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Review Article

Comprehensive Review on Fast Mouth Dissolving Film As Novel Drug Delivery System

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ABSTRACT

Fast mouth dissolving films are solid dosage types that, when placed in the mouth, dissolve or disintegrate over the course of a few seconds. They are not manufactured or palatable. Fast-dissolving films are becoming more popular as an alternative to quick-dissolving tablets in order to reduce patients' concerns about choking and to overcome patients' obstacles. A complex alternative to the traditional pills, capsules, and liquids often associated with prescription and over-the-counter drugs is the quickly disintegrating thin film. Thin film strips are often intended for oral administration, with the individual placing the strip on or below the tongue or on the inside of the cheek. They are similar in size, shape, and thickness to an item. Drugs can be administered intragastrically, buccally, or sublingually thanks to thin films. Thin-film organ and buccal administration of a medicine has the potential to accelerate the beginning of action, reduce dosage, and improve the medication's efficacy and safety profile. The invention of quick-dissolving buccal films, which dissolve or disintegrate quickly on the patient's buccal membrane, is a wholly novel technology that addresses the steadily rising need for patient comfort and compliance-related analyses. This fast-acting drug delivery method is appropriate for medications with high first-pass metabolism. It increases bioavailability while decreasing dosage frequency to reach oral plasma peak levels, which gradually reduces side effects and also makes it cost-effective. The present review compiles recent developments and research on quick-dissolving buccal films and argues that several pharmaceutical businesses may use this delivery technique in the future on a large basis. Many products are now being developed that might use thin films as dosage forms to deliver medications.

INTRODUCTION

Granules, liquids, powders, and tablets are all common kinds of pharmacological dosage forms. For patients to receive a precise amount of medication, pills are designed to be chewed or swallowed whole. However, some patients, particularly those who are young and old, find it difficult to swallow or chew solid dose forms like

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tablets and capsules. Despite their quick disintegration period, some patient groups still have a phobia of swallowing solid pills and a danger of choking. Hence oral film medication administration is preferable solution in such instances. Pharmaceutical researchers from all across the world are investigating thin film as a cutting-edge medication delivery method. Alternative methods to traditional dose forms have been found. Due to their flexibility, mouth-dispersing films and fast-dispersing films are the most sophisticated solid dosage forms. In comparison to tablets, it increases the effectiveness of active medicinal substances dissolving in short-term oral cavities following contact with saliva.1 Fast-disposing technology is a revolutionary medicine delivery method that has just come to light. It offers a highly practical way to take vitamins and prescription drugs. These systems collapse in a matter of seconds. The drug is delivered via a thin film that is applied to the patient's tongue or mucosal tissue, promptly moistened by saliva, quickly disintegrated, and then released for absorption through the oral mucosa. In the saliva of the oral cavity, they disintegrate and release the active component.2 utilising a number of processes, such as freeze-drying, wet granulation, and direct compression Drug delivery methods that dissolve quickly can be produced. Some people utilise various disintegrating mechanisms, such as high levels of dissolving or effervescent chemicals, to quickly dissolve the dose form in the mouth. Fast dissolving drug delivery systems have lately begun to acquire favour as innovative medication delivery methods due to their simple administration and improved compliance. These rapidly dissolving medication delivery systems can dissolve or disintegrate in the patient's mouth in a matter of seconds or minutes without the patient having to chew or use water to help in swallowing. Even though oral films have short disintegration/dissolution times, oral solid tablets are still preferred over them for some patient populations due to patient anxiety and the risk of choking. Additionally, oral solid tablets have poor oral availability due to the pH of the stomach, the presence of enzymes, and extensive first-pass metabolism, all of which can be overcome by creating oral films. Parenteral drug delivery systems have been used to dispense these medications, but because to low patient compliance, the pharmaceutical industry is looking for alternate drug administration methods, such as film drug delivery. The floor or top of the tongue is used for an intraoral fast-dissolving medication delivery method. It quickly releases the active ingredient for local and/or systemic absorption while being maintained at the application location. They also provide distinctive product distinction, making it possible to employ them as line extensions for already-available commercial goods. Improved solubility/stability, biological half-life, and bioavailability increase of pharmaceuticals are further benefits of this innovative drug delivery system that can help it fulfil the demands of the industry today.26

Benefits of mouth dissolving film

- Due to its versatility, films are less brittle than orally disintegrating pills.
- Since films are more expansive, they encourage the Rima's rapid and swift breakdown and destruction.
- Choking is not a possibility.
- Films increase a patient's level of compliance
- There is no lack of water for film breakdown, which has led to improved patient satisfaction among the dysphasic population.
- Films break down on the patient's tongue in a matter of seconds, allowing the active medicinal component to be released quickly.

- The patient may watch films whenever and wherever it is most convenient for them.
- Molecules that survive the initial pass result have improved oral bioavailability thanks to it.
- Bypassing the primary pass leads to a decrease in molecule-related side effects as a result of a dosage reduction.
- Films have a sophisticated sense.
- They can manage themselves easily.
- Stability over a lengthy period of time because the medicine is stable and available indefinitely until it is eaten. It thereby combines the benefits of a liquid indeterminate amount kind with the stability and bioavailability of a solid indefinite quantity kind.

