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## A COMPREHENSIVE REVIEW ON FAST DISSOLVING BUCCAL FILM

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### ABSTRACT

Standard oral drug delivery systems encounter many challenges in the gastrointestinal tract, including inefficient drug release and decreased effectiveness of the dose administered. Many efforts have been undertaken to increase medicine's efficacy and bioavailability. Drugs delivered through the buccal mucosa of the oral cavity are called buccal medication drug delivery systems. In pediatric and geriatric patients, buccal films are more effective, since they reduce the frequency of dose administration, ensures plasma peak values, reduce side effects, and make drugs with high first-pass metabolism more affordable. This review outlines the composition, formulation, formulation technologies, buccal film packaging, and future prospect related to the fast dissolving drug delivery system.

**Key words: Buccal film, Polymer, Solvent Casting, Swelling index, Folding endurance, Bioavailability**

### INTRODUCTION

Fast-dissolving oral films are ultra-thin films made of hydrogen-based polymers that disintegrate rapidly on the tongue surface or buccal cavity. It is a postage stamp-sized, ultrathin strip (50–150 microns less) with an active ingredient designed to be convenient,

and they efficiently address problems with medications and nutraceuticals taken internally in a solid dosages [1]. The ultra-thin oral strip is applied to the tongue, or tongue mucous membrane, the saliva immediately moistens the strip and adheres

to the mucous membrane that dissolves in seconds for oral mucosal absorption. Fast dissolving oral films are a well proven and worldwide accepted technology for the systematic distribution of active pharmaceutical ingredients (APIs) [2].

Patients in paediatrics and the elderly have trouble swallowing tablets. To overcome this difficulty brand-new oral fast-dissolving dosage form has been produced. The novel dosage form combines the advantages of simple dosing with the convenience of administering without water or fluid, which disintegrates quickly. Most of the fast-acting medication delivery systems dissolve or disintegrate within seconds without chewing or swallowing and the film overcomes the danger of choking. A wide range of medications, including analgesics, cardiovascular medications, antihistamines, and antiasthmatics, for erectile dysfunction are fabricated into fast-dissolving film [3].

#### **Unique property of mouth dissolving film:[4][5]**

- Excellent mucoadhesion
- A gently textured thin film
- Un-obstructive
- Rapid release
- various sizes and shapes
- Rapid disintegration or dissolution

#### **Ideal properties of Fast Dissolving buccal film [5]**

The most desirable film should have the following qualities:

- It should also be thin and elegant
- It should be tolerant of changes in temperature and humidity
- It should release the medicine quickly
- It should be less fragile and able to endure handling strain during shipping.
- It should be capable of rapid disintegration and dissolution without water
- The pH value of the film should be between 6.2 and 6.52 to prevent irritation

#### **Advantages [6]**

- Improvements in stability and patient compliance
- Administration without use of fluids
- No chance of choking
- Quick action with few adverse effects
- Accurate dosing
- Taste destruction
- Improves the systemic bioavailability
- The acidic environment and GI enzymes may protect drugs from a failure.

#### **Disadvantages**

- Unpleasant taste drugs are not suitable candidates.

- Large doses cannot be administered.
- Drug dilution due to continuous saliva secretion.
- Small surface area for absorption.
- Minimal dose medications
- As saliva is constantly produced, the medication is further diluted and administered frequently, promoting fast drug clearance
- Absorption via passive diffusion
- Consuming meals and drinks may be prohibited

### Oral dissolving film drawbacks [7, 8]

There are several challenges involved in the administration of medication via oral dissolving films. These challenges might be listed as follows:

Table:1 Summarization of properties of different types of oral films [9]

Property	Flash release films	Mucoadhesive melt-away films	Mucoadhesive sustained release films
Area (cm <sup>2</sup> )	2-8	2-7	2-4
Thickness (µm)	20-7	50-500	50-250
Structure (Film)	Single layer	Single or multilayer system	Multilayer system
Excipients	Soluble, highly hydrophilic polymer	Soluble, hydrophilic polymer	Low/insoluble polymer
Drug phase	Solid solution	Solid solution or suspended drug particles	Suspension and/or solid solution
Application	Tongue	Gingival or buccal region	Gingival(other regions in oral cavity)
Dissolution	Minimum 60 sec Maximum 8-10hrs	Disintegration in few mins. Forming gel	Maximum 8-10 hrs.
Site of action	Systemic or local	Systemic or local	Systemic or local

### Composition and Formulation of Fast Dissolving Buccal film:

The oral dissolving film has a surface area of 1 to 20 cm<sup>2</sup> depending on the dose and drug loading. The maximum of 30 mg drug

will be loaded in a single strip. The mechanical properties of films have reportedly been impacted by the formulation issues like Plasticizers, Polymers and surface-active agents etc.

