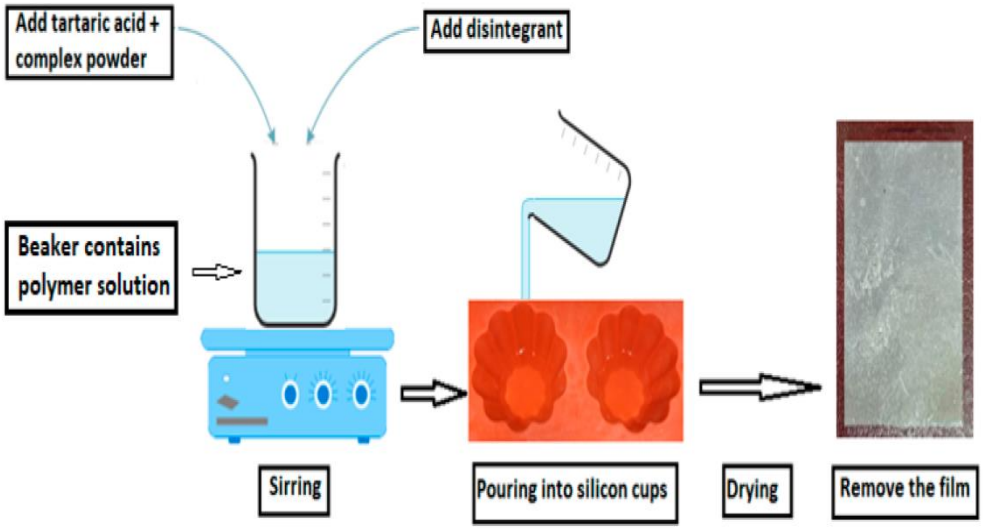
>Sweetening agent

> Saliva stimulating agent

> Surfactants

> Coloring agent

> Flavouring agent



Formulation of FDFs involves the intricate application of aesthetic and performance characteristics such as taste masking, fast dissolution, physical appearance, mouth feel etc. From the regulatory perspectives, all excipients used in the formulation of OS should be Generally Regarded as Safe (i.e. GRAS-listed) and should be approved for use in oral pharmaceutical dosage forms. A typical composition includes various ingredients which are described.

Sr.no	Agents	Concentration
1	Drug	1-25%
2	Water soluble polymer	40 -50%
3	Plasticizers	0-20%
4	Fillers,colours,Flavours	0-40%

Active Pharmaceutical Ingredient : [6]

The film composition contains 1-30% active ingredient w/w. Always use small doses of effective medications, as higher doses are difficult to integrate into the film quickly. Antibiotics, antibiotics, antibiotics, vasodilators, antibiotics, antibiotics, etc. There are many drugs that are quickly found in the mouth, including: Dimenhydrinate may also be included in ODF to mask the taste. Examples of drugs belonging to ODF are

albuterol sulfate, rizatriptan benzoate, verapamil, onasetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, and others. Micronizing the API is always beneficial to both improve the texture of the film and improve the resolution and compatibility of OFDF. Many APIs are competitive with OFDF technology but have a bitter taste. This makes the formulation particularly unsuitable for children's formulations. Therefore, the smell needs to be covered before submitting the API to OFDF. Various methods can be used to enhance the palatability of formulations. Among the methods of operation, the simplest is the mixing and integration of bitter APIs with pleasant-tasting additional products. This is often called masking.

List of few drugs can be incorporated in fast dissolving film . (6)

Sr.No.	Drug	Dose	Therapeutic action
1	Azatidine Maleate	1mg	Anti histamine
2	Nicotine	2mg	Smoking cessation
3	Loperamide	2mg	Anti diarroheal
4	Ondensetron	2.5 mg	Anti emetic
5	Zolmitripan	2.5 mg	Anti migraine
6	Salbutamol	4mg	Anti histamine
7	Cetrizine	5- 10mg	Anti histamine
8	Omiprazole	10-20mg	Proton Pump Inhibitor
9	Loratidine	10mg	Anti histamine
10	Ketoprofen	12.5mg	Analgesic

Film Forming Polymers (7)

Polymers are the main and most basic components of FDOF. A variety of polymers are available for the preparation of oral films and are used in amounts of approximately 40-45% w/w of the total film weight, but can be increased individually or together up to 65% w/w film weight. Get what you need for spoken word videos. The resulting film must be sturdy enough to not cause damage during handling or shipping. The strength of the film depends on the type of polymer and its content in the composition. The physicochemical properties of the polymer or polymers selected for film formulation play an important role in determining the final disintegration of the prepared film. Plasticizers Formulation decisions (plasticizers, etc.) are reported to be important factors affecting the properties of films. By adding plastic, the mechanical properties of the film, such as tensile strength and elongation, are also improved. Changes in their concentrations will affect these products. Commonly used plastics include glycerin, dibutyl phthalate, polyethylene glycol, etc. is available. The most commonly used natural and synthetic polymers are presented in the table.

