



Fast Dissolving Oral Thin Film: An Innovative Drug Delivery System

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ABSTRACT

Compared to traditional dose forms, Fast Dissolving Films offer a number of benefits. Because of their enhanced dissolution and quick disintegration, they are now regarded as one of the most significant drug delivery systems. They bridge the gap between the two concepts by combining the advantages of both solid and liquid dosage forms into a sophisticated, stable, and efficient delivery system. They do this by combining the better stability of a solid dosage form with the good application of a liquid. Therefore, they are crucial in emergency situations like allergic responses and asthma attacks when prompt action is required. They bridge the gap between the two concepts by combining the advantages of both solid and liquid dosage forms into a sophisticated, stable, and efficient delivery system. They do this by combining the better stability of a solid dosage form with the good application of a liquid. Therefore, they are crucial in emergency situations like allergic responses and asthma attacks when prompt action is required. As a result, the majority of pharmaceutical companies are finding it difficult to create oral films for a variety of active pharmaceutical ingredients due to the rapid growth of this technology.

Key Words: Fast Dissolving Films, Traditional Dose Forms, Drug Delivery.

Introduction

Patients tend to choose oral dosing over other delivery methods. Oral drug delivery research has led to the creation of new dosage forms, including fast-dissolving oral thin films and fast-disintegrating versions of traditional tablets and capsules (OTF). As an alternative to traditional dosage forms, fast dissolving drug delivery methods were initially developed in the late 1970s. "a solid dosage form containing therapeutic chemicals that disintegrates fast, generally within a couple of seconds when put onto the tongue," is how the Centre for Drug Evaluation and Research (CDER) describes ODTs. U.S. Food and Drug Administration (FDA) guidelines define OTFs as "a thin, flexible, non-friable polymeric film strip containing one or more dispersed active pharmaceutical ingredients that is intended to be placed on the tongue for rapid disintegration or dissolution in the saliva prior to swallowing for delivery into the gastrointestinal tract" [1]. Pharmaceutical OTFs are maturing into established market niches. In 2010, Zuplenz (Ondansetron hydrochloride- 4 mg, 8 mg) became the first OTF available via prescription. Quickly after that, Suboxone was given a second green light (Buprenorphine and Naloxone). According to the data, 80% of patients would rather take a pill that dissolves in their mouth than a pill that stays in their mouth [2]. These characteristics, together with the benefits of convenience and compliance, have been (and will continue to be) the driving force behind the expansion of ODT and OTF pharmaceuticals. Designed to dissolve quickly in the mouth, oral thin films are supplied as a flat sheet directly into the mouth. This is a helpful dose form since the drug's effects may be felt very instantly upon contact with the oral mucosa. According to the European Pharmacopoeia, these tablets are "orodisperse" since they are meant to be dispersed quickly in the mouth before being swallowed. Fast dissolving films are a well-proven and well approved technique for the systemic medication administration of active pharmaceutical ingredients (API) [3]. Oral thin films are produced as a large sheet, which is then sliced into smaller pieces that make up a single dose unit before being packaged. When a quick, targeted effect is needed in the mouth, such when treating a toothache, an oral ulcer, a cold sore, or teething, a thin film may be placed directly within the mouth. You may put just about any medicine in this dose form, including those for coughing, asthma, allergies, ED, sore throat, GI issues, nausea, pain, and the central nervous system. Oral thin films may

also be used to make coffee strips, multivitamins, sleeping pills, snoring remedies, etc. [4]. History of film formulation Researchers nowadays always seek for new approaches to creating cutting-edge, modern dosage designs that are not only foolproof and highly effective, but also economical and straightforward to create. Patient-friendly dosage forms are in high demand. Medicines that may be taken by mouth are generally regarded as the best and most sought after among the several common dose types [5]. While the introduction of oral quick dissolving tablets in the 19th century was a step in the right direction toward addressing the problems associated with liquid formulations, the drawbacks of the tablet form paved the way for the development of an entirely new technology: mouth dissolving films. Though rapid dissolving oral films have been in the spotlight recently, the vast majority of fast-dissolving pharmaceutical medications come in tablet form and dissolve within minutes. Fast-dissolving films placed on the tongue dissolve instantly without the need for water or chewing. Figure 1 depicts the original concept for this groundbreaking medication delivery system, which was developed in the 1970s.

