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Fast dissolving film: As advanced Venture for an Oral route Drug Delivery System

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Abstract

Finding and perfecting novel compounds is a lengthy and resource-intensive process. This is why the healthcare sector is investing so much in the advancement of new methods of administering current medications. The rapid dissolving oral film is a kind of delivery technology that has seen increasing use in both young children and elderly people. Fast dissolving films have the potential for industrial use because of their advantages over fast disintegrating tablets. However, the lack of friability and the risk of choking are more likely to occur in paediatric and elderly patients, who may benefit from quick dissolving tablets. The oral film dosage form not only improves upon the strengths of existing quick disintegrating systems, but also responds to the needs of the market that have previously gone unfulfilled. The potential for further research of orally rapid- dissolving films, as well as their design and development, is emphasised in the current review.

Keywords: - Mouth Dissolving, Films, Super Disintegrants, Polymers, Plasticizers

Introduction

Oral medication delivery systems still need some improvements due to their a few drawbacks related to unique class of sufferers, such as elderly people, paediatric, dysphasic unconscious patients, emetic patients, bowel movements, and individuals experiencing an acute episode. people with several medical issues who have trouble gulping or chewing large pills. People with busy lifestyles are more likely to have allergic responses or sneezing episodes. It may also be used locally for anaesthetic in cases of tooth pain, mouth sores, fever blisters, or teething[1]. It is estimated that half of the population has been impacted by this problem, leading to a higher likelihood of noncompliance and poor treatment. The tablet form of even quick dissolving pills poses a choking hazard. 26 percent of 1576 patients studied had difficulty taking their medications because of difficulty swallowing. To get past this As a replacement for traditional medication delivery methods such as pills, pills, syrup, etc., the late 1970s saw the introduction of oral rapid disintegrating drug delivery systems. These doses may be taken orally without the use of water, since they dissolve or disintegrate within three minutes. Oral fast dissolving doses have begun to gain popularity as an alternative

method of administering medications. A novel method of administering medication by mouth involves films that dissolve quickly in the mouth[2].

It's based on transdermal patch technology, which inspired its creation. Because salivary fluid travels down into the stomach, very few medicines are absorbed by the mouth, throat, and oesophagus. When this occurs, the drug's bioavailability is much higher than what would be expected from the conventional dose method. The films used as part of a fast-dissolving delivery method should include enough ingredients to disguise the active ingredient's taste. Saliva, coupled with the soluble and insoluble excipients, helps the patient ingest the disguised active ingredient. Fast buccal dissolving films are films that dissolve in the mouth, allowing for sublingual and buccal absorption of tablets, as well as enteric absorption in the small intestine[3]. A completely thin oral strip is used in the delivery method; it is placed and held firmly on the patient's tongue or other oral mucosal tissue, where it is quickly hydrated by saliva and adheres to the point of application. It rapidly dissolves and disintegrates to allow for Oro-mucosal and intragastric absorption of the medicine. The breakdown rate and kind of polymer utilised determine the film's durability. In accordance with the Pharmacopoeia, the period for orally dissolving film is 5-20 minutes. A new oral dosage form that maximises absorption, initiates action rapidly, and requires little patient monitoring is the holy grail of the pharmaceutical industry. Therefore, rapid dissolving tablets are made with hydrophilic components and superdisintegrant/s. The first rapid medication delivery device was created in the late 1970s. Fast dissolving oral films [FDOFs] are the most cutting-edge kind of oral solid dose form because of their improved versatility and patient convenience. It enhances API efficiency since it dissolves in the mouth just minutes after coming into touch with saliva (chewing is not necessary, and neither is water)[4]. The oral mucosa has a blood flow and permeability that are 4-1000 times larger than skin, allowing for rapid absorption and fast bioavailability of the medicine. One such cutting-edge approach is oral fast dissolving film (OFDF), which allows patients to self-administer their medication without the need for water or chewed and so increases consumer acceptability. When it comes to intraoral fast-dissolving drug delivery systems, this film checks all the boxes: it's easy to handle and administer, comes in handy packaging, has no aftertaste, and is straightforward to produce. The tip of your tongue or the back of your mouth will hold the film. It stays there where it's applied and quickly releases the medicine for local and/or systemic effect. The development of a fast-dissolving film might open up new channels of distribution for a variety of pharmaceuticals (such as neuroleptics, cardiovascular treatments, anaesthetics) and even be suitable for the administration of antihistamines, asthma meds, and ED therapies. It is possible to create films that dissolve in the mouth for a wide variety of medications. Novel goods have the potential to expand treatment options for the following condition: Antitussive, expectorant, and antihistamine medications for children. Anticonvulsants and expectorants for the elderly Illnesses of the digestive tract Pain (migraine) Nausea (from cytostatic treatment)Central Nervous System (Antiparkinsonism Treatment)[5].

Oro-mucosal absorption of the medication occurs immediately from the site of administration to the systemic circulation, bypassing primary-hepatic first pass metabolism, resulting in a rapid beginning of action in a matter of seconds. Strip-forming polymers, plasticizers, active pharmaceutical ingredients, sweeteners, a saliva-stimulating agent, flavorants, colourants, stabilisers, and thickeners are used in the preparation of rapid dissolving films for their aesthetic and functional qualities[6].

It's not shocking that thin-film dosage forms of pharmaceuticals are so popular, given their convenience and efficacy. Both well-established drugmakers and upstarts are interested in this technique. Significant sales goals in the United States and Europe have been met. The market for pharmaceuticals using oral thin-film formulations increased from 2007's $500 million to 2010's $2 billion. A study also predicts that by 2024's conclusion, the

worldwide market for thin-film pharmaceutical goods would have grown from 2015's $7 billion to over $15 billion[7]. That's why we anticipate a 117 percent boom over the next decade as shown in figure 1.

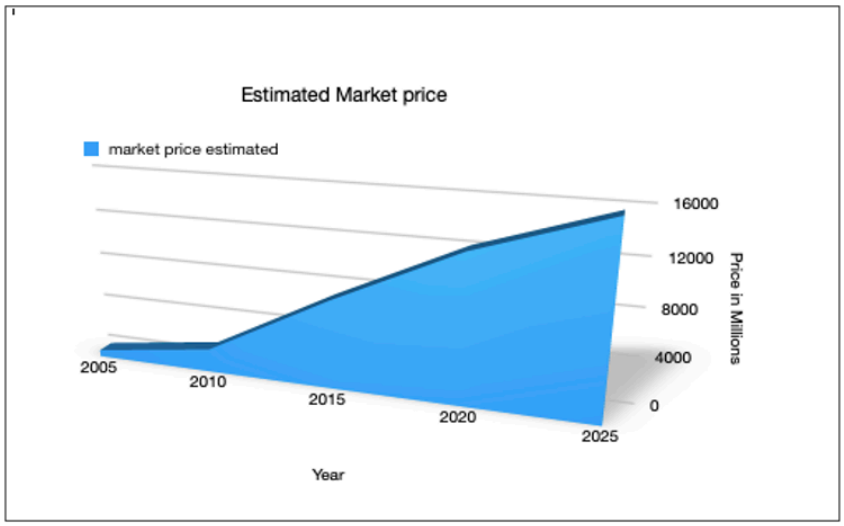

Figure 1: Marketed growth of film

Release Mechanism

A patient's tongue, or other oromucosal tissue, serves as the delivery site. The hydrophilic polymer and other excipients in the film make it instantly moist by saliva, allowing it to affix to the site of application before dissolving and releasing the drug for oromucosal absorption. It has fast dissolving capabilities, allowing for oral GIT absorption, and dissolves quickly to release the drug for mucosal absorption[8].

Special features[9],[10],[11]

- Sizes and forms may be customised.
- A beautiful, thin film.
- Un-obstructive.
- rapid breakdown .or dissolution.
- Quick dissolving, mucoadhesive, and rapid release.
- Criteria for Fast Dissolving Film.
- The mouthfeel of an oral dissolving film should be pleasant.
- It shouldn't be hard to swallow, and it shouldn't take more than a few seconds to dissolve or disintegrate in the mouth without water.
- Good for covering up unpleasant flavours.
- After oral use, there should be little to no aftertaste.
- display a lack of sensitivity to changes in temperature and humidity.

Ideal properties of oral films [12],[13]

- ✓ The tongue gel and flavour should to be pleasing.
- ✓ It should have a high mechanical strength and be less prone to breaking during post-production handling if it is to survive.
- ✓ The medicine must have a long shelf life, be soluble in water and saliva, and be stable.
- ✓ it shouldn't leave any unpleasant aftertaste in your tongue.
- ✓ It must to dissolve rapidly enough to provide instantaneous medication release in the mouth.
- ✓ it must work well with the other component.