Disadvantages of mouth dissolving film

- You cannot incorporate high dosages.
- Dose homogeneity is a difficult technological issue.
- Ideal characteristics of suitable drug candidate
- The medication must be stable and water soluble, even as spittle.
- A reduced or moderate relative molecular mass is required for the medication.
- The medicine should have a pleasing appearance.
- The medicine should only be used in small doses, up to forty milligrammes.
- The medication should be able to penetrate the oral tissue layer tissue.
- At Rima's concentration of hydrogen ions, it should be somewhat unionised.
- It should be perishable and non-nephrotoxic.
- It should be capable of loading drugs sufficiently.
- It should be less sensitive to external factors like humidity and temperature.2

Structural features of Oral Mucosa

The outermost layer of stratified squamous epithelial tissue makes up the mouth membrane. A foundation membrane, a plate propria, and connective tissue—the deepest layer—are located underneath this. The epithelial tissue progresses from a mitotically active basal cell layer through several differentiating intermediate layers to the superficial layers, where cells are shed from the epithelial tissue's surface. This is similar to stratified squamous epithelia found throughout the rest of the body. The buccal epithelial tissue has a calculable turnover time of 5–6 days, which is most likely indicative of the mouth membrane as a whole. The buccal membrane measures at 500-800 m, but the membrane thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and also the gingivae live at around 100-200 m. Depending on where it is located inside the Rima, the epithelial tissue's composition also changes. The mucosae of the gingivae and surface are keratinized, much like the cuticle, and contain neutral lipids called ceramides and acyl ceramides that are associated to the function of the barrier. However, the membranes of the palate, organ, and buccal areas aren't keratinized, which are rather water-resistant to water and contain only very little levels of ceramide. They also include trace quantities of neutral yet polar lipids, primarily glucosyl ceramides and steroid alcohol salt. It is discovered that the nonkeratinized epithelia are substantially more water-leaky than the keratinized epithelia.

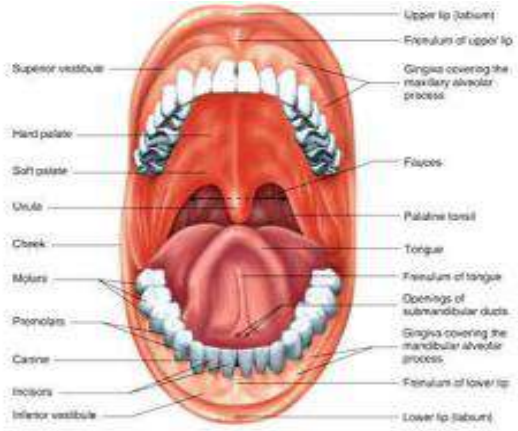

Fig. 1: Anatomy of buccal cavity

Mechanism of absorption through oral mucosa

For passive drug transport over the oral mucosa, there are two permeation routes: transcellular (passing inside the cell) and paracellular (passing around the cell). Both of these pathways may be used simultaneously by a medicine, however depending on the chemical scientific features of the drug, one route is usually preferred over the other. Oleophilic chemicals would have minimal solubility in this environment since the living body parts and protoplasm are hydrophilic in nature. However, due to a rare partition constant, the cytomembrane's oleophilic composition might make it difficult for hydrophilic solutes to pass through it. As a result, the cytomembrane serves as the main transport barrier for hydrophilic chemicals, while the living tissue serves as the primary barrier to the permeability of oleophilic substances. Since the oral epithelial epithelium is stratified, a combination of those 2 pathways may be used for substance penetration. But often, the path with the fewest obstructions to passage is the one that prevails.3

Classification of Fast Dissolve Technology

Fast-dissolve technologies may be divided in to 3 broad groups:

- Lyophilized systems.
- Compressed tablet-based systems.
- Thin film strips.

The lyophilized systems

When it comes to sales value, volume, and the variety of products that have received approval throughout the world, this method is the most successful of them all. Drugs in suspension or resolution with different structural excipients can be transformed into tablet-shaped units by using a mound or packing. The units or pills are then lyophilized and frozen inside the pack or mould. High consistency subsequent units are to responsible for exceptionally quick disintegration and rapid water or spittle penetration Depending on whether the active components are soluble or insoluble, these systems have different dose-handling capacities, with the former having slightly lower capacities than systems based on a few tablets. The devices are able to incorporate a variety of flavor-masked ingredients and disintegrate much more quickly than tablet-based solutions.

Compressed tablet-based systems

This technique was developed by directly compressing excipients using conventional pill technology. Depending on the manufacturing process, the pill technologies have completely varied levels of hardness and breakability. The formulation of fast-dissolve tablets uses water soluble excipients, or superdisintegrant or effervescent portions, to enable rapid penetration of water into the pill's core, resulting in a faster rate of disintegration than a conventional tablet. The only exception to the current strategy for tablets is the Fuisz technology from Biovail. It provides drug-loaded candy floss using the exclusive Shear kind method, which is subsequently utilised to make tablets using different excipients. These devices should be able to handle relatively high concentrations of pharmacological substance as well as style-masked coated particles. They may be less effective than thin-film or lyophilized dosage forms because they take longer to dissolve. For the internal development of line extension and generic rapid dissolve dosage forms, various technological homes, branded companies and generic pharmaceutical corporations have gradually used the loose compression pill technique.30

Oral thin film strips

Oral films, sometimes referred to as oral wafers in the related literature, are a collection of flat films that are injected into the Rima. Although oral film systems, the third type, have been around for a while, they have just lately gained attention as a

novel method of fast-acting pharmaceutical drug administration. Dissoluble oral thin films, also known as oral strips, have developed over the past several years from the confection and oral care industries in the form of breath strips and have since established themselves as a distinctive and widely popular type of product for supplying vitamins and personal care items. The possibility to adapt this technique to oral thin film forms was seized by companies with experience in the manufacture of chemical compound coatings containing active pharmaceutical components for stratified drug delivery. Oral thin films are now in the early to intermediate phases of research for pharmaceuticals and are a proven and approved method for the broad delivery of insect genus for over-the-counter drugs. This is mostly a result of Listerine Pocket Parks' popularity in the American consumer market for client, buyer, and patron breath-thing products. These methods provide a fabric coating between 50 and 200 millimetres thick using a variety of deliquescent polymers. According to reports, this movie will include soluble, insoluble, or flavor-masking pharmacological ingredients. The film is manufactured at a factory as an enormous sheet, from which individual dosage units are removed and packaged in a wide range of pharmaceutically approved shapes.