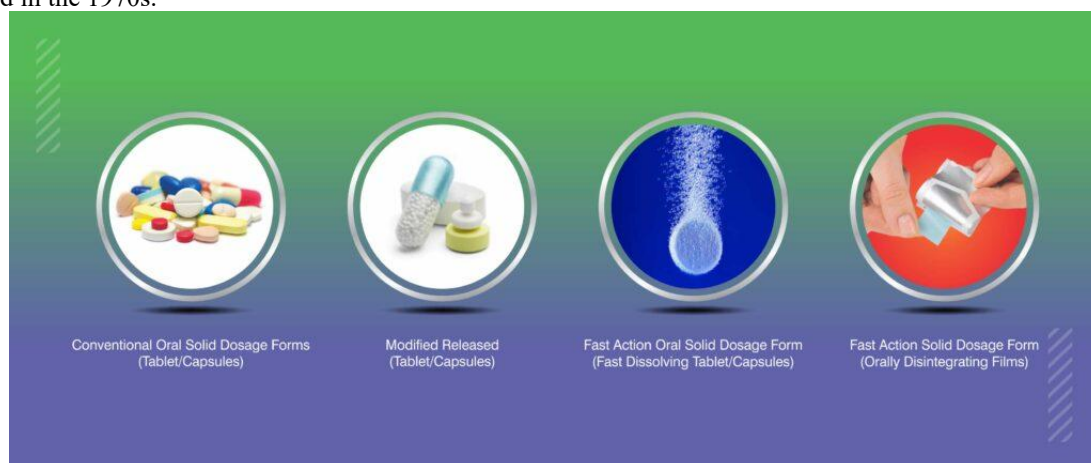


Fig.1 Progress in oral Dosage Form

Merits

- Several benefits set oral quick dissolving thin films apart from other oral preparations
- Large areas of exposed surface aid in both disintegration and breakdown [7].
- Unlike orodispersible tablets, rapid dissolving thin films do not need special packaging and may be stored and transported with ease. Each film strip assures accurate dose administration [9, 10].
- The drug-containing film rapidly dissolves in the mouth, and it doesn't even need to be mixed with water before administration [11].
- Any special practice of administration is not required in the case of oral thin films [12].
- The dosage form provides the best systemic absorption to drugs that experience the first effect [13], hence improve their bioavailability [14] therefore in this way promotes rapid therapeutic action [15].
- Due to the escape of first-pass metabolism, this delivery system can reduce dose and side effects [16].
- This dosage form is extremely patient compliant as it is non-invasive [17,18], suitable for paediatrics and geriatrics [19] uncooperative and unconscious patients with different illnesses [20], for cardiovascular patients, for people with respiratory ailments and chemotherapy patients, patients having swallowing problems [21]
- It is exceptionally useful in cases where a local action and an ultra-rapid drug onset are needed [22].
- It delivers a pleasant mouth feel and also valued for masking the taste, moreover, well favorable for travelling patients [23].
- The oral bioavailability of drugs also gets enhanced in this dosage form because of lesser drug decomposition. [24]
- Fast dissolving oral thin film has longer and improvised stability. It has the advantage of both the solid and liquid dosage forms concerning solubility and bioavailability respectively. The unique packaging of OFDTF enhances product stability.
- There is an immediate release of one or more drug ingredients, as these films disintegrate within seconds once taken orally [25].
- The dosage form is technically advantageous since its excipients include sugars and belong to the GRAS category [25].
- Business benefits concerning product differentiation and promotion, as well as patent extension, are also provided. An unprecedented business structure is not required for industry [26] Clinical Advantages [27, 28, 29].
- As oral thin films are given by oral route their administration is easy as it employs the oral route.
- In pediatric and geriatric patients the risk of choking or suffocation is reduced.
- Oral Thin Films are a better alternative for patients with nausea.
- Oral Thin Films do not required to be swallowed with water.