1.3. Advantages[14]

- In order to prevent choking,
- It allows for a faster beginning of action at less dosages while avoiding first-pass metabolism.
- Delicious
- Solid foundation
- Water is not necessary.
- The fast breakdown and dissolution in the mouth is made possible by the large surface area.

- The convenience of film for individuals with swallowing difficulties, nausea, and mental issues
- Accurate dosing

Disadvantages[15],[16]

- The film cannot feature such a high dosage.
- The movie package is rather pricey.
- Drugs that irritate the mucous membranes are prohibited.
- Because it is delicate and has to be kept dry,
- Unique packaging is required.

limitation of oral fast dissolving films:

A patient's tongue, or other oromucosal tissue, serves as the delivery site. The presence of saliva causes instant wetting. Since it is difficult to maintain the same dosage over all strips, the FDOFs have significant drawbacks in this regard. One downside is that not all pharmaceuticals can be loaded onto the FDOFs because to constraints such as the drug concentration/dose. Not all drugs may be placed onto the film due to a maximum allowable dosage of 75 mg. In addition, there are constraints on how the strips may be packed, which calls for certain criteria to be met so that the pack does not contact with the film throughout the packing process[17].

Types of fast dissolving oral film[18]

There are three different subtypes as shown in figure 2.

1. Flash release 2. Mucoadhesive melt release 3. Mucoadhesive Sustained release

Classification of fast dissolving technology

For case description, fast dissolving technologies can be divided into three broad group.

I. Lyophilized system: Forming tablet-shaped units from a medication suspension or solution with additional structural additives utilising a moulding device or blistering package is the technology underlying these methods. The pills or units are frozen in the mould or pack before being lyophilized. The final components are so porous that they dissolve quickly in the presence of saliva or water[19].

II. Compressed tablet- : This system is manufactured utilising regular tablet manufacturing techniques and directly compressed excipients. Depending on the production process, tablet technology may be either firm or soft. Fast dissolve tablets are formulated with either water soluble excipients superdisintegrant or effervescent components, enabling water to quickly penetrate the core of the tablet, resulting in faster disintegration compared to a conventional tablet[20].

III. Thin film strips: Oral films, also known as oral wafers, have emerged as an innovative and generally accepted form by consumers over the last several years, having developed from the confection and oral care sectors in the form of breath strips. For the systemic distribution of active pharmaceutical ingredients (APIs), FDFs are currently a validated and recognised technique in OTC medicines, and are in the early to middevelopment stages for prescription treatments. This is said to be due to the popularity of breath mints in the United States, namely Listerine Pocket Paks. Such systems use a wide range of hydrophilic polymers to produce a film with a thickness of 50 mm to 200 mm. The film is produced in long rolls, from which individual doses are sliced for packing in a pharmaceutically acceptable form[21].

Benefits of oral fast dissolving films

Since films have a larger surface area, they melt and disintegrate rapidly in the mouth. OFDFs are convenient in that they may be easily transported, handled by customers, and stored. People with dysphagia, those on strict diets, and the sick may all benefit from this. The film is useful for alleviating symptoms of motion sickness, extreme discomfort, allergy attacks, and coughing fits, all of which need immediate intervention. The drug stays stable for a long time before it is consumed since it is administered in solid dose form. Therefore, it has the advantages of both solid and liquid dose forms, namely, stability and portability[22].

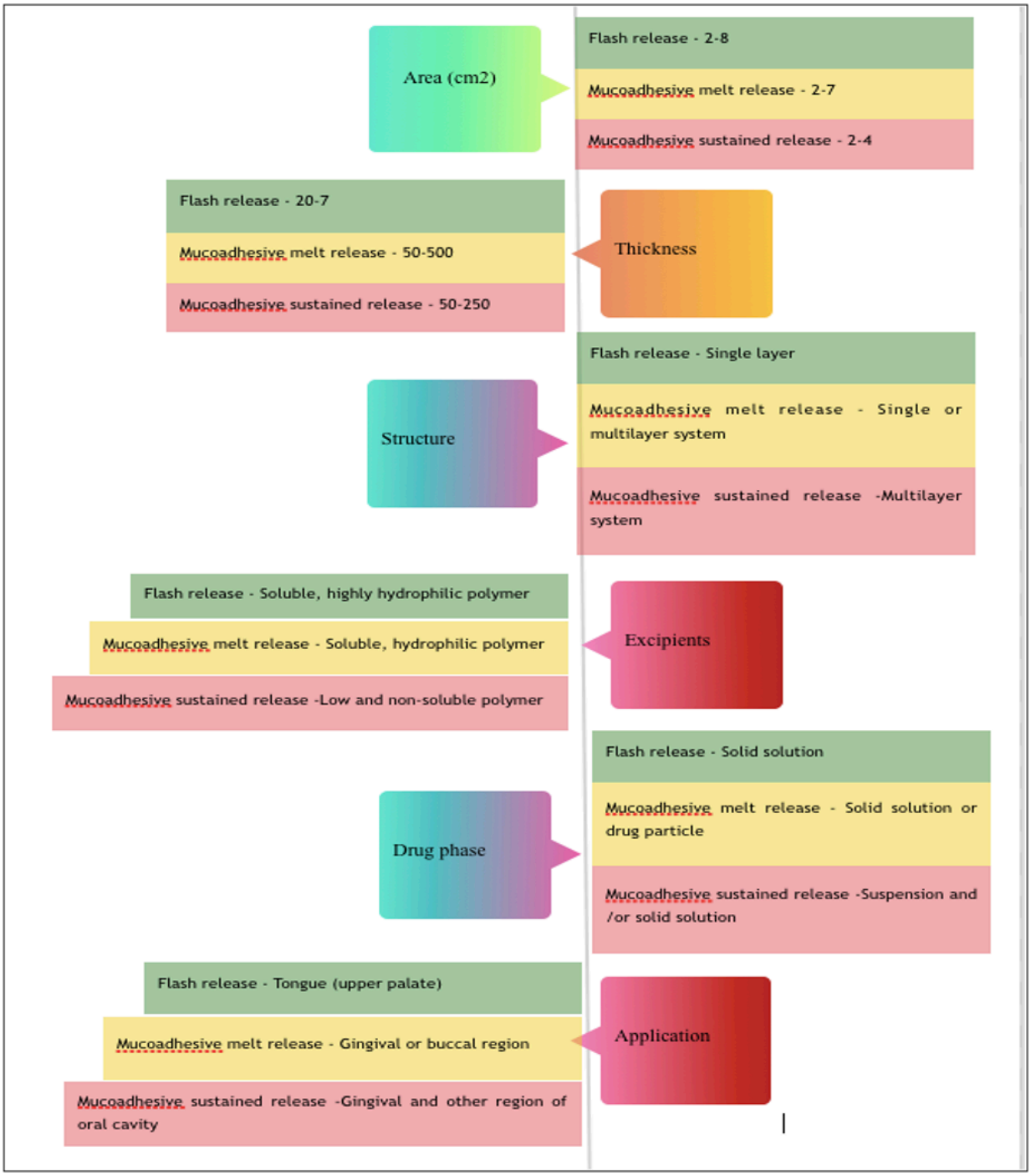

Figure 2: Different characteristics of three types of film

Table 1: Comparison between oral films and oral disintegrating tablet[23], [24]

Fast dissolving films	Fast dissolving tablet
Greater dissolution due to large surface Lesser	Lesser dissolution due to less surface area
Better durable than oral disintegrating	Less durable as compared with oral films
More patient compliance	Less patient compliance than films
Low dose can be incorporated	High dose can be incorporated
No risk of choking	Fear of choking

Structural feature of oral mucosa

Buccal mucosa structure: The total length of the oral cavity is around 100 centimetres. approximately a third of this area is the buccal surface, which is coated by epithelial measuring approximately 0.5 mm in thickness . Keratinized and non-keratinized regions of the oral epithelium have different lipid profiles. Polar lipids, such as lipoprotein sulphates and glucosylceramides, are in little supply in the non-keratinized epithelium, whereas neutral lipids (such as ceramides) predominate in the keratinized epithelium. The buccal membrane contains several elastic dermal fibres that also function as a barrier to the passage of drugs over the membrane. To enter the general blood supply through a system of capillaries and arteries. Lymphatic drainage and venous vascularization are almost parallel[25].

Permeability:

Although the buccal membrane is thicker and more porous than other oral regions, the oral mucosa as a whole has a relatively modest permeability overall. It's so buccal The mucosa acts as a barrier to both the absorption of medicines and their subsequent effects. This is a barrier, and buccal absorption is another aspect. influencing the delivery of pharmaceuticals. The buccal mucosa's permeability is thought to be four to ten thousand times that of the skin. Buccal and sublingual mucosa are more permeable than palate and gingival mucosa, in that order. The degree of keratinization and relative thickness were used to create this order. The permeability coefficient is a measure of how accessible a substance[26].