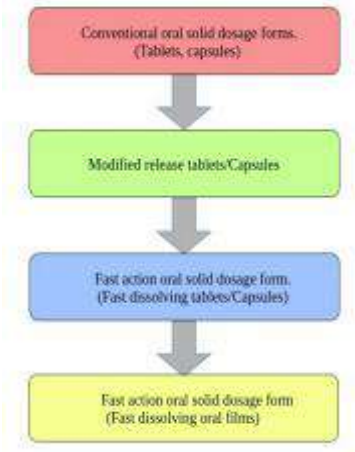

Fig. 2: Development of fast dissolving oral film

Formulation consideration

- A pharmacological active component.
- Polymer that forms films.
- Plasticizers.
- Agent for disintegrating.
- A soluble substance.
- Sweetening substance.
- A stimulant for saliva.
- Flavouring substance.
- A colourant.

Active pharmaceutical ingredients

A typical film composition has 1-25% weight/weight of the medication. Quick-dissolving films can be used to deliver a range of pharmaceutical substances. The easiest choices to be included in a mouth-dissolving film are small dosage compounds. For mouth-dissolving films, different classes of medications such as neuroleptics, vessel agents, analgesics, anti allergic, anti epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and medications used for dysfunction, anti-alzheimers, and expectorants are suitable.5,6 List of the pharmaceutical molecules that will be included in the mouth film48

Table 2: Pharmaceutical ingredients incorporated in mouth film

Drug	Dose	Therapeutic category
Loratadine	10 mg	Anti histaminic
Chlorpheniramine maleate	4 mg	Anti allergic
Famotidine	10 mg	Antacid
Azatadine maleate	1 mg	Anti histaminic
Sumatriptan succinate	35-70 mg	Anti migraine
Ketoprofen	12.5mg	Analgesic
Ondansetron	2.5 mg	Antiemetic
Nicotine	2 mg	Smoking cessation
Acrivastine	8 mg	Anti histaminic

Film forming polymer

The film-forming component, which accounts for 20–75% (w/w) of the mouth-dissolving film's total dry weight, determines the physical and mechanical qualities of the mouth-dissolving film. Therefore, one of the most important and challenging factors for the formulation's effective development is the choice of chemical. The polymers utilised should have the right mechanical characteristics, quick disintegration, smart mouth feel, and smart hydrophilicity. Along with being intelligently soluble, the molecule must also possess further mechanical, chemical, and porous qualities. A movie has to have a high mechanical strength with room for elongation and physical property qualities in order to maintain its integrity against the internal and external stresses created during storage and in especially once exposed to environmental conditions.4,5

Ideal properties of the film forming polymers

1. It should have astute wetting and spreading capabilities.
2. There shouldn't be any leachable contaminants in it.
3. It shouldn't cost a much.
4. It should have a respectable amount of time.
5. It should have a sophisticated mouth feel.
6. The substance must be strong and have ample peeling capacity. an inventory of the polymers used in twin films.4,5

Table 3: Film forming polymer used in mouth film

Group	Class	Example
Natural	Protein	Polymerized resin
	Resin	Pullulan, Pectin, Sodium alginate ,Maltodextrin,
	Carbohydrate	Sodium starch glycolate
Synthetic	Cellulose Derivative	[E3,E5,E15,K3,K 15,K50] Hydroxypropyl Methylcellulose Secekol30, carboxy methyl cellulose, methyl cellulose [A3,A6,A15], Sodium Croscarmellose, carboxymethyl cellulose Sodium
	Vinyl	Polyvinyl Pyrrolidone(K-
	Polymer	90,K-30) Polyvinyl alcohol
		Poly ethylene oxide
	Acrylic Polymer	Eudragit (RD100,9,10,11,12 and RL100

Plasticizer

Plasticizers are employed to lower the glass transition temperature and enhance polymer flow. It aids in enhancing the strip's suppleness and lowering its brittleness. It also affects how quickly the medicine is absorbed. The proper usage of plasticizers can have a number of impacts, including cracking, blooming, pilling, and spitting of the strip.

Several polymers that are plasticized with other polymers include,

1. With the help of hydroxyl-containing plasticizers including glycerol, polyols, propylene glycol, and PEG, cellulose hydrophilic polymers were easily plasticized.
2. Citric acid and phthalic acid esters were used to plasticize less hydrophilic cellulose polymers.
3. The table below includes examples of several medications that include various plasticizers.

Table 3: Plasticizer used in mouth film

oral film	Plasticizer
Montelukast sodium	Glycerin
Triclosan	Propylene Glycol
Sertraline	Propylene Glycol or PEG-400
Telmisartan	Propylene Glycol
Amlodipine Besylate	Glycerol

Levocetirizine Dihydrochloride	Glycerine, Dibutyle Phthalate

Saliva stimulating Agent

This substance will promote saliva production, which might hasten the breakdown of the oral thin film. Water-soluble vitamins, malic, tartaric, citric, and lactic acids are a few examples. Between 2 and 6 w/w of the strip, one of these agents will be utilised alone or in combination.7

Flavouring agent

The type of medicine that will be included in the formulation will influence the flavour choice. The kind and strength of the flavour will determine how many flavours are required to complete the assignment. Any flavour that has received US FDA approval will often be used to cover up the formulation's bitter flavour. Examples include essential oils, menthol, strong mints like pepper, sweet, spear, wintergreen, cinnamon, and clove, as well as sour fruits like lemon and orange and sweet confectionery flavours like vanillin and chocolate.2,8

Sweetening Agent:

Sweeteners are typically used to cover up the bitter flavour of binding drugs. Both natural and artificial sweeteners may be used separately or in combination.9

Table 4: sweetening agents used in mouth film.

Sweeteners	**Example**
Natural	Xylose, Glucose, Mannose, Fructose, Dextrose, Sucrose, Maltose, Comsyrup solids
Artificial	1stgeneration: Saccharin, aspartame, Cyclamate

Surfactant

Surfactants are employed in formulations as a solubilizing or wetting agent to breakdown films quickly and release active ingredients. Examples include Tweens, Benzalkonium chloride, and Sodium Lauryl Sulphate.