Natural Polymer	Synthetic Polymer
Starch	Hydroxy propyl methyl cellulose
Pectin	Poly vinyl pyrolidone
Gelatin	Polyvinyl alcohol
Sodium alginate	Sodium carboxy methyl cellulose
Pullulan	Methyl cellulose
Xanthum	Hydroxy ethyl cellulose

Plasticizer [8]

Plasticizer is an important component of melt film. Plasticizers help soften the strip and reduce the brittleness of the film. It increases film performance by lowering the glass transition temperature of the polymer. The chemical structure and concentration of the polymer play an important role in reducing the glass transition temperature of the polymer. The choice of plasticizer will depend on its compatibility with the type of polymer and solvent used in the casting film. The use of plasticizers allows the polymer to flow better and increases its strength. Phthalate derivatives such as glycerin, propylene glycol, low molecular weight polyethylene glycol, dimethyl phthalate, diethyl phthalate and dibutyl phthalate, and citrate derivatives such as tributyl ester, triethyl ester, acetyl citrate, triacetin and castor oil are frequently used in plastics. .

Plasticizers are generally used at 0–20%; w/w dry weight of polymer. However, using the wrong plastic wrap will cause the film to crack, crack, and strips to peel off. It is also reported that the use of plastic may affect the absorption of the drug.

Sweetening agents [8]

Sweeteners have become the important part of the formulation intended to be disintegrated or dissolved in the oral cavity. Generally sweeteners are used in the concentration of 3 to 6 %w/w either alone or in combination. Both natural sweeteners as well as artificial sweeteners are used in the formulation of these fast dissolving films. Polyhydric alcohols such as sorbitol, mannitol, and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation. However it should be noted that the use of natural sugars in such preparations need to be restricted in people who are on diet or in the case of diabetic patients. Due to this reason, the artificial sweeteners have gained more popularity in food and pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame-K and sucralose have more than 200 and 600 time sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Aspartame was used for the preparation of oral strips of valdecoxib. Sucralose and neotame was reported to be used in the suppression of the bitter taste of fast dissolving films of diclofenac and ondansetron respectively.

Flavoring Agents. [2]

Flavoring agents can be selected from the synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. Any flavor can be added such as essential oils or water soluble extracts of menthol, intense mints such as peppermint, sweet mint, spearmint, wintergreen, cinnamon, clove, sour fruit flavor such as lemon, orange or sweet confectionary flavors such as vanillin, chocolate ,or fruit essence like apple, raspberry, cherry, pineapple. The amount of flavour needed to mask the taste depends on the flavor type and its strength. Preferred different flavors as per the type and taste of the drugs are mentioned .

Drug	Preferred Flavour
Antibiotics	Cherry , maple ,pineapple, orange, raspberry, banana – vanilla , vanilla
Antihistamines	Aprricot , cherry, cinnamon, grape, honey, lime, raspberry

Decongestants & Expectorants	Anise , apricot, butterscotch,cherry, strawberry, coriander, pineapple,raspberry

Saliva stimulating agent [9]

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Eg. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. These agents are used alone or in combination between 2 to 6%w/w of weight of the strip25

Surfactants [10]

Surfactants are used as solublising or wetting or dispersing agent so that the film is getting dissolved. Some of the commonly used are sodium lauryl sulfate, benzalkonium chloride, bezthonium chloride, tweens etc. One of the most important surfactant is polaxamer 407 that is used as solubilizing, wetting and dispersing agent.

Coloring agents [9]

FD & C approved coloring agents are used (not exceeding concentration levels of 1 percent; w/w) in the manufacturing of orally fast dissolving films. Eg. Titanium dioxide

Manufacturing Methods [11] [12]