Standard composition of oral fast dissolving film:

Thin films containing a medication and designed for oral dissolution typically have an area between 5 and 20 cm2. A maximum of 30 milligrammes (mg) of the medicine may be taken at once. All excipients included in the formulation must be GRAS and authorised for use in oral pharmaceutical dosage form in accordance with regulatory guidelines(24)(25)(26)(27). The following are substances included in a typical formulation. Drug, Polymer, Plasticizer, Substances that make you salivate, Substitute for sugar , Flavouring component , Surfactant, Adhesives, dyes[27].

Active pharmaceutical ingredient:

Drug content ranges from 0.15% to 0.25% by weight in a typical film formulation. A variety of active pharmaceutical ingredients (APIs) may be delivered through rapidly disintegrating films. The most promising options for inclusion in OFDFs are small dosage compounds. Multivitamins up to 10% w/w of dry film weight were added into the films, and the dissolution time was shorter than 60 seconds. Better film texture, faster dissolving, and more consistent OFDFs are all possible thanks to micronized API. Many APIs that have the potential to be used with OFDF technology leave a bad taste in the mouth. This makes the formulation unpleasant, even in child-friendly forms. Therefore, it is necessary to conceal the API's flavour before merging it into the OFDF. There are a number of approaches that may be used to enhance flavour. due to the way it was formulated The easiest method is to combine API with excipients that do not have an unpleasant taste and then process them together. This is an example of a method called "obscuration"[28].

Film forming polymer

The dosage form's intended use dictates the polymer type used. The film's stability in respect to these key characteristics may be altered by the presence of polymers. Many different kinds of polymers may be used to make OFDFs. OFDFs may have their hydrophilicity, flexibility, mouth feel, and solubility enhanced by using either one or a mix of polymers. The formulation's kind of polymer and its quantity of polymer influence the film's stiffness. The ideal polymer would have excellent wetting and spreading qualities, be non-toxic, and not cause any irritation. The polymer must be easily accessible and at a fair price. Natural gums like xanthan, guar, acacia, and tragacanth gums are examples of water-soluble polymers; other options include cellulose or cellulose derivatives, hydroxyl propyl methyl cellulose (HPMC) in a variety of grades (e.g., HPMC E15, HPMC E5, HPMC K4M, HPMC K100), hydroxy ethyl cellulose, hydroxy propyl cellulose, carboxy The technique also makes use of modified starches. Many polymers exist, each with its own unique set of physical characteristics. When making oral films, it's important to choose a polymer

that is: Water-soluble and low-molecular-weight Free of leachable contaminants Non-irritant[29].

Plasticizers:

The oral film formulation requires the use of plasticizer. As a result, the strip's flexibility is enhanced and its brittleness is reduced. Strip properties may be enhanced with the use of plasticizers since they reduce the polymer's glass transition temperature. Both the polymer and the solvent used in film casting will have a role in deciding which plasticizer to utilise. Adding a plasticizer to a polymer makes it more malleable and boosts its strength. Glycerol, propylene glycol, di-butylpthallate, and polyethylene glycols are just some of the plasticizers that see regular usage. Film splitting or cracking might result from improper usage of plasticizer[30]. Some plasticizers may slow down the body's ability to absorb drugs. The plasticizer should give the strip a lasting quality. The glass transition temperature of polymers may be lowered by plasticizer characteristics to temperatures between 40 and 60 degrees Celsius in non-aqueous solvent systems and to temperatures below 75 degrees Celsius in aqueous systems. It is important that plasticizers used in strip manufacturing be compatible with both the medicine and any other excipients that may be present. Plasticization of hydrophilic polymers made from cellulosic materials was straightforward using hydroxyl-containing plasticizers such polyethylene glycol, propylene glycol, glycerol, and polyols. Plasticizers for both hypromellose and polyvinyl alcohol films, glycerol is preferable to diethylene glycol[31].

Saliva stimulating agent: Rapid dissolving strip formulations may include a saliva stimulating ingredient to encourage more frequent saliva production and hasten the pace at which the strips dissolve. Saliva may be stimulated by several different acids found in the kitchen, including citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid. These agents are applied to the strip at a rate of 2%-6%w/w, either alone or in combination[32].

Sweetening agent: As formulations have progressed towards the goal of disintegration or dissolution in the oral cavity, sweeteners have become an integral part of these processes. Fast dissolving films may be made using either natural or artificial sweeteners. In formulations, sweeteners are commonly utilised at percentages between 3% and 6% w/w. A pleasant mouthfeel and refreshing experience may be achieved by combining polyhydric alcohols like sorbitol, mannitol, and isomalt. However, it is important to highlight that this study was conducted on a paediatric population. Natural and synthetic foods and medicines Artificial and natural sweeteners are used to make mouth dissolving formulations more palatable by disintegrating or dissolving in the oral cavity. Valdecoxib oral strips were sweetened with aspartame, whereas piroxicam oral strips were sweetened with maltodextrin[33].

Flavouring agent: Flavouring up to 10%w/w is acceptable in OFDF formulations. The initial flavour quality experienced during the first few seconds after ingestion, as well as the after taste of the formulation, which persists for at least 10 minutes, play a significant role in determining an individual's acceptability of an oral disintegrating or dissolving formulation. Which medicine is included in the formulation influences the taste profile selected. It was found that the degree to which one enjoys a certain flavour changes significantly with age. Younger people like fruit punch, raspberry, and so on, whereas the elderly prefer mint or orange tastes. Synthetic flavour oils, oleo resins, and plant-based extracts are all viable options for use as flavouring agents. Vegetation that has leaves, flowers, and fruit You may use a single flavouring agent or combine many. Fruity tastes include vanilla, cocoa, coffee, chocolate, and citrus, while flavoured oils include peppermint oil, cinnamon oil, spearmint oil, and nutmeg oil. Apple, raspberry, cherry, and pineapple essences are just a few examples of the many available[34].

Surfactatnt: Solubilizing, wetting, or dispersion agent surfactants enable the film to disintegrate in seconds, releasing the active component instantly. Common chemicals such as sodium lauryl sulphate, benzalkonium chloride, bezthonium chloride, tweens, and more Solubilizer, wetting agent, and dispersant(8) all fall under the category of "surfactant," of which polaxamer 407 is one of the most notable examples[35].

Colouring agent: FD&C colours, EU colours, Natural colours, and bespoke Pantone-matched

colours are just some of the options you have. Disintegration and release may be enhanced by including saliva-stimulating substances. Some examples of such chemicals are citric acid, tartaric acid, malic acid, ascorbic acid, and succinic acid[36].

METHODS OF PREPARATION OF FILM:

Solvent casting method
Semisolid casting method
Hot melt extrusion method
Rolling method
Solid dispersion method

Solvent casting method: Solvent casting is the method of choice for formulating fast-dissolving films; in this process, the water-soluble ingredients are dissolved to form a clear viscous solution, the drug and excipients are dissolved in a suitable solvent, and the two solutions are combined before being casted into a Petri plate, dried, and subsequently cut into the desired size pieces. The qualities of the API are essential for making the right choice of solvent. Hydroxypropyl methyl cellulose (HPMC), hydroxypropyl cellulose (HPC), pullulan, sodium alginate, pectin, carboxy methyl cellulose (CMC), and polyvinyl alcohol (PVA) are all examples of water-soluble hydrocolloids used to create RDFs[37]. for possible, utilise solvents from the ICH Class 3 solvent list for making a solution or suspension. Specialised tools, including rollers, are needed to pour the solution over the inert foundation. The gap between the roller and the substrate specifies how thick the film must be. Drying the film is the last process step and helps get rid of the solvent. In film casting, inert bases made of glass, plastic, or teflon are employed. Transferring manufacturing technologies from the lab to the production scale is not without its challenges. Some examples of such problems include improper sample drying and uneven film thickness during casting. Selecting the best drier for the job is the last stage in drying. The films may be trimmed, stripped, and spliced once they have dried. We have completed the packing[38]. Cut the film to the right size and shape. There are two standard film sizes, both of which are 3 x 2 cm2. A process flow for solvent casting is shown in Figure 3.

Advantages[39]

- ✓ Clearer and more consistent in thickness than extrusion.
- ✓ Films should be high-gloss and devoid of flaws like die lines.
- ✓ more malleable and has better physical qualities.