Table 2: A typical composition contains the following: [10]

Sr.no	Ingredient	Amount(w/w)
1	Drug	5-50%w/w
2	water-soluble polymer	45%w/w
3	Plasticizers	0-20%w/w
4	Surfactants	q.s
5	Sweetening agent	3-6%w/w
6	Saliva-stimulating substance	2-6%w/w
7	Colour, flavour, and filler	q.s

### A. Drug

- Various category of API's are loaded into buccal films. API's can be loaded into the film from 5% w/w to 30% w/w. Water soluble and water

insoluble drugs can be used for fabrication of buccal film, water soluble API'S are incorporated in dissolved state, and water-insoluble APIs are dispersed using water-

soluble polymers. The cyclodextrins mixed with the poorly soluble drug will lead to complexation and enhances the solubility. Milled, micronized, particle or nano crystal form of API can be utilised based on release profile. Micronized API can be used to get a better film texture and content uniformity.

- The medication should be stable and simple to dissolve in saliva.
- It is advised to use medications with a low or moderate molecular weight.
- At the pH of the oral cavity, it should be able to partially unionise and enter oral mucosal tissue.
- Several classes of medications, such as NSAIDs (such as paracetamol, meloxicam, and valdecoxib), anti-ulcers (such as omeprazole), antiasthmatics (such as salbutamol sulphate), antitussives, expectorants, and antihistaminics, can be produced as mouth-dissolving films [11, 12].

### **B. Polymer:**

The majority of the oral quick-dissolving film is made of polymers. The toughness of the film depends on the total amount of polymer present in each strip. Based on the overall weight of the dry film, 45% w/w polymer is often used. The majority of the oral strip is fabricated of hydrophilic polymers, which break down quickly after

coming into contact with saliva in the mouth [13].

### **C. Plasticizers:**

It has been found that formulation considerations have an impact on film mechanical properties. Plasticizers were added to the films, which increased their mechanical properties including tensile strength and elongation. These features may be affected by variations in their concentration. Glycerol, dibutyl phthalate, and polyethylene glycols are some of the most used plasticizers.

### **D. Surfactants:**

Surfactants, commonly referred to as wetting or solubilizing agents. Addition of surfactant caused the increase in tensile strength and decrease in elongation of the films. It is effective at the range of 2 to 6 % and it can be used alone or in combination.

### **E. Sweetening Agent:**

Sweeteners have become the important excipients for oral disintegration drug delivery system. Sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose are the most prevalent sweeteners. Polyhydric alcohols with a pleasant mouthfeel and a cooling effect, such as sorbitol, mannitol, and isomalt, can be blended. Saccharin, cyclamate, and aspartame are examples of first generation artificial sweeteners, while acesulfame-k, sucralose, alitame, and neotame are examples of second-generation artificial sweeteners. Sweeteners are widely

used in concentrations of 3 to 6% w/w, either alone or in combination.

#### F. Saliva Stimulating Agent:

Fast-dissolving films dissolve more quickly due to increased salivation. Therefore, the formulations should contain acids that are commonly used to make food as salivary stimulants. The most popular salivary stimulant is citric acid, lactic acid, malic acid, tartaric acid, and ascorbic acid.

#### G. Flavoring Agents:

Flavoring agents include synthetic flavor oils, oleoresins, and extracts derived from various parts of plants, such as leaves, fruits, and flowers. Flavors are used either alone or

in combination. Menthol essential oils or water-soluble extracts, strong mints such as spearmint, sweet mint, peppermint, wintergreen, cinnamon, and clove, sour fruit flavors such as lemon, orange, or sweet confectionery flavors such as vanillin, chocolate, or fruit essences such as apple, raspberry, cherry, and pineapple can all be used to mask the taste [18].

#### H. Coloring agent

Coloring agents can be added to improve elegance. The most often used pigments include silicon dioxide, titanium oxide, and their concentration should not be more than 1%.

Table 3: List of excipients and their characteristics

Category	Example	Properties
Polymers	Hydroxypropyl Methylcellulose (HPMC) [14]	HPMC has great film forming property and is widely accepted. Other -grade varieties of HPMC, like Methocel E3, E5, and E15, are less viscous frequently utilized for MDFs.
	Hydroxypropyl cellulose (HPC)	HPC is a non-ionic, water-soluble thermoplastic polymer. Because films created with high glass transition temperature polymers are stiff. Commercially, HPC is available in several of grades, each with a particular solution viscosity. The molecular weight of HPC varies from 50,000 to 1,250,000.
	Poly Ethylene Oxide (PEO)	A non-ionic, highly molecular-weighted, water-soluble polymer is called poly ethylene oxide. Due to the unusual flexibility of the PEO structure, allowing expansion of the polymer chains and building up interpenetration between PEO and mucin, PEO films display increased bio adhesivity. A polymer called Polyox N-80 might be utilized in the oral film.
	Carboxymethyl cellulose (CMC)	CMC, or modified cellulose, produces films with exceptional clarity and a neutral flavour.
	Pectin	Pectin is an organic polymer that can be found in apples and citrus fruits. Pectin's are excellent film formers, well-suited for low pH applications, and these medications have a good capacity to transmit within the mouth. The <i>in-vivo</i> dissolution time 141 seconds, and <i>in-vivo</i> disintegration time is 15-second required for pectin film.
	Gelatin	The natural protein collagen is the source of gelatin, which is a common ingredient for food, growth and absorption in the pharmaceutical industries. Gelatin comes in brittle flakes or powder form and is transparent, odorless, colorless or slightly yellow.
Plasticizers	Propylene Glycol [15]	Propylene glycol has a flavour similar to glycerine and is a clear, colourless, thick, virtually odorless liquid. Propylene glycol is a substance that is not harmful and is commonly used in aqueous film-coating formulations as a plasticizer. PG as a plasticizers having good appearance.
	Polyethylene Glycol (PEG)	Polyethylene glycol is non-toxic and non-irritant material and is used in variety of pharmaceutical formulations. PEG 400, 1,450, 8,000 and 20,000, decrease the tensile strength of fast dissolving films. PEG is the most effective plasticizer for the fast-dissolving film.
	Dibutyl Phthalate	Dibutyl phthalate is an odorless, oily, colorless, viscous liquid and relatively non-toxic material which is used as plasticizers in films and film coatings.