Manufacturing methods

There are several methods for producing rapid-disposing film, which are categorised as follows: 8

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

A. Method of preparation of film:

Solvent casting method

Excipients are dissolved in water for the solvent casting procedure before water soluble polymers are added, followed by the medicine and stirring to create a homogenous solution. The fluid is then dried after being cast into the Petri dish.11

Advantages:

1. 1.More flexibility.
2. 2.Better physical properties.
3. 3.Finished film thickness is 12-100um.
4. 4.great clarity then extrusion.
5. 5.great uniformity of thickness.

Disadvantage: polymer must be soluble in a volatile solvent or water viscosity should be formed.2

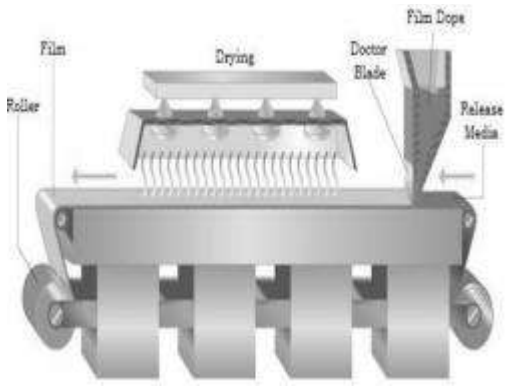

Fig. 3: Solvent casting method for preparation of mouth films.

Fig. 4: Solvent casting method for preparation of film at laboratory

Semisolid casting

When acid-insoluble polymers are required for the film production, this approach is preferred. Gel mass is cast in to the films or ribbons using heat-controlled drums in the semisolid casting process. Gel mass is created by mixing a film-forming solution with an acid-insoluble polymer solution in sodium hydroxide or ammonium hydroxide. The polymers cellulose acetate phthalate and cellulose acetate butyrate are acid-insoluble and are used to create films. The ratio of acid-insoluble polymer to film-forming polymer should be 1:1.12.

Hot melt extrusion

In the hot melt extrusion procedure, the medication and carriers are first combined in solid form. The extruder is then fed with dry, granular material. To process the granules inside the extruder barrel for around 3–4 minutes, the screw speed should be set at 15 rpm. Zones 1, 2, 3, and 4 should each have processing temperatures of 800 C, 1150 C, 1000 C, and 650 C. After pressing the extrudate (T = 650 C) onto a cylindrical calendar, a film was produced. Hot melt extrusion has several advantages28, 29. Less operational units -Better homogeneity of content -Anhydrous procedure Extrusion with solid dispersion Immiscible components are extruded with the medication in this process, and solid dispersions are subsequently made. Finally, dies are used to mould the solid dispersions into films.12

Advantages:

1. Cost effective process with reduced production time and reduced number of unit operation.
2. Improved bioavailability of poorly soluble compounds.
3. Capability of sustained, modified and targeted release.
4. Have stability at varying pH and moisture levels.
5. Rolling Method

In the rolling procedure, a prepared medication solution or suspension containing a film-forming polymer is put into the roller. Specific rheological considerations should be made for the solution or suspension. Water and an alcohol-water combination make up the majority of the solvent. The film is cut into the required shapes and sizes once it has dried on the rollers.12

Application of oral strip in drug delivery

for quick absorption is sought, such as for treating pain, allergies, sleep issues, and diseases of the central nervous system, oral mucosal distribution via buccal, sublingual, and mucosal routes by use of OTFs may become the preferred delivery strategy. Dissolvable oral thin films, originally in the shape of breath strips for the confection and oral care sectors, have developed over the past several years into an innovative and well-liked delivery method for vitamins and personal care items.28

Topical applications:

The distribution of active substances, such as analgesics or antibacterial compounds for wound care and other purposes, may be possible using dissolvable films.

Retentive dosage systems:

Dissolvable films are being studied for dosage forms that incorporate molecules with a range of molecular weights that are both water-soluble and poorly soluble in a film format. The gastrointestinal tract's pH or enzyme secretions may cause the films to dissolve, which may be utilised to treat gastrointestinal diseases. 29

Diagnostic device :

Dissolvable films can be filled with delicate chemicals to permit controlled release when

exposed to biological fluids or to construct isolation barriers for dividing numerous reagents to enable a timed reaction inside a diagnostic device.28,29

EVALUATION PARAMETERS

Weight variation test

Each formulation batch is subjected to a random examination of films. Each film strip's weight was measured using a digital analytical balance, and both the weight variation and the mean deviation of the films were computed and recorded.1

Fig. 5: Digital analytical balance

Thickness

The thickness was measured using tools including dial gauges, Vernier callipers, screw gauges, and microscopes. To determine the average thickness of the film, thickness is measured at several locations. As long as the sample is equal to the dose of the medicine that was consumed, the thickness may be determined using a Vernier calliper. After ensuring that the pointer was adjusted to zero and lifting the anvil of the thickness gauge, the film was inserted, held against the anvil, and the reading on the dial was recorded.A three-reading average was computed. It is crucial to confirm the uniformity of the film's thickness since it has a direct impact on the accuracy of the dosage in the strip.18

Fig. 6: Electronic digital caliper

Folding endurance:

The folding endurance value is calculated as the number of folds the film can withstand without breaking. The number of folds necessary to produce cracks—300 in certain cases—gives the value of folding endurance. The folding is done at the same location repeatedly.1,11

