Original Article

A Comprehensive Review On Orally Dissolving Film Drug Delivery System

Swetha.M[1]*, Janaki Devi Sirisolla[2]

*[1]Research Scholar, GITAM School of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam- 530045, India, Assistant professor, CMR College Of Pharmacy, Kandlakoya (V, Medchal Rd, Hyderabad, Telangana 501401, India.
[2] Assistant Professor, GITAM School of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam- 530045, India

***Corresponding author:** - Swetha.M

*Research Scholar, GITAM School of Pharmacy, GITAM (Deemed to be University), Rushikonda, Visakhapatnam- 530045, India, Assistant professor, CMR College Of Pharmacy, Kandlakoya (V, Medchal Rd, Hyderabad, Telangana 501401, India.
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Abstract

Orally dissolving films are one of the prevailing oral dosage form as these drug delivery systems release the active pharmaceutical ingredient quickly in oral cavity as soon as it comes in contact with the saliva. The advantages like rapid melting in the mouth to give immediate release, avoiding first pass metabolism makes orally dissolving films a predominant dosage form. The current study emphasis about the fundamental understanding of formulation of films, use of various polymers, standard measurements of basic types of films. In the present review compiled evaluation procedures and some of the marketed products to show the demant of the market for orally dissolving films.

Keywords: oral films, oral cavity, formulations, evaluation studies.

INTRODUCTION

Oral route for administration of drugs is one of the most convenient one among all other dosage routes. At the same time administration into paediatrics, geriatrics is observed as a difficult condition. Another stumbling block in case of oral route of administration is disintegration and dissolution time for the release of drug from the dosage form to exhibit the therapeutic effect immediately. Over all other oral dosage forms such as tablets, capsules, pellets are going to the gastrointestinal tract and undergoing disintegration and dissolution for giving pharmacological activity, where in case of orally dissolving films are showing immediate release excluding interaction with stomach contents, long time to release and first pass metabolism. Oral dissolving films also advantageous for patience with dysphagia, bedridden, suffering from parkinson's disease. Natural and synthetic excipients can be used to make the formulation more efficient in releasing to treat patients disease or disorders.

A few different names of these oral films have been shown up; for instance, oro-dispersible films (ODFs), oral soluble films, mucoadhesive films, oral strips, oral thin films, buccal films, wafers, ophthalmic films, and transmucosal films. It is an ultrathin strip (50-150 microns thick) of postage stamp size with a functioning specialist and different excipients created based on transdermal patch technology.(7)

ANATOMY OF ORAL CAVITY

The physiology and anatomy of oral cavity is studied for understanding the environment provided for delivering drugs [Fig. 1]. The oral mucosa allows direct access of drug to the systemic circulation and avoids first pass metabolism. The epithelium of the oral cavity is quite similar to that of the skin, with slight differences with regard to keratinization, protective and lubricant mucous which is spread across its surface.[19] The permeability of oral mucosa is 4–1000 times greater than that of the skin. The oral cavity is divided into two regions: outer being the oral vestibule bounded by the lips and cheeks; the hard and soft palates, the floor of the mouth and tonsils.(6) Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms.[1]

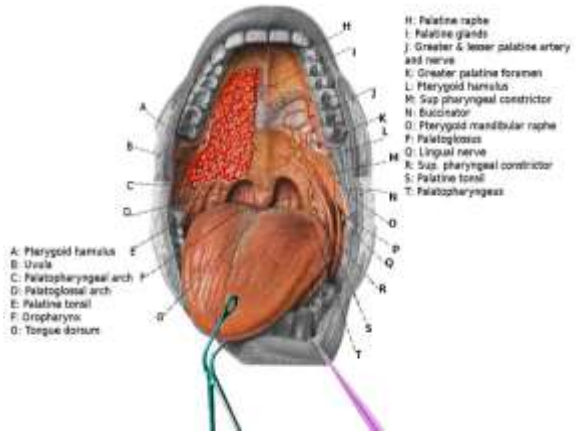

Figure 1 (5)

APPLICATIONS OF ORAL FILMS IN DRUG DELIVERY

Oral drug delivery by sublingual, mucosal and buccal become preferable for therapies in which immediate absorption is required including those used to manage pain, allergies, sleep problems and CNS disorders. Topical applications, the oral films are ideal in the delivery of active agents like analgesic or antimicrobial ingredients for the care of wound and other applications. Gastroretentive dosage systems, poorly soluble and water soluble molecules of different molecular weights are found in film format (Barnhart and Sloboda, 2007a). Dissolution of oral films could be initiated by the pH or enzymatic secretion of GIT and are used to treat gastrointestinal disorders. Diagnostic devices, Oral films loaded with sensitive reagent to allow controlled release faced to biological fluid for separating multiple reagents to allow a timed reaction within diagnostic device (2).