1. Solvent casting

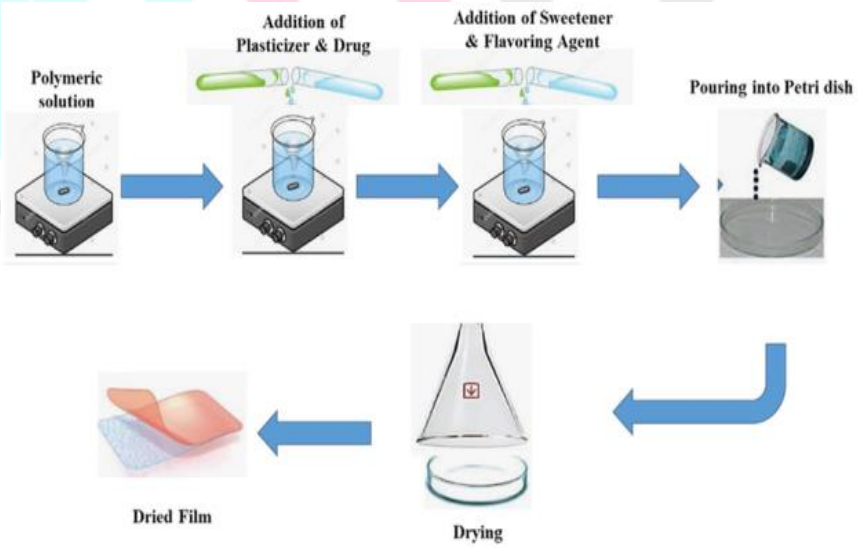
2. Semisolid casting

3. Hot melt extrusion

4. Solid dispersion extrusion

5. Rolling

1) Solvent casting method [13]



Fast dissolving buccal films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable Ingredients that are water soluble are dissolved in water. Drug and other ingredients are dissolved in a suitable solvent to form a clear viscous solution. Both solutions are mixed. degass under vaccume The resulting solution casted as a film..

Advantage:

• The film have great uniformity of thickness and better clarity than extrusion.

• Films have fine gloss & freedom from a defect such a die liners.

• Films have a lot of flexibility & good physical properties.

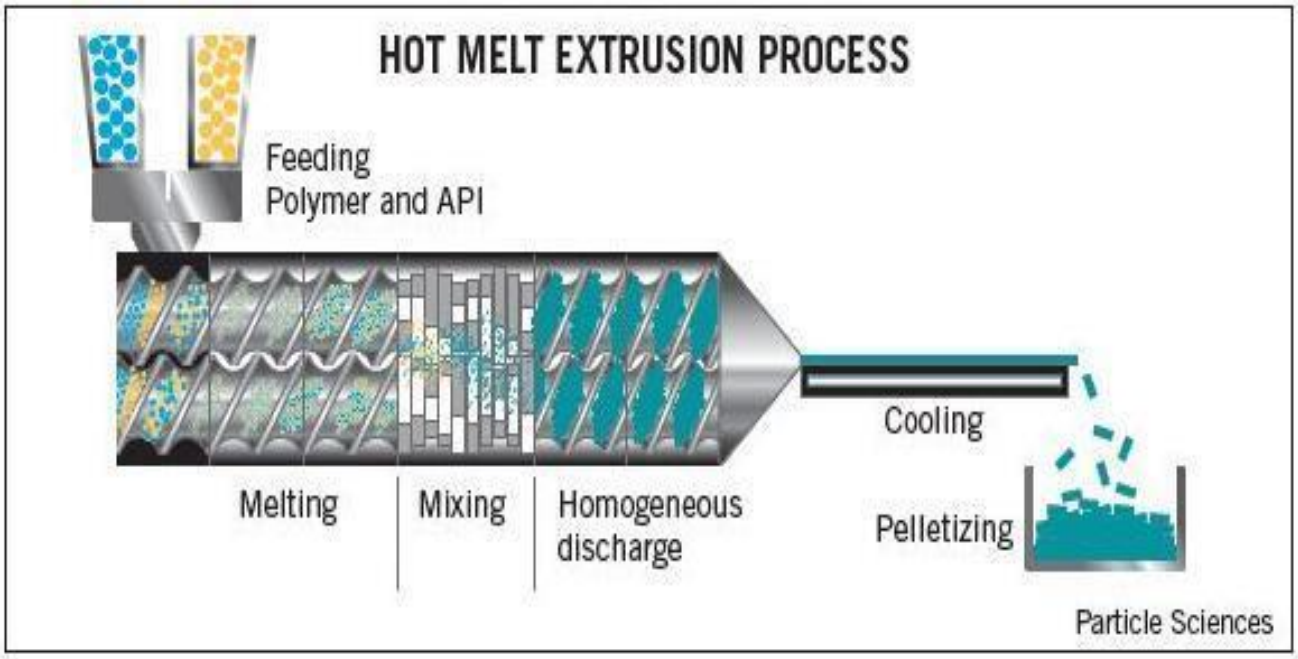
Disadvantage:

• The polymer must be soluble in volatile solvent or water.

• The stable solution with reasonable minimum solid content.

Hot melt extrusion [14]

Hot metal extrusion is commonly used to prepare granules, sustained release tablets, transdermal and transmucosal drug delivery systems. Melt extrusion was used as a manufacturing tool in the pharmaceutical industry as early as 1971.