Market Advantages [30]

- This novel drug delivery system presents pharmaceutical companies with patents on the verge of expiration to increase the revenue cycles.
- OTFs dissuade the misuse, tampering and abuse related to some prescribed drugs because the film is loaded with an exact amount of drug.
- The oral thin films market is currently in its embryonic stages and limited only to certain over the counter drugs available within the American, Japanese and EU Markets. Thus, researches and corporations have a great scope in formulating drugs that haven't been previously formulated into OTFs and developing newer and cheaper technologies.
- In India, per Indian demographics for 2017 roughly 13.39% of the population is senior citizens while 45.7% are children. Thus, Indian investors have a good consumer range and this technology is inchoate in our country Demerits [31,32].
- Special moisture-resistant packaging is required as fast dissolving thin films are sensitive to moisture, and this particular packing is costly.
- From the technical aspect, dose uniformity in the strip is a serious risk.
- A significant manufacturing difficulty that confronts manufactures is that the drying time required for the OTFs. Since thermo labile drugs prohibit the utilization of hot air ovens and high temperatures, it takes each day for the films to dry at room temperature thereby reducing the production rate.
- As the films are highly hygroscopic and tend to lose stability in environments having high relative humidity.
- Drugs which are unstable at the buccal pH or irritate the mouth mucosa cannot be formulated into thin films.
- The co-administration of multiple drugs remains to be a challenge because the dissolution time is affected.
- Drug with small dose requirement can only be administered.
- Taste masking is required for bitter taste drugs.
- Special packaging is required for OTFs, so as to protect it from water. Limitations [33].
- Drugs with unpleasant taste must be avoided or inert substances needed to mask the taste of bitter API.
- There is a limitation in administration or incorporation of higher doses.
- Mucosal irritants shouldn't be administered following this route.
- Saliva contains a proteolytic enzyme, inhibition of which is required in case of protein-based drugs, with the help of enzyme inhibitors. Absolute characteristics

Fast dissolving films must possess the following properties: [34]

- Adequate taste/ must not be bitter.
- A pleasant sensation in the mouth.
- Having lesser friability and appropriate mechanical capacity to combat postproduction handling.
- Good stability in natural conditions.
- The drug must not have a higher dose.
- No or minimum residue should be left in the mouth
- It should dissolve rapidly and release drug content instantly in the oral cavity.
- It should possess compatibility with other ingredients
- The drugs having smaller or moderate molecular weight are preferred.
- The drugs having better stability and solubility in water & saliva are selected.
- It should not completely ionize at the pH of oral cavity.
- The drugs should permeate through the oral mucosal membrane.

It's no surprise that thin-film dosage forms of pharmaceuticals are so popular, given their convenience and efficiency. Both well-established pharmaceutical firms and start-ups are interested in this technology. Sales have surpassed significant milestones in both the United States and Europe. In 2007, the market for pharmaceutical items in oral thin-film formulations was valued at \$500 million. By 2010, this figure was projected to rise to \$2 billion. Furthermore, a study projects that the worldwide market for thin-film pharmaceutical products would grow from \$7.1 billion in 2015 to \$15.9 billion by the end of 2024. Consequently, a rise of 117% is predicted during the next decade (see Figure 2) [35].

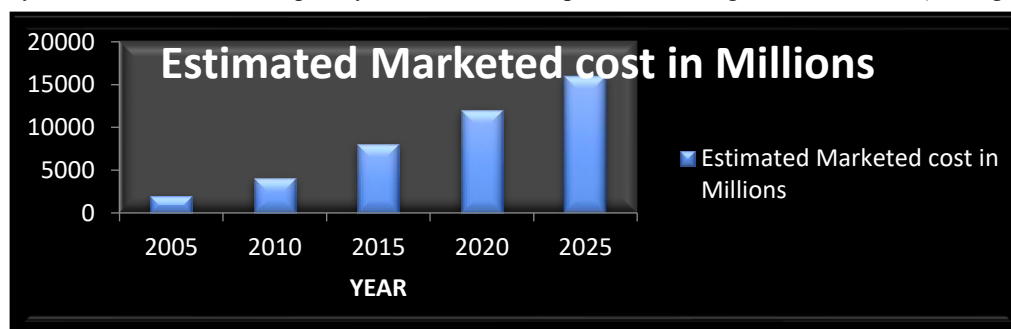


Fig.2 Estimated demand of thin film in market.