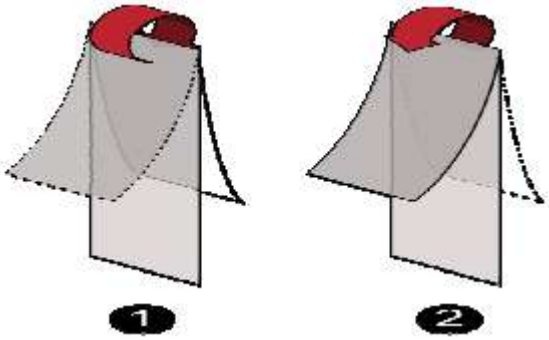

Fig. 7: Folding endurance test

Tensile strength

Tensile strength is the amount of tension needed to rip the film. It is determined as follows by dividing the load at rupture by the cross-sectional area of the film.22

$$\text{Tensile strength} = \frac{\text{load at failure} \times 100}{\text{Film thickness} \times \text{Film width}}$$

To achieve the best results, use a film that is physically flawless. The film was pulled at a rate of 5 to 10 mm/min while being held 10 mm apart between two clamps. Three times the entire experiment is conducted.2,13

Fig. 8: Tensile strength detector

Percent elongation

The film extends after being under stress, which is referred to as strain. The term "strain" refers to the division of a film's changed length by its original or first length. The percentage of elongation is quantitatively proportional to the volume of plasticizer added during the film's formulation. A film with greater elongation qualities is produced by adding additional plasticizer to the formulation. These variables decide it23

$$\text{Percentage elongation} = \frac{\text{change in length} \times 100.}{\text{Initial length}}$$

Drug uniformity

Any chosen assay technique specified for that specific API in any of the standard pharmacopoeia is used to conduct the test to establish whether there is a drug uniformity in all the films that are made. By measuring the API content in each individual strip, content consistency is assessed. 85–115% is the maximum content homogeneity. In the case of loperamide, each film is dissolved in 50 ml of methanol-filled volumetric flask. It is further filtered using Mann Filter Paper No. 41.A portion of 1 ml of filter solution was added to a 25 ml volumetric flask that had been filled with 6 ml of phosphate buffer. The solution is tested in an ultraviolet spectrophotometer at 223 nm using a phosphate buffer solution at pH 6.8 as a blank. Drug homogeneity Any chosen assay technique specified for that specific API in any of the standard pharmacopoeia is used to conduct the test to establish whether there is a drug uniformity in all the films that are made. By measuring the API content in each individual strip, content consistency is assessed. 85–115% is the maximum content homogeneity. In the case of loperamide, each film is dissolved in 50 ml of methanol-filled volumetric flask. It is further filtered using Mann Filter Paper No. 41.A portion of 1 ml of filter solution was added to a 25 ml volumetric flask that had been filled with 6 ml of phosphate buffer. The solution is tested in a phosphate buffer pH 6.8 solution as a blank in a UV spectrophotometer at 223nm.

Surface pH

To study side effects, the pH of the film was determined. The oral mucosa becomes irritated by an acidic or alkaline pH, hence a film must have a surface pH that is near to neutral. For 30 minutes, the film was allowed to swell in a Petri dish at room temperature. To determine the film's surface pH, 1 ml of the solution was then placed under a digital pH metre. 1,15

Fig. 9: Digital pH meter

Swelling test

Insert the wire mesh into a Petri dish filled with 40 ml of 6.8 phosphate buffer. After then, the film's weight rise was monitored at regular intervals until a steady weight was reached. The following formula was used to determine the film's hydration ratio:25,1

Swelling index (SI) = (Wt-Wo)/Wo

Where,

Wt=weight of film at 't' time.
Wo=weight of film at '0' time.

In vitro disintegration test

Disintegration time refers to the period of time when a film begins to dissolve or disintegrate. A single unit disintegration equipment holding 900 ml of 6.8 phosphate buffer was used to conduct the disintegration test for quick mouth dissolving film. The thermostat was set at 37.50.5°C. The temperature at which the film must break is reached, and the time it takes for the film to begin breaking is recorded as the disintegration time of a certain film.26,16

There are two other ways to calculate disintegration time.39,40,41

Slide frame method:

On a petri dish with slide frames fastened onto it, distilled water is dropped onto the film. Disintegration time is the amount of time it takes for the film to dissolve.39,41

Petri dish method:

In a Petri plate filled with 2 ml of distilled water, a film is added. The length of time it takes for the film to totally dissolve is referred to as the disintegration period.39,42\

Fig. 10: Disintegration apparatus

In vitro dissolution study

Fast-dissolving film's in vitro dissolution was investigated using a USP paddle dissolution test device and 900 cc of phosphate buffer with a pH of 6.8. The experiment was conducted at a constant temperature of 37.5%C and 50 rpm. A 5 minute withdrawal of a 5 ml sample was made. and phosphate buffer with a pH of 6.8 was substituted for the same amount. With the use of a UV visible spectrophotometer, the proportion of medication released was calculated.14.

Fig. 11: Dissolution apparatus

Technologies44

SOLULEAVES

This is used to products that release flavours, such as victuals, candy, and mouth fresheners. Using SOLULEAVES technology, active chemicals are frequently delivered to the tongue quickly, in a pleasant manner, and with minimal effort. In order to swiftly release the flavours and active components, SOLULEAVES films are frequently made to dissolve rapidly when they come into contact with saliva. This characteristic makes edible films a fantastic delivery method for a wide range of goods needing fast disintegration in the mouth. For pharmacological purposes, this method of administration is especially beneficial for young patients or elderly patients who may have difficulty ingesting antiquated pills or capsules. Along with providing organic process products, the delivery systems are frequently employed for the treatment of pain, gastrointestinal, and cough/cold-related disorders. Additionally, SOLULEAVES films can be made to adhere to mucous membranes and release the active component gradually over the course of a quarter-hour.

WAFERTAB

It can be a proprietary delivery system that employs a cutting-edge technique to organise drug-loaded thin films for topical or oral

treatment.When casting a drug delivery system with pharmaceutical actives into an ingestible filmstrip, active components are included into the film. When saliva contacts the strip within the mouth, the system quickly dissolves and releases the active ingredients. The WAFERTAB filmstrip frequently have enhanced style masking and are elegant. The precise treatment and integration of the active component into a pre-fabricated XGEL film's body prevents exposure to excessive heat and moisture and may even increase product stability. The WAFERTAB technology opens up a variety of opportunities for cutting-edge product design by permitting the secure association of several films containing various active ingredients. WAFERTAB are frequently available in a variety of sizes and forms, making them the ideal delivery method for medications that require rapid release or for usage by patients who have difficulty swallowing.