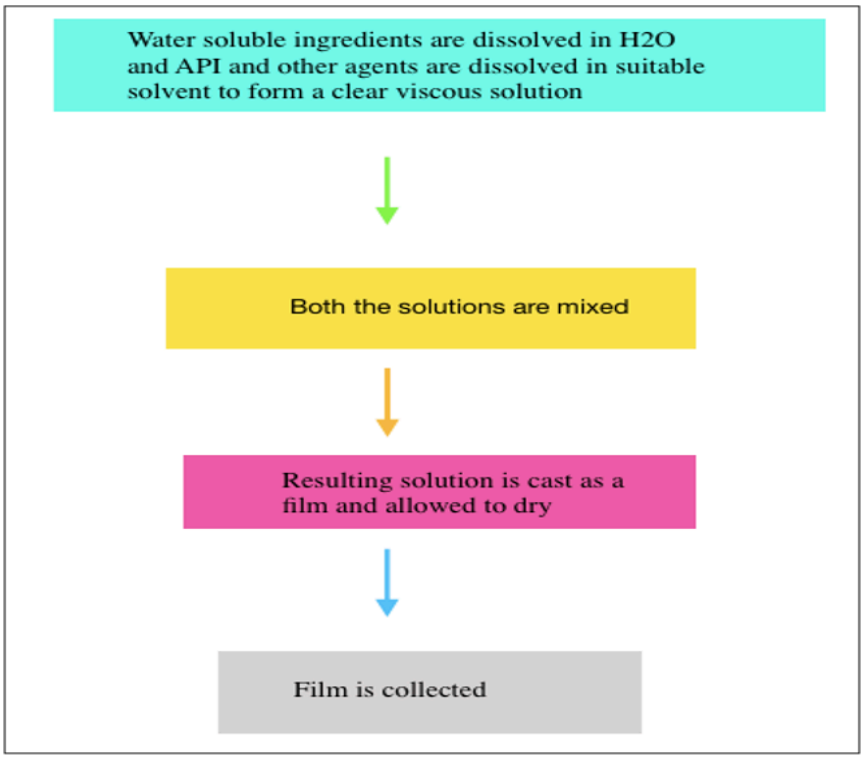

Figure 3: Flow chart of solvent casting method

Disadvantages[40]

- ✓ Polymer solubility in water or volatile solvents is required.
- ✓ A stable solution must be developed with a minimal solid content and viscosity that is acceptable.

Semisolid casting method

This process involves combining two solutions: an acid-insoluble polymer (such as cellulose acetate phthalate or cellulose acetate butyrate) dissolved in ammonium or sodium hydroxide, and a water-soluble film-forming polymer solution. The mixture should then have plasticizer added to it in order to produce a gel. The gel mass is then cast into the films or ribbons using drums that may be heated to a certain temperature. The produced film will have a thickness anywhere between 0.015 and 0.05 inches. A 1:4 ratio of acid insoluble polymer to film-forming polymer is required for this technique[41]. A process flow for Semisolid casting method is shown in Figure 4.

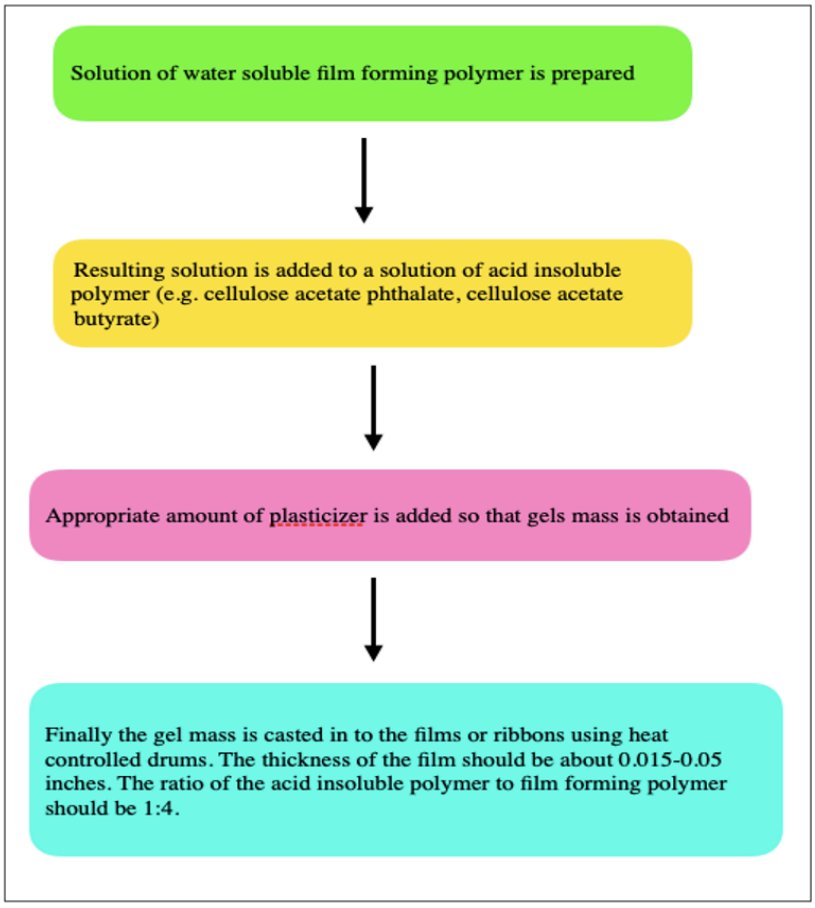

Figure 4: Flow chart of Semisolid casting method

Hot melt extrusion method:

As can be seen in Fig.5, the first step in the hot melt extrusion process is to dry and obtain the initial mass with carriers, as the drug is mixed with carriers and obtained as solid mass. Next, the mass is fed into an extruder for plastic divided into four zones with varying degrees of temperature, zone 1 at 800°C, zone 2 at 150°C, zone 3 at 1000°C, and zone 4 at 650°C. Set the extruder speed to 15 rpm and let the granules sit in the barrel to be processed for three to four minutes. The film is obtained by being crushed within a cylinder-shaped calendar. One of the benefits of hot melt extrusion is that it requires fewer machines to run. Because of intensive mixing and agitation, using a solvent or water (anhydrous) results in consistent content while minimising waste[42]. A process flow for Hot melt extrusion method is shown in Figure 5.

Advantages[43]

- ✓ A few of functional measures.
- ✓ Updated for better internal consistency.
- ✓ Hydro-free methods

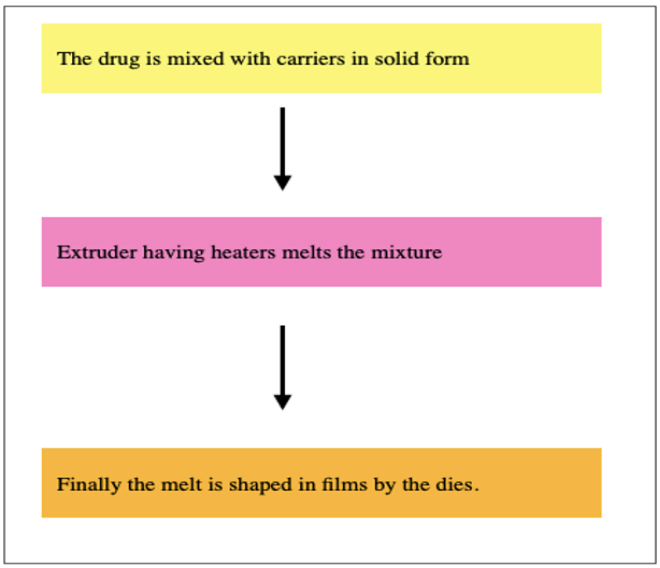

Figure 5 : Flow chart of Hot melt extrusion method

Rolling method:

In the rolling technique, a medication solution or suspension is rolled onto a carrier. Water or a water-alcohol combination is often used as the solvent. After being cured on the rollers, the film is then cut to the specified dimensions. The active agent and the other components are dissolved in a tiny quantity of aqueous solvent using a high shear processor. Dispersible hydrocolloids that turn water into a uniformly thick paste[44].A process flow for Rolling method is shown in Figure 6.