Advantage:

➢ Fewer operation units

➢ Better content uniformity

➢ An anhydrous process

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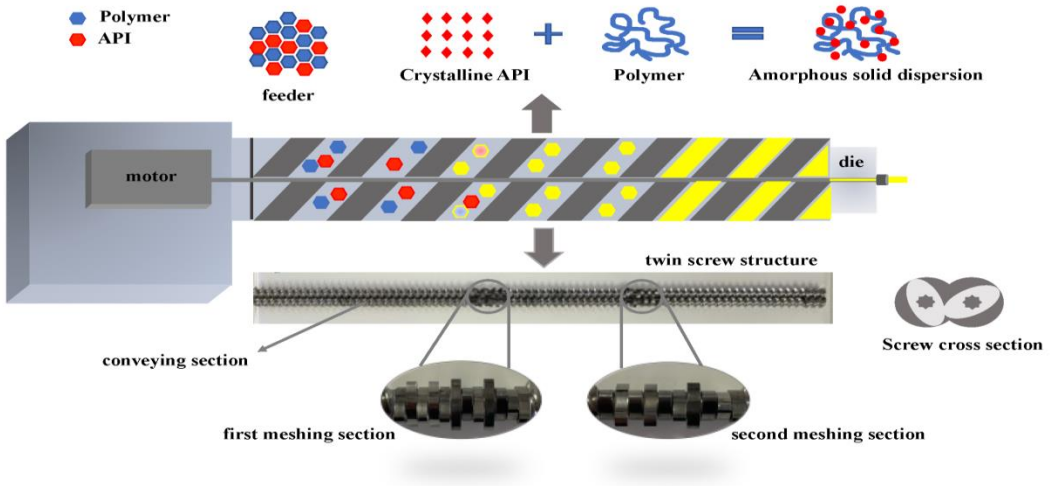
Semisolid Casting. [13]

Solution of water soluble film forming polymer is prepared. Resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate). Appropriate amount of plasticizer is added so that gels mass is obtained. Finally the gel mass is casted into the films and ribbons using heat controlled drums. The thickness of the film should be about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

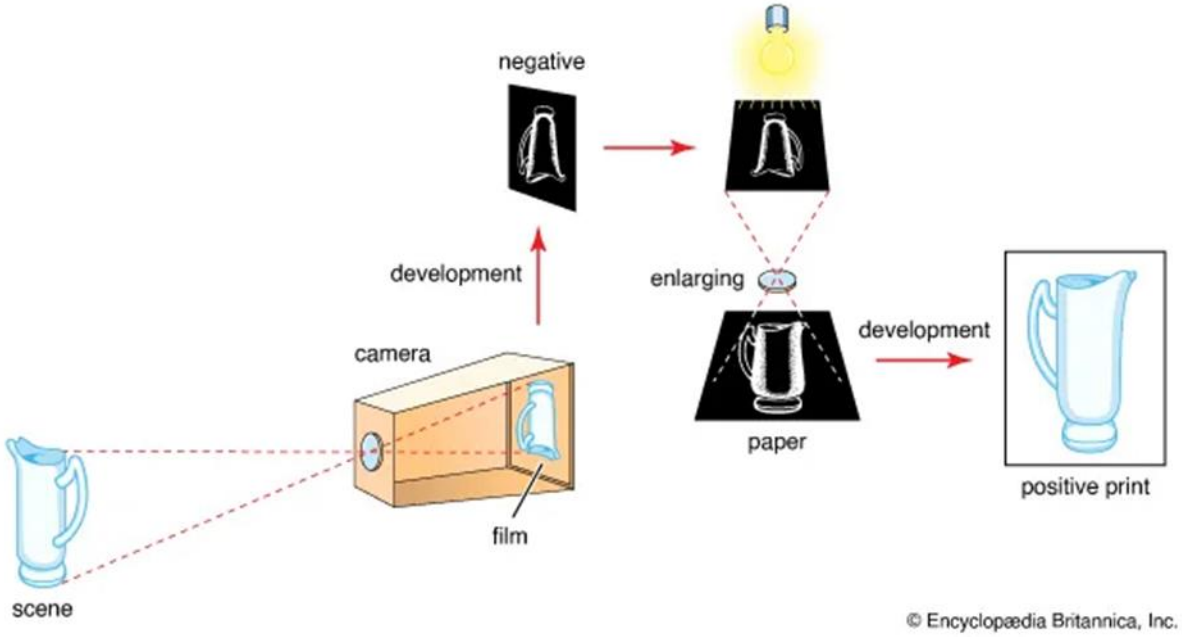
Solid Dispersion Extrusion [14]

The term solid dispersions refer to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers. Drug is dissolved in a suitable liquid solvent. Then solution is incorporated into the melt of polyethylene glycol, obtainable below 70◦ C Finally the solid dispersions are shaped into the films by means of dies.



Rolling method : [12]

In this method the film is prepared by preparation of a pre-mix, addition of an active and subsequent formation of a film. Prepare pre-mix with film forming polymer, polar solvent and other additives except a drug Add pre mix to master batch feed tank. Fed it via a 1st metering pump and control valve to either or both of the 1st and 2nd 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 2nd metering pumps. The film is finally formed on the substrate and carried away via the support roller. The wet film is then dried using controlled bottom drying.