FOAMBURS

It is a unique variation of the SOLULEAVES technology used whenever a chemical is introduced into the film while it is being produced. This results in a movie with a pitted structure that disintegrates quickly and creates a distinctive mouth experience. Food and candy manufacturers are interested in FOAMBURST as a means of storing and releasing flavours.

XGEL

This film, which is used in all of Meldex International's film systems and ingestible infinite quantity delivery technologies, is the foundation of the company. With its nonanimal origin, spiritual approval, and suitability for vegetarians, XGEL film offers particular product advantages for care and pharmaceutical goods. Its continuous production method also offers a financially and strategically advantageous foundation for production. In addition to having the ability to be enteric, XGEL films are frequently styled to be opaque, coloured, layered, and capable of containing active medicinal substances. The XGEL film systems may be dissolved in either cold or difficulty and are frequently designed to encapsulate any oral indeterminate quantity kind. XGEL film is made up of a range of different soluble polymers that have been specially tailored for the intended function. All of the components in XGEL are listed and generally regarded as safe. The pharmaceutical industry is now seeing a transformation in terms of product offers and production methods thanks to Bio Progress's X Gel film Technology.

Storage and Packaging45

Drug manufacturers benefit from more product flexibility throughout the changing and packaging stages. As needed for the appliance, the rolled film may be sliced into smaller rolls or die-cut into any shape or size. Converting companies sometimes want to print information directly onto the film unit dosages before packing in order to comply trade rules and stigmatisation purposes. The need for unit-dose packaging, barcode labelling and the content of usage instructions, child-resistant sealing, and packaging that is senior-friendly are all considerations.27 In the pharmaceutical industry, it's crucial that the package effectively preserves the product's integrity. To protect the dosage of different quick-dissolving dose forms, expensive packaging, particular processes, and extra attention are required during production and storage. There are several packing options available for quickly disintegrating films. For films, which are medicinal materials, solitary packaging is required; the most popular type of packaging is a metallic element bag. Specifically created for the quick films, APR-Labtech has created the speedy card, a patented and exclusive packaging solution. Three raid videos are stored on each side of the fast card, which is the same size as a Mastercard. It is possible to take each dosage

alone. The chosen cloth should have the following qualities:

- They must protect the preparation from the environment.
- They have to be Food and Drug Administration approved.
- They have to meet applicable tamper resistant demand.
- They have to be non-toxic.
- They have to not be reactive with the merchandise.
- They have to not impart to the merchandise tastes or odors.31

Foil, paper or plastic pouches

The adaptable pouch may be a packaging concept that can offer a package that is not only temperature-resistant but also, with the correct fabric selection, a product with a high level of environmental protection. A multifunctional pouch is often formed by a vertical or horizontal forming, filling, or waterproofing instrumentation during the goods filling process. The bags might be single bags or bags for metallic elements. Single pouch and metallic element pouch: A peelable soluble film drug delivery pouch for "quick dissolve" soluble films with good barrier qualities is also possible. Clear packaging allows for product display. Using a two-structure combination enables one side to be transparent and provides the option of using a low-cost foil lamination. The foil lamination essentially has no gas or moisture transfer. The container offers a flexible narrow film that may be used for pharmaceutical and nutraceutical purposes. Each substance and dose are protected by the sole dose bag. The most often used bag is made of a metallic material.

Blister card with multiple units

The blister tool is made up of two parts: the blister, which is the formed chamber that houses the product, and the lid stock, which is the substance that seals to the blister. The thermoplastic rosin sheet used to make the blister packaging is softened by heat before being vacuum-drawn into a mildewed shape. The sheet is free of mildew and pays off to the packing machine's petrol station when it is cooling. The previously formed semi-rigid blister is filled with the product and has a heat-sealable material lid. The level of security required should primarily guide the film selection. Tin foil is typically used as the material for the lid. Plastic is frequently the material chosen to form the cavity because it may be used to protect the dosage form from moisture.31

Barrier Films

Since many pharmacological formulations are extremely sensitive to moisture, strong barrier coatings are required. Numerous materials, such as plastic and Polychlorotrifluoroethylene (PCTFE) film, are also known to provide moisture protection. Under any circumstances, plastic does not stress fracture. It is an excellent vapour and gas barrier. Clarity issues still provide a challenge.

Applications of quick dissolving buccal films46

Vaccines

buccal films that dissolve quickly. Film can be administered in the form of a vaccine that is stable at room temperature; as a result, it dissolves fast in the mouth and in spittle. The temperature-stable, fast-dissolving buccal film delivery device for the reovirus vaccine, which is now available in the United States, will make being immunised almost as simple as brushing your teeth. The benefits of this delivery system include increased patient compliance, increased bioavailability, and decreased costs for handling, administration, storage, and distribution.46,49

Controlled and Sustained release film

prolonged release Numerous polymers, including derivatives of polyose and chitosan, are employed as excipients in buccal film, which is useful in hospital preparations. By virtue of their release

qualities and stickiness, they help to increase application, minimise toxicity, wound dressings, oral mucoadhesive, and water-resisting adhesive.32,35

Taste masking

A crucial need for the commercial success of quickly dissolving pills is taste masking. Quickly dissolving buccal films dissolve or break down in the patient's mouth, releasing the active components that are in touch with the style buds. A soluble chemical substance supports buccal films that dissolve quickly. The film's ability to dissolve fast without the need for water offers patients with swallowing issues and patients who suffer from nausea, such as those undergoing treatment, an alternative. Table No. 536, 37, and 38 lists the various commercially available quick-dissolving film formula This attribute is crucial for patient compliance. By using solvent evaporation and solvent extraction procedures, a drug with an unfavourable bitter flavour may be microencapsulated into acrylic polymers that are pH scale sensitive. These polymer microspheres demonstrated total dissolving in a remarkably short period of time and a cost-effective masking method.33,35