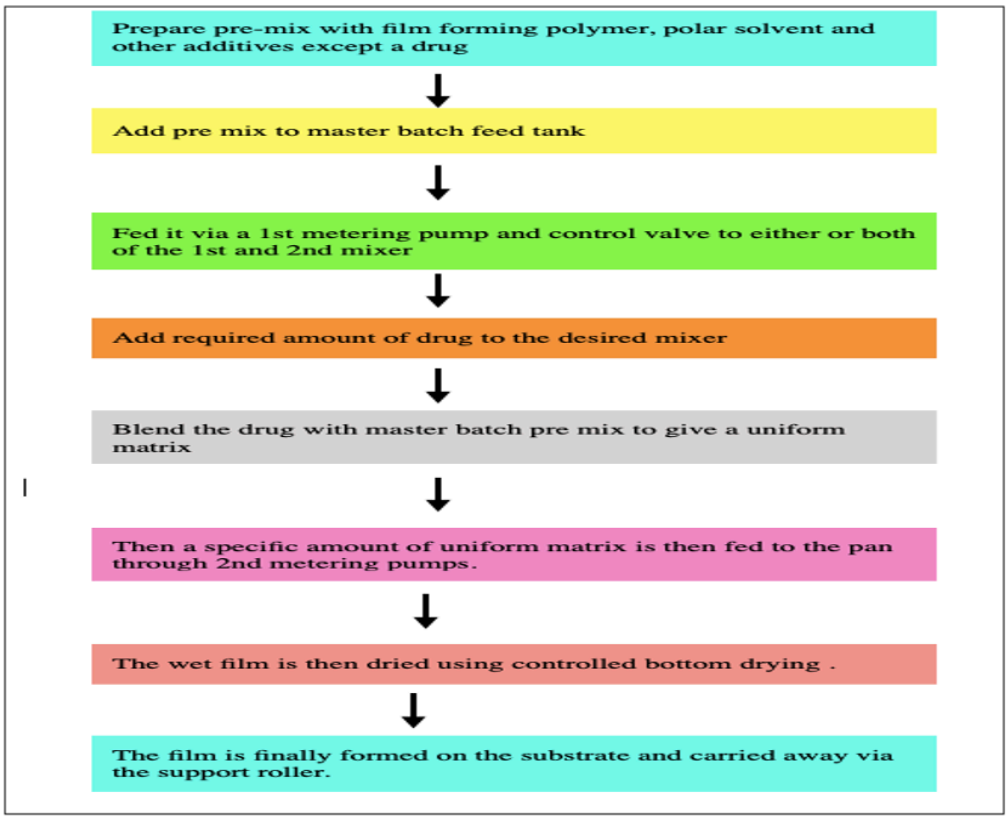

Figure 6: Flow chart for Rolling method

Solid dispersion method: Immiscible components are extruded with drug in this method, and then solid dispersions are prepared. Finally, dies are used to shape the solid dispersions into films[45].

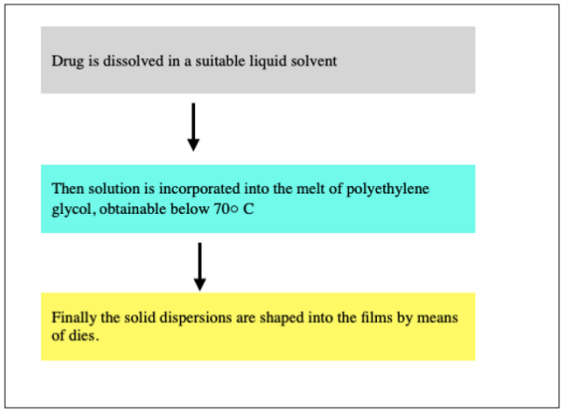

Figure 7: Flow chart for Solid dispersion method

EVALUATION PARAMETER FOR ORAL FILMS[46],[47],[48],]49]

1. Morphology study
2. Weight variation
3. Thickness
4. Surface pH
5. Dissolution test
6. Disintegration time
7. Folding endurance
8. Tensile strength
9. Percent elongation
10. In vitro drug release
11. Swelling property
12. Storage and packaging

Morphology study:

Oral strip morphology is examined using scanning electron microscopy (SEM) at a fixed magnification. Compare the top and bottom of the films to see how they vary. It's also useful for figuring out how widely used an API

Weight variations:

Variations in weight are measured by applying random weights to each weight in turn. The average should be around the same as the weighted average of 10 films.

Thickness:

Film thickness is measured using a micrometre screw gauge at five locations (the film's centre and four corners) and the average thickness is then determined. The thickness of 5 randomly selected films is measured at many locations for each formulation to determine how consistent the film's thickness really is. There should be less than a five percent range in film thickness. Unaccounted for.

Dissolution test:

Dissolution tests may be performed at 370.5°C using the usual basket or paddle equipment specified in any of the pharmacopoeias in a simulated saliva solution or pH 6.4 phosphate buffer. A UV-Visible spectrophotometer is used to evaluate samples at predetermined intervals.

Surface Ph:

To examine the potential for adverse effects in vivo, the films' surface pH was measured by putting them on a surface of 1.5% w/v agar gel and then placing pH paper (pH range 1-11) on them. It was seen that pH paper turned a different shade.

Disintegration time:

Time required for disintegration: a USP disintegration device is required for the disintegration of orally rapid dissolving films. Fast dissolving oral films may adhere to the CDER recommendation disintegration time restriction of 30 seconds or less for orally disintegrating pills. The time it takes to disintegrate is formula dependent, but is normally between 5 and 30 seconds. However, fast-dissolving films for the mouth do not have any formal recommendations.

Folding endurance:

The ability to withstand repeated folding at the same location was measured by seeing how many times the film could be folded before snapping. How many times a film can be folded before it breaks is known as its folding endurance value.

Tensile strength:

The tensile strength of a film is its ability to withstand a certain amount of stress before tearing. The films' mechanical strength is measured by this procedure. The following equation shows how to get it from the applied load at cleavage and the film's cross-sectional

area: Failure load divided by strip thickness and breadth yields tensile strength.

Tensile strength = (load at failure / strip thickness / strip width)

Percent elongation:

Strain, measured in percentage elongation, is the result of applying force to a film sample and observing the resulting length change. Strain is the amount by which a film has been stretched relative to its initial size. Increase in length as a percentage is calculated as follows: 100 increased length decreased length.

In vitro drug release:

Film dissolution investigations for in vitro drug release typically use approved, industry-standard basket or paddle equipment. It is important to maintain the sink conditions when dissolving. Sometimes film can float over the medium and make it impossible to conduct the test as intended. The paddle approach is more prone to this issue, hence the basket device is often used instead. Phosphate buffer with a pH of 6.8 (300 ml) and 0.1 N HCl (900 ml) are the solvents used. Typically, the speed of rotation is fixed to 50 rpm and the temperature is maintained at 37 0.5 _C. At regular intervals, a UV spectrophotometer is used to evaluate samples of the dissolved medication.

Swelling property:

To measure the swelling property, we first weigh and position each film sample in a mesh made of preweighed stainless steel wire. The film sample and its accompanying mesh are then placed in a plastic container with 15 ml medium (simulated saliva solution). At regular intervals, the film's weight was gradually raised until a steady state was reached.

Swelling degree = (Wt. - W0 /W0)

Storage and packaging:

Pharmaceutical companies gain from adaptability in the warehousing and packaging of their products. The rolled film may be sliced into thinner rolls or die-cut to any shape or size as required by the application. Before packing, converters may choose to print information directly onto film unit dosages for branding reasons and to meet industry rules. Unit-dose packaging, barcode labelling, and content in directions for use are all optional considerations; child-resistant sealing and packaging designed with the elderly in mind are mandatory[50].

PACKAGING OF FAST DISSOLVING FILM

It is critical that pharmaceutical products be packaged in a way that prevents contamination. Other quick dissolving dose forms need expensive packaging, unique processing, and extra care during manufacture and storage to safeguard the dosage. Fast dissolving films may be packaged in a number of different ways. Films, which are considered medicinal items, must be packaged individually and, often, an aluminium bag is used for this. The Rapid card is APRLabtec's unique packaging technique, created specifically for use with their Rapid films. Similar in size of a credit card, the fast card can store three Raid films on each of its two sides. Each dosage may be removed separately[51].

The material selected must have the following characteristics[52], [53]

- ✓ The preparation has to be shielded from the elements.
- ✓ They need to meet FDA requirements.
- ✓ They need to be tamper-proof as specified by law.
- ✓ They have to be safe to use.
- ✓ The product must not cause any reactions in them.
- ✓ No off-flavors or odours should be transferred to the final product.

Foil, paper or plastic pouches

The flexible pouch is an environmentally friendly packaging option that can also withstand extreme temperatures. This is because of the materials used to create the pouch. During the product filling process, a flexible pouch is typically manufactured using vertical or horizontal forming, filling, or sealing machinery. Single pouches or aluminium pouches are also acceptable for use[54] .

Single pouch and Aluminum pouch

Peelable bag for "quick dissolve" soluble films with good barrier qualities; used for medication administration. To better showcase the contents, the bag is see-through. One side may be transparent while the other is laminated with inexpensive foil thanks to our 2-in-1 design. Gas and moisture transfer via the foil lamination is almost nonexistent. The packaging offers a thin film alternative that is flexible for use in the pharmaceutical and nutritional

supplement industries. The product and dosage are both safeguarded by the single-use bag. The most popular kind of bag is made of aluminium[55].

