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INNOVATIVE FAST-DISSOLVING ORAL FILM DRUG DELIVERY SYSTEM

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ABSTRACT

Fast-dissolving films (FDFs), which take advantage of the benefits of rapid absorption and simplicity of administration, have become a promising drug delivery option. This study looks at the formulation, benefits, drawbacks, and technologies used in different preparation techniques as well as the difficulties faced during the formulation and development of FDFs. FDFs are made using five main techniques, which can be applied singly or in combination. These techniques allow for the creation of thin, quickly dissolving films that are appropriate for oral administration and provide flexibility in formulation design. However, there are several difficulties in the formulation and development of FDFs. To overcome unpleasant drug flavors, these include taste masking; maintaining stability against moisture sensitivity; achieving uniformity in drug content and dissolution profiles; resolving issues with loading complex formulations or high doses; and managing manufacturing complexities connected to specialized tools and procedures.

Keywords: Fast-dissolving oral film, Solvent casting method, Polymer.

INTRODUCTION

Fast-acting dissolving films have gained popularity as a novel form of drug delivery. They are simple to use and allow for a sudden start of the medication's effects because they dissolve under the tongue. Due to its thin membrane and high perfusion, the sublingual mucosa allows for quick drug absorption and instant bioavailability, which causes the drug's action to start quickly. First-pass effect and gastrointestinal (GI) tract degradation can be avoided because the drug is absorbed directly into the systemic circulation. Furthermore, since this system does not need to be swallowed like a traditional tablet does, it is anticipated that patient compliance will improve.[1]

One new drug delivery system for oral drug delivery, mouth dissolving films, was created using the transdermal patch's technology. The delivery method is a skinny oral strip that is applied directly to the patient's tongue or any other oral mucosal tissue. Saliva quickly hydrates the film, which then sticks to the application site. After that, it quickly dissolves and disintegrates to release the medication for oromucosal absorption, or, if the formula is changed, it will retain the fast-dissolving qualities to enable gastrointestinal absorption upon swallowing.[2]

Oral disintegrating film or strip can be defined as, "A dosage that employs a water dissolving polymer which allows the dosage form to quickly hydrate by saliva, adhere to mucosa, and disintegrates within a few seconds, dissolves and releases medication for oromucosal absorption when placed on the tongue or oral cavity." The sublingual mucosa having a thin membrane and large veins is more permeable. It gives instantaneous bioavailability of drugs due to rapid blood flow.[3]

ADVANTAGES OF MOUTH DISSOLVING FILM: [4-7]

1. When FDFs come into contact with saliva, they dissolve easily and facilitate quicker absorption of the active pharmaceutical ingredient (API) into the bloodstream, which causes the therapeutic effects to start working immediately.

2. FDFs are simple to use and don't need water to be ingested, they are especially good for elderly, pediatric, and dysphagic patients who might have trouble swallowing regular pills or capsules.

3. The API can be added to FDFs at exact doses, reducing the possibility of dose variability and guaranteeing reliable therapeutic effects.

4. Potentially higher bioavailability than with conventional oral dosage forms. The uniform dispersion of API in FDFs promotes effective absorption through the oral mucosa.

5. Patients can carry FDFs easily when traveling or on the go because they are small, discrete, and lightweight.

6. In the oral cavity, a larger surface area encourages quicker dissolution and disintegration.

7. Compared to ODTs, oral films are less fragile because they are more flexible. This makes handling and storing by consumers and transportation easier.

8. No choking hazard.

9. Drugs that are not crushed or injected by patients can be administered to patients with the aid of a mouth-dissolving film drug delivery system.

10. The dosage form can be taken whenever and wherever it is convenient for the individual.

11. Compared to other areas of the skin, the oral cavity's striated squamous epithelia, thin membranes, and intricate capillary network allow for 4 – 4000 times higher absorption.

12. Because the medication enters the systemic circulation directly, it avoids the first-pass metabolism, increasing its bioavailability and enabling dose reductions that may lessen the molecules' side effects.

13. Leave little to no trace in the mouth.

DISADVANTAGES OF ORALLY DISINTEGRATING FILMS: [8-10]

1. FDFs are thin and water-soluble, they are usually sensitive to moisture. This can cause problems with stability, such as physical degradation, loss of potency, and changes in the kinetics of drug release over time.
2. Some active pharmaceutical ingredients (APIs) have an unpleasant taste or bitterness that can be difficult to mask in full-dose formulations (FDFs), which could jeopardize patient acceptability and adherence.
3. FDFs' limited ability to load APIs may limit their use for medications requiring complicated formulations or high dosages.
4. Producing FDFs can be expensive and time-consuming due to the technical difficulties and potential need for specialized tools and knowledge.