Classification of Oral Films

There are three different subtypes of oral films:

- i. Flash release
- ii. Mucoadhesive melt-away wafer
- iii. Mucoadhesive sustained-release wafers

Types of oral films and their properties are described in Table 1 Classification of Fast Dissolving Technology For ease of description, fast-dissolve technologies can be divided into three broad groups:

i. Lyophilized systems:

The technology around these systems involves taking a suspension or solution of drug with other structural excipients, through the use of a mould or blister pack, forming tablet shaped units. The units or tablets are then frozen and lyophilized in the pack or mould. The resulting units have a very high porosity, which allows rapid water or saliva penetration and very rapid disintegration.

ii. Compressed tablet-based systems:

This system is produced using standard tablet technology by direct compression of excipients. Depending on the method of manufacture, the tablet technologies have different levels of hardness and friability. The speed of disintegration for fast dissolve tablets compared with a standard tablet is achieved by formulating using either water soluble excipients, superdisintegrant or effervescent components, to allow rapid penetration of water into the core of the tablet.

iii. Thin film strips:

Oral films, also called oral wafers, evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products. Today, FDFs are a proven and accepted technology for the systemic delivery of APIs for over-the counter (OTC) medications and are in the early- to mid development stages for prescription drugs. This has been attributed to the success of the breath freshener products by consumers such as Listerine Pocket Paks in the US consumer market. Such systems use a variety of hydrophilic polymers to produce a 50- 200 mm film. The film is manufactured as a large sheet and then cut into individual dosage units for packaging in a range of pharmaceutically acceptable formats. [36]

Table 1: types of Oral Film and their Properties

Property/Sub Type	Flash Release Water	Mucoadhesive Melt-Away Wafer	Mucoadhesive Sustained Release wafer
Area (cm ²)	2-8	2-7	2-4
Thickness (µm)	20-70	50-500	50-250
Structure	Film:single layer	Single or multilayer system	Multilayer system
Excipients	Soluble,highly hydrophilic polymers	Soluble,hydrophilic polymers	Low/ non-soluble polymers
Drug phase	Solid solution	Solid solution & suspended	Suspension and and/or solid solution
Application	Tongue(upper palate)	Gingival or Buccal region	Gingival,other region in the oral cavity
Dissolution	Maximum 60 sec.	Disintegration in a few minutes, forming gel	Maximum 8-10hr

Table 2 : List of marketed products of films

Product Category	Ingredients	Application
Appetite suppressant	Fucus vesiculosus & guarana Extract, garcinia cambogia	These are top selling natural ingredients associated with weight loss. Cambogia helps to reduce the food intake by suppressing appetite
Breath freshener strip, (antibacterial strip)	Contain mint flaver & antibacterial agent, cetylpridiniumchloride	It is used as mouth freshner& to stop bad breath
Donezepil rapid film	Donezepil Hydrochloride 5mg & 10mg	Treatment of mild to moderately severe dementia of the Alzheimer's type
Suppress cough stirips with menthol	Artificial flavors ,ascorbic acid,aspartame,a sulfame potassium,cargeenan,diglycerides,fatty acid ester etc.	Temporarily suppresses coughs due to minor throat and bronchial irritation.
Saliva promoting strips	Fruit acid extracts,range of flavours	Its used for dry mouth as a side effect of other medications.
Energy boosters	Caffeine ,green tea extract & gaurana	The product maintains the energy levels.
Smoking cessation	Nicotine	Used to reduce the smoking habit
Vitamins and food supplements	Various vitamins,minerals and supplements	It is use for people who do not pop up the tablets or soluble supplements.
Labtec GmbH ondansetronRapidfilm	Ondansetron (4mg & 8mg)	It is used in the prevention of chemotherapy/radiation-induced nausea and vomiting; prevention of postoperative nausea/vomiting.
Chloraseptic Kids Sore Throat Relief strips	Benzocaine (2 mg) and menthol, grape flavor, BHT, corn starch, erythritol, FD&C Blue 1, FD&C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monoammoniumglycyrrhizinate, polyethylene oxide, sucralose	Occasional minor irritation, pain, sore throat, and sore mouth in children.
InnozenIncChloraseptic Relief Strips	Benzocaine (3 mg), BHT, corn starch, erythritol, FD&C Red 40, hydroxypropyl methylcellulose, malic acid, menthol, monoammoniumglycyrrhizinate, cherry flavors, polyethylene oxide, sucralose.	Occasional minor irritation, pain, sore throat, and sore mouth.