Surfactants	Sodium lauryl sulphate	Freely soluble in water, producing an opalescent solution; almost insoluble in ether and chloroform. At 308°C, the spreading coefficient is 7.0 (0.05 percent by weight of an aqueous solution). Surface tension for a 0.05 percent w/v aqueous solution at 308°C is 25.2 mN/m (25.2 dynes/cm). Wetting time is 118 seconds at 308°C (0.05 percent w/v aqueous solution) [16].
	Benzalkonium chloride	Acidity/alkalinity for a 10% w/v aqueous solution, pH = 5-8. Anti-microbiological action: A number of bacteria, yeasts, and fungi can be effectively eliminated by benzalkonium chloride solutions. In the case of Gram-negative and acid-fast bacteria, activity is weaker against bacterial endospores and stronger against Gram-positive bacteria. The similar mixture of benzalkonium chloride and alkyl determines the antibacterial activity capacity [16].
	Tweens	It is available mainly as polysorbate 20, 60 and 80. According to reports, polysorbate 80's In pure water, 0.012 mM is the essential micelle concentration.
	Spans	Span-20 has an HLB of 8.6 and is soluble in water, cottonseed oil, mineral oil, tetra carp, and xylene to varying degrees. It is also soluble in liquid paraffin to varying degrees, but not completely.
Sweeteners	Aspartame	Acidity/alkalinity: pH is 4.5–6.0 (Aqueous solution, 0.8% w/v) index of 1.05 for brittle fracture.
	Saccharin	Acidity/alkalinity: pH is 6.6 (Aqueous solution, 10% w/v) Saturation in water at 20° C is 1 in 1.2.
	Mannitol	True density is 1.514 g/cm <sup>3</sup> Solubility in water at 20° C is 1 in 5.5.
Saliva stimulating agent	Citric acid	Soluble 95% ethanol ether; just moderately soluble in 1.5 parts ethanol and less than 1 part water. For a 50% weight-to-volume aqueous solution at 258 °C is 6.5 mPa s (6.5 cP).
	Tartaric acid	Density is 1.76 g/cm <sup>3</sup> , Dissociation constant, pKa = 2.93 at 258°C; pKa = 4.23 at 258 °C.
Flavors	Peppermint	Menthol content must be less than 50% and the peppermint flavor's methyl acetate content must not be less than 5% [15].
	Fruit flavors	Apple: Manzanate (Ethyl 2-methylpentanoate) Pineapple: Allyl Hexanoate or Allyl Caproate Orange: d-Limonene, Ethyl Butyrate
Color	Annatto extract	Orange-Red, including both external and internal medicines. The water soluble pigment is called norbixin.
	β-Carotene	Precursor of the vitamin A compound retinol. Red-orange, medications that are external and generally ingested.

### METHOD OF PREPARATION:

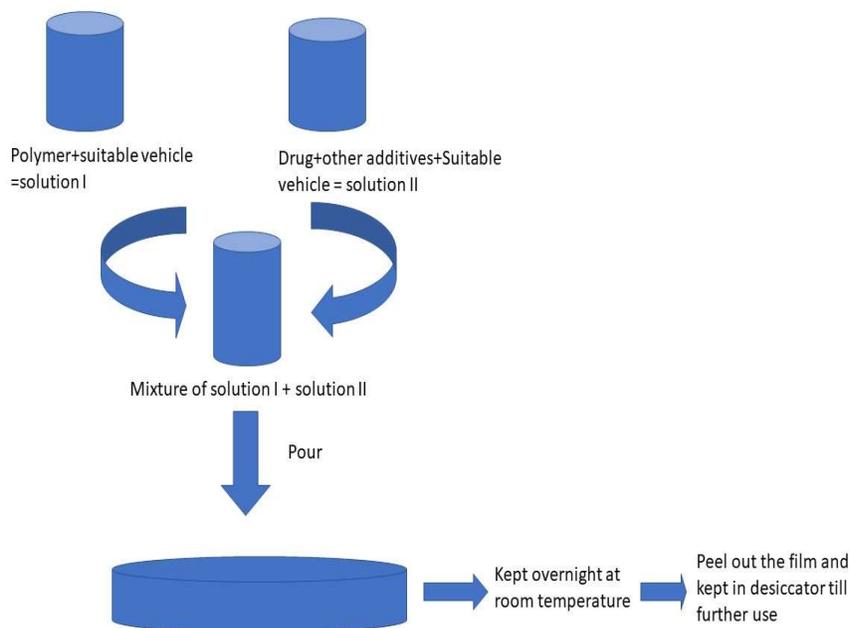
The following methods alone or in combination with other methods can be used exclusively to prepare the film.

