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A Detailed Account On Novel Oral Fast Dissolving Strips: Application And Future Prospects

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ABSTRACT:

Orally Fast Dissolving Strips (OFDS) is a novel drug delivery dosage form designed and developed as an alternative to orally conventional drug delivery system (tablets, capsules, syrups). Many drawbacks like gastrointestinal destruction of liable molecules, slow onset of action, low absorption of macromolecules and unavoidable fluctuation in the concentration of drug which may either leads to under-or-over medication. To overcome these difficulties, recent trends are shifting towards developing an innovative drug delivery system to improve safety, efficacy & patient compliance by fast dissolving technologies, which dissolves within a minute in oral cavity. This dosage form is an alternative plate form for molecules that undergoes high first-pass metabolism. OFDS are useful in patient such as pediatrics, bedridden or developmentally disabled, geriatric, who faces difficulty in swallowing solid dosage forms like tablets & capsules. Now-a-days this technology became a novel and widely accepted formulation by consumers. Various approaches are employed for formulating OFDS's and among which solvent casting is widely used method. The present review attempts to focus on formulation aspects, manufacturing methods, evaluation parameters & an overview on packaging available and some marketed products.

Key words: Fast dissolving films, hydrophilic polymers, solvent casting, disintegration, patient compliance.

INTRODUCTION:

The oral route is one of the most popular medication administration methods since it is more convenient, cost-effective, and easy to administer, resulting in high patient compliance.[1] Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing. [2] Fast-dissolving drug delivery-systems (FDDDS), were developed in the last 1970's as an alternative to conventional oral dosage forms to deliver the drugs under emergency conditions and where pediatric and geriatric patients who experience difficulties in swallowing the oral dosage forms like tablets and capsules.[4] Fast Drug Delivery System is rapidly gaining interest in the pharmaceutical industry. These systems either dissolve or disintegrate rapidly within a minute without needing water or chewing, the ability to manage without swallowing makes these systems particularly beneficial for children, the elderly and non-assisted patients. The large capillary network beneath the oral mucosa is rapidly absorbed and increases the bioavailability of drug with respect to oral administration.[5] Orally Fast Dissolving Strips (OFDS) are a novel dosage form that disintegrates or dissolve in the oral cavity. These dose forms go on the tongue or any other mucosal tissue. When wet with

saliva, the films rapidly hydrates and adheres onto the site of application. [3] It rapidly dissolves to release the medicine for mucosal absorption. An important benefit of these dosage forms is accurate dosing as compared to liquid dosage form, no more water is needed and there is no fear of choking as compared to tablets and capsules. This technique allows for faster drug absorption from the pre-gastric region, potentially resulting in a faster beginning of action. In such cases, bio-availability of drug is significantly greater than those observed from conventional tablet dosage form.[6,7] Fast dissolving buccal film drug delivery systems have lately acquired popularity as an essential new method of drug administration. Pharmaceutical and nutraceutical goods are typically made with them. It is the newest frontier in drug delivery technology that provides a very convenient means of taking medications & supplements. Therefore, they are very suitable for pediatric patients; bedridden patients or patients suffering from dysphagia, Parkinson's disease, mucositis, or vomiting. [8]

OFDS's are strip type preparations with active molecules dissolved are dispersed in film forming materials. It gives quick dissolution, absorption and instant bioavailability of drugs due to high blood flow and permeability of buccal mucosa of 4-1000 times greater than that of skin.[2] OFDS is also known as fast dissolving film, Quick dissolving film, Rapid dissolving film, Oral thin film (OTF), Mouth Dissolving Films (MDF). Formulation of fast dissolving oral film involves material such as strip-forming polymers, plasticizers, active pharmaceutical ingredient, sweetening agents, saliva stimulating agent, flavoring agents, coloring agents, stabilizing and thickening agents, permeation enhancers, and superdisintegrants. According to regulatory perspectives, all excipients used in the composition of rapid dissolving film should be permitted for use in oral pharmaceutical dosage forms. [9]

SPECIAL FEATURES OF MOUTH DISSOLVING FILM: [10]

- Film should be thin and elegant.
- Available in various size and shapes.
- Unobstructive.
- Excellent mucoadhesion.
- Should processes fast disintegration without water
- Rapid release.