Formulation Aspects for Fast Dissolving Films

- 1) Drug Category
- 2) Film Forming Polymers
- 3) Plasticizers
- 4) Sweetening Agents
- 5) Saliva Stimulating Agents
- 6) Cooling Agent
- 7) Flavoring Agent
- 8) Coloring Agent
- 9) Surfactants

10) Stabilizing and thickening agents

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 in the Table 3. [37]

Table 3: A typical composition contains the following ingredients

Agents	Concentration
Drug	1-25%
Water Soluble Polymer	40-50%
Plasticizers	0-20%
Fillers ,Colours ,Flavours Etc	0-40%

i. Drug Category:

This technology has the potential for delivery of variety of APIs. However since the size of the dosage form has limitation, high dose drugs are difficult to be incorporated in films. Several classes of drugs can be formulated as fast dissolving films including antiulcer, antiasthmatics, antitussives, expectorants, antihistaminics, NSAID'S etc.

ii. Film Forming Polymers:

Water-soluble polymers are used as film formers as they provide rapid disintegration, good mouth feel, and mechanical strength to the films. The robustness of the strip depends on the type of polymer and its amount in the formulations. Water-soluble polymers film, adheres to the buccal mucosa and rapidly delivers medication into the systemic circulation. A variety of polymers are available for preparation of films of which pullulan, gelatin and hypromellose are most commonly used. At least 45%w/w of polymer should generally be present based on the total weight of dry film [38].

Examples of water-soluble polymers include:

Pullulan, Gelatin, guar gum, Xanthum gum, Hydroxyl propyl methyl cellulose, Modified starches, Hydroxyl ethyl cellulose etc.

iii. Plasticizers:

Plasticizer is a vital ingredient of the oral films. The selection of plasticizer depends upon its compatibility with the polymer and also the type of solvent employed in the casting of film. It helps to improve the flexibility of the film and reduces the brittleness of the film. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. Typically the plasticizers are used in the concentration of 1 - 20%w/w of dry polymer weight.

Examples include: Glycerol, Propylene glycol, Low molecular weight polyethylene glycols, Citrate derivatives like triacetin, acetyl citrate, Phthalate derivatives like dimethyl, diethyl, dibutyl derivatives, Castor oil etc.

iv. Sweetening agents:

Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Suitable sweeteners include:

(a) Water soluble natural sweetener: xylose, ribose, glucose, sucrose, maltose, stevioside etc.

(b) Water soluble artificial sweetener: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc.

(c) Dipeptide based sweetener: aspartame

v. Saliva stimulating agent:

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster dissolution of the film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them.

vi. Cooling agents:

Cooling agents like monomethyl succinate can be added to improve the flavor strength and to enhance the mouth-feel effect of the product. Other cooling agents like WS3, WS23 and Utracoll II can also be used in conjunction with flavors .

vii. Flavoring agents:

Perception for the flavour changes from individual to individual depending on the ethnicity and liking. It was observed that age plays a significant role in the taste fondness. Flavoring agents can be selected from synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Peppermint oil, cinnamon oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence type. The amount of flavor needed to mask the taste depends on the flavor type and its strength.

viii. Coloring agents:

Pigments such as titanium dioxide or FD & C approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in OS when some of the formulation ingredients or drugs are present in insoluble or suspension form.

ix. Surfactants:

Surfactants are used as solubilizing or wetting or dispersing agents so that the film gets dissolved within seconds and release active agent immediately. Surfactants also improve the solubility of poorly soluble drugs in fast dissolving buccal films. Some of the commonly used are polaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc.

x. Stabilizing and thickening agents:

The stabilizing and thickening agents are employed to improve the viscosity and consistency of dispersion or solution of the strip preparation solution or suspension before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivatives can be used in the concentration up to 5%w/w as thickening agents and stabilizing agents.