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

#### 1) Solvent casting method: [19]

The standard technique for producing buccal films is solvent casting method. The following steps make up this process:

- Water is used to dissolve water-soluble polymers, resulting in the formation of a viscous solution.
- An appropriate solvent is used to dissolve API and other excipients to create a viscous clear solution.
- The two solutions are combined, and the combined product is then molded into a film and allowed to dehydrate.



## 2) Semisolid casting: [8]

The steps involved in the semisolid casting process are as follows:

- A solution is prepared from a water-based, film-forming polymer.
- A solution of an acid-insoluble polymer, such as cellulose acetate phthalate or cellulose acetate butyrate, is then added to the resultant solution.
- To generate a gel mass, the necessary quantity of plasticizer is used.
- The mass of gel is transformed taking films or strips in the last stage using heat-controlled drums. The film should be around 0.015 to 0.05 inches in diameter. The proportion ratio of film-forming polymer to

acid-insoluble polymer should be 1:4.

## 3) Hot Melt Extrusion: [20]

The hot melt extruder technique utilizes heat to transform into a polymer film. A hot melt extruder is used for a dry or mix of pharmaceutical components, using API, delivered to the extruder, heated and mixed, and the molten mixture is subsequently forced out of the hopper. The resulting molten mass is used to make the film. A critical stage in the casting process is drying. The lack of continuous use, availability of organic solvents, minimal product waste, proper operating parameter management, and quickly scaling up are a few advantages of this process. Additional advantages include lower temperatures shortening the remains of residents and medication-mixed carriers.

#### 4) Solid dispersion extrusion:

- The term "solid dispersions" describes the solid-state of one or more active entities dispersed hydrophilic amorphous polymers in a carrier that is chemically inert.
- The drug is dissolved in a suitable liquid solvent, heated to a temperature of over 70 °C, and then added to the liquid polyethylene glycol.
- The solid dispersions films are formed by using dies.

There are a few safety measures that must be considered when using this procedure. For instance, the selected solvent or drug may not combine with liquid polyethylene glycol, and the liquid solvent may alter the polymorphic form of the drug that precipitated in the solid dispersion.

#### 5) Rolling:

The creation of a premix, active addition, and subsequent film development are the different steps in the process as it rolls. Except for the API provided to the masterbatch feed. Polar solvent, a film-forming polymer, and other chemicals make up the pre-mix batch. The first sampling device and control valve are then used to feed the master batch in a predefined amount. The mixer is filled with the necessary amount of medication, and the mixture is carefully combined to generate a homogenized matrix. The second metering

pump feeds the pan with a precise amount of matrix. The metering roller measured the thickness of the film. The support roller eventually removes the film once it has been created on the substrate. After being produced on the substrate, the film is eventually removed by the support roller [21].

#### Newer Technologies to develop Oral Fast Dissolving Films:[22]

##### XGel™

XGel is the core of Meldex international's intellectual property and is used in all medicinal aluminum foil and ingestible delivery techniques. The XGel technology developed by BioProgress, his XGel sheet technology is modifying the products and manufacturing methods currently available in the pharmaceutical industry. X gel film may improve product stability. It was also created for non-ingestible uses such as cosmetics, ostomy bags, sanitary and healthcare products. A process called "solution casting" is used to develop and manufacture XGel films.

##### Soluleaves™

In this technology, the film is made to release the active ingredient upon contact with saliva. This applies to goods that release flavours, such as sweets, candy, and vitamin supplies. Active compounds can be efficiently, pleasantly, and conveniently supplied to the oral cavity using the soluleaves technology.

Both nutritional products and remedies for gastrointestinal disorders, cough/cold, and pain complaints can be addressed by using this method. Additionally, soluble films may be created to comply with mucosal membranes and slowly release active ingredients over 15 minutes.

#### **Wafertab™**

A pharmaceutical active ingredient is contained in an ingestible film via the drug delivery technology WAFERTAB. It is a proprietary delivery system that uses a unique method to create a thin film that contains drugs and it can be applied topically or orally. Active ingredients are incorporated into the film after casting. The WAFERTAB system offers many opportunities for innovative drug design by connecting multiple films with different active ingredients.