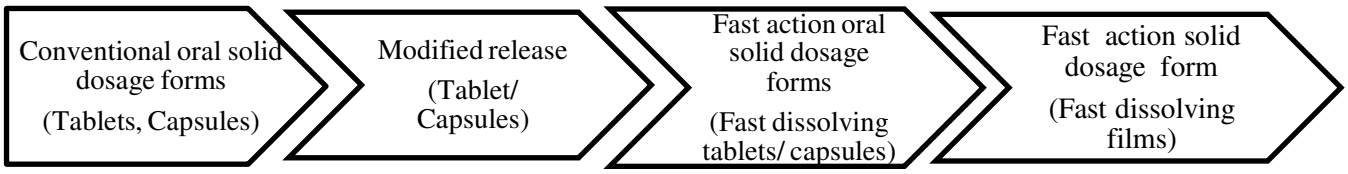
ADVANTAGES OF FAST DISSOLVING FILMS: [11]

- Convenient dosing
- No water needed
- No risk of chocking
- Taste masking
- Enhanced stability
- Improved patient compliance
- More flexible, easily handled storage and transportation.
- Because the medicine enters the systemic circulation immediately, it has the quickest beginning of therapeutic activity. [12]
- It provides the ease of administration of pediatrics and geriatrics patients who face the problem of dysphasia
- With a diminished hepatic first-pass impact, the medication penetrates the systemic circulation. Site specific and local action
- Large surface area available, resulting in fast disintegration and dissolution within the oral cavity
- Dose accuracy in comparison to syrup.

DISADVANTAGE OF ORAL FILMS:

- High dose cannot be incorporated into the strip.
- Dose uniformity is a technical challenge.
- Drugs that irritate the oral mucosa and which are unstable at mucosal pH cannot be administrated.[12]
- Oral strips are sensitive and must be protected from water, they require specific packaging.

MODIFICATION IN ORAL DOSAGE FORM



OVERVIEW OF ORAL MUCOSA

An outer layer of stratified squamous epithelium makes up the oral mucosa. Underneath this lie a foundation membrane, a lamina propria, and the sub-mucosa, the innermost layer as shown in fig.1. The epithelium begins with a mitotically active basal cell layer and goes through a succession of growing intermediate layers to the superficial layers, where cells are shed from the epithelium's surface, similar to the rest of the body's stratified squamous epithelia.

The trans-cellular or Para-cellular pathways can both be used to take drugs from the buccal pit. In terms of permeability, the oral mucosa falls somewhere between the epidermis and the intestinal mucosa. The wafer dissolves quickly in the mouth, and the active moiety is absorbed into the circulation via the gastrointestinal tract. [15]

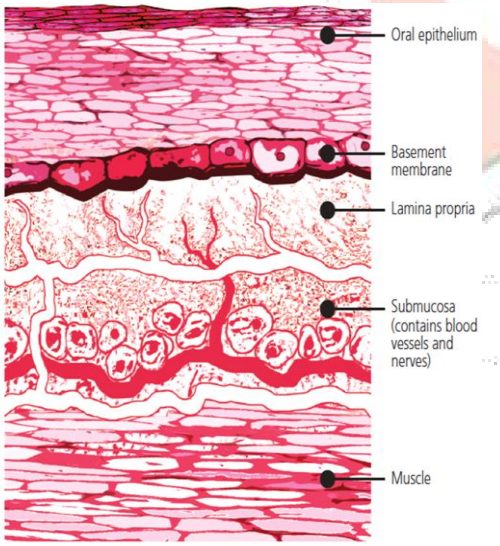


Fig: 1. OVERVIEW OF ORAL MUCOSA

MECHANISM OF ACTION: The delivery system is simply placed on a patient's tongue or any oro-mucosal tissue. Instantly wet by saliva due to presence of hydrophilic polymer and other excipients, the film rapidly hydrates and dissolves to release the medication for oro-mucosal absorption. [18]

CLASSIFICATION OF FAST DISSOLVING TECHNOLOGY

The three types of fast-dissolving technology are as follows. [14]

- Lyophilized systems
- Compressed tablet-based systems
- Oral thin film

Lyophilized systems

This approach includes forming tablet-shaped units from a medication suspension or solution with various structural excipients using a mould or blister pack. Following that, the units or tablets are frozen and lyophilized in a pack or mould. The resultant units have a high porosity, allowing water or saliva to penetrate quickly and disintegrate quickly.