The Following Classification of Drugs that are incorporated in the film formulation : [15] [16]

Fast dissolving films (FDFs) are thin, oral dosage forms that dissolve rapidly in the mouth, allowing for quick absorption of the active pharmaceutical ingredient (API). These films are especially beneficial for patients who have difficulty swallowing tablets or capsules. Here are some types of drugs that can be incorporated into fast dissolving films along with examples:

1. Antihistamines: [15]

1. Loratadine: Used to treat allergic conditions such as hay fever, Loratadine can be incorporated into FDFs for quick relief of allergy symptoms. Loratadine is a second-generation antihistamine that is often used to treat allergy symptoms such as sneezing, itching, watery eyes, and runny nose. It works by blocking the action of histamine in the body. In oral thin film formulations, loratadine is typically formulated to dissolve quickly in the mouth, providing rapid relief from allergy symptoms without the need for water. 1. **Selection of Ingredients**:

- Active Ingredient: Loratadine

- Film-Forming Polymer: Typically, a hydrophilic polymer like hydroxypropyl methylcellulose (HPMC) or polyvinyl alcohol (PVA) is used.

- Plasticizer Such as glycerin or propylene glycol to improve film flexibility.

- Surfactant:To aid in wetting and uniform spreading of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Loratadine is dissolved in a suitable solvent, often ethanol or a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

3. Film Casting:

- The loratadine solution is then mixed with the polymer-plasticizer-surfactant mixture to form a homogenous solution.

- This solution is then cast onto a suitable substrate like a glass plate using a film applicator or similar equipment. The thickness of the film can be controlled by adjusting the gap of the applicator.

- The cast film is allowed to dry at a controlled temperature to evaporate the solvent, leaving behind a solid film.

4. Film Drying and Conditioning:

- The cast film is left to dry in a controlled environment, often at room temperature or under reduced pressure to speed up the drying process.

- Once dry, the film is cut into suitable sizes or shapes for packaging and storage.

2. Antiemetics: [17]

Ondansetron: This drug is commonly used to prevent nausea and vomiting, particularly in patients undergoing chemotherapy. Fast dissolving film Ondansetron provide a convenient dosage form patients who may have difficulty swallowing tablets during nausea episodes. Ondansetron oral thin films are thin, flexible strips that dissolve rapidly in the mouth, delivering the medication directly into the bloodstream for quick action.

Method of Preparation:

1.Ingredients:

- Ondansetron hydrochloride (active pharmaceutical ingredient)

- Polyvinyl alcohol (PVA) or hydroxypropyl methylcellulose (HPMC) (polymer matrix)

- Flavoring agents (to improve taste)

- Sweeteners (to enhance palatability)

- Plasticizers (such as glycerin or propylene glycol, to improve film flexibility)

2. Film Preparation:

a. Preparation of Polymer Solution:

- Dissolve the polymer (PVA or HPMC) in purified water under stirring and heating until a clear solution is obtained.

- Add plasticizers to the polymer solution to enhance film flexibility.

b. Drug Incorporation:

- Dissolve ondansetron hydrochloride in a small amount of purified water or a suitable solvent.

- Add the drug solution to the polymer solution and mix thoroughly to ensure uniform drug distribution.

c. Additives:

- Incorporate flavoring agents and sweeteners into the polymer-drug mixture to improve taste and palatability.

d. Film Casting:

- Pour the prepared mixture onto a clean, flat surface (such as a glass plate) to form a thin, uniform layer.

- Allow the mixture to dry and form a solid film under controlled temperature and humidity conditions.

e. Cutting and Packaging:

- After drying, cut the solid film into individual strips of appropriate size.

- Package the ondansetron oral thin films in blister packs or pouches to protect them from moisture and maintain stability.

3. Analgesics/NSAIDs: [18]

1.Ibuprofen:A nonsteroidal anti-inflammatory drug (NSAID) used for pain relief and reducing inflammation, Ibuprofen can be formulated into fast dissolving films for quick action in conditions like headaches, dental pain, or muscle aches.

1. Selection of Ingredients

- Active Ingredient: Ibuprofen

- Film-Forming Polymer: Typically, a hydrophilic polymer like hydroxypropyl methylcellulose (HPMC) or polyvinyl alcohol (PVA) is used.

- Plasticizer: Such as glycerin or propylene glycol to improve film flexibility.

- Surfactant: To aid in wetting and uniform spreading of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Ibuprofen is dissolved in a suitable solvent, often ethanol or a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

3. Film Casting:

- The ibuprofen solution is then mixed with the polymer-plasticizer-surfactant mixture to form a homogenous solution.

- This solution is cast onto a suitable substrate, such as a glass plate, using a film applicator or similar equipment. The thickness of the film can be controlled by adjusting the gap of the applicator.