#### **Foamburst™**

FOAMBURST is a foam film capsule patent issued in September 2004. During production, gas is blown into the film to produce a honeycomb film. The voids in a film can empty, gas-filled, or containing additional ingredients to produce particular flavor-blasting qualities and release the active substances. Due to the light honeycomb structure, the capsules melt quickly, providing a melt-in-your-mouth agitation. FOAMBURST has attracted confectionary producers as a way of delivering and releasing flavours.

#### **Micap™**

Micap entered to integrate its understanding of microencapsulation technology with the water-soluble Bio Progress films, it entered into an option agreement in 2004. For the \$1.4 billion global market for smoking cessation products (SCP), the advances were created to develop new delivery systems.

#### **Evaluation of films:**

##### **Morphology study:[23]**

Scanning electron microscopy (SEM) is used at a specific magnification to analyse the morphology of the films.

##### **General appearance: [24-29]**

The visual characteristics of the strip, such as its transparency and semitransparency, are utilised to assess the quickly dissolving films.

##### **Weight of film:**

Using an analytical balance, oral fast-dissolving films can be weighed to determine their average weight. It is ideal for films to maintain an amount of weight practically consistent. It is beneficial to make sure that the appropriate amount of excipients and APIs are present in a film.

##### **Organoleptic evaluation:**

For many pharmaceutical components, colour is a key indicator of identity and is typically crucial for consumer approval. The product's color must match consistent throughout the dose form. The odour of the films can be utilized to assess their quality, it is particularly significant for assessing

consumer approval of oral dose forms. The existence of an odour could be a sign that drug (like vitamins), other substances (like flavoring compounds). Consumer acceptability is dependent on taste, and lots of companies use tasting panels to determine how much the public prefers specific flavors when developing new products. For the psychophysical assessment of the product, specialized use of regulated human taste panels will be used. Taste sensors are used in *in-vitro* applications that make use of specifically created equipment.

#### **Thickness:**

Thickness of the film is measured by using calibrated set of digital vernier calipers or a micrometer screw gauge. Five spots on the film, including the Centre and all four corners, should be measured in order to determine the mean thickness. It must be developed since the precise dosage of a film is directly impacted by thickness uniformity.

#### **Dryness test/tack tests:[30]**

Tack describes how strongly a strip adheres to a component (like a piece of paper) when the two are brought into contact. Also, this study's instruments are available.

#### **Mechanical properties:**

There are three mechanical qualities that are calculated: Young's modulus, percentage elongation, and tensile strength.

#### **Tensile strength:**

The amount of force that may be applied to a strip specimen before it breaks is known as

the tensile strength. A formula is used to determine it:

$$\text{Tensile strength} = \frac{\text{Load at Failure} \times 100}{\text{Film Thickness} \times \text{Film Width}}$$

#### **Percent Elongation:**

A film sample stretches when pressure is applied; which is known as strain. In essence, Strain is the film's distortion divided by the initial sample dimension. In general, the elongation of the film accelerates with increasing plasticizer concentration.

$$\text{Percentage elongation} = \frac{\text{Increase in length} \times 100}{\text{Original Length}}$$

#### **Young's modulus:**

The stiffness of a film determined by the elastic modulus, sometimes referred to as young's modulus. The ratio of the applied stress to the strain in the elastic deformation area using the following formula:

$$\text{Young's modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{Cross head speed}}$$

Film that is rigid and brittle has a high young's modulus and tensile strength.

#### **pH value:**

The pH of the consequent solution is calculated after dissolving the film in 10 ml distilled water. The resulting solution's pH value must should be almost constant.

#### **Swelling property:**

Film should be bioadhesive in nature and should get hydrated in buccal cavity. It indicates the hydrophilic polymers were used while formulating. The buccal film is preweighed (W1) and it is allowed to swell in a medium and at specific time interval film is recovered from the medium and weighed (W2). The amount of swelling is determined by

$$\text{Swelling Index \%} = \frac{W2 - W1}{W1} \times 100$$

Where, W1 = initial weight, W2 = weight of swelled film [31].

#### **Assay/Uniformity of drug content:**

The content uniformity of the homogeneity of the material carried out by estimating the API quantity for each strip by utilizing specific assay method. The allowed range for content consistency is 85-115%.

#### **Stability Studies:**

To ascertain the impact of temperature and humidity on the drug's stability, stability experiments are being conducted on the optimized oral fast-dissolving film. The film is kept in an aluminium foil and maintained at room temperature. The sample can be removed and subjected to *in-vitro* dissolution studies at three and six months to evaluate the disintegration time, and cumulative percentage drug release.

#### **Weight variation: [32-36]**

By weighing each of the 10 randomly chosen oral films individually and

determining out their average weight, the weight variation is analyzed.

#### **Transparency:**

The UV spectrophotometer can be used to determine the transparency of the film. In order to fit within the spectrophotometer cell, rectangles are cut out of the film samples and placed. The transmittance of the film is measured at 600 nm.