5. Different FDF formulations and batches may have dissimilar dissolution profiles, which can make it difficult to achieve consistent drug release and bioavailability and call for stringent quality control procedures.
6. Due to their temperature, special packaging is needed and susceptible to moisture.

Ideal Characteristics of a Suitable Drug Candidate.[11]

- The drug should have a pleasant taste.
- The drug to be incorporated should have a low dose of up to 40 mg.
- The drugs with smaller and moderate molecular weight are preferable.
- The drug should have good stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of the oral cavity.
- It should have the ability to permeate oral mucosal tissue.

COMPONENTS OF AN ORAL FILM FORMATION:

A typical composition contains the following

- Drug
- Water soluble polymer
- Plasticizers
- Sweetener
- Fillers
- colors
- Flavors

Active pharmaceutical ingredients:

Many drug classes, including antihistamines, antidiarrheal, vasodilators, antidepressants, anti-emetic, anti-asthmatic, and others, can be found in ODFs. Moreover, flavors in ODFs can be concealed by adding dimenhydrinate. ODFs frequently contain drugs such as salbutamol sulfate, rizatriptan benzoate, verapamil, ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc. Oral fast-dissolving films can potentially deliver a range of APIs Oral Fast Dissolving Film (OFDF). The most suitable candidates for incorporation into ODFs are small dose molecules. There is potential for this

technology to deliver multiple APIs. A micronized API is always advantageous since it improves the uniformity and dissolution of the ODFs and the film's consistency. Additionally, an ODF of the anti-emetic drug prochlorperazine was produced using microcrystalline cellulose and additional film-forming polymers.[12]

Water soluble polymer:

Polymers may be utilized separately or in combination to produce the necessary film qualities. Since water-soluble polymers give films good mechanical properties, a fast rate of disintegration, and a pleasant mouthfeel, they are commonly used as film formers. The strength of the film is determined by the type and amount of polymers used in the formulation. Increasing the molecular weight of the polymer film bases slows down the rate of polymer disintegration. HPMC E3, E5, E15, cellulose ether, polyvinyl alcohol, polysaccharides, polyvinylpyrrolidone K-90, polyethylene glycols, pullulan, gelatin, carboxy methyl cellulose, hydroxy propyl methyl cellulose E-3 and K-3, methylcellulose A-3, A-6, and A-15, pectin, sodium alginate, hydroxyl propyl cellulose, maltodextrins, and eudragit are a few of the water-soluble polymers used as film formers.[13]

Plasticizers:

The mechanical properties of films are significantly impacted by formulation factors, such as plasticizers. Plasticizer addition has also improved the films' mechanical properties, including elongation and tensile strength.[14] Flexibility is the most important factor to consider when making an oral film. The pliability of the film is determined by the selection of plasticizer. Changes in their concentration may affect these characteristics. Plasticizers that are commonly used include triacetin, glycerol, di-butyl phthalate, and polyethylene glycol.[15]

Surfactants:

Surfactants play a crucial role in film dissolution by acting as a dispersing, wetting, and solubilizing agent, thereby releasing the integrated medication faster. Surfactants that are frequently used include benzethonium chloride, tweens, sodium lauryl sulfate, and benzalkonium chloride. Plaxamer 407 is widely used due to its advantages.[16,17]

Flavors:

The sickening or bitter taste of integrated drugs is disguised by flavors. The kind of drug that will be included in the formulation determines the flavor choice. Its type and potency affect taste intensity. You can use any flavor that has been approved by the US FDA, like vanilla or sweet orange flavor, or even mint, sour, or sweet. According to one study, the flavors of licorice, mint, and a sucralose mixture successfully mask the bitterness.[18]

Sweetening agents:

Sweeteners are now a common ingredient in both food and medicine products that are meant to dissolve or disintegrate in the mouth. When it comes to the pediatric population, the formulation's sweet taste is more crucial.[19] The purpose of sweetening agents is to break down or dissolve in the mouth. Mannitol and sorbitol are used to make ODFs. Compared to sucrose, sucralose was 600–1000 times sweeter. Aspartame

and saccharin sodium are likely 200 and 300–500 times sweeter than sucrose, respectively. It was also observed that sweeteners and flavors had minimal effect on the film's pliability.

(a) Natural sweeteners that dissolve in water, such as xylose, ribose, glucose, sucrose, maltose, and stevioside.

(b) Artificial sweeteners that dissolve in water, such as cyclamate salts, acesulfame-K, sodium or calcium saccharin salts, etc.

