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REVIEW ARTICLE

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A Path for Horizing Your Innovative Work

A REVIEW ON FAST DISSOLVING FILM

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Abstract: Fast-dissolving oral delivery systems are solid dosage forms, which disintegrate or dissolve within 1 min when placed in the mouth without drinking water or chewing. More recently, fast-dissolving films are gaining interest as an alternative to fast-dissolving tablets to definitely eliminate patient's fear of chocking and overcome patent impediments. Orally fast dissolving film is the type of drug delivery system which when placed in the oral cavity, disintegrate or dissolve within few seconds. Fast dissolving films are very similar to postage stamp in their shape, size and thickness. These films have a potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action. Fast dissolving films are formulated using polymers, plasticizers, sweeteners, flavors and colors. Fast dissolving film is manufactured using solvent casting method, rolling method, extrusion method and solid dispersion method. The films evaluated for disintegration dissolution, tensile strength, thickness, folding endurance, elastic modulus.

Keywords: Fast dissolving films (FDFs), Oral strip, Disintegration, Dissolution.

INTRODUCTION

Among the various routes, oral route drug administration is considered to be most effective and acceptable form due to its better therapeutic efficacy and acceptable good patient compliance. Peroral dosage forms can be distinguished as solid or liquid oral dosage forms in which the prior fall in category of pills, capsules, granules and powder while the latter include solution/suspension or emulsion offering more advantages over monolithic solid dosage form. However they also possess certain disadvantages finding non toxic excipients and need preservatives which might cause adverse effects in children, microbiology stability and also shows problems with the taste masking and dose accuracy. To overcome these problems associated with the liquids dosage forms, fast dissolving tablets were designed in early 19th Century, which slowly led to their further development and thus came the existent of fast dissolving films.[1]

So, fast-dissolving drug-delivery systems came into existence in the late 1970's as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms. These systems consist of the solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water. Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to fast disintegrating tablet (FDT) to wafer to the recent development of oral fast dissolving films (FDFs). Amongst the plethora of avenues explored for the rapid drug releasing products, oral strip technology is gaining much attention.[2, 3]

SPECIAL FEATURES [4]

- Thin elegant film
- Various sizes and shapes
- Unobstructive
- Mucoadhesion
- Fast disintegration
- Quick dissolving
- Rapid release

The fast dissolving films has also a clear advantage over the fast dissolving tablets (FDTs):

- FDTs are sometimes difficult to carry, store and handle (fragility and friability).

- Many FDTs are prepared by using the expensive lyophillisation process.

A large number of drugs can be formulated as fast dissolving films. Innovative products may

- Increase the therapeutic possibilities in the following indications.
- Pediatrics (antitussives, expectorants, antiasthamatics)
- Geriatrics (antiepileptic, expectorants)
- Gastrointestinal diseases
- Nausea (e.g. due to cytostatic therapy)
- Pain (e.g. migraine)
- CNS (e.g. antiparkinsonism therapy)

Improved patient compliance is a primary benefit of the fast-dissolving drug delivery systems. The main difference between the Quick-Dis ™ (Example) drug delivery system and most conventional fast-dissolving dosage forms is that it is not a tablet. Rather, the Quick-Dis ™ drug delivery system is a thin film that alleviates the fear of swallowing and the risk of choking commonly associated with a conventional tablet. This fast-dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment. These additional, superior benefits allow patients to take their medication anytime and anyplace under all circumstances. Quick-Dis ™ however, comprises a tough, solid, soft, flexible film and does not require special packaging. It is thin and can be carried in a patient's pocket, wallet, or pocket book.

GENERAL PROPERTIES & RELEASE MECHANISM [4]

The Quick-DisTM drug delivery system comprises a thin, printable, low-moisture, non-tacky film that is convenient for dosing, suitable for labelling, and flexible for easy packing, handling and application. The thickness of a typical film ranges from 1 to 10 mil and its surface area can be 1 to 20 cm2 for any geometry. At the same time, the rapid hydration rate facilitates an almost immediate softening of the Quick-DisTM film upon application in the oral cavity. The wet-tack and mucoadhesive properties of the system are designed to secure the film to the site of application. The flexibility and strength of the film may be selected/modified to facilitate automatic rewinding, die cutting, and packaging during manufacturing.