Methods of Manufacturing Fast Dissolving Films [39]

Following are the methods of manufacturing for fast dissolving films. One or combination of the following process can be used to manufacture the fast dissolving films –

i. Solvent casting method

- ii. Semisolid casting method
- iii. Hot melt extrusion
- iv. Solid dispersion extrusion
- v. Rolling method

Generally the solvent casting method is employed for manufacture of strips.

1) Solvent Casting

Technique Fast dissolving 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 solvent then both the solutions are mixed and finally casted in to the Petri plate and dried, which is then cut into pieces of the desired size. The properties of the API play a critical role in the selection of a suitable solvent. Water-soluble hydrocolloids used to prepare RDFs include: hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose (HPC), pullulan, sodium alginate, pectin, carboxy methyl cellulose (CMC), polyvinyl alcohol (PVA). Solvents used for the preparation of solution or suspension should ideally be selected from ICH Class 3 solvent list [40]. Specific types of equipment such as rollers are required for pouring the solution on an inert base. The clearance between the roller and the substrate determines the required thickness of the film. The final step, drying the film, removes the solvent and helps to obtain the finished product. Usually, glass, plastic, or teflon plates are used as an inert base for film casting. When the manufacturing technology is transferred from laboratory scale to production scale, several problems can be encountered. These problems can include the casting of the film, obtaining uniform thickness of the film, and proper drying of the sample. The selection of the proper type of dryer is needed in the final step of drying. Once the films are dried, cutting, stripping, and packaging is done. Suitable size and shapes of films can be cut. The commonly available sizes of films are 3 x 2 cm² and 2 x 2 cm². Flowchart showing the solvent casting method is described in figure.1.

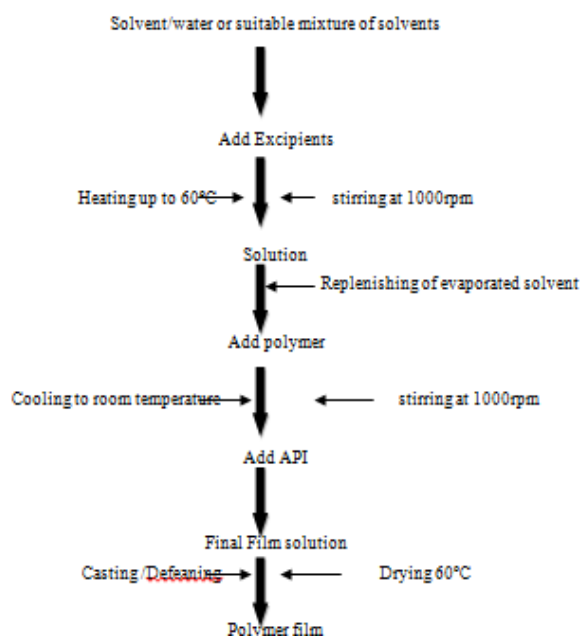


Fig.1;Flow chart of solvent casting method for the preparation of fast dissolving film

2) Semisolid casting

In semisolid casting method, firstly a solution of water soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which can be prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

3) Hot melt extrusion

Hot melt extrusion is commonly used to prepare granules, sustained-release tablets, and transdermal and transmucosal drug-delivery systems. In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies. Usually, when designing RDFs, polymers with low molecular weight or viscosity, such as HPMC E5 or pullulan PI.20, are preferred. A combination of various grades of polymers may also be used to achieve desired physical properties. Mixing polymers of high and low viscosity produces a film with good mechanical strength and high drug solubility in the film. The manufacturing process for the wafers in the pharmaceutical industry is divided into different steps.

Generally, the mass is prepared first under the control of temperature and steering speed. Afterwards, the wafers are coated and dried in a drying tunnel, once again the temperature, air circulation and line speed are controlled. Then follows a slitting and in the last step the wafers are punched, pouched and sealed. Other ways of manufacturing oral wafers are spraying process or extrusion, in particular hot-melt extrusion

There are certain benefits of hot melt extrusion.