Orally disintegrating films

Table 5: Marketed Films available in market.43

Brand name	Manufacturer /Distributer	API(strength)	Uses
Gas-X	Novartis	Simethicone (62.5 mg)	Anti Flatulating
Benadryl	Pfizer	Diphenhydramine HCL (12.5mgor 25mg)	Anti allergic
Chlorase ptic	Prestige	Benzocaine/menthol (3 mg/3 mg)	Sore throat
Orajel	Del	Menthol/pectin(2mg/ 30 mg)	Mouth ulcer
Triaminic	Novartis	Diphenhydramine HCL (12.5 mg)	Anti allergic
Listerine Cool Mint Pocket Paks	Pfizer, Inc.	Cool mint	Mouth fresheners
Klonopin Wafer	Solvay Pharmaceuticals	Clonazepam In five strength (0.125mg,0.25 mg, 0.5 mg, 1 mg and 2 mg.)	Treatment of anxiety

CONCLUSION

The current research demonstrates that one of the cutting-edge methods in the world of pharmaceutical sciences is the use of oral quick-dissolving films. In comparison to traditional indefinite quantity forms, they need better patient compliance and acceptability while posing no choking danger. The primary goal of developing oral disintegrating films was to address the difficulty that disturbed paediatric, geriatric, and mental patients had eating conventional oral indeterminate quantity forms. Oral dissolving films are currently widely available for conditions such as pain, acidity, allergies, and cardiovascular disease. reflects their significance. Major advantages of such indefinite quantity types include their administration without the use of water, which meets the needs of the target population for ease in drug administration while also avoiding internal organ metabolism, leading to an improved therapeutic response.

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REFERENCES

1. Pawar R, Sharma R, Sharma P, Darwhekar GN, A Review on Mouth Dissolving Film, Journal of Drug Delivery and Therapeutics. 2019; 9(6):206-210
2. Deepak Sharma, daljitkaur, Shivani Verma, Davinder Singh,Mandeep Singh, Gurmeet Singh, Rajeev Garg, Fast Dissolving Oral Films Technology: a recent trend for an innovative oral drug delivery system.international journal of drug delivery 7(2015)60-75
3. Sharma Pravin kumar, Sharma Pankaj kumar. An overview about novel fast dissolving oral films. International Journal of Drug Regulatory Affairs; 2018, 6(1), 1-7
4. Nagar P,Chauhan L,Yasir m.A Review:Insights into Polymers:Film Formers in Mouth Dissoloving Films, Drug Invention Today,2011;3(12):280- 289
5. Garima B, Vipin G, Siddiqui MN. Investigation of polymers alone and in combination for the development of oral thin film. Int.J. Invent Pharmaceutical sci.2013;(3):231-235
6. Patil P, Shrivastava SK, Fast Dissolving Oral Films: An Innovative Drug Delivery System Int. J.Sci.Res. 2014,3(7) :2088- 2093
7. Ghodake PP, Karande Km , Osmani RA, Bhosale RR, Bhargav ,HarkareR,Kale BB. A Review : Mouth Dissolving Film Innovative Vehicle For Oral Drug Delivery ,Int J Pharmceutic Res. 2013; 2(10): 41-47
8. Puja Chaurasiya et.al.Asian Journal of Research in Chemistry and Pharmaceutical sciences.4(4),2016,165- 175.
9. Julie Mariam Joshua, R Hari, Fithal K Jyothish, Saritha A Surendran : Fast Dissolving Oral Thin Film: An effective Dosage Form For Quick Releases ,Int.J. Pharm. Sic .Rev. Res. 38(1) May- June 2016,282-289
10. Kumar RK, Sulochana MM. Fast Dissolving Films; A unique strategy for Drug Delivey, Asian J.pharmaceut, Res.2014;4(1);47-55
11. M Nishimura, K Matsuura, T Tsukioka, H Yamashita, N Inagaki, T Sugiyama, Y Itoh, In Vitro And In Vivo Characteristics Of Prochlorperazine Oral Disintegrating Film. International Journal Of Pharmaceutical Scienses. 368(2): 2009: 98–102
12. Bhupinder Bhyan,Saritajangra,Mandeepkaur, Harmanpreetsingh,Orally Fast Dissolving Films: Innovations In Formulation And Technology,International Journal Of Pharmaceutical Sciences Review And Research.Volume 9, Issue 2, July – August 2011; Article-009
13. Sagar Kishor Salve ,Formulation And Evaluation Of Mouth Dissolving Film Containing Vildagliptin; Asian Journal Of Biomaterial Research 2017; 4(2):23-38
14. Shelke PV, Dumbare AS, Gadhave MV, Jadhav SL, Sonawanne AA, Gaikwad DD. Formulation and evaluation of rapidly disintegrating film of Amlodipine bedylate.Journal of Drug Delivery & Therapeutics. 2012; 2(2): 72-75.
15. Narasimha Rao R. Formulation and evaluation of rapidly dissolving film Etophylline.International Journal of Pharmacy and Biological Sciences. 2011; 1: 145-159.
16. Patil. Development and evaluation of fastdissolving film of montelukast sodium. World Journal of Medical Pharmaceutical and Biological Sciences. 2011: 6-12.
17. Yellanki SK, Jagtap S, Dissofilm: A Novel Approach for Delivery of Phenobarbital;Design and Characterization. Jonrnal of Young Pharmacist.2011: 181–188.
18. Panchal MS, Patel H, Bagada A, Vadalia KR. Formulation and evaluation of mouth

dissolving films of Ropinirole hydrochloride by using pullulan polymers. International Journal of Pharm Res & All Science. 2012; 1(3): 60-72.