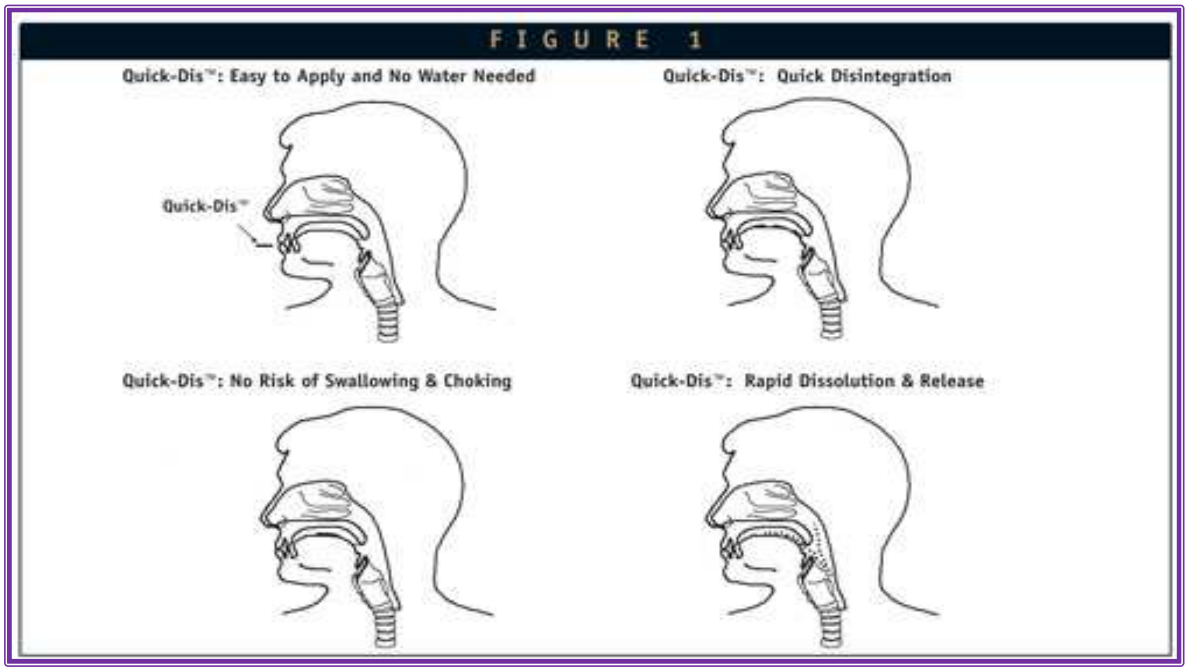
The typical disintegration time, which is defined as the time at which the film begins to break?

When brought into contact with water, is only 5 to 10 seconds for the Quick-Dis ™

film with a thickness of 2mil. The dissolving time, which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for Quick Dis ™ film with a thickness of 2 mil.

The drug is released from the dosage form upon disintegration and dissolution. The disintegration and dissolving times are prolonged as the film thickness increases as shown in the

Figure1.The disintegration and dissolving times may be further influenced, by varying the formulation composition of the film.



Fast dissolving film is a thin film with an area of 5- 20 cm^2 containing an active ingredient. The immediate dissolution, in water or saliva respectively, is reached through a special matrix from water-soluble polymers. Drugs can be incorporated up to a single dose of 15mg. formulation considerations (plasticizers etc.) have been reported as important factors affecting mechanical properties of the films, such as shifting the glass transition temperature to lower temperature.