#### **Tear resistance:**

The maximal force or stress, which is determined by the pressure required to break the film, is typically observed near the start of the tearing process (or pounds -force).

#### **Disintegration time:**

The CDER guidance's 30 second or shorter disintegration time requirement for orally disintegrating tablets can be applied to fast dissolving oral strips. Although there is no formal recommendation for oral rapid dissolving films/strips, this can be used as a qualitative guidelines for quality control tests or during the development stage. A petri dish was filled with 10 ml of pH 6.8 phosphate buffer, and the film was placed on top of it. The disintegration time was noted as soon as the film breaks and slowly disintegrates. The readings were measured along with mean and standard deviation.

#### **Dissolution test:**

The pharmacopoeia's dissolution testing processes are carried out utilising a standard paddle or basket device. The maximum API dosage and sink conditions will be

considerations while selecting the is attached to the dissolving liquid makes the dissolving medium. The tendency for the dissolution test difficult. strip to float when the paddle apparatus

Table 4: List of Patents on fast dissolving buccal film

Researchers/ Year	The work's title	Summary of the work and results
Bodkhe O. G <i>et al</i> 2023	Fast Dissolving Oral Film: A Review [22].	Since, the modified-release dosage forms become standard dosage forms for oral medications, and more recently, quickly dissolving films have replaced orally disintegrating tablets. This type of technology provides an affordable way for distributing pharmaceuticals to the general public as well as particular populations such as young children, the elderly, disabled patients, and others with psychiatric conditions. It applies a film on or under the tongue, which quickly dissolves and releases the medicine. The drug then dissolves in saliva and passes to the stomach. The drug's bioavailability is enhanced in such situations.
Tarun Patel <i>et al</i> (December 2022)	Fast Dissolving Oral Film: An Approach To Enhance Patient Compliance [37].	The novel oral films that dissolve quickly is effective, safe, and preferred by patients. Mouth dissolving films are solid oral dosage forms that dissolve when placed in the mouth and it break down immediately without water and chewed. The medication's bioavailability may be increased by avoiding first pass metabolism using this dosage form. The use of oral dissolving film could speed up the onset of effect, lower the dosage, and minimize any choking problems.
Ze-yu Qin <i>et al</i> (2019)	Fast dissolving oral films for drug delivery prepared from chitosan/pullulan electrospinning nanofibers [38].	In this study, electrospinning technique was used to create Chitosan/Pullulan composite nanofiber fast dissolving oral films (FDOFs). The solution properties and nanofiber morphology were both affected by the chitosan/pullulan (C/P) ratio; as chitosan concentration increased, the viscosity and conductivity of the solutions also increased. According to findings from scanning electron microscopy, the diameter of the nanofibers initially decreased before increasing. Chitosan and pullulan molecules interacted through hydrogen bonds, as shown by the Fourier transform infrared spectra. The electrospinning technique lowered the crystallinity of the materials, according to study of X-ray diffraction. Thermal study revealed that the addition of chitosan content to the FDOF increased the melting point, degradation temperature, and transition glass temperature. The FDOF can completely dissolve in water in less than 60 seconds, according to a water solubility test.
Gamal M. Zayed <i>et al</i> (2020)	<i>In-vitro</i> and <i>in-vivo</i> characterization of domperidone-loaded fast dissolving buccal films [39].	For drugs with a low bioavailability, fast-dissolving films are a reliable replacement for other delivery systems. When combined with PVP K-90 in various ratios, the muco-adhesive and low water solubility antiemetic domperidone can have a potent first-pass impact. In addition, when compared to standard tablets, the buccal film formulation produced had a greater absorption rate, a quicker higher bioavailability, and an earlier onset of the action.
Patil D, <i>et al</i> (2018)	Design and development of fast dissolving film of telmisartan [40].	The main objective was to promote the release of telmisartan from the dosage form at the site of absorption in order to increase absorption and bioavailability. Polyvinyl pyrrolidone was used as a film-forming agent in the creation of six formulations. Plasticizers included propylene glycol and polyethylene glycol 400. The solvent casting technique was used in the preparation. The thickness, dissolving time, folding durability, and dissolution investigations of the films were evaluated.
Ehtezazi T <i>et al</i> (2018)	The application of 3d printing in the formulation of multilayered fast dissolving oral films [41].	Fast-dissolving oral films (FDFs) offer a different strategy to increase consumer acceptance because of their fast dissolution and without water administration. Usually, FDFs need taste-masking substances. The addition of these excipients, however, can make it difficult to develop the formulation. In order to create single-layered FDFs (SLFDFs) or multilayered FDFs (MLFDFs) films with taste-masking layers separated from drug layer, this work used fused-deposition modelling three-dimensional printing. Ibuprofen or paracetamol were used as model pharmaceuticals in the preparation of polyethylene oxide (PEO)-containing filaments at 60° C. Additionally, filaments containing polyvinyl alcohol and paracetamol were created at 130°C. Furthermore, a strawberry powder- and PEO-based filament was developed as a taste-masking layer. Plain or mesh designs were printed on FDFs at temperatures of 165°C (PEO) or 190°C (polyvinyl alcohol). Active ingredient stability was shown by high-performance liquid chromatography and mass spectroscopy investigation during the film-making process. MLFDFs had thicknesses beginning at 298± 15 m, whereas SLFDFs had thicknesses as low 197±21 m. Mesh SLFDFs had a disintegration time as low 42±7 s, while mesh MLFDFs had a disintegration time of 48±5 s, depending on formulation and design. Drug content homogeneity in SLFDFs ranged from 106.0% to 112.4%.