Advantages Of Orally Dissolving Films (16)

1.Convenient dosing.
2. No water needed.
3. No risk of chocking.
4. Taste masking.
5. Enhanced stability.
6. Improved patient compliance.
7. The drug enters the systemic circulation with reduced hepatic first pass effect.
8. Site specific and local action.
9. Availability of large surface area that leads to rapid disintegration and dissolution within oral cavity.
10. Dose accuracy in comparison to syrup.

Disadvantages of orally dissolving films

1. The disadvantage of orally dissolving film is that high dose cannot be incorporated into the strip.
2. The dose should be between 1-30 mg.
3. There remain a number of technical limitations with use of film strips; the thickness while casting the film.
4. Glass Petri plates cannot be used for casting.
5. The other technical challenge with these dosage forms is achieving dose uniformity.
6. Packaging of films requires special equipments and it is difficult to pack.

Ideal characteristics of a suitable drug candidate (17, 18)

1. The drug should have pleasant taste.
2. The drug to be incorporated should have low dose up to 40 mg.
3. The drug should have smaller and moderate molecular weight.
4. The drug should have good stability and solubility in water as well as saliva.
5. It should be partially unionized at the pH of oral cavity.
6. It should have ability to permeate the oral mucosal tissue.

Classification of fast dissolving technologies (18)

Orally dissolve technologies can be divided in to three broad groups.[3]

- Lyophilized systems.
- Compressed tablet-based systems.
- OTF

Classification of fast dissolving technologies

Properties	Lyophilized system	Compressed tablet based system	Oral thin films
Composition	Solution or suspension of drug with excipients	Active pharmaceutical ingredient with superdisintegrants	Hydrophilic polymers with drug and other excipients
Technology used	Lyophilization	Direct compression	Solvent casting, hot melt extrusion
Characteristics	High porosity which allow rapid water or saliva penetration and disintegration	Different levels of hardness and friability these result in varying disintegration and packaging needs	Large surface area leads to rapid disintegration
Packaging	Blister pack	High density polyethylene bottles	Blister cards with multiunits

Classification of orally dissolving films

1. Flash releasing oral films
2. Mucoadhesive Melt-away wafers
3. Mucoadhesive sustained-release wafers

S.No	Property/Sub/Type	Flash Release films	Mucoadhesive Melt - away wafer	Mucoadhesive sustained - release wafer
1	Area (cm2)	2-8	2-7	2-4
2	Thickness (μm)	20-70	50-500	50-250
3	Structure	Film, single layer	Single or multilayer system	Multi-layer system
4	Excipients	Soluble, highly hydrophillic polymers	Soluble, hydrophillic polymers	Low/Non-solid solution
5	Drug phase	Solid solution	Solid solution or suspended drug particles	Suspension and/or solid solution
6	Application	Tongue (upper palate)	Gingival or buccal region	Gingival, (other region in the oral cavity)
7	Dissolution	Maximum 60sec	Disintegration in a few mins, forming gel	Maximum 8-10 hrs

Ideal Properties of the Film Forming Polymers. (4)

1. The polymer employed should be non-toxic, nonirritant and devoid of any leachable impurities.
2. It should be tasteless.
3. It should have good wetting and spreadability property.
4. The polymer should exhibit sufficient peel, shear and tensile strengths.
5. The polymer should be cheap and readily available.
6. It should have long shelf life.
7. It should not cause any secondary infections in the oral mucosa/ dental region.
8. It should have a good mouth feel property.
9. It would be ideal to have a polymer that would have local enzyme inhibition action.