- Fewer operation units
- Better content uniformity
- An anhydrous process

Disadvantages:

- Thermal process so drug/polymer stability problem
 - Flow properties of the polymer are essential to processing
 - Limited number of available polymers
- Comparison of solvent-casting and HME for the manufacturing of ODFs is described in the Table 4.

Table 4: Compares solvent-casting and HME for the manufacturing of FDFs.

Process Parameters	Solvent Casting	Hot Melt Extrusion
API selected	Thermoliable ,thermostable	Thermostable
Solvent required	Yes	No
Process	Hydrous	Anhydrous
Equipment required	Rollers, coaters	Hot –melt extruder
Scale-up	May create problems	May not be difficult
Chance of air entrapment	High chance	Low chance

4) Solid dispersion extrusion

The term solid dispersion refers to the dispersion of one or more APIs in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers using methods such as HME. In this method, immiscible components are extruded with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

5) Rolling Method

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water or a mixture of water and alcohol. The film is dried on the rollers and cutted into desired shapes and sizes. Three roll coating unit Diagram is shown in fig 3.

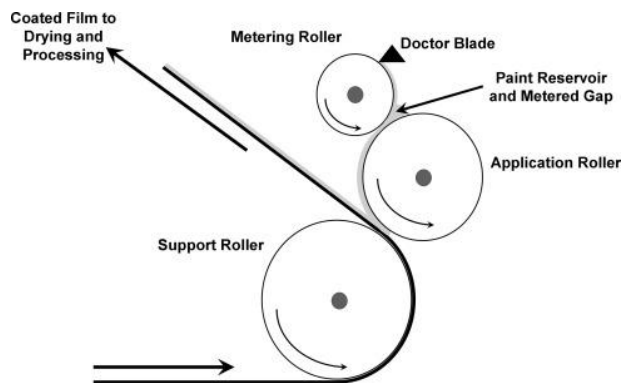


Fig.3 Three roll coating unit

Objective of Formulation of Fdfs

The aim of the present research work is development and characterization of mouth dissolving oral films of a suitable drug candidate so as to achieve following objectives:

- To improve patient compliance.
- To provide a rapid onset of action.
- To reduce the extent of hepatic first pass metabolism.
- To reduce the dose administered and thus the side effects associated with it.
- To enhance the oral bioavailability of molecules.

Patented Technologies [41]

1) XGel:

XGel is at the heart of Meldex international’s intellectual properties used in all its film system and its ingestible delivery technologies. XGel film Technology developed by Bio Progress is bringing a revolution in the product offerings and manufacturing methods now available to the pharmaceutical industry. X Gel film, potentially enhance the product stability. It has also been developed for non-ingestible applications such as cosmetic, ostomy pouches, sanitary and healthcare devices. The development and manufacture of XGel films uses a means called “solution casting”.

2) Soluleaves:

In this technology, the film is produced in order to release the active ingredients on coming in contact with saliva. This is applied to flavour-release products such as mouth fresheners, confectionery and vitamin products. SOLULEAVES technology can be used to deliver active ingredients to oral cavity efficiently and in a pleasant and easily portable form. The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas as well as nutritional products. SOLULEAVES films can also be designed to adhere to mucous membranes and to release the active ingredients slowly over 15 minutes.

3) Wafer tab:

WAFERTAB is a drug delivery system that incorporates pharmaceutical actives into ingestible films. It is a patented delivery system that uses a unique process to prepare drug-loaded thin films which can be used in topical or oral application. Active ingredients are incorporated into the film after casting. WAFERTAB system lends itself to many possibilities for innovative drug design, enabling multiple films with different actives to be bonded together.

4) Foam burst:

FOAMBURST is a patent granted in September 2004 which is for capsules made of foamed film. Gas is blown into the film during production, resulting in a film with a honeycombed structure. The voids in the film may be gas-filled, empty or filled with other materials to produce specific taste burst characteristics or to deliver active drugs. The light honeycombed structure results in capsules that dissolve rapidly, causing a melt-in-the-mouth sensation. FOAMBURST has attracted from and confectionary manufactures as a mean of carrying and releasing flavours.