(c) Dipeptide-based sweetener: aspartame.[20]

Saliva-stimulating agent:

To speed up the breakdown of the fast-dissolving strip formulations, saliva stimulation agents are used to increase the rate of saliva production. Salivary stimulants are generally acidic. Saliva-stimulating agents that are commonly used include tartaric acid, ascorbic acid, lactic acid, malic acid, and citric acid. The salivary flow rate increases and salivary enzyme production, including amylase, is stimulated by citric acid. Citric acid accelerates the breakdown of the film matrix and facilitates the release of active pharmaceutical ingredients by encouraging the hydration and swelling of film-forming polymers.[21]

Coloring agent:

Pigments are used to make coloring agents. Titanium dioxide is the colorant most frequently used in ODFs and other pharmaceutical preparations. In addition to titanium dioxide, a broad range of colors are available, including FD and C, natural, and custom Pantone-matched colors.[22]

Table 1: Percentage of components in oral thin film

Ingredients detail	Quantity % (w/w)	Example
Active pharmaceutical ingredients	1-25%	Antiemetic, Antiallergic, etc.,
Polymer	40-50%	HPMC E5, E3, pectin, gelatin, etc.,
Plasticizer	0-20%	Glycerol, polyethylene glycol, etc.,
Saliva stimulating agent	2-6%	Citric acid, malic acid, lactic acid
Surfactant	Q. S	Sodium lauryl sulfate, tween, etc.,
Flavoring agent	2-5%	FDA approved flavors
Sweetener	2-10%	Saccharin, aspartame, etc.,

METHOD OF PREPARATION:

Five methods are used alone or in combination with the following process for the manufacture of the dissolving oral films

i) Solvent casting method

ii) Semisolid casting

iii) Hot melt extrusion

iv) Solid dispersion extrusion

v) Rolling

Solvent casting method:

Solvent casting is among the oldest methods of producing ODFs. Drugs that need to be taken in a dosage form that is both thermostable and thermolabile are prepared using this hydrous method.[23] A clear, viscous solution is formed by dissolving the water-soluble film-forming polymer. After dissolving in a different solvent, the active medication and the other excipients are added to the bulk viscous solution. To create a uniformly thick film, any air trapped in the viscous solution during mixing is evacuated using a vacuum. After the mixture is transferred to plates, the solvent is allowed to evaporate completely in an oven, and the resulting films are then divided into the desired shapes. In large-scale production, specialized tools like rollers are needed to pour the drug and polymer mixed solution onto an inert base, which is typically Teflon, glass, or plastic plates. The film's thickness is determined by the gap or clearance between the roller and the base. The solvent is eliminated from the film as it dries, assisting in the creation of the final product. [24,25]