List of some synthetic and natural polymers useful in film forming (8)

Natural polymer	Synthetic polymer
Starch	Hydroxy propyl methyl cellulose
Pectin	Poly vinyl pyrolidone (PVP)
gelatin	Polyvinyl alcohol (PVA)
Sodium alginate	Sodium Carboxy methyl cellulose
Maltodextrin	Poly ethylene oxide (PEO)
Pullulan	Kollicoat IR
Xanthan	Hydroxy propyl cellulose (HPC)
Polymerized rosin	Hydroxy ethyl cellulose (HEC)
Gum acacia	Methyl cellulose (MC)

SOME QUALITY PARAMETERS OF SOME DIFFERENT NATURAL POLYMERS

1. Pullulan

Water soluble. Neutral, non-toxic, non-immunogenic, biodegradable, nonmutagenic, non-carcinogenic, impermeable to oxygen, high adhesion and film forming abilities, non-ionic polysaccharide and is blood compatible. It is flexible and

spinnable, being a good adhesive and binder. Pullulan can be made into films of high elasticity and which are oil and grease resistant.(9, 10, 11,12)

2. Sodium Alginate

Practically insoluble in ethanol and ether, also insoluble in other organic solvents and acid. It's stabilizing agent; suspending agent; tablet and capsule disintegrant; tablet binder; viscosity-increasing agent.(9, 10)

3. Pectin

Pectin is partially soluble in cold water. It is insoluble in organic solvents and alcohol. Stabilizing agent; gelling agent; thickening agent.(9, 10,13,14)

4. Gelatin

Practically insoluble in acetone, chloroform, ethanol (95%), ether, and methanol. Soluble in glycerine, acids, and alkalis, although strong acids or alkalis cause precipitation. It's a coating agent, film former, gelling agent, suspending agent, tablet binder, viscosity increasing agent.(9, 10,15)

5. Rosin

Films prepared from the plasticizer-free solutions were smooth and transparent yet brittle. The addition of plasticizers plays an important role in the presentation of film coating, which brings about diminished tensile strength, decreased Tg, and expanded elongation and flexibility of the films.(9, 12)

STANDARD COMPOSITION OF FAST DISSOLVING FILMS (19)

Ingredients	Amount	Examples
Drug	5-30%w/w	Antiallergic, antiemetic, antiepileptic, antimigrant
Water soluble polymer 45%w/w	45%w/w	HPMC E3, E5 and E15 and K-3, Methyl cellulose A-3, A-6 and A-15, Pullulan, carboxmethylcellulose cekol 30, polyvinylpyrollidone PVP K-90, pectin, gelatin, sodium, alginate, hdroxypropylcellulose, polyvinyl alcohol, maltodextrins
Plastisizers	0-20%w/w	Glycerol, dibutyl pthallate, polyethylene glycol, etc.,
Surfactants	q.s.	Sodium lauryl sulfate, benzalkonium chloride, Tween, etc.,
Sweetening	3-6%w/w	Saccharin, cyclamate, and aspartame
Saliva stimulating agents	2-6%w/w	Citric acid, malic acid, lactic acid, and ascorbic acid
Fillers, colors, flavors	q.s.	FD and C colors, US FDA approved flavors

APPROACHES USED FOR THE FORMULATION OF FAST DISSOLVING FILMS (20)

Conventional approaches

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

Solvent casting method

In this method, firstly the water soluble polymers are dissolved in water at 1,000 rpm and can be heated up to 60°C. All the other excipients like colors, flavoring agent, sweetening agent, etc., are dissolved separately. Then both the solutions obtained are mixed thoroughly stirring at 1,000 rpm. The obtained solution is incorporated with the API dissolved in suitable solvent. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size.

Hot-melt extrusion

In hot melt extrusion method, the initial mass is formed with the help of carriers. To form initial mass, the drug is mixed with carriers and a solid mass is obtained and dried. Then dried granular material is introduced into the extruder. The extruder is divided into four zones having following degrees of temperature: 800 (zone 1), 1150 (zone 2), 1000 (zone 3), and 650°C (zone 4). The speed of extruder screw speed should be set at 15 rpm in order to process the granules inside the barrel of extruder for approximately 3-4 min so that mass should be properly melted. The extrudate (T = 650°C) obtained is then pressed into a cylindrical calendar in order to obtain a film. There are certain benefits of hot melt extrusion: Fewer operation units, minimum product wastage, possibility to scale up, an anhydrous process, absence of organic solvents, include shorter temperature and shorter residence time of the drug carrier mix, and better content uniformity (21).