Blister card with multiple units

The blister, the created chamber that stores the product, and the lid stock, the substance that closes to the blister, make up the blister container. Blister packaging is created by vacuum forming a heated sheet of thermoplastic resin into a predetermined shape. Once the sheet has cooled, it is removed from the mould and sent on to the packing machine's filling station. After forming a semi-rigid blister, the product is placed inside and the blister is sealed using heat. The level of security needed should inform the choice of film. Aluminium foil is a common material for the stock of lids. Typically, a plastic is used to shape the cavity, since it may be engineered to keep the dosage form dry[56].

Barrier Films

High barrier films are necessary for the packaging of many pharmaceutical preparations because of their great vulnerability to moisture. Waterproofing may be accomplished using a variety of materials, including Polychlorotrifluoroethylene (PCTFE) film, Polypropylene, and others. Under any tension, polypropylene will not fracture. It effectively blocks the passage of gases and vapours. The problem of ambiguity persists[57].

APPLICATION OF FAST DISSOLVING FILM

Therapies used to treat pain, allergies, sleep problems, and central nervous system illnesses may soon have a preferred delivery method: oral mucosal distribution through Buccal, sublingual, and mucosal route using FDFs. After years of development in the breath strip industry for sweets and dental care, dissolvable FDFs have emerged as an innovative and highly recognised form for consumers to get vitamins and personal care goods[58].

Topical applications

Active substances, such as analgesics or antibacterial components, may be delivered through dissolvable films in wound care and other contexts.

Gastro retentive dosage systems

Water-soluble and poorly soluble compounds of varying molecular weights are being studied for inclusion in dissolvable films for use in dosage formulations. Potentially useful for the treatment of gastrointestinal problems, the films' dissolution might be triggered by the pH or enzyme secretions of the gastrointestinal system[59].

Diagnostic devices

In order to time a reaction between numerous reagents inside a diagnostic instrument, dissolvable films may be loaded with sensitive reagents for controlled release upon exposure to a biological fluid[60] .

Vaccines:

Vaccines that are stable at room temperature may be provided in the form of buccal films that dissolve rapidly in the mouth and in saliva. The United States-made rotavirus vaccine is a fast-dissolving buccal film that can be stored at room temperature, making immunisations as easy as brushing one's teeth. There are a number of benefits to this delivery method, including higher rates of patient compliance and bioavailability and lower costs connected with logistics[61].

Controlled and Sustained release film:

Long-term release Different polymers, such as chitin and chitosan derivatives, are employed as excipients in medical preparations, and buccal film is one such example. Because of their release properties and adherence, they are useful in a variety of contexts, including wound dressings, oral mucoadhesive, and water-resistant adhesive[62].

Taste masking:

For fast dissolving pills to be commercially successful, taste masking is a must. It is essential for patient compliance that fast dissolving buccal films melt or disintegrate in the mouth, releasing the active components that come into touch with the taste receptors. By using solvent evaporation and solvent extraction methods, medicines with an intolerably bitter taste may be microencapsulated into pH-sensitive acrylic polymers for use in taste masking. These polymer microspheres completely dissolved in a short amount of time and demonstrated effective flavour masking [63].

Orally disintegrating films:

The polymer used to make fast-dissolving buccal films may be dissolved in water. Patients with swallowing problems or nausea, including those undergoing chemotherapy, may find this

film useful since it dissolves quickly without the need for water [64].

Stability studies

Whether or whether the final formulation is stable is the primary goal of stability testing. First, the formulation is wrapped in butter paper, then in aluminium foil, and finally, the whole thing is put in an aluminium bag and heat sealed, all so that the influence of temperature and humidity on the stability of the medicine can be determined. A three-month shelf life may be expected when the formula is kept at 45 degrees Celsius and 75% relative humidity. Films should be assessed for physical changes and drug content three times over the stability study period, with samples obtained at 0, 1, and 3 month intervals in duplicate[65].

Marketing Status And Products Available For Oral Thin Film Dosage Form

Since 2002, when quick dissolve product sales were projected at roughly $850 million, they have skyrocketed to an estimated $1.4 billion in 2005 (IMS Data). After the breath freshener industry adopted the thin film format, the lifestyle and nutraceuticals sector followed suit with a variety of fast-dissolving strip products that included actives including vitamins, herbal extracts, and non herbal extracts. There is more than $15 billion in the global market for these goods. The global market for pharmaceuticals using quick dissolve technology is now worth over $1 billion, and is growing at a rate of over 40% per year. Demand from patients is driving this expansion; research suggests that 88% of people would rather take fast-dissolving versions of common prescriptions than the more cumbersome regular pills, which are difficult to swallow for 40% of the population. Various products are available in market as shown in figure 8. Nine pharmaceuticals are now available over-the-counter. There were predictions in 2001 and 2002 that several major therapeutic treatments using this technology will enter the market during the next two to three years. In spite of a global growth of fivefold in the number of thin film strips since 2002, hardly none of them have made it into the ethical prescription market. There are currently 47 OTF products under development by 12 different firms. Oral thin film formulations of pharmaceuticals were estimated to be worth $500 million in 2007 and might rise to $2 billion by 2010, according to research by Technology Catalysts.In addition, TCI's study includes specifics on the research and development initiatives of 25 firms working on Orally- Disintegrating Tablet technologies and 17 companies working on Oral Film technologies [66, 67].

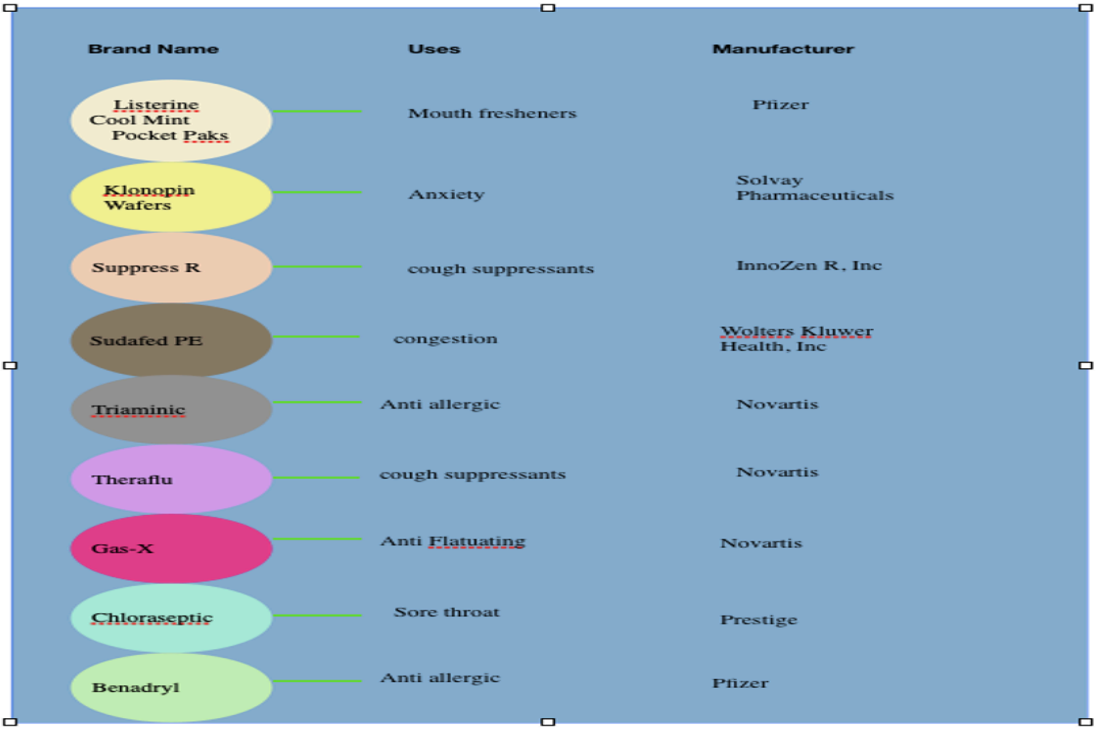

Figure 8: Marketed products in form of film

Patented technologies of fast dissolving oral films

XGel

BioProgress's XGel film technology has brought about a sea change in the range of products and production techniques accessible to the pharmaceutical sector. These films were designed for use with non-edible products, such as cosmetics, ostomy pouches, sanitary and healthcare pouches, and they may be coloured or printed during production for branding and tagging, which is very beneficial for product identification . The use of these sheets improves product consistency[68].