19. Nidhi P. Sapkal, Vaishali A. Kilor. Development of fast dissolving oral thin films of ambroxol hydrochloride: Effect of formulation variables. Journal of Advanced Pharmaceutical Research. 2011: 102-109.
20. Raju S. Oral films of Metoclopramide hydrochloride for pediatric use: Formulation and in-vitro evaluation. Journal of Chemical and Pharmaceutical Research. 2011: 636-646.
21. Gupta MM, Patel Mitul G, Madhulika Kedawat. Enhancement of dissolution rate of rapidly dissolving oral film of meclizine hydrochloride by complexation of Meclizine hydrochloride with βcyclodextrine. Journal of Applied Pharmaceutical Science. 2011:150-153.
22. Sapkal NP, Kilor VA, Daud AS, Bonde MN. Development of fast dissolving oral thin films of Ambroxol hydrochloride: Effect of formulation variables. Journal of Advanced Pharmaceutical Research. 2011; 2(2):102-09.
23. Doaa A, Nevine S. Formulation of a novel Tianeptine sodium orodispersible film. Journal of Pharmaceutical Science & Technology. 2010; 11(3):1018-25.
24. Yoshinori Itoh. Preparation of a fast dissolving oral thin film containing dexamethasone:A possible application to antiemesis during cancer chemotherapy. European Journal of Pharmaceutics and Biopharmaceutics. 2009: 361–365.
25. Renuka Mishra, Avani Amin. Formulation and Characterization of Rapidly Dissolving Films of Cetirizine hydrochloride using Pullulan as a Film Forming Agent. Indian Journal of Pharmaceutical Education and Research. 2011; 45: 71-77.
26. Bhanushali AK, Chaudhary PM, Sonawane TD, Solanki ND. Formulation and evaluation of mouth dissolving tablet of isosorbide mononitrate. International Research Journal of Pharmacy. 2011; 2(3): 149-53.
27. Frey P. ìFilm Strips and Pharmaceuticals,î Pharma. Mfg. & Packag. Sourcer, winter, 2006: 92-93.
28. Barnhart S.D, Sloboda M.S. The Future of Dissolvable Films. Drug Delivery Technol. 2007;7 (8): 34-37.
29. Meathrel B, Moritz C. Dissolvable Films and Their Potential in IVDs. IVD Technol. 2007; 13(9): 53-58.
30. Vondrak B, Barnhart S. Dissolvable Films for Flexible Product Format in Drug Delivery. Pharmaceutical Technology Supplement. April 2008.
31. L Lachmann. In The Theory & Practical of Industrial Pharmacy, 3rd ed, Varghese Publishing house, Fourth Indian Reprint, 1991, page no 344-348.
32. W Habib; R Khankari; J Hontz. Drug Carrier Systems, 2000, 17(1), 61-72.
33. SS Biradar; S Bhagavati; The Internet Journal of Pharmacology, 2006, 4, 135- 136.
34. Y Kato; H Onishi; Y Machida. Current Pharmaceutical Biotechnology, 2003, 4 (5), 303-309.
35. Apoorva Mahajan et al Der Pharmacia Lettre, 2011, 3(1):152-165
36. Vondrak B, Barnhart S. Dissolvable Films for Flexible Product Format in Drug Delivery, Pharmaceutical Technology Supplement. April 2008.
37. Verena Garsuch. Preparation and characterization of fast-dissolving oral films for pediatric use [dissertation]. D¸sseldorf, Heinrich- Heine University (2009) pp13.

38. Alpesh. R. Patel et al: Fast Dissolving Films.Int.J.Drug Dev. & Res., April-June 2010, 2(2):232-246.
39. Pawar R, Sharma R, Sharma P,Darwhekar GN, A Review on Mouth Dissoving Film, Journal of Drug Delivery and Therapeutics, 2019; 9(6):206-210.
40. Laohakunjt N,Noomhorm A. Effect of plasticizers on Mechanical and Barrier properties of rice Starch film, Starch/Staerice 2004;56:348-356.
41. Wu Y, Weller C, Hamouze F, Cuppett S, Schnepf M. Moisture Loss and Lipid Oxidation for Precooked Ground-Beef Patties packaged in Edible Starch-Aginate Based Composit films. Journal of Food Science 2001;66(3):486-493.
42. El-Setouchy El-Malak N.Formulation of a Novel Tianeptine Sodium Orodispersible Film, AAPS Pharm Sci Tech. 2010;11(3) 1018-1025.
43. Rajani Bala, Pravin Pawar,Sandeep Arora; Orally dissoving strips: A new approach to oral drug delivery system; Int. Journal of Pharmaceutical Investigation.2013 Apr-Jun; 3(2):67-76.
44. Heena Mulla Muzawar, Viresik.k.Chandur, A.R. Shabaraya; Formulation, Evaluation and optimization of Fast Dissolving Oral Strips of Isosorbide Mononitrate, Am.J.Pharm Tech Res. 2014;4(3).
45. Vishwkarma DK, Tripathi AK, Yogesh P and Maddheshiya B, Review Article on Mouth Dissolving Film. Journal of Global Pharma Technology, 2011; 3(1): 1-8.
46. Patel AR, Prajapati DS and Raval JA: Fast dissolving films (FDFS) as a newer venture in fast dissolving dosage forms. International Journal of Drug Development and Research, 2010.
47. Aggarwal J, Singh G, Saini S and Rana AC. Fast dissolving films: A novel approach to oral drug delivery. Int Res J Pharm, 2011; 2(12): 69-7.
48. Dhere PM, and Patwekar SL. Review on conventional dosage forms. So they are of preparation and evaluation of oral disintegrating films greatimportance during the emergency condition like, 2011: IJPT, 3(4): 1572-1585. allergy, Short term spasm and asthma.
49. N.G.Raghavendra Rao, Priyanka Gupta, Amruta Bisht; Fast Dissolving Oral Film: A Comprehensive Review; WJPMR 2019 5(7),116-127.

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