Semi-solid casting

This method is mostly preferred when film ingredient involves acid insoluble polymer. In this firstly, the water soluble polymers are dissolved in water. The obtained solution is added to the acid insoluble polymer solution which is separately formed. Both the solutions are mixed properly. After mixing the two solutions, appropriate amount of plasticizer is added to the obtained final solution so that gel's mass can be obtained. At last, the gel mass is casted onto the films or ribbons using heat controlled drums. The thickness of the film should be about 0.015-0.05". The ratio of the acid insoluble polymer to film forming polymer should be 1:4. Examples of acid insoluble polymers are cellulose acetate phthalate and cellulose acetate butyrate.

Solid dispersion extrusion

Method involves the solid dispersion of drug incorporated in melted polymer solution so that drug can be loaded. The drug is dissolved in suitable liquid solvent and obtained solution is added to the melt of suitable polymer, obtainable below 70°C without removing the liquid solvent to obtain the solid dispersion. Finally the obtained solid dispersions are shaped into films by means of dyes.

Rolling method

In rolling method, both the drug solution and film forming polymer solution are mixed thoroughly and the resultant solution or suspension is subjected to the roller. The solution or suspension should have specific rheological consideration. The film is dried on rollers and cut into desired shapes and sizes.

PATENTED APPROACHES [22]

XGel XGel™ film provides unique product benefits for healthcare and pharmaceutical products: It is nonanimal derived, approved on religious grounds, and is suitable for vegetarians; the film is genetically modified organism (GMO) free and continuous production processing provides an economic and competitive manufacturing platform. XGel™ film can be taste masked, colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGel™ film systems can be made to encapsulate any oral dosage form and can be soluble in either cold or hot water. XGel™ film is comprised of a range of different water soluble polymers, specifically optimized for the intended use.

SOLULEAVES

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

WAFERTAB

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

FOAMBURST

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

MICAP

Micap plc signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water soluble films. The developments will be aimed at providing new delivery mechanisms for the $1.4 billion global market for smoking cessation products (SCPs).

EVALUATION PARAMETERS

Thickness

The thickness of film is measured by micrometer screw gauge or calibrated digital Vernier Calipers. The thickness of film should be in range 5-200 µm.[24] The thickness should be evaluated at five different locations (four corners and one at

centre) and it is essential to ascertain uniformity in the thickness of film as this is directly related to accuracy of dose distribution in the film.

DRYNESS/TACK TEST

In all there have been eight stages identified for film drying and these are set-to-touch, dust-free, tack-free (surface dry), dry-to touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat, and dry print-free. Tack is the tenacity with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with strip. Instruments are also available for this study.[25]

TENSILE STRENGTH (18)

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

Tensile strength = Load at failure × 100/Strip thickness × Strip width

PERCENT ELONGATION [26]

When stress is applied on a film (2 × 2 cm2) sample it gets stretched, this is referred to strain. Strain is basically the deformation of strip before it gets broken due to stress. It is measured by using hounsfield universal testing machine. Generally elongation of strip increases as the plasticizer content increases. It is calculated by the formula:
% Elongation = Increase in length of strip × 100/Initial length of strip

TEAR RESISTANCE [27]

Tear resistance is the resistance which a film offers when some load or force is applied on the film specimen. The load mainly applied is of very low rate 51 mm/min. The unit of tear resistance is Newton or pounds-force. In other words it is the maximum force required to tear the specimen.

YOUNG'S MODULUS

Young's modulus or elastic modulus is the measure of stiffness of strip.[25] It is represented as the ratio of applied stress over strain in the region of elastic deformation as follows: Young's modulus = Slope × 100/Strip thickness × Cross head speed
Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation.

FOLDING ENDURANCE

Folding endurance gives the brittleness of a film. The method followed to determine endurance value is that the film specimen (2 × 2 cm2) are repeatedly folded at the same place until it breaks or a visible crack is observed. The number of times the film is folded without breaking or without any visible crack is the calculated folding endurance value.[28]

IN VITRO DISINTEGRATION TEST

Disintegration time is the time when an oral film starts breaking when brought in contact with water or saliva. For a fast dissolving film, the time of disintegration should be in range of 5-30 s. United State Pharmacopoeia (USP) disintegration apparatus can be used to study disintegration time.[29] In another method, the disintegration time can be visually determined by dipping the film in 25 ml water in a beaker. The beaker should be shaken gently and the time was noted when the film starts to breaks or disintegrates.[30]