Soluleaves

In this method, the film adheres to the mucosal membrane and releases the medicine gradually over the course of 15 minutes after coming into contact with saliva. Those who have trouble swallowing regular pills might benefit from this strategy [45]. Vitamins, candies, and breath mints are just some of the flavoured goods that have benefited from this technique [69].

Wafertab

Wafertab is an orally consumable film strip that contains pharmaceutically active substances. When the film comes in contact with saliva, the active component is quickly dissolved and released [47]. Flavouring the Wafertab film strip is an option for better flavour concealment. A fused body incorporates the active substance into its structure[70].

Foamburst

The Foamburst patent was issued in September 2004 for formed film capsules. Producing a film with a honeycomb structure as a capsule that dissolves quickly and causes a melt-in-your-mouth feeling requires blowing an inert gas into the film during creation. Gas, air, or another substance might be used to fill the film's vacuum and provide a targeted flavour burst or medicine delivery system [71]. .

Micap

Micap plc, a leader in micro encapsulation technology, and BioProgress, a manufacturer of water-soluble films, entered into a partnership in 2004. The primary goal of these studies is to develop innovative delivery modalities for the $1.4 billion worldwide market for smoking cessation products (SCPs) [72].

Rapid film™

Applied Pharma Research (APR), a prominent Swiss R&D business whose major emphasis is breakthrough medication delivery, collaborated with Labtec GmbH to create this groundbreaking thin film technique. This technology is crucial when immediate action is needed, according to Dr. Paulo Galfetti, Head of Licencing & Business Development. According to Galfetti's recommendation, this approach may even be used to poorly soluble pharmaceuticals. [48] A rapid film has an area of 1 cm 2 to 10 cm 2 and contains the medication. The whole process of disintegration takes about 20 seconds. For example: Donepezil Rapidfilm®, Olanzapine Rapidfilm®. [73]

Table. 2: Some patents on oral thin films[74,75]

Country	Patent Number	Title
US	20110305768A1	Quick dissolving oral thin film for targeted delivery of therapeutic agents
WO	2012103464A2	Oral thin film vaccine preparation
WO	2013085224A1	Bitter taste masked oral thin film formulation of Sildenafil citrate
US	6177096B1	Water soluble film for oral administration with instant wettability
EP	1680079A2	Rapidly disintegrating films for delivery of pharmaceutical and cosmetic agents
EP	2509631A4	Ph sensitive compounds in taste masking within oral thin film strips
WO	2012053006A2	Improved oral fast dissolving films comprising combination of polymers and method of preparation thereof
US	6596298B2	Fast dissolving orally consumable films
WO	2014183054A1	Thin film with high load of active ingredient

Conclusion

FDF is the most well-liked and precise oral dose form since it may avoid the hepatic system without compromising efficacy. Pharmaceutical firms use this dose form because of high patient compliance (particularly among elderly and paediatric patients) and widespread industry acceptance. They're a hybrid between the more long-lasting stability of a solid dosage form and the convenient use of a liquid. Oral films may compete with and even displace OTC, generic, and brand-name drugs on the market. The use of this technology in product life cycle management has the potential to extend the protection afforded by current patents.

References

1. Bhura N, Sanghvi K, Patel U, PARMAR B. A review on fast dissolving film. The International Journal of Pharmaceutical Research and Bio-Science. 2012;1(3).
2. Bhyan B, Jangra S, Kaur M, Singh H. Orally fast dissolving films: innovations in formulation and technology. Int J Pharm Sci Rev Res. 2011 Jul;9(2):9-15.
3. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of ChemTech Research. 2010 Jan 1;2(1):576-83.
4. Thakur N, Bansal M, Sharma N, Yadav G, Khare P. Overview “a novel approach of fast dissolving films and their patients”. Advances in biological research. 2013 Aug;7(2):50-8.
5. Siddiqui MN, Garg G, Sharma PK. A short review on “A novel approach in oral fast dissolving drug delivery system and their patents”. Adv Biol Res. 2011 Nov;5(6):291-303.
6. Siddiqui MN, Garg G, Sharma PK. A short review on “A novel approach in oral fast dissolving drug delivery system and their patents”. Adv Biol Res. 2011 Nov;5(6):291-303.
7. Kunte S, Tandale P. Fast dissolving strips: A novel approach for the delivery of verapamil. Journal of pharmacy and bioallied sciences. 2010 Oct;2(4):325.
8. Garsuch V, Breitkreutz J. Comparative investigations on different polymers for the preparation of fast-dissolving oral films. Journal of Pharmacy and Pharmacology. 2010 Apr;62(4):539-45.
9. Liang AC, Chen LL. Fast-dissolving intraoral drug delivery systems. Expert opinion on therapeutic patents. 2001 Jun 1;11(6):981-6.
10. Juluru NS. Fast dissolving oral films: A review. Int. J. Adv. Pharm. Biol. Chem. 2013 Jan;2:108-12.
11. Mahaparale MA, Shivnikar SS, Pawar KV, Prashant N. Fast dissolving oral films: An innovative drug delivery system. IJRRPAS. 2012;2(3):482-96.
12. Keshari A, Sharma PK, Parvez N. Fast dissolving oral film: a novel and innovative drug delivery system. International Journal of Pharma Sciences and Research. 2014;5(3):92-5.
13. Joshua JM, Hari R, Jyothish FK, Surendran SA. Fast dissolving oral thin films: An effective dosage form for quick releases. Drugs. 2016;11:12.
14. Mahajan A, Chhabra N, Aggarwal G. Formulation and characterization of fast dissolving buccal films: A review. Der Pharm Lett. 2011;3(1):152-65.
15. Ketul P, Patel K, Patel M, Patel N. Fast dissolving films: A Novel approach to oral drug dilivery. Safety. 2013;4:6.
16. Padamwar PA, Phasate PP. Formulation and evaluation of fast dissolving oral film of bisoprololfumarate. International Journal of Pharma Sciences And Research (IJPSR). 2015 Jan;6(01):135-42.
17. Ali MS, Vijendar C, Kumar SD, Krishnaveni J. Formulation and evaluation of fast dissolving oral films of diazepam. Journal of pharmacovigilance. 2016 May 28;4(3):1-5.
18. Chaturvedi A, Srivastava P, Yadav S, Bansal M, Garg G, Kumar Sharma P. Fast dissolving films: a review. Current drug delivery. 2011 Jul 1;8(4):373-80.
19. Yadav G, Kapoor A, Bhargava S. Fast dissolving tablets recent advantages: A review. International journal of pharmaceutical sciences and research. 2012 Mar 1;3(3):728.
20. Kshirsagar T, Jaiswal N, Chavan G, Zambre K, Ramkrushna S, Dinesh D. Formulation & evaluation of fast dissolving oral film.