Table 5: List of marketed fast dissolving buccal film products [42-44]

Sr. No	Product name	Manufacture	Active Pharmaceutical Ingredient (API)	Brand name	Application
1.	Theraflu	Novartis	Dextromethorphan HBr	Triaminic	Cough suppressants
2.	Fresh meltz	Pfizer, Inc	Cool mint	Listerine	Mouth freshener
3.	Robitussin	Innozen, Inc	Menthol (2.5mg)	Suppress	Cough suppressan
4.	Vomiboon MD	LTS Vestiq Pharmaceuticals	Ondansetron	Setofilm Zuplenz	Antiemetic
5.	Simekon	Novartis	Simethicone	Gas X	Anti-Flatulence
6.	Donezil-10	Meda Pharmaceuticals LTS	Donepezil	Donepezil Rapid Film	Alzheimers disease
7.	klonopin Wafers	Solvay Pharmaceuticals	The strengths of clonazepam are 1 mg, 2 mg, 0.5 mg, and 0.125 mg.	Klonopil	Anxiety
8.	Benadryl	Novartis	Diphenhydra mine HCl (12.5)	Triaminic	Antiallergic
9.	sudafed	Wolters Kuwer Health, Inc	Phenylepinephrine	Wal-profen	congestion
10.	Niquitin	LTS	Nicotine	Niquitin	Smoking cessation
11.	Fentora	Meda Pharmaceuticals LTS	Fentanyl Citrate	Breakyl Onsolis	Pain management
12.	Chloraseptic	Prestige	Benzocaine/ menthol(3m g/3mg)	Chloraseptic	Sore throat

### Buccal Film Packaging:

To maintain the film's integrity, at most care should be taken while selecting materials for packing. These dosage forms must be produced and stored with particular regard, through processing, and in high-quality packaging. The best qualities for choosing a packaging materials are:

- ✓ It shouldn't be impacted by the environment outside
- ✓ It must not be harmful
- ✓ It should be authorized by FDA
- ✓ It shouldn't affect the product in any way
- ✓ It must fulfil the requirements for tamper-resistance

Oral film packaging often consists of barrier films, pouches made of foil, paper, or plastic, single pouches, aluminium pouches, blister package containing multiple units,

and aluminium pouches. Quick Film technology is a major packaging material created by Labtec GmbH that comprises of a sealable bag with lots of instructions, logos, codes, and other informational areas are provided [45].

### Plastic, paper, or foil pouches: [46, 47]

The flexible pouch is a specific kind of packaging. It cannot provide only a package that is temperature-resistant but also, with the right material choice, a product that has high levels of environmental protection. Typically, horizontal or vertical shaping, such as filling or sealing machinery creates a flexible pouch throughout the product filling process. Aluminum or single-use pouches are both acceptable options.

### Aluminium pouches and single pouches:

Peelable packaging for "fast dissolve" superior barrier qualities for soluble films is called a medicine delivery pouch made of

soluble film. For product display, the pouch is transparent. By combining two structures, an aspect can be precise and other can be laminated with affordable foil. Transport of gases and moisture through the foil lamination are basically non-existent. The container offers a versatile thin film substitute for pharmaceutical and nutraceutical applications. The most common form is a aluminium pouch.

**Multiple-unit blister card:**

The blister container consists of two components: the blister, which is formed cavity that holds the product, and the lid stock, which is the material that seals to the blister. Heat is used to soften a sheet of thermoplastic resin, which is then vacuum-drawn into a moulded shape to create the blister packaging. The sheet is taken out of the mould after cooling and brought to the filling station for the packing machine. The pre-developed semi-rigid blister, which has a backing material that can be heat-sealed covering the top, is then filled with the substance. The type of film to use should be decided based on the required level of protection. The stocks for lids frequently created from aluminium foil.

**Film barriers:**

Strong barrier coatings are required due to the high sensitivity of many pharmaceutical compositions to moisture. Two materials that can be used to protect against moisture

are polypropylene and polychlorotrifluoroethylene (PCTFE) film. Polypropylene plastic cannot fracture under any condition. It's significant as a vapour and gas barrier. Clarity issues continue to be problematic.