IN VITRO DISSOLUTION STUDIES

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent concentration. The standard basket or paddle apparatus described in any of the pharmacopoeia can be used for dissolution testing. The selection of dissolution medium will essentially depend as per the sink conditions and highest dose of API. The temperature of dissolution medium should be maintained at 37 ± 0.5°C and rpm at 50. When the paddle apparatus is employed, it has a disadvantage that oral films have a tendency to float over the dissolution medium. Stainless steel wire mesh with sieve opening of approximately 700 µm used to dip salbutamol fast dissolving film inside the dissolution medium.[31,32]

DRUG CONTENT UNIFORMITY

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85-115%.[33]

ORGANOLEPTIC TEST

The desired organoleptic properties a fast dissolving formulation should have are color, flavor, and taste. As the formulation will disintegrate in the oral cavity so it should provide acceptable organoleptic palatable characteristics. Color makes a formulation acceptable among the patients and moreover oral films should have attractive color as they are administered to children. Hence, color of formulation should be uniform and attractive. Color can be evaluated by visual

inspection. The other organoleptic property is the odor. The flavor used in the formulation should provide good odor to the formulation. The odor of the polymer, drug, and any other excipient should be masked with use of flavoring agent. Taste is also an important factor which has to be evaluated. To evaluate the taste, special human taste panels are used. Experiments using electronic tongue measurements have also been reported to distinguish between sweetness levels in taste masking formulation.[33] Electronic tongue technique works on the principle of potentiometric titration method. In this liquid samples can be analyzed directly, whereas solid samples need to be dissolved in a suitable solvent before analyzing. In this method, reference electrode and sensors are dipped in a beaker containing a test solution for 120 s and a potentiometric difference between each sensor and a reference electrode is measured and recorded by the E-tongue software.[34,35]

SURFACE PH TEST

The surface pH of fast dissolving strip can cause side effects to the oral mucosa, so it is necessary to evaluate the surface pH of film. The surface pH of film should be 7 or close to neutral. For this purpose, a combined pH electrode can be used. With the help of water, OS was made slightly wet and the pH was measured by bringing electrode in contact with surface of oral film. This study should be done on at least six films of each formulation and their mean ± SD can be calculated.[36] In another method to determine the surface pH, the films are placed on the 1.5%w/v agar gel and then the pH paper are placed on the film, change in color of pH paper gives surface pH of the film.

CONTACT ANGLE

Contact angle measurement predicts the wetting behavior, disintegration time, and dissolution of oral film. These measurements are performed with help of goniometer (AB Lorentzen and Wettre, Germany) and the measurements should be done at room temperature. The water used to determine contact angle should be double distilled water.[8] A drop of double distilled water is placed on the surface of dry film. Images of water droplet are recorded within 10 s of deposition by means of digital camera. Digital pictures can be analyzed by imageJ 1.28v software (NIH, USA) for angle determination.

TRANSPARENCY

To determine transparency of oral film, a simple ultraviolet (UV) spectrophotometer can be used. The film specimen is placed on the internal side of spectrophotometer cell. The transparency of films is calculated as follows:

$$\text{Transparency} = (\log T600)/b = -\epsilon c$$

Where T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration.[37]

SCANNING ELECTRON MICROSCOPY

To study the surface morphology of film between different excipients and drug scanning, electron microscopy can be used. The film sample should be placed in sample holder and at ×1000 magnification, various photomicrographs can be taken using tungsten filament as an electron source.[38]

PERMEATION STUDIES

Even though permeability of oral mucosa is 4-1000 times greater than that of skin, permeation studies should be carried out. To study the permeability, modified Franz diffusion cell can be used along with porcine buccal mucosa. The Franz diffusion cell consists of a donor and a receptor compartment. In between the two compartments, mucosa is mounted and the size of the mucosa should be of the same size as that of the head of receptor compartment. The receptor compartment is filled with buffer and maintained at 37 ± 0.2°C and to maintain thermodynamics a magnetic bead stirring at a speed of 50 rpm is used. A film specimen moistened with a few drops of simulated saliva should be kept in contact with mucosal surface. The donor compartment should consist of 1 ml simulated saliva fluid of pH 6.8. At particular interval, samples are withdrawn and replaced by same amount of fresh medium. By suitable analytical method, percentage of drug permeated can be determined.[39]