A typical composition contains the following

Drug 1-25%

Water soluble polymer 40-50%

Plasticizers 0-20%

Fillers, colours, flavours etc. 0-40%

COMPOSITION [5, 6, 7]

- Active pharmaceutical ingredient
- Film forming polymers
- Plasticizer
- Sweetening agent
- Saliva stimulating agent
- Flavoring agent
- Coloring agent

Active Pharmaceutical Ingredient [5, 6]

A typical composition of the film contains 1-25% w/w of the drug. Variety of APIs can be delivered through fast dissolving films. Small dose molecules are the best candidates to be incorporated in Oral fast dissolving film. Multivitamins up to 10% w/w of dry film weight was incorporated in the films with dissolution time of less than 60 seconds. It is always useful to have micronized API which will improve the texture of the film and also for better dissolution and uniformity in the Oral fast dissolving film. Many APIs, which are potential candidates for fast dissolving film technology, have bitter taste. This makes the formulation unpalatable especially for pediatric preparations. Thus before incorporating the API in the fast dissolving film, the taste needs to be masked. Various methods can be used to improve the palatability of the formulation. Among the techniques employed, the simplest method involves the mixing and co-processing of bitter tasting API with excipients with pleasurable taste.

Some of the examples of suitable drug molecule that can be incorporated in the fast dissolving films are listed in Table

API	Therapeutic category	Dose
Nicotine	Smoking Cessation	1.0–15.0 mg
Nitroglycerin derivatives	Vasodilator	0.3–0.6 mg
Zolmitriptan	Anti migraine	2.5 mg
Loratidine	Antihistaminic	5–10 mg
Desloratidine	Antihistaminic	5.0 mg
Diphenhydramine hydrochloride	Antihistaminic	25.0 mg
Loperamide	Antidiarroheal	2.0 mg
Famotidine	Antacid	10.0 mg
Flurazepam	Anxiolytic, Anticonvulsant	15.0–30.0 mg
Chlorpherinamine maleate	Antihistaminic	4.0 mg
Acrivastine	Antihistaminic	8.0 mg
Oxycodone	Opoid Analgesic	2.5–10.0 mg
Diclyclomine	Muscle Relaxant	25.0 mg
Omeprazole	Proton pump inhibitor	10.0–20.0 mg
Cetrizine	Antihistaminic	5.0–10.0 mg
Ketoprofen	Anti–inflammatory	12.5–25.0 mg
Azatidine maleate	Antihistaminic	1.0 mg
Sumatriptan succinate	Antimigraine	35.0–70.0 mg
Chlorhexidine gluconate	Antimicrobial	0.12%
Tiprolidine hydrochloride	Antihistaminic	2.50 mg

Film forming polymer[6]

Since the primary use of all fast dissolving film oral dosage forms relies on their disintegration in the saliva of the oral cavity, the final film that is used must necessarily be water soluble. In order to prepare a film formulation that is water-soluble, excipients or polymer must be water soluble with low molecular weight and excellent film forming capacity. The polymer employed should be non-toxic, non-irritant and devoid of leachable impurities. It should have good wetting and spread ability property. The polymer should exhibit sufficient peel, shear and tensile strengths. The polymer should be

readily available and should not be very expensive.

Some of the examples of suitable polymer that can be incorporated in the fast dissolving films are listed in Table

Property	**Hydoxy propyl methyl cellulose (Hypromellose)**	**Hydroxy propyl cellulose**	**Pullulan**	**Starch and modified starch**	**Gelatin**	**Carboxy methyl cellulose**
Synonym	HPMC, Methocel, Metolose, Benecel	Hydroxyl propyl ether, Hyprolose, Klucel, Nisso HPC.	Pullulane, 1, 6 α linked maltotriose	Amido, amylum, PharmGel, Fluftex W, Instant pure-Cote, Melogel etc.	Byco, cryogel, Instagel, Solugel	Akulell, Blanose, Aquasorb, CMC sodium
Description	It is a odourless, tasteless and white or creamy white fibrous or granular powder	It is a white to slightly yellow colored, odourless and Tasteless powder. It is stable material	It is available as white, odourless tasteless, stable powder	It is an odourless, tasteless, Fine, white powder.	It occurs as light amber to faintly yellow colored, Vitreous, brittle solid. It is Odourless, tasteless.	It is white, odourless powder
Molecular weight	10,000–1,500,000	50,000–1,250,000	8000–2,000,000	50,000–160,000	15,000–250,000	90,000–700,000