**Future prospect:**

In the pharmaceutical industry, major advancements have been made in oral drug delivery technologies. The market has come a long way from the conventional tablet/capsules and fast disintegration tablet and film. Various limitations such as oral solid drugs has a lower bioavailability, the administration of injections is inconvenient, inaccurate dosing by liquid formulations base which has turned the focus of pharmaceutical companies to develop novel oral dosage forms that eliminate these limitations. Fast dissolving oral thin films are designed to meet most of these challenges. The transformation of prescription medications into oral thins has been facilitated by consumer acceptance and a rise in demand for over-the-counter oral film products. This emerging area is gaining awareness from both established and start-up pharmaceutical companies. Companies are using their oral thin film technologies to create different types of oral thin films. (e.g. oraldispersible, sublingual, buccal).

The different method of administration can improve bioavailability while also offering quick and direct absorption into the

bloodstream, ease of accessibility, and greater patient compliance. The most popular buccal film advanced and frequently used drug delivery technology because it attaches to buccal mucosa easily, conforms to the mucosal surface better, and has longer retention duration than other buccal dosage forms [48].

The lercanidipine due to its weak low permeability, high first pass metabolism, and solubility, it has a 10% bioavailability for the treatment of angina pectoris and hypertension. By improving oral transmucosal absorption, lercanidipine nanoparticles added to fast-dissolving oral films increase *in-vivo* bioavailability [49].

With reference to improving the quality of life and good health of all people, nutrients and nutraceuticals with well-known capabilities in illness prevention and elimination are becoming more important. It may stand for a fresh perspective on cutting-edge methods of delivering drugs useful for health benefits [50].

Therapeutic peptides and proteins have unique, unparallel pharmacological qualities, that is superior biological

modeling of physiological mechanisms and strong receptor selectivity, which make them preferable to conventional chemically produced drugs in terms of therapeutic index. Since, proteins also have limitations on their natural bioavailability. There are many effective methods, with focus on oral polymeric films as oral delivery machinery, to improve the stability, permeability, and pharmacokinetics of protein/peptide therapies. The function of proteins and peptides in biology, as well as other advantages, can be considerably improved by oral films [51].

This explains the significant research presently being undertaken on this technology. As a result, the development of oral dissolving films using a wide selection of active pharmaceutical ingredients has become increasingly difficult due to technology's rapid growth.

Wafertab<sup>TM</sup>, Soluleaves<sup>TM</sup>, and Foamburst<sup>TM</sup> are a few novelties that have been added to the ODF preparation procedures that give greater precision and, as a result, improve patient compliance.

Table 6: Recent studies on fast dissolving buccal films

Drug	BCS	Drawbacks with drugs	Polymers	Method of preparation	Conclusion	Refs.
Naproxen particle and Anthraquinone	II	15.9 mg/l and 1.35 mg/l, very poor solubility in water was determined.	Glycerol, PVP K-30, SDS, HPMC	Stirred media mill and solvent casting technique.	High dissolving rate and particle loading ODF; optimal formulation solutions for particle-loaded ODFs	52
Buspirone HCL	I	Due to substantial first-pass metabolic activity, there is a	PEG-400, PVA, PLGA, PVA, Poloxamer	Solvent casting and nanoprecipitation	prolonged drug release in vitro for up to 48 hours	53

		low bioavailability of only 4%.	188, and HPMC E15			
Carvedilol	II	Poor bioavailability (25%) Very weak solubility in water (0.00444 mg/mL).	Polysorbate 80, or PEO	Electrospinning and solution casting	30minute dose release that is 86.40% faster and has a higher bioavailability than pure drug	54
Domperidone	II	Oral bioavailability (10–15%) is poor.	Propylene glycol, HPMC E5, and Carbopol 934P	Fast homogenizer and casting using solvent	Good appearance and enhanced medication in vitro release	55
Griseofulvin	II	Extremely weak hepatic and water-soluble first pass metabolic activity	Pullulan, glycerin, and SDS	With solvent film casting and wet stirred media milling	About 80% of the drugs release in 30 minutes, and strips that are 120 mm thick show potential for extended release.	56
Medoxomilol mesartan	II	Oral bioavailability is poor (26%).	Pluronic F127, Pectin, HEC, PG, and PEG 400	Ultrasonication, solvent casting, and antisolvent precipitation	When compared to a market drug, the relative bioavailability was 209.28 %.	57

## CONCLUSION

Fast-dissolving films were considered by pharmaceutical companies as an acceptable and practical alternative for conventional medications. FDOFs have special qualities which makes them an effective pharmaceutical delivery form for patients with dysphasia, geriatric conditions, or who have trouble swallowing tablets and capsules. A pharmaceutical company utilizes this unique novel technology to manage the product life cycle and extend the patent life of existing products. These combined potentials promote shifting from over-the-counter to prescription products. The FDOFs fill the gap between consumer desires and manufacturers. Hence within the patient population and formulators, fast dissolving oral films leads to be an ideal dosage form. This review is an effort to

combine the knowledge available in fast dissolving buccal film.

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