World J. Pharm. Res. 2021 May 27;10(9):503-61.
21. Juluru NS. Fast dissolving oral films: A review. Int. J. Adv. Pharm. Biol. Chem. 2013 Jan;2:108-12.
22. Liang AC, Chen LL. Fast-dissolving intraoral drug delivery systems. Expert opinion on therapeutic patents. 2001 Jun 1;11(6):981-6.
23. Reddy TU, Reddy KS, Manogna K, Thyagaraju K. A detailed review on fast dissolving oral films. Journal of Pharmaceutical Research. 2018;8(06).
24. Karthik DR, Keerthy HS, Yadav RP. A Review on Fast Dissolving Oral Films. Asian Journal of Pharmaceutical Research and Development. 2021 Jun 15;9(3):122-8.
25. Kushwaha V, Akhtar J, Usmani S, Singh SP. A review on fast dissolving formulation technologies. World Journal of Pharmacy and Pharmaceutical Sciences. 2015 May 10;4(7):574-85.
26. Mushtaque M, Muhammad IN, Ali SK, Khalid F, Masood R. Novelty and Compliance of Oral Fast Dissolving Thin Film–A Patient Friendly Dosage Form. Clin. Pharmacol. Biopharm. 2021;10(2):211.
27. Ratnaparkhi MP, Mohanta GP, Upadhyay L. Review on: Fast dissolving tablet. Journal of pharmacy research. 2009 Jan;2(1):5-12.
28. Mostafa DA. Fast dissolving oral film: overview. European Journal of Biomedical. 2018;5(8):86-101.
29. Kulkarni NS, Wakase PS, Indore PS, Dhole SN. A systematic review on Oral drug delivery as a fast dissolving film to improve therapeutic effectiveness. Research Journal of Pharmacy and Technology. 2021;14(3):1771-8.
30. Kumar S, Garg SK. Fast dissolving tablets (FDTs): Current status, new market opportunities, recent advances in manufacturing technologies and future prospects. Int J Pharm Pharm Sci. 2014;6(7):22-35.
31. Reddy MR. An Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems: A Review. Journal of Pharmaceutical Sciences and Research. 2020 Jul 1;12(7):925-40.
32. Prajapati BG, Ratnakar N. A review on recent patents on fast dissolving drug delivery system. International Journal of PharmTech Research. 2009 Jul;1(3):790-8.
33. Banarjee T, Ansari VA, Singh S, Mahmood T, Akhtar J. A review on fast dissolving films for buccal delivery of low dose drugs. Int. J. Life Sci. Rev. 2015;1:117-23.
34. Pawar R, Sharma R, Sharma P, Darwhekar GN. A review on mouth dissolving film. Journal of Drug delivery and Therapeutics. 2019 Nov 15;9(6):206-10.
35. Balaji A, Poladi KK, Vookanti AR. Fast dissolving oral films for immediate drug release: a review. World J Pharm Res. 2014 Feb 1;3(2):3751-75.
36. Mehta AP, Patil MP, Patil PR, Gadhari VS, Ghuge VD. Fast Dissolving Films: Brief review on preparation methods, ingredients and technology used. Advance Pharmaceutical Journal. 2021;6(2):52-8.
37. Kumar S, Yagnesh TN. Fast dissolving systems an alternative approach for enhanced therapeutic action. Indo Am J Pharm Res. 2018;8:1464-72.
38. Bilal Q, Unhale S, Shelke S, Kale P, Sarode P, Biyani D. A review on mouth dissolving films. Eur. J. Pharm. Med. Res. 2020;7:232-8.
39. Meher A, Dighe NS. An Overview of Fast Dissolving Oral Film. Journal of Drug Delivery and Therapeutics. 2019 Aug 29;9(4-s):822-5.
40. Saharan VA, editor. Current advances in drug delivery through fast dissolving/disintegrating dosage forms.
41. Heer D, Aggarwal G, Kumar SH. Recent trends of fast dissolving drug delivery system–an overview of formulation technology. Pharmacophore. 2013 Jan 1;4(1):1-9.
42. Gauri S, Kumar G. Fast dissolving drug delivery and its technologies. The pharma innovation. 2012 Apr 1;1(2, Part A):34.
43. Selmin F, Franceschini I, Cupone IE, Minghetti P, Cilurzo F. Aminoacids as non-traditional plasticizers of maltodextrins fast-dissolving films. Carbohydrate polymers. 2015 Jan 22;115:613-6.
44. Bhattarai M, Gupta AK. Fast dissolving oral films: a novel trend to oral drug delivery

system. Sunsari Technical College Journal. 2015;2(1):58-68.
45. Rezaee F, Ganji F. Formulation, characterization, and optimization of captopril fast-dissolving oral films. AAPS PharmSciTech. 2018 Jul;19:2203-12.
46. Karthik DR, Keerthy HS, Yadav RP. A Review on Fast Dissolving Oral Films. Asian Journal of Pharmaceutical Research and Development. 2021 Jun 15;9(3):122-8.
47. Jain A, Ahirwar HC, Tayal S, Mohanty PK. Fast dissolving oral films: a tabular update. Journal of Drug Delivery and Therapeutics. 2018 Jul 14;8(4):10-9.
48. Gali AK. Fast dissolving dosage forms. Int J Pharm Sci Inv. 2013;2(11):14-7.
49. Garsuch VI. Preparation and characterization of fast-dissolving oral films for pediatric use. Cuvillier Verlag; 2009 Jun 24.
50. Saini S, Nanda A, Hooda M, Chaudhary K. Fast dissolving films (FDF): innovative drug delivery system. Pharmacologyonline. 2011;2:919-28.
51. Reddy TU, Reddy KS, Manogna K, Thyagaraju K. A detailed review on fast dissolving oral films. Journal of Pharmaceutical Research. 2018;8(06).
52. Sharma I, Sharma V. A comprehensive review on fast dissolving tablet technology. Journal of applied pharmaceutical science. 2011 Jul 30(Issue):50-8.
53. Prasanthi NL, Krishna CS, Gupta ME, Manikiran SS, Rao NR. Design and development of sublingual fast dissolving films for an antiasthmatic drug. Der Pharmacia Lettre. 2011;3(1):382-95.
54. Mushtaque M, Muhammad IN, Ali SK, Khalid F, Masood R. Novelty and Compliance of Oral Fast Dissolving Thin Film–A Patient Friendly Dosage Form. Clin. Pharmacol. Biopharm. 2021;10(2):211.
55. Dangre PV, Phad RD, Surana SJ, Chalikwar SS. Quality by design (QbD) assisted fabrication of fast dissolving buccal film for clonidine hydrochloride: Exploring the quality attributes. Advances in Polymer Technology. 2019 May 5;2019:1-3.
56. Jadhav YG, Galgatte UC, Chaudhari PD. Challenges in formulation development of fast dissolving oral films. J. Pharm Res. 2013;3(8).
57. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. International journal of pharmaceutical investigation. 2013 Apr;3(2):67.
58. Prabhu SC, Parsekar SD, Shetty A, Monteiro SS, Azharuddin M, Shabaraya AR. A review on fast dissolving sublingual films for systemic drug delivery. Int J Pharm Chem Sci. 2014;3(2):501-11.
59. Kaza R, Yalavarthi PR, Ravouru N. Design and characterization of fast dissolving films of Valsartan. Turk J Pharm Sci. 2014 Jul 1;11(2):175-84.
60. Mostafa DA. Fast dissolving oral film: overview. European Journal of Biomedical. 2018;5(8):86-101.
61. Sadique S, Ramya SS. Preparation and evaluation of fast dissolving oral film of losartan potassium. Research journal of pharmaceutical dosage forms and technology. 2020;12(1):13-6.
62. Arunachalam A, Karthikeyan M, Kumar SA, Konam K, Prasad PH, Sethuraman S, Manidipa S. Fast dissolving drug delivery system: a review. Journal of global trends in pharmaceutical sciences. 2010 Oct;1(1):92-110.
63. Kulkarni NS, Wakase PS, Indore PS, Dhole SN. A systematic review on Oral drug delivery as a fast dissolving film to improve therapeutic effectiveness. Research Journal of Pharmacy and Technology. 2021;14(3):1771-8.
64. Reddy MR. An Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems: A Review. Journal of Pharmaceutical Sciences and Research. 2020 Jul 1;12(7):925-40.
65. Kaur P, Garg R. Oral dissolving film: present and future aspects. Journal of Drug Delivery and Therapeutics. 2018 Nov 15;8(6):373-7.
66. Kapadia YD, Trambadiya DA, Patel AV, Patel VP. FORMULATION AND EVALUATION OF FAST DISSOLVING SUBLINGUAL FILM OF METOPROLOL SUCCINATE. Pharma Science Monitor. 2013 Apr 16;3(3).

67. Banarjee T, Ansari VA, Singh S, Mahmood T, Akhtar J. A review on fast dissolving films for buccal delivery of low dose drugs. Int. J. Life Sci. Rev. 2015;1:117-23.
68. Lodhi DS, Verma M, Golani P, Patra P, Nagdev S, Pawar AS. Fast-dissolving oral film of anti-migraine drug. Nat. J. Pharm. 2021;1(2):40-8.
69. Vaidya MM, Khutle NM, Gide PS. Oral fast dissolving drug delivery system: A modern approach for patient compliance. World J Pharm Res. 2013 Mar 2;2(3):558-77.
70. Ehtezazi T, Algellay M, Hardy A. Next steps in 3D printing of fast dissolving oral films for commercial production. Recent Patents on Drug Delivery & Formulation. 2020 Mar 1;14(1):5-20.
71. Jain S, Pillai S, Mandloi RS, Namdev N, Birla N. Formulation and evaluation of fast dissolving film of labetalol hydrochloride. Research Journal of Pharmacognosy and Phytochemistry. 2021;13(1):1-4.
72. Bahrainian S, Abbaspour M, Kouchak M, Moghadam PT. A review on fast dissolving systems: from tablets to nanofibers. Jundishapur Journal of Natural Pharmaceutical Products. 2017 May 31;12(2).
73. Balaji A, Poladi KK, Vookanti AR. Fast dissolving oral films for immediate drug release: a review. World J Pharm Res. 2014 Feb 1;3(2):3751-75.
74. Ratnaparkhi MP, Karnawat GR, Andhale RS. Natural polymers in fast dissolving tablets. Research Journal of Pharmacy and Technology. 2021;14(5):2859-66.
75. Dahiya M, Saha S, Shahiwala AF. A review on mouth dissolving films. Current drug delivery. 2009 Oct 1;6(5):469-76.