Solubility	Soluble in cold water, forming a viscous colloidal solution, insoluble in Chloroform , ethanol.	It is freely soluble in water below 38 °C forming a smooth, clear, colloidal Solution. Hydroxypropyl cellulose is soluble in many cold and hot polar organic solvents such as absolute ethanol, methanol, isopropyl Alcohol and propylene glycol.	It is soluble in hot as well as cold water	Starch is insoluble in cold Water and ethanol. It swells in water by about 5 to 10% at 37 °C	Soluble in glycerine, acid and Alkali. Swells in water and Softens. It is soluble in hot Water.	It is easily dispersed in water to form a clear or colloidal Solution.
Film forming capacity	It has a film forming ability in	It has a good film forming	5–25%w/w solution forms	Modified starches have a	It has a very good film Forming	The enzymatically

	2–20%w/w concentrations.	property and 5%w/w solution is generally used for film Coating.	Flexible films. Films are low Permeable to oxygen, stable.	property to form quick Dissolving films.	ability.	modified carboxymethyl cellulose has Good film forming property.
Viscosity	A wide range of viscosity grades are commercially Available. Viscosity of various grades ranges from 3 mPa s–100,000 mPa s	A wide range of viscosity types Are commercially available. The viscosity of solutions ranges from 75 mPa s–6500 mPa s depending upon the polymer grade.	The viscosity (10%w/w, 30 °C) of pullulan was 100–180 mm2/s.	2%w/v aqueous dispersion of starch provides 13 mPa s Viscosity.	4.3–4.7 mPa s for a 6.67%w/v Aqueous solution at 60 °C.	The 1%w/w aqueous solution has viscosities in the range of 5–13,000 mPa s.
Melting	Browns at	It softens	107 °C	It	–	Browns at

point	190–200 °C. glass transition temperature is 170–180 °C	at 130 °C; chars at 260–275 °C		decomposes at 250 °C		227 °C and chars at 252 °C.
Moisture content	It absorbs moisture from the air. The amount of moisture absorption depends on initial moisture content, temperature and humidity of Surrounding air.	It absorbs moisture from the Air. Typical equilibrium moisture content values at 25 °C/50% RH are 4%w/w and 12%w/w at 84%RH.	It contains less than 6%w/w of moisture.	Starch is very hygroscopic And readily absorbs moisture. Commercial grades are having moisture content in the range of 10–14%w/w.	9–11%w/w	Moisture content of the Polymer is less than 10%.
Application/s	Hypromellose is widely used in oral, ophthalmic and Topical formulation	Hydroxypropyl cellulose acts as a tablet binder in the range of 2–8% of	It is used extensively in food industry to provide bulk and Texture. The	Starch is used widely in the solid oral dosage forms as a binder,	It is widely used in an Implantable delivery system. It is used for the preparation	It is used widely in oral and Topical formulation. It is used mainly as

	s. Hypromellose is primarily used as a tablet binder, film coating agent, film forming agent and as a matrix for use in extended release Formulations. Hypromellose is also used as a suspending and thickening agent. Hypromellose is also used as an emulsifier, suspending	tablet weight. The polymer is also used for preparation of modified Release dosage form. Hydroxy propyl cellulose is most suitable for water soluble Drugs. It is also used for the Preparation of microcapsules. It is used as a thickening agent in the oral	hydrophobic grades of pullulan are used for preparation of nanoparticles for targeted Delivery. Pullulan can be used as a replacement to dextran as a plasma expander. Pullulan films are strong therefore used for decoration of food products, in confectionaries. It acts as an ideal	diluents and Disintegrant. Starch is used extensively in topical preparation such as dusting powders, ointments. It is used therapeutically for the treatment of iodine Poisoning. Modified starches are used for coating of immediate release dosage forms. These are the	of hard and soft gelatin Capsule. It is used for Microencapsulation of drugs. It is used topically in wound Dressing. Absorbable gelatin is available as sterile film, ophthalmic film, sterile sponge etc.	a viscosity Increasing agent. It is used as a stabilizer for preparation of Suspensions and emulsions. It can be utilized as a binder or disintegrant depending on the grade and concentration Used in the formulation. It is also reported as a Cryoprotec