PERCENTAGE MOISTURE LOSS

To determine percentage moisture loss films of area 2 × 2 cm2 are cut and weighed accurately on an electronic balance. After weighing, the films were kept in desiccators containing fused anhydrous calcium chloride. The films should be kept for 72 h in the desiccator. After 72 h, they are taken out and again weighed and the percentage moisture loss of films was measured by using the formula:

$$\text{Percent moisture loss} = (\text{Initial weight} - \text{Final weight})/\text{Initial weight} \times 100$$

The percentage moisture loss studies are done to determine physical stability and integrity of the film.[40]

Determination of % yield of buccal patches [41]
Percentage yield of buccal patches can be calculated by the following formula:

% yield = Mass of the buccal patches obtained/Total weight of drug and polymer × 100

Stability study

Stability study should be carried out according to the International Conference on Harmonization (ICH) guidelines. The prepared formulation was wrapped in a special way. Firstly, it was wrapped in a butter paper then above it an aluminum foil was wrapped and the packing should be placed in an aluminum pouch and make it heat sealed. The storage conditions at which formulations are kept should be 30°C/60% relative humidity (RH) and 40°C/75% RH. After 3 months, the films were evaluated for drug content, disintegration time, and physical appearance observation.[42]

Storage and packaging

Orally dissolving strips can be packed using single pouches, blister card with multiple units, multiple-unit dispenser, and continuous roll dispenser. There are certain patented packaging systems for fast dissolving films such as Rapid card by Labtec and Core-peel by Amcor flexible. The rapid card is of same size as a credit card and holds three films on each side. Every dose can be taken out individually.[43]

MARKETED PRODUCTS OF ORAL FILMS

Different products of oral films are summarized in the following table Marketed Products of Oral Films (3) (Arya et al., 2010)

Product category	Ingredients	Indication /Application
1. Bio Films		
Energy boosters	Caffeine, green tea extract and guarana	The product maintains the energy level
Saliva promoting strip	Fruit acid extract	It is used in the dry mouth as a side effect of the other medication
Detoxification strip	Green tea extract	Green tea has been used as a traditional medicine commonly used in blood sugar, wound healing, regulating body temperature and promoting healthy digestion
Breath freshener strip (anti-bacterial strip)	It contains mint flavor and anti-bacterial agent, cetylpyridinium chloride	It is used as mouth freshener and to stop bad odor of breath.
2. Bio Delivery Sciences International		
Onsolis	Fentanyl /buccal soluble film	Pain in Opioid tolerant patients
BEMA buprenorphine	Buprenorphine	Therapeutic alternative for patient with incomplete pain relief or those unable to tolerate
3.Hughes Medical Corporation		
Caffeine	2.5mg	CNS Stimulant
Diphenhydramine Hcl	2.5mg-5mg	Antihistaminic
Folic acid	1m-5mg	Needed for formation of healthy red blood cells and used in anemia
Loratidine	10mmg-15mg	Allergy
4. Innozen Inc		
Chloraseptic relief strip	Benzocaine 3mg, BHT, corn starch, erythritol, FD&C Red 40, hydroxypropyl methylcellulose mallicacid, menthol monoammonium glycyrrhizinate, cherry flavor, polyethyleneoxide, sucralose	Occasional minor irritation, pain, sore throat and sore mouth
Chloraseptic kids sore throat relief strips	Benzocaine 2mg & menthol, grape flavor,BHT,cornstarch,erythritol,FD&C Red 40,hydroxypropyl methylcellulose, mallicacid,menthol,menthol,mono ammonium glycyrrhizinate,polyrthyleneoxide,sucralose	Occasional minor irritation, pain, sore throat and sore mouth
5. Labtec Gmb H		
Ondensetron rapid film	Ondensetron 4mg and 8mg	It is used to prevent chemotherapy and radiation induced nausea, vomiting
Donezepil rapid film	DonezepilHcl 5mg and 10mg	It is used in the treatment of mild to moderately severe dementia of the Alzheimer's type
6. Paladin Labs(bioenvelop)		
Smoking cessation	Nicotine	To reduce smoking habit
Food supplements	Benzocaine, caffeine, melatonin, menthol, vipocetina	Neutraceuticals

CONCLUSION

This review highlights the importance of orally dissolving films and various advantages over other dosage forms. It aids the fast release of the medicament in the mouth when it is placed on tongue or in the cheeks.It enumerates basic role of various natural and synthetic polymers used in formulating orally dissolving films along with formulation approaches. It gives information about procedures to perform evaluation tests. At last concludes that how efficiently orally dissolving films are being used in market by patients for immediate relief from the disease or disorder.