- The cast film is allowed to dry at a controlled temperature to evaporate the solvent, leaving behind a solid film.

4. Film Drying and Conditioning:

- The cast film is left to dry in a controlled environment, often at room temperature or under reduced pressure to speed up the drying process.

- Once dry, the film is cut into suitable sizes or shapes for packaging and storage.

3. Lidocaine: [19] Lidocaine is a local anesthetic used to numb specific areas of the body to reduce pain or discomfort. Oral thin films containing lidocaine can be applied directly to the a 1. Selection of Ingredients:

- Active Ingredient: Lidocaine

- Film-Forming Polymer: Hydroxypropyl methylcellulose (HPMC) or polyvinyl alcohol (PVA) are commonly used film-forming polymers for oral or topical films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant:Added for uniform spreading and wetting of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Lidocaine is dissolved in a suitable solvent, often ethanol or a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation:Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface. ffected oral mucosa for quick relief from mouth sores, toothaches, or other oral pain.

The formulation of these analgesics into oral thin films involves combining the active ingredient with a suitable polymer matrix, plasticizers for film flexibility, flavoring agents, sweeteners, and other additives as necessary to enhance taste, palatability, and drug release properties. The prepared mixture is then cast into thin films, dried, cut into individual doses, and packaged for distribution and use.

4. Antibiotics: [20]

1. Amoxicillin: Amoxicillin is a broad-spectrum penicillin antibiotic used to treat a wide range of bacterial infections, including respiratory tract infections, urinary tract infections, and skin infections. Oral thin films containing amoxicillin are designed for rapid dissolution in the mouth, providing systemic antibiotic therapy

1. Selection of Ingredients:

- Active Ingredient: Amoxicillin

- Film-Forming Polymer: Hydroxypropyl methylcellulose (HPMC) or ethyl cellulose are commonly used film-forming polymers for oral films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant: Added for uniform spreading and wetting of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Amoxicillin is dissolved in a suitable solvent, often water or a water-alcohol mixture.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

3.Film Casting:

- The amoxicillin solution is mixed with the polymer-plasticizer-surfactant mixture to obtain a homogenous solution.

- This solution is then cast onto a suitable substrate, such as a glass plate, using a film applicator or similar equipment. The thickness of the film is controlled by adjusting the applicator gap.

- The cast film is allowed to dry at a controlled temperature to evaporate the solvent, resulting in a solid film.

4. Film Drying and Conditioning:

- The cast film is dried in a controlled environment, such as at room temperature or under reduced pressure, to expedite drying.

- After drying, the film is cut into appropriate sizes or shapes for packaging and storage.

5. Azithromycin: Azithromycin is a macrolide antibiotic used to treat respiratory tract infections, skin infections, and sexually transmitted infections. Oral thin films of azithromycin offer a convenient alternative to oral suspensions or tablets, particularly for pediatric patients or individuals with swallowing difficulties

1. Selection of Ingredients:

- Active Ingredient: Amoxicillin

- Film-Forming Polymer: Hydroxypropyl methylcellulose (HPMC) or ethyl cellulose are commonly used film-forming polymers for oral films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant: Added for uniform spreading and wetting of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Amoxicillin is dissolved in a suitable solvent, often water or a water-alcohol mixture.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

3. Film Casting:

- The amoxicillin solution is mixed with the polymer-plasticizer-surfactant mixture to obtain a homogenous solution.

- This solution is then cast onto a suitable substrate, such as a glass plate, using a film applicator or similar equipment. The thickness of the film is controlled by adjusting the applicator gap.

- The cast film is allowed to dry at a controlled temperature to evaporate the solvent, resulting in a solid film.

4**. Film Drying and Conditioning:**

- The cast film is dried in a controlled environment, such as at room temperature or under reduced pressure, to expedite drying.

- After drying, the film is cut into appropriate sizes or shapes for packaging and storage.

The formulation of these antibiotics into oral thin films involves combining the active ingredient with a suitable polymer matrix, plasticizers for film flexibility, flavoring agents, sweeteners, and other additives as

necessary to enhance palatability and drug release properties. The prepared mixture is then cast into thin films, dried, cut into individual doses, and packaged for distribution and use, ensuring effective antibiotic therapy with ease of administration.

6. Antiasthmatics: [21]

Oral thin film formulations for antiasthmatic drugs offer convenience and ease of administration, especially for patients who may have difficulty swallowing pills or tablets. Here are some examples of antiasthmatic drugs that are available in oral thin film formulations:

1.Montelukast: This is a leukotriene receptor antagonist used to manage asthma and allergic rhinitis. Montelukast oral thin films dissolve quickly in the mouth, making them suitable for patients who h Here's a detailed method for preparing a film formulation of montelukast, an anti-asthmatic drug:

1.Selection of Ingredients:

- Active Ingredient: Montelukast

- Film-Forming Polymer: Hydroxypropyl methylcellulose (HPMC) or ethyl cellulose are commonly used film-forming polymers for oral films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant: Added for uniform spreading and wetting of the formulation.