	agent and stabilizing agent in gels and ointments. Hypromellose is also used to manufacture capsules, as an adhesive in plastic bandage and as a wetting agent in contact lenses	and topical formulations. Due to its non ionic nature, it is used as an emulsifier in the cosmetic Formulations. It imparts low surface and interfacial tension to its solution and thus can be used for the preparation of flexible films alone or in combination with Hypromellose.	carrier system for flavors, colors and drugs. Pullulan is used in coating for immediate release tablets and it is also used for Preparation of capsule shells.	aqueous preparations used for aesthetic purpose, light and Moisture barrier. It is also used in the treatment of Dehydration.		tive agent. It has a mucoadhesive property which is utilized in some of the topical as well as oral Preparation. It is reported for use in combination with other film forming polymers for preparation of oral films or for coating the tablets. It can be used for preparatio

						n of micro particles as it forms complex coacervats with Gelatin and pectin.
Safety and regulatory status	GRAS listed and included in FDA Inactive Ingredient Guide.	Generally regarded as a nontoxic and non-irritant Material. It is GRAS listed and included in the FDA Inactive Ingredient Guide.	GRAS listed.	Generally regarded as a nontoxic and non-irritant Material. It is GRAS listed and included in the FDA Inactive Ingredient Guide.	Included in FDA Inactive Ingredient Guide.	GRAS listed and included in the Inactive Ingredients Guide.

Plasticizer[7]

Plasticizer is a vital ingredient of the fast dissolving films. Plasticizer helps to improve the flexibility of the strip and reduces the brittleness of the films. It significantly improves the film forming properties by reducing the glass transition temperature of the polymer. The chemical structure and concentration of plasticizers play an important role in alleviating the glass transition temperature of the polymers.

The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of film. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such astributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients. Typically the plasticizers are used in the concentration of 0–20 % w/w of dry polymer weight. However, in appropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug.

Sweetening agents[7]

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 Ondensteron respectively.

Saliva stimulating agent[7]

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. e.g. 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 strip.

Flavoring agents[5]

Preferably up to 10%w/w flavors are added in the Fast dissolving film formulations The acceptance of the oral disintegrating or dissolving formulation by an individual is largely depends on the initial flavor quality which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min. The selection of flavor is dependent on the type of drug to be incorporated in the formulation. It was observed that age plays a significant role in the taste fondness. The geriatric population like mint or orange flavors while younger generation like flavors like fruit punch, raspberry etc. Flavoring agents can be selected from 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. Peppermint oil, cinnamon oil, spearmint 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.

Coloring agents[5]

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.

CRITERIA FOR SELECTION [8]

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasant mouth feel.
- Leave minimum or no residue in the mouth after oral administration.
- Exhibit low sensitive to environmental condition as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipments at low cost.

SELECTION OF DRUGS [8]

The ideal characteristics of a drug to be selected

- No bitter taste
- Dose lower than 20mg
- Small to moderate molecular weight
- Good stability in water and saliva

- Partially non ionized at the oral cavities pH
- Ability to diffuse and partition into the epithelium of the upper GIT (log p>1, or preferably>2)
- Ability to permeate oral mucosal tissue

ADVANTAGES [5]

- Oral dissolving films can be administered without water, anywhere, any time.
- Due to the presence of larger surface area, films provide rapid disintegrating and dissolution in the oral cavity.
- Oral dissolving films are flexible and portable in nature so they provide ease in transportation, during consumer handling and storage.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, acute pain, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- As compared liquid formulations, precision in the administered dose is ensured from each strip of the film.
- The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect.
- The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
- Provide new business opportunity like product differentiation, product promotion and patent extension.

DISADVANTAGES [5]

- High doses cannot be incorporated.
- Dose uniformity is a technical challenge.