REFERENCES

1. Theory and Practice of Contemporary Pharmaceutics. Ghosh TK, Jasti BR, editors. CRC Press, 2005; 282–367: 150–155.
2. Meathrel, B., Moritz, C., (2007). Dissolvable films and their potential in ivds. IVD Technol, 13(9), 53-58. [DOI]

3. Arya, A., Chandra, A., Sharma, V., Pathak, K., (2010). Fast dissolving oral films: An innovative drug delivery system and dosage form. International Journal of Chem Tech Research, 2(1), 576-583.
4. Priyanka Gupta, Amrita Bisht and Dr. N. G. Raghavendra Rao.FAST DISSOLVING ORAL FILMS: A COMPREHENSIVE REVIEW.WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH, wjpmr, 2019,5(7), 116-127
5. Payvand Kamrani; Nazia M. Sadiq.Anatomy, Head and Neck, Oral Cavity (Mouth), NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.PMID: 31424855
6. Gandhi SD, Pandya PR, Umbarkar R, Tambawala T, Shah MA. Mucoadhesive drug delivery systems an unusual maneuver for site-specific drug delivery system.. Pharm Sci Monit an Int J Pharm Sci., 2011; 2(3): 132–52
7. Arya Arun, Chandra Amrish, Sharma Vijay and Pathak Kamla, Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form, International Journal of Chemtech Research, 2(1), 2010, 576-583.
8. Patel A, Prajapati DS, Raval JA. Fast dissolving films: as a newer venture in fast dissolving dosage forms. Int. J. Drug Dev. Res., 2010; 2: 232-246.
9. Nagar Priyanka, Chauhan Iti, Yasir Mohd, Insights into Polymers: Film Formers in Mouth Dissolving Films, Drug Invention Today, 3(12), 2011, 280-289.
10. Bala Rajni, Pawar Pravin, Khanna Sushil, Arora Sandeep, Orally Dissolving Strips: A New Approach to Oral Drug Delivery System, International Journal of Pharmaceutical Investigation, 3(2), 2013, 67-76.
11. Hanif Muhammad, Zaman Muhammad & Chaurasiya Vesh, Polymers used in Buccal Film: A Review, Designed Monomers and Polymers, 18(2), 2015, 105-111.
12. Pathare Yogyata S., Hastak Vishakha S., Bajaj Amruta N., Polymers used for Fast Disintegrating Oral Films: A Review, International Journal of Pharmaceutical Sciences Review and Research, 21(1), 2013, 169-178.
13. Kaur Gaganjot, Grewal Jasleen, Jyoti Kiran, Jain Upendra K., Chandra Ramesh, Madan Jitendra, Chapter 15- Oral Controlled and Sustained Drug Delivery Systems: Concepts, Advances, Preclinical, And Clinical Status, Drug Targeting and Stimuli Sensitive Drug Delivery Systems, 2018, 567-626.
14. Mudgil Deepak, Chapter 3- The Interaction between Insoluble and Soluble Fiber, Dietary Fiber for the Prevention of Cardiovascular Disease, 2017, 35-59.
15. Liu Dasong, Nikoo Mehdi, Boran Gokhan, Zhou Peng and Regenstein Joe M., Collagen and Gelatin, Annual Review of Food Science and Technology, 6, 2015, 527-557.
16. Bhura N, Sanghivi K, Patel U, Parmar B. A review on fast dissolving film. Int J Res Bio Sci 2012; 3:66-9.
17. Fulzele SV, Satturwar PM, Dorle AK. Polymerized rosin: Novel film forming polymer for drug delivery. Int J Pharm 2002; 249:175-84.
18. Rajni Bala, Pravin Pawar, Sushil Khanna, Sandeep Arora, Orally dissolving strips: A new approach to oral drug delivery system, International Journal of Pharmaceutical Investigation, April 2013, Vol 3, Issue 2: 67-76.
19. Deshmane SV, Joshi UM, Channwar MA, Biyani KR, Chandewar AV. Design and characterization of carbopol-HPMC-ethyl cellulose based buccal compact containing propranolol HCl. Indian J Pharm Educ Res 2010;44:67-78.