2. Preparation of Film Formulation:

- Dissolution: Montelukast is dissolved in a suitable solvent, often ethanol or a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

3. Film Casting:

- The montelukast solution is mixed with the polymer-plasticizer-surfactant mixture to obtain a homogenous solution.

- This solution is then cast onto a suitable substrate, such as a glass plate, using a film applicator or similar equipment. The thickness of the film is controlled by adjusting the applicator gap.

- The cast film is allowed to dry at a controlled temperature to evaporate the solvent, resulting in a solid film.

4. Film Drying and Conditioning:

- The cast film is dried in a controlled environment, such as at room temperature or under reduced pressure, to expedite drying.

- After drying, the film is cut into appropriate sizes or shapes for packaging and storage. ave trouble swallowing.

7. Antifungals: [22]

Oral thin film formulations of antifungal drugs offer a convenient and effective way to treat various fungal infections, especially for patients who may have difficulty swallowing pills or tablets. Here are some examples of antifungal drugs that are available in oral thin film formulations:

1.Miconazole: Miconazole is an antifungal medication commonly used to treat oral thrush (candidiasis) and other fungal infections. Oral thin film formulations of miconazole are designed to dissolve quickly in the mouth, allowing the drug to come into direct contact with the affected area for effective treatment.

1. Selection of Ingredients:

- Active Ingredient: Miconazole

- Film-Forming Polymer: Polyvinyl alcohol (PVA) or hydroxypropyl methylcellulose (HPMC) are commonly used film-forming polymers for topical films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant: Added for uniform spreading and wetting of the formulation.

- Penetration Enhancer:Optional, such as propylene glycol or isopropyl myristate, to enhance drug penetration into the skin.

2. Preparation of Film Formulation:

- Dissolution: Miconazole is dissolved in a suitable solvent, often a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

- Penetration Enhancer (if used):Optionally, a penetration enhancer is added to the formulation to improve drug delivery through the skin.

3. Film Casting:

- The miconazole solution is mixed with the polymer-plasticizer-surfactant mixture (and penetration enhancer, if used) to obtain a homogenous solution.

- This solution is then cast onto a suitable substrate, such as a silicone-coated release liner, using a film applicator or similar equipment. The thickness of the film is controlled by adjusting the applicator gap.

- The cast film is allowed to dry at a controlled temperature, often at room temperature or under reduced pressure, to evaporate the solvent and form a solid film.

4. Film Drying and Conditioning:

- After drying, the film is conditioned to ensure proper mechanical properties (e.g., flexibility, tensile strength).

- The film is then cut into appropriate sizes or shapes for packaging and storage.

2. Clotrimazole: [21] Similar to miconazole, clotrimazole is used to treat fungal infections such as oral thrush, vaginal yeast infections, and skin infections like athlete's foot. Oral thin films containing clotrimazole provide targeted treatment and are easy to administer, especially for oral conditions.

1. Selection of Ingredients:

- Active Ingredient: Clotrimazole

-Film-Forming Polymer: Polyvinyl alcohol (PVA) or hydroxypropyl methylcellulose (HPMC) are commonly used film-forming polymers for topical films.

- Plasticizer: Glycerin, propylene glycol, or polyethylene glycol (PEG) can be used to improve film flexibility.

- Surfactant:Added for uniform spreading and wetting of the formulation.

- Penetration Enhancer:Optional, such as propylene glycol or isopropyl myristate, to enhance drug penetration into the skin.

2. Preparation of Film Formulation

- Dissolution: Clotrimazole is dissolved in a suitable solvent, often a mixture of ethanol and water.

- Polymer Solution: A separate solution of the film-forming polymer is prepared by dissolving it in water or a water-alcohol mixture.

- Plasticizer Addition: The plasticizer is added to the polymer solution to enhance film flexibility.

- Surfactant Incorporation: Surfactant is added to the polymer-plasticizer mixture to ensure uniform spreading of the formulation on the film-forming surface.

- Penetration Enhancer (if used): Optionally, a penetration enhancer is added to the formulation to improve drug delivery through the skin.

3. Film Casting:

- The clotrimazole solution is mixed with the polymer-plasticizer-surfactant mixture (and penetration enhancer, if used) to obtain a homogenous solution.

- This solution is then cast onto a suitable substrate, such as a silicone-coated release liner, using a film applicator or similar equipment. The thickness of the film is controlled by adjusting the applicator gap.

- The cast film is allowed to dry at a controlled temperature, often at room temperature or under reduced pressure, to evaporate the solvent and form a solid film.