APPLICATION [9]

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of FDFs could become a preferential delivery

method for therapies in which rapid absorption is desired, including those used to manage pain, allergies, sleep difficulties, and central nervous system disorders. Dissolvable FDFs 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.

1) Topical applications: The use of dissolvable films may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications.

2) Gastro retentive dosage systems: Dissolvable films are being considered in dosage forms for which water-soluble and poorlysoluble molecules of various molecular weights are contained in a film format. Dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially be used to treat gastrointestinal disorders.

3) Diagnostic devices: Dissolvable films may be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic device.

METHODS [4]

One or combination of the following process can be used to manufacture the fast dissolving films.

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Solid dispersion extrusion
5. Rolling

1) Solvent casting method

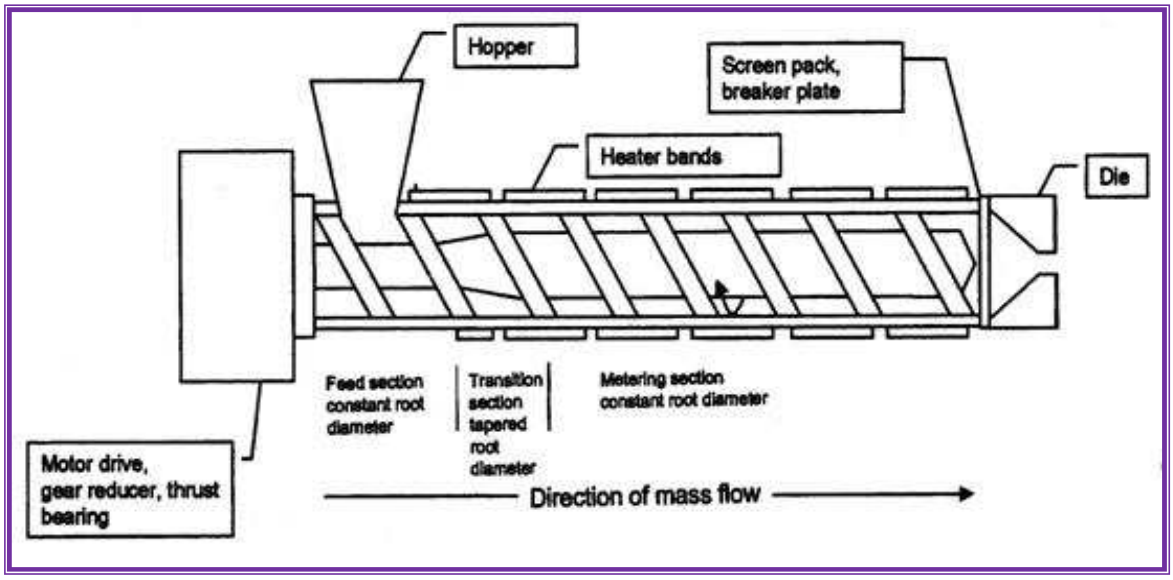
In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate dried and cut in to uniform dimensions.

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 was 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



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.

There are certain benefits of hot melt extrusion.

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

4) Solid dispersion extrusion

In this method immiscible components are extrude 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 and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes.

PATENTED TECHNOLOGY [8]

SOLULEAVES™ technology is used to produce a range of oral delivery films that can incorporate active ingredients, colors and flavors. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. For pharmaceutical uses this method of administration is especially useful for pediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas as well as delivering nutritional products. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes.

WAFERTAB™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a pre-manufactured XGEL™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The WAFERTAB™ system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. WAFERTAB™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release, or for use by patients who have difficulty swallowing.

FOAMBURST™ is a special variant of the SOLULEAVES™ technology where an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. FOAMBURST™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

XGEL™ film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. XGEL™ film provides unique product benefits for healthcare and pharmaceutical products: it is non animal- derived, approved on religious grounds and is suitable for vegetarians; the film is GMO free and continuous production processing provides an economic and

competitive manufacturing platform. XGEL™ film can be taste masked, colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGEL™ film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water. XGEL™ film is comprised of a range of different water-soluble polymers, specifically optimized for the intended use. All of the XGEL ingredients are well known and generally regarded as safe (GRAS).