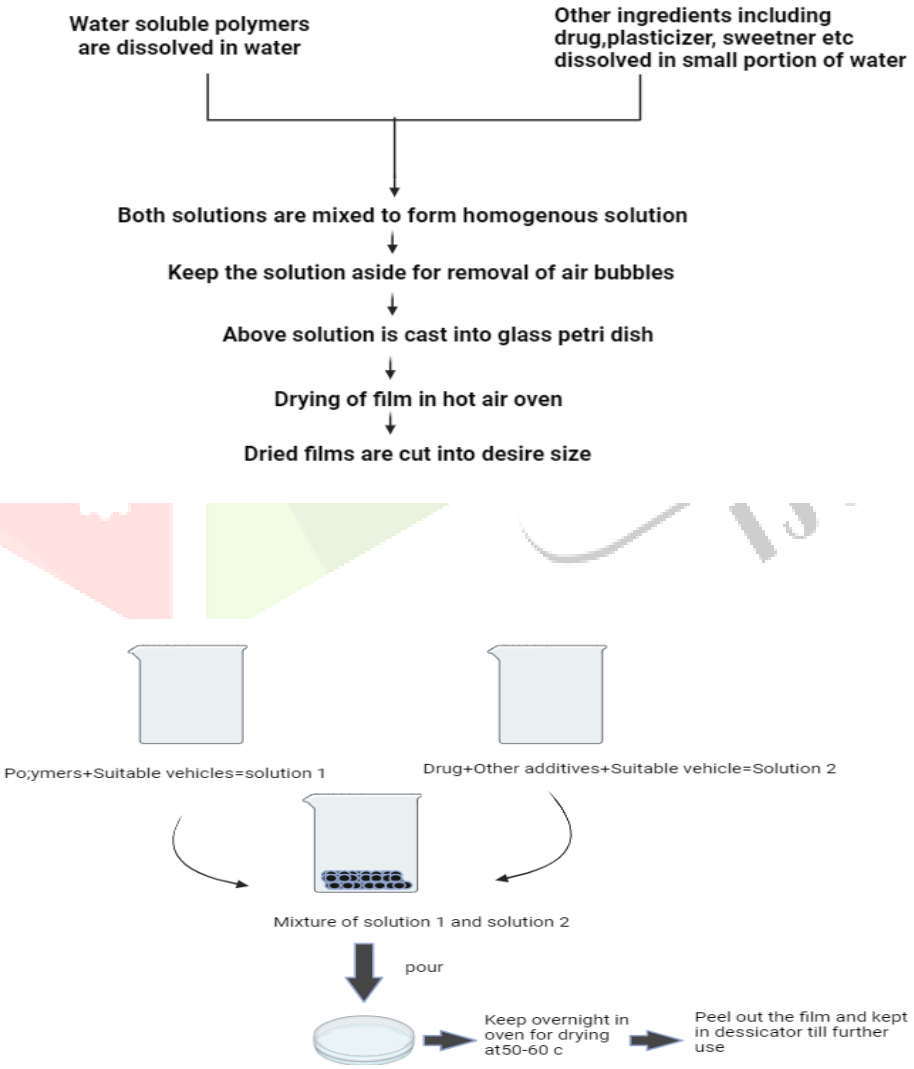

Figure 1: Solvent Casting Technique

Semisolid casting:

This method begins with the preparation of a water-soluble film-forming polymer solution. The resulting solution is then mixed with an acid-insoluble polymer solution (such as cellulose acetate phthalate)

made with sodium or ammonium hydroxide. The acid-insoluble polymer to film-forming polymer ratio ought to be 1:4. A gel mass is produced when the appropriate quantity of plasticizer is added. Eventually, the gel mass is cast into the films or ribbons using heat-controlled drums.[26]

Hot melt extrusion:

HME technology has proven to be a dependable means of developing a range of drug delivery systems, and the pharmaceutical sector has also found application for it. To produce a uniform density and form product, raw materials are forced through a heated barrel at a high, controlled temperature and pressure during the extrusion process. Although Breitenbach was the first to introduce the melt extrusion process in pharmaceutical manufacturing operations, Follonier, and his colleagues were the first to examine the use of hot-melt technology to produce sustained-release polymer-based pellets of various freely soluble drugs. HME involves the processes of compaction and granular mix conversion into a homogenous product. Polymers are formed into products of different sizes and shapes, like plastic sheets, pipes, and bags, by forcing polymeric components and active substances, like any additives or plasticizers, through an orifice or die under controlled temperature, pressure, feeding rate, and screw speed. Nonetheless, the following categories can be used to summarize the theoretical framework (Figure 2) for understanding the melt extrusion process: HME compaction as a whole.[27]

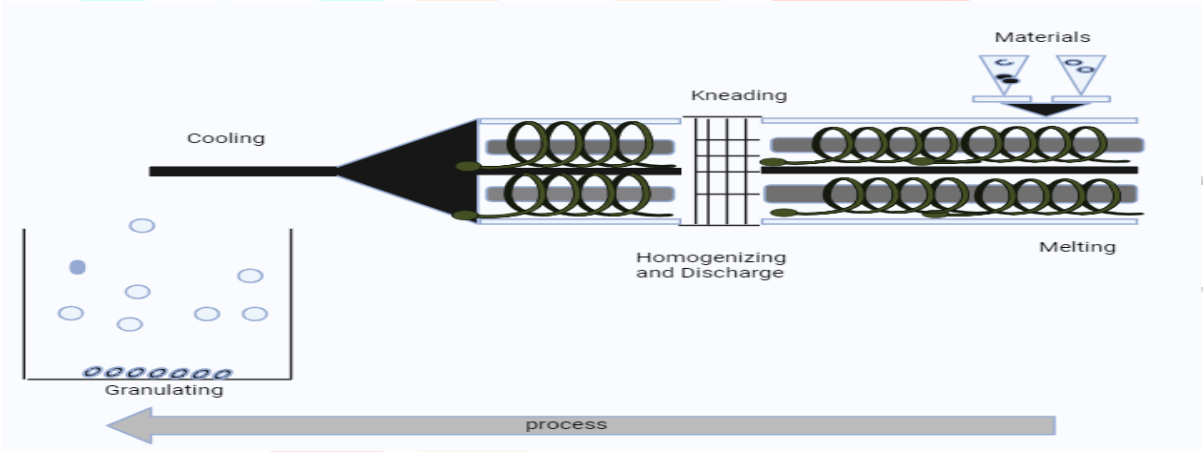

Figure 2: Hot melt extrusion method

Solid dispersion method:

In the presence of amorphous hydrophilic polymers, one or more active ingredients are dispersed in a solid state within an inert carrier using this technique. API is dissolved in the proper solvent to form a solution. Without draining the liquid solvent, the solution is added to a suitable polymer (PEG) melt at temperatures lower than 70 °C. In the end, dies are used to form solid dispersions into films.[28]

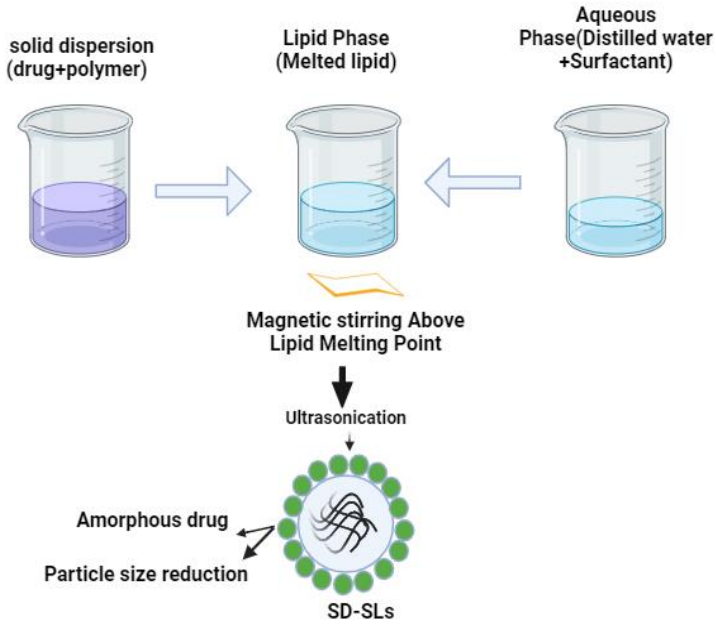

Figure 3: Solid Dispersion Method

Spray Coating:

This method involves misting a substrate with a polymer suspension or solution along with other ingredients. The substrate could be a pre-formed film or a mold. After spraying, the solvent is extracted from the coated substrate by drying it, leaving behind a thin layer.[29]

Rolling technique:

This method forms the film by first preparing a pre-mix, adding an active, and then forming the film. To prepare the pre-mix, incorporate additional additives, polar solvents, film-forming polymers, and medications as needed. Pour pre-mix into the master batch feed tank. It can be fed to either the first mixer or both the first and second mixers using the first metering pump and control valve. Add the required amount of medication to the mixer of your choice. Combine the medication with the master batch pre-mix to form a homogenous matrix. The second metering pump then fills the pan with a preset volume of homogenous matrix. Eventually, the support roller removes the film that has formed on the substrate. Next, regulated bottom drying is applied to finish drying and wet the film.[30]

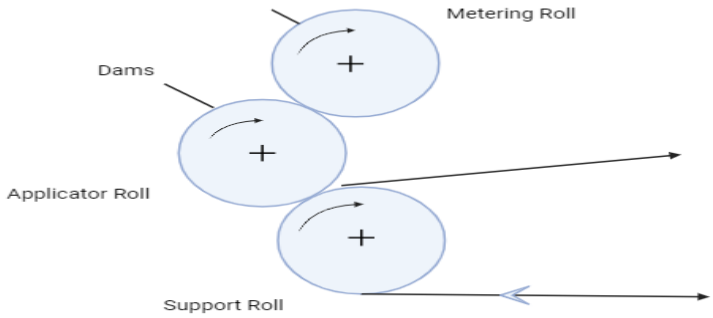

Figure 4: Rolling Technique

Printing:

An innovative method of creating film preparations is to print APIs onto a base film layer (obtained, say, from a previous solvent casting procedure). Thus, the drug load can be changed by printing additional layers of ink that have been loaded with API. The most effective printing technique was flexographic printing. Printed films are advantageous to industrial manufacturing because they use only APIs in the printing process. The pre-manufacturing of film bases is exempt from the same safety protection regulations as operations involving extremely potent drug substances or APIs with unknown toxicity.[31]

TECHNOLOGIES FOR FAST-DISSOLVING FILMS:

The technology used in formulating ODF is listed below

- Soluleaves.
- Wafertab.
- Micap.
- Foam burst.
- Xgel

SOLULEAVES:

Using this technology, the film is made so that when it comes into contact with saliva, the active ingredients will be released. A variety of oral delivery films with active ingredients, colors, and flavors can be made using this technology. When soluleave films come into contact with saliva, they can be made to dissolve quickly, releasing the flavors and active ingredients. Because of this feature, edible films are a great way to deliver a wide variety of products that need to be released quickly in the mouth. When it comes to pharmaceutical applications, this mode of administration is particularly helpful for young patients or the elderly who might have trouble swallowing regular tablets or capsules. The delivery system can be applied to nutritional product delivery as well as the therapeutic areas of cough/cold, gastrointestinal, and pain. Additionally, soluleave films can be made to stick to mucous membranes and release the active ingredient gradually over 15 minutes.[32]