4. Film Drying and Conditioning:

- After drying, the film is conditioned to ensure proper mechanical properties (e.g., flexibility, tensile strength).

- The film is then cut into appropriate sizes or shapes for packaging and storage.

3.Fluconazole: Fluconazole is a broad-spectrum antifungal medication used to treat various fungal infections, including yeast infections of the mouth, throat, and esophagus (oral candidiasis). While fluconazole is more commonly available in tablet or liquid forms, oral thin film formulations may offer additional convenience for certain patients.

4. Ketoconazole: Although ketoconazole is primarily used in topical formulations for skin and scalp fungal infections, there are oral formulations available, including oral thin films, for systemic fungal infections such as oral thrush or esophageal candidiasis.

5. Itraconazole: Itraconazole is another antifungal medication used to treat a range of fungal infections, including oral and esophageal candidiasis, as well as systemic fungal infections. Oral thin film formulations of itraconazole provide an alternative to traditional capsules or tablets.

These oral thin film formulations of antifungal drugs are designed to dissolve rapidly in the mouth, ensuring effective drug delivery and absorption for the treatment of fungal infections in various parts of the body.

Evaluation parameter. (23)

> **Mechanical properties**

> Thickness

> Dryness/tack test

> Tensile strength

> Percent elongation

> Young's modulus

> Tear resistance

> Folding endurance

> Organoleptic test

> Swelling test

> Surface pH test

> Contact angle

> Transparency

> Assay/Content Uniformity

> Disintegration test

> In-vitro Dissolution test

Thickness (11)

As the thickness of film is directly concern with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital Vernier Calipers at different strategic locations.

Dryness test/tack tests (24)

About eight stages of film drying process have been identified and they are set-to-touch, dust-free, tack-free (surface dry), Dry-to touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat and dry print-free. Although these tests are primarily used for paint films most of the studies can be adapted intricately to evaluate pharmaceutical OFDF. The details of evaluation of these parameters can be checked elsewhere and are beyond the scope of this review. Tack is the tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with the strip. Instruments are also available for this study.

Tensile strength (24)

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

$$\text{Tensile strength} = \frac{\text{Load at breakage}}{\text{Strip thickness} \times \text{Strip Width}}$$

Percent elongation

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases30

$$\% \text{ Elongation} = \frac{\text{Increase in length} \times 100}{\text{Original length}}$$

Young's modulus [25]

Young's modulus or elastic modulus is the measure of stiffness of strip. It is represented as the ratio of applied stress over strain in the region of elastic deformation

Tear resistance [25]

Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. Basically very low rate of loading 51 mm (2 in)/min is employed and is designed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newtons (or pounds-force).

Folding endurance [25]

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.

Organoleptic evaluation [26]

For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are being used for this purpose. These in-vitro taste assessment apparatus and methodologies are well suited for high-throughput taste screening of oral pharmaceutical formulations.

Surface pH of film [26]

Surface pH of the films was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the colour of pH paper was observed and reported.

Swelling property [26]

Film swelling studies is conducted using simulated saliva solution. Each film sample is weighed and placed in a preweighed stainless steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weight of the film was determined at preset time interval until a constant weight was observed.

The degree of swelling was calculated using parameters

$\alpha = wt - wo/wo$

wt is weight of film at time

t, and wo is weight of film at time zero.

Transparency [27]

The transparency of the films can be determined using a simple UV spectrophotometer. Cut the film samples into rectangles and placed on the internal side of the spectrophotometer cell. The determine transmittance of films at 600 nm. The transparency of the films was calculated as follows:

Transparency = (logT600)/b = - €c

Where T600 is the transmittance at 600 nm and

b is the film thickness (mm) and c is concentration

Assay/ Content uniformity [27]

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85–115 percent.

Disintegration time [26]

Disintegration of orally fast dissolving films requires USP disintegration apparatus. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Disintegration time will vary depending on the formulation but typically the disintegration range from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films strips.

Dissolution test [23]

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.

CONCLUSION [28]

Recently FDF has gained popularity as dosage form and is most acceptable and accurate oral dosage form which bypass the hepatic system and show more therapeutic response. The pharmaceutical companies prefer this dosage form due to both patient compliance (especially pediatric and geriatric) as well as industrial acceptability. They combine the greater stability of a solid dosage form and the good applicability of a liquid. Oral films can name from market due to lower cost and consumer preference. This technology is a good tool for product life cycle management for increasing the patent life of existing products. OFDFs are also having great potential of delivering the medicinal agent systemically as well locally and have several advantages over many dosage forms even over the fast disintegrating tablets. This explains the extensive research actively going on this technology. So this technology is growing in fast pace challenging most of the pharmaceutical companies to develop oral films for a wide range of active pharmaceutical ingredients.

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