EVALUATION PARAMETERS [1,5,7,8,10]

Organoleptic Evaluations

Color is a vital means of identification for many pharmaceutical products and is also usually important for consumer acceptance. The color of the product must be uniform within a dosage form.

Odor is also be important for consumer acceptance of oral dosage forms and can provide an indication of the quality of oral strips or films as the quality of oral strips or films as the presence of an odor in a batch could indicate a stability problem. However, the presence of an odor may be characteristic of the drug added ingredients.

Taste is also essential factor for the consumer acceptance and many companies utilize taste panels to judge the preference of different flavors and flavor levels in the development of a product. Taste preference is however subjective and the control of taste in the production of oral soluble films is usually based on the presence or absence of a specified taste.

Tensile Strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks 14. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

% Elongation

It is calculated as =

$$\frac{\text{Increase in length X 100}}{\text{Original length}}$$

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.

Disintegration time

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.

***In vitro* drug release**

Dissolution studies of films were performed by USP XXIII type II apparatus in 6.8 phosphate buffer (500ml) and 0.1N HCl (500ml). The temperature (37±0.5°C) and the rotation speed was 50 rpm. The samples were withdrawn at various time intervals and analyzed spectrophotometrically.

Content Uniformity

The test for the content uniformity is carried out taking a sample film of size 2×2cm^2 which is placed in a beaker containing 10 ml of a suitable medium. The contents were stirred in a cyclo-mixer to dissolve the film which was transferred to a volumetric flask (10ml). The absorbance of the solution was measured against the corresponding blank solution at particular wavelength using a standard assay method described for the particular API mentioned in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%

Stability studies

Stability study was carried out for all the batches at accelerated condition (65% relative humidity and 35 ºC temperature) in the humidity chamber for the three months. After 3 months the films were evaluated for the drug content, disintegration time and physical appearance observation.

COMPARISON BETWEEN FAST DISSOLVING FILMS AND FAST DISSOLVING TABLETS [5]

Fast Dissolving Films	Fast Dissolving Tablets
It is a film	It is a tablet
Greater dissolution due to larger surface area	Lesser dissolution due to less surface area
Better durable than oral disintegrating tablets	Less durable as compared with oral films
More patient compliance	Less patient compliance than films
Low dose can only be incorporated	High dose can be incorporated
No risk of chocking	It has a fear of chocking

MARKETED PRODUCT OF FAST DISSOLVING FILM [7,8]

Distributor	Brand	API	Strength
Del	Orazel	Menthol/pectin	2mg/30 mg
InnoZen	Suppress	Menthol	2.5 mg
Novartis	Gas-X	Simethicone	62.5 mg
Novartis	Theraflu	Phenylepherine HCl/Dextromethorphan HBr	10 mg/20 mg
Novartis	Theraflu	Phenylepherine HCl/Diphenhydramine HCl	10 mg/25 mg
Novartis	Theraflu	Dextromethorphan HBr	15 mg
Novartis	Theraflu	Diphenhydramine HCl	25 mg
Novartis	Triaminic	Diphenhydramine HCl	12.5 mg
Novartis	Triaminic	PhenylepherineHCl	2.5 mg
Novartis	Triaminic	Phenylepherine HCl/Diphenhydramine HCl	5 mg/12.5 mg
Novartis	Triaminic	Dextromethorphan HBr	7.5 mg
Novartis	Benadryl	DiphenylhydramineHCl	12.5 mg
Pfizer	Benadryl	DiphenylhydramineHCl	25 mg
Pfizer	Suldafed	Phenylephrine HCl	10 mg
Prestige	Chloraseptic	Benzocaine/menthol	3mg/3mg
Labtec GmbH	Ondensteron Rapdifilm	Ondensteron	4mg/8 mg
Labtec GmbH	Donepzil Rapdifilm	DonepzilHCl	5mg/10 mg

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