WAFERTAB

Wafertab is an exceptional, cutting-edge, and extremely stable edible film dosage form. Wafertab is a patented delivery system that creates drug-loaded thin films for oral or topical use using a special technique. Wafertab is a medication delivery system that combines ingestible film strips with pharmaceutical active ingredients. The active pharmaceutical ingredients dissolve and release quickly when the strip comes into contact with saliva in the mouth. Choring the Wafertab film strip for even better taste masking is also possible. The active component is incorporated into the fused body. The film is prepared in a range of sizes and forms, making it a perfect way to administer medications that need to be released quickly as well as for patients who have trouble swallowing.[33]

MICAP:

Micap used to combine its expertise in microencapsulation technology with the Bio Progress water-soluble films. The developments will be aimed at providing new delivery mechanisms for smoking cessation products (SCPs).[34]

FOAMBURST:

A recent patent, Foamburst, relates to foamed film capsules. During the manufacturing process, gas is blown into the film to give it a honeycomb structure. The film's voids can be gas-filled, empty, or packed with different substances to deliver active medications or create particular taste-burst effects. The capsules dissolve quickly due to the light honeycomb structure, leaving a melt-in-your-mouth feeling.

XGEL:

With its non-animal origin, religious approval, and vegetarian suitability, Xgel film offers special product benefits for pharmaceutical and healthcare products. It is also free of genetically modified organisms (GMOs), and its continuous production processing offers a competitive and cost-effective manufacturing platform. Xgel film can incorporate active pharmaceutical ingredients and can be taste-masked, colored, layered, and have enteric properties. Any oral dosage form can be encapsulated in XgelTM film systems, which are soluble in both hot and cold water. A variety of distinct water-soluble polymers that have been specially tailored for the intended use of Xgel film make up this widely recognized and widely accepted safe ingredient (GRAS). The pharmaceutical industry was now able to take advantage of the revolutionary changes in product offerings and manufacturing methods brought about by BioProgress technology. Xgel film may improve product stability. The films can be printed or colored during the manufacturing process for branding and coding, which is a helpful way to improve product identification. They have also been developed for non-ingestible uses, like ostomy pouches, cosmetics, sanitary products, and medical equipment.[35]

CHALLENGES IN FORMULATION DEVELOPMENT OF FAST-DISSOLVING ORAL FILMS:

The insolubility of drug:

Solubility plays a rate-limiting parameter to get the desired concentration of drug of orally administered formulation in the systemic circulation. The problem of solubility is a main challenge for the

formulation of oral film of BCS class II drugs having low solubility and high permeability. It is the most important preference of a drug candidate to be selected for formulation of oral film. In the case of oral film, solubility plays an important role in two stages i.e. solubility of the drug in the solvent during formulation and solubility or dissolution of the drug in saliva after putting the film in the oral cavity. So, the solubility behavior of the drug remains one of the most challenging aspects in the formulation of oral film.[36]

Taste masking of the bitter and obnoxious drug:

Taste is an important parameter in the case of fast-dissolving oral film. Oral film has to remain in contact with oral mucosa until it completely dissolves in saliva in the oral cavity. For this, the taste of bitter drugs should be masked. So, taste masking becomes a prerequisite for bitter drugs used in the fast-dissolving oral film to improve patient compliance, especially in the pediatric and geriatric populations.

Taste masking techniques:

Addition of flavors and sweeteners, coating, microencapsulation, ion exchange resin, inclusion complexes, granulation, adsorption, prodrug approach, bitterness inhibitors, multiple emulsion, and gel formation.[37]

Reduction in drying time of film:

Drying time plays an important role in oral film formulation and also in the case of the rate of production of oral film in industries. Generally, a hot air oven is not used for drying an oral film of thermo-labile drugs. So, the oral film is dried at room temperature. But, it takes more time to dry (about one day).