5) Micap:

Micap signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water-soluble films. The developments aimed at providing new delivery mechanisms for the \$1.4bn global market for smoking cessation products (SCPs). Pharmacopoeial Status of Oral Films Monographs of common dosage forms are provided by the pharmacopoeias (e.g. Ph. Eur., USP). Even though dosage forms for application in the oral cavity such as Medicated chewing gums, Oromucosal preparations, Orodispersible tablets or oral Lyophilisates are included, monographs and specifications for oral films of diverse dissolution kinetics has not yet been established. There are inadequate pharmaceutical technical procedures for analysis in development and quality control of oral films as well. For instance, disintegration and dissolution testing procedures may be provided, but the recommended conditions such as volumes of media do not reflect the natural conditions in the oral cavity.

Evaluation of Fast Dissolving Films [42]

1) Organoleptic evaluation

2) Mechanical properties

a) Thickness

b) Dry test/tack test

c) Tensile Strength

d) Percent Elongation

e) Tear Resistance

f) Young's modulus

g) Folding endurance

3) Swelling properties

4) Transparency

5) Contact angle

6) Assay/Content uniformity

7) Disintegration time

8) In-vitro Dissolution test

1) Organoleptic evaluation:

For evaluation of the product, special controlled human taste panels are used. Invitro methods of utilizing taste sensors, are being used for this purpose. These invitro taste assessment apparatus and methodologies are well suited for high-throughout taste screening of oral films.

2) Mechanical properties:

Thickness is the thickness of strip can be measured by micrometer screw gauge at different strategic locations. This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip. Dryness test/tack test 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. Tensile Strength 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: $\text{Tensile strength} = \frac{\text{Load at failure}}{\text{Strip thickness} \times \text{Strip width}}$ 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 increases. $\% \text{ Elongation} = \frac{\text{Increase in length of strip}}{\text{Initial length of strip}} \times 100$ Tear Resistance 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 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 Newton's (or pounds-force). Young's Modulus 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 as follows: Young's modulus= Slope \times 100 Strip thickness \times cross-head speed Folding Endurance 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.

3) Swelling property:

Film swelling study 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 is determined at preset time interval until a constant weight is observed. The degree of swelling is calculated using formula $\alpha = (wt - wo)/wo$ wt is weight of film at time t, and wo is weight of film at time zero.

4) Transparency:

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. Determine the transmittance of films at 600 nm. The transparency of the films can be calculated as follows: Transparency = $(\log T_{600})/b = -\epsilon c$ Where T_{600} is the transmittance at 600 nm, b is the film thickness (mm) and c is concentration [43].

5) Contact Angle:

Contact angle measurements are performed at the room temperature with a goniometry. A drop of double distilled water was placed on the surface of the dry film. Images of the water droplet were recorded by means of digital camera, digital images are analyzed by the image 1.28v software for angle determination.

6) Assay/ Content uniformity:

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.

7) Disintegration Time:

The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips [44]. Although, no official guidance is available for oral fast disintegrating films/strips, this may be used as a qualitative guideline for quality control test or at development stage. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for strips is 5–30 s [45].

8) In-vitro Dissolution Test:

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 dissolution test can be difficult due to tendency of the strips to float on the dissolution medium where paddle system is used. Storage and Packaging of Films A variety of storage and packaging options are available for fast dissolving films. The packaging stage provides product flexibility to the drug manufactures. Single packaging is mandatory for films, which are pharmaceutical products; an aluminum pouch is the most commonly used packaging format. APRLabtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for the Rapid films. The rapid card has same size as a credit card and holds three rapid films on each side. Every dose can be taken out individually.

Conclusion

Fast Dissolving Films have several advantages over the conventional dosage forms. They are considered as a most important drug delivery system today because of their rapid disintegration, improved dissolution. They combine the greater stability of a solid dosage form and good applicability of the liquid and thus bridge the gap between the two ideas, incorporating positive elements from both solid and liquid dosage forms into an elegant, stable and effective delivery vehicle. So they are of great importance during the emergency cases such as allergic reactions and asthmatic attacks whenever immediate onset of action is desired. 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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