20. Khairnar A, Jain P, Bhaviskar D, Jain D. Development of mucoadhesive buccal patches containing aceclofenac: In vitro evaluation. Int J Pharm Sci 2009;1:91-5.
21. Shinde AJ, Garala KC, More HN. Development and characterization of transdermal therapeutics system of tramadol hydrochloride. Asian J Pharm 2008;2:265-9.
22. Chi Fai Cheung Randy, Bun Tzi Ng, Wong Jack Ho and Chan Wai Yee, Chitosan: An Update on Potential Biomedical and Pharmaceutical Applications, Marine Drugs, 13, 2015, 5156- 5186.
23. Peh KK, Wong CF. Polymeric films as vehicle for buccal delivery: Swelling, mechanical, and bioadhesive properties. J Pharm Pharm Sci 1999;2:53-61.
24. Sani S, Nanda A, Hooda M, Komal. Fast dissolving films (FDF): Innovative drug delivery system. Pharmacologyonline 2011; 2:919-28.
25. Mashru RC, Sutariya VB, Sankalia MG, Parikh PP. Development and evaluation of fast dissolving films of salbutamol sulphate Drug Dev Ind Pharm 2005;31:25
26. Borsadia SB, O'Halloran D, Osborne JL. Quick dissolving films-a novel approach to drug delivery. Drug Deliv Technol 2003;3:63-7.
27. Ali S, Quadir A. High molecular weight povidone polymer-based films for fast-dissolving drug delivery applications. Drug Deliv Technol 2007;7:36-43
28. Kalyan S, Bansal S. Recent trends in the development of oral dissolving film. Int J PharmTech Res 2012; 4:725-33.
29. Dahiya M, Saha S, Sahiwala AF. A review on mouth dissolving films. Curr Drug Deliv 2009;6:469-76.
30. Vishwkarma DK, Tripathi AK, Yogesh P, Maddheshiyab B. Review article on mouth dissolving film. J Glob Pharm Technol 2011; 3:1-8.
31. Dinge A, Nagarsenker M. Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. AAPS Pharm Sci Tech 2008;9:349-56.
32. Rathi V, Senthil V, Kammili L, Hans R. A brief review on oral film technology. Int J Res Ayurveda Pharm 2011; 2:1138-47.
33. Sharma R, Parikh RK, Gohel MC, Soniwala MM. Development of taste masked film of valdecoxib for oral use. Indian J Pharm Sci 2007; 69:320-3.
34. Tomar A, Sharma K, Chauhan NS, Mittal A, Bajaj U. Formulation and evaluation dissolving oral film of dicyclomine as potential route of buccal delivery. Int J Drug Dev Res 2012; 4:408-17.
35. Kumar SV, Gavaskar B, Sharan G, Rao YM. Overview on fast dissolving films. Int J Pharm Pharm Sci 2010; 2:29-33.
36. Parmar D, Patel U, Bhimni B, Tripathi A, Daslaniya D, Patel G. Orally fast dissolving films as dominant dosage form for quick release. Int J Pharm Res Bio Sci 2012;1:27-41.
37. Corniellio C. Quick dissolving strips: From concept to commercialization. Drug Deliv Technol 2006;6:68-71.
38. World Health Organization Working document 2008, QAS/08.257.
39. Patel AR, Prajapati DS, Raval JA. Fast dissolving films (FDFs) as a newer venture in fast dissolving dosage forms. Int J Drug Dev Res 2010;2:232-46.
40. Kulkarni AS, Deokule HA, Mane MS, Gadhe DM. Exploration of different polymers for use in the formulation of oral fast dissolving strips. J Curr Pharm Res 2010;2:33-5.
41. Peppas NA, Buri PA. Surface, interfacial, molecular aspects of polymer bioadhesion to soft tissues. J Control Release 1985;2:257-75.
42. Sakellariou P, Rowe RC. Interactions in cellulose derivative films for oral drug delivery. Prog Polym Sci 1995;20:889-942.
43. Browhn GL. Formation of film from polymer dispersions. J Polym Sci 1956;22:423-34.