Reduction in drying time can be achieved in the following ways:

By increasing in temperature without developing cracks to film. Selection of ingredients in the film especially type and concentration of polymer and plasticizer i.e. addition of those polymers and plasticizers which form less viscous solution so that drying time will be minimal and prevention of the use of those polymers and plasticizers which form highly viscous solution so that drying time will be increased. The use of suitable dryers can minimize drying time. An increase in the area of film will expose a large surface to a drying environment and further will reduce drying time.[38]

Co-administration of drugs:

The use of more than one drug i.e. Co-administration of drugs is a very difficult task in oral film formulation. Because it may affect disintegration time as well as the dissolution rate of the formulation. Combination of more than one drug can be possible in two ways

- Multilayered oral film
- Co-adjacent oral film

Stability of film against humidity and temperature:

Fast-dissolving oral film consists of about 45% of polymer which is hydrophilic. In the humid atmosphere, the film will absorb water and get liquefied due to the dissolution of the film in water. So, the stability of film against humidity is a very difficult and challenging task.[39]

Packing:

In the pharmaceutical industry, the package must be selected adequately to preserve the integrity of the product. Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast-dissolving dosage forms. A variety of packaging options are available for fast-dissolving oral films.[47] The stability of oral films is affected by moisture and temperature, the selection of an appropriate primary packaging container is an important decision for manufacturers of oral films. The packaging container should provide sufficient mechanical protection to the film from external factors such as mechanical abrasions, impacts, light, temperature, and humidity either during storage or transportation. Aluminum foil, paper, or plastic pouches or combinations of them have been used for packing oral films.[40]

Dose uniformity:

The film which is to be made in a container has to be cut into a desired area containing the required dose of the drug. So, to get a uniform dose in all films that cut into the desired area is a challenging task.[41]

Table 2: Examples of marketed oral thin film formulation.

Product	**Manufacturer**	**API**	**Use**
Listerine	Pfizer	Cool mint	Mouth fresheners
Triaminic	Novartis	Dextromethorphan HBr	Cough suppressants
Suppress®	InnoZen.Inc	Menthol	Mouth fresheners
Chloraseptic	Prestige	Benzocaine Menthol	Local anesthetic
Gas-X	Novartis	Simethicone	Anti-flatuating
Theraflu	Novartis	Dextromethorphan HBr	Anti-allergic
Setofilm	Bioalliance Pharma	Ondansetron	Prevention of Nausea and Vomiting
Zuplenz®	MonoSol Rx	Ondansetron	Prevention of Nausea and Vomiting
Donepezil Rapid film	Labtec	Donepezil	Alzheimer's diseases
Klonopin Wafer	Solvay Pharmaceuticals	Clonazepam	Treatment of Anxiety
Thin film strip	Novartis	Phenylephrine HCL/Diphenylhydramine HCL	Cough suppressants

Orajel	Del	Menthol/Pectin	Mouth fresheners

EVALUATION OF FILM

Visual inspection

Properties such as homogeneity, color, transparency, smell, and surface of the oral films were evaluated for all the prepared formulas visually. [42,43]

Weight variation

Take the 20 films and individually weigh each film. The mean and standard deviation were computed.[44]

Thickness

Randomly 10 films were selected and thickness was measured using a digital screw gauge. The individual film was placed between two anvils of the screw gauge and the sliding knob was rotated until the film was fitted. The digital reading displayed was noted.[45]

Surface pH Determination:

A glass electrode was utilized to determine the surface pH. Water was used to moisten the oral film just a little. After exposing the film to distilled water (pH 6.8±0.1) the film was allowed to swell. The electrode was then placed against the patch's surface and left to equilibrate for one minute. To look into any potential side effects in the oral cavity, the surface pH of the film was measured. A conscious effort was made to maintain the film surface pH near neutral because an acidic or alkaline pH is certain to irritate the buccal mucosa.[46]

Folding endurance:

The folding endurance was measured manually for the prepared films. A strip of film was cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without breaking gave the value of folding endurance.[47]

Tensile strength

An analog tensile tester was used to measure the tensile strength. For tensile testing, films devoid of air bubbles or physical flaws were chosen. The upper clamp of the tensile tester was moved to adjust the distance between the two clamps to 3 cm. The top clamp pulled the strips at 100 mm per minute during the measurement process, and the force applied was recorded until the film broke. The film samples that broke at the clamping point rather than in the space between the clamps weren't incorporated into the computation. Results in triplicate for every movie were taken into account. The following formula can be used to calculate tensile strength from the applied load at rupture as the mean of three measurements and the cross-sectional area of the fractured film.[48]

$$\text{Tensile strength } (N/mm^2) = \frac{\text{breaking force (n)}}{\text{Cross-sectional area of the sample } (mm^2)}$$

Disintegration time:

A disintegration test apparatus was used to measure the disintegration time. An area of two square inches of film was inserted into the basket and adjusted so that it moved up and down thirty times per minute. The amount of time the film required to completely disappear above the gauze was observed.[49]

In vitro dissolution

Dissolution test equipment was used to investigate drug release from OFDFs. The intended formulation of OFDFs was inserted into the dissolution apparatus vessels. At intervals of 5, 10, 15, 20, 25, 30, 40, and 60 minutes, samples were taken and then replenished with an equal volume of the blank solution. The samples underwent prompt filtration, followed by an analysis to determine the drug concentration and the percentage (%) of the drug that had been released or dissolved. Three films were subjected to release studies, and mean values were obtained.[50]

Moisture loss

To verify the integrity of films in a dry state, a percentage moisture loss test was also conducted. Three films with a diameter of one centimeter were cut out, precisely weighed, and stored in desiccators that held fused anhydrous calcium chloride. Following 72 hours, the films were taken out and weighed. Three films' average percentage moisture loss was determined.[51]

$$\text{Moisture loss} = \frac{(\text{Initial weight} - \text{Final weight})}{\text{initial weight}} \times 100$$

Percentage elongation

Using the following formulas, the percentage elongation was computed by measuring the film's length increase following the measurement of its tensile strength.[52]

$$\text{Percentage Elongation} = \frac{[L - L0]}{L0} \times 100$$

Where L = Final length

L0 = initial length.

Transparency

The transparency of the films can be determined using a simple UV spectrophotometer. The film samples are cut into rectangles and placed on the internal side of the spectrophotometer cell.[53] This determines the transmittance of films. The transparency of the film is calculated as:

$$\text{Transparency} = \frac{(\log T600)}{b} = -\varepsilon c$$

Where T600 is the transmittance at 600 nm, b is the film thickness (mm) and c is concentration.

Swelling property

Research studies on film swelling are carried out with a simulated saliva solution. A stainless steel wire mesh that has been previously weighed is used to hold each weighed film sample. In a plastic container, 15ml of medium is added to the film sample mesh. The weight of the film was observed to increase at predetermined intervals until a constant weight was reached. The formula for calculating the degree of

swelling was wt-w0/wo, where wt is the weight of the film at time t and wo is the weight of the film at time zero.[54]

Dryness and tackiness

Tack refers to how firmly the strip sticks to an object, such as a piece of paper pressed against the strip. The film drying process has been divided into eight stages: dry-to-touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat, dry print-free, dust-free, and dry-to-touch. There are several tools available to carry out this test. none.[55]

Stickiness determination

According to the texture method typically used to measure the tack of pressure-sensitive adhesives, the stickiness of the film was assessed. A flat dish plate was covered with a 2.54 cm2 sample film. On top of the sample, a 2.04 kg cylinder with an 8 mm diameter hole was positioned, making sure the film was centered around the cylinder hole. After that, the cylinder and sample were clamped into the testing position of a dynamometer I) that was software-controlled and had a 5 DaN cell. After lowering the stainless steel probe into the cylinder, the sample was subjected to a constant force of 0.05 N for 5 s. Afterward, the probe was removed at a constant speed of 100 mm/min. The debonding velocity was set at 5 mm/s.[56]

Uniformity of drug content

100 ml of distilled water was placed in a graduated flask along with a fast-dissolving film. In a mechanical shaker, the flask was shaken for four hours. Following the filtering of the solution and appropriate dilutions with distilled water, the drug content was computed by measuring the absorbance value with the placebo film (film without drug) solution serving as a blank.[57]

Drug Excipient Compatibility studies

Differential Scanning Colorimetry (DSC) and Fourier Transmission Infrared Spectroscopy (FTIR) were the methods used to conduct the drug excipient compatibility studies.

Fourier Transform Infrared Spectroscopy (FTIR)

A Fourier transform infrared spectrophotometer was used to record the FTIR spectra of pure drugs, physical mixtures, and optimized formulations. Using KBr (spectroscopic grade) disks and a hydraulic pellet press operating at seven to ten tons of pressure, the samples' infrared spectra were prepared.[58]

Stability studies

Stability studies were carried out for 45 days at 2–8°C (45% RH) and 25–30°C (60% RH). The films were observed for physical changes, the percentage of drug content, and the percentage of drug release. Fast-dissolving films of lisinopril were found to be physically and chemically stable and showed no significant change in terms of physical characteristics, the percentage of drug content, and the percentage of drug release.[59]

CONCLUSION

Fast-dissolving films have shown great promise as a drug delivery method that can improve therapeutic outcomes and patient compliance. This oral dosage form is particularly useful for achieving an immediate onset effect and in emergencies. Better therapeutic results and a quicker onset of action may result from their capacity to dissolve rapidly in the oral cavity and directly transfer medication into the bloodstream. Therefore, it can be concluded that fast-dissolving films with superior patient compliance and numerous benefits have cutting-edge and forward-thinking prospects. Overall, oral fast-dissolving films hold great promise for the future of pharmaceutical delivery, offering a convenient, effective, and patient-friendly option for medication administration.

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