Compressed tablet- based systems

This method is made using normal tablet technology, which involves direct compression of excipients. Depending on the technique of manufacturing, tablet technologies have varying degrees of hardness and friability**.** The speed of disintegration for fast-dissolving tablets compared with a standard tablet is achieved by formulating it using water soluble excipients, or super-disintegrate or effervescent components, to allow quick water penetration into the tablet's core. [17]

Oral thin films

Oral films are a collection of flat films that are placed in the mouth. Dissolvable oral thin films (OTFs) or oral strips (OS) originated from the confection and oral care sectors in the form of breath strips during the last several years and have become a unique and highly recognized method of delivering vitamins and personal care items to consumers. To create a 50-200mm film, these methods utilize a range of hydrophilic polymers. [16]

CLASSIFICATION OF OTF: [13]

Oral quick dissolving films are divided into three categories:

- Flash release
- Mucoadhesive melt-away wafer
- Mucoadhesive sustained release wafers

Table 1: Types of Oral Thin Films with Their Properties

Orally disintegrating film types and their characteristics			
Properties	**Flash release**	**Mucoadhesive melt-away wafers**	**Mucoadhesive sustained released wafers**
Area(cm_2)	2-8	2-7	2-4
Thickness(µm)	20-70	50-500	50-250
Structure	one layer	one or more than one layer	Multilayer system
Drug phase	Solid phase	Solid phase or suspended drug particle	Suspension or solid phase
Application	Tongue(upper plate)	Gingival or buccal region	Gingival(other region in the oral cavity)
Dissolution	60's	In few minutes forming gel	Maximum8-10h

COMPOSITION OF ORALLY FAST DISSOLVING STRIPS

- Active Pharmaceutical Ingredients (API) / Drug
- Water soluble polymers
- Plasticizer
- Surfactants
- Sweetening agents
- Saliva stimulating agents
- Fillers, Colours, and flavors.

Active Pharmaceutical Ingredients/ Drug

1-30% w/w of API is used for a standard composition of orally dissolving strips. Generally, small dose molecules are the best candidates to be incorporated in orally fast dissolving strips. Micronization of APIs is highly effective for improving strip dissolving, which leads to rapid absorption and immediate therapeutic action of the medication. This technology has the ability to offer a wide range of APIs. However, there are several restrictions, such as the size of the dosage form and the difficulty of incorporating high-dose medications into films. In the distribution of water soluble APIs, consistency is not an issue. Water-insoluble APIs, on the other hand, must be dispersed uniformly to achieve acceptable content uniformity. Anticancer drugs, anti-asthmatics, anti-tussives, antihistamines, anti-epileptics, anti-anginal drugs, anti-emetics, cardiovascular drugs, neuroleptics, analgesics, anxiolytics, anti-allergic drugs, hypnotics, sedatives, antibacterial drugs, anti-drugs, Alzheimer's diuretics, and expectorants are all examples of drugs. [19, 20]

Table 2: Examples of suitable drug molecule and its category

Category	Examples
Anti-emetics	Granistron,pionostron,dronabinol,aprepitant,ramostron,trimethobezamide,nabilone,metoclopramide Dolasetron, dimenhydramine, Ondasetran
Serotonin inhibitors	Fluoxetine, setraline, paroxetine,fluxoamine,citalopram and alaproclate
SHT3antagonists	Alosetron,ondansetron,grainsetron,palonosetron,rmosetron,tropisetron
Anti-epileptics	Carbamezapine,clonazepalm,diazepam,divalproex sodium,fosphenyloin,gabapentin,lamotrigine, Levetiracetam,oxacarbazepine,phenyton,primidone and valproate sodium
Anti-migraines	Almotriptan,dihydrogotamine,mesylate,eletriptan,frovateiptan,naratriptan,rizatriptan,sumatriptn and Zolmitriptan
Dopamine D1 andD2antagonists	Amisulpride,bromperidol,cabergoline,domeperidone,fenoldopam,haloperidol,metoclopramide,metopimazine Pergolidemesylate,prochlorazine,quetiapine,ropinirole hydrochloride,sulpiride,tiapride and zotepine
No tropics	AlmitrineDimesylate and raubasine,cevimeline Hydrochloride,codergocrinemesylate,donepezil,galantamine, GinkgoBilobaextract(egb761),memantine,nicergoline,piracetam,rvastigmine,tacine and vinpocetine
Statins	Atorvastatin,cerivastatin,fluvastatin,lovastatin,pitavastatin,rosuvastatin and simvastatin

Film- forming polymers

Selection of polymer is very important parameter and most critical one in the successful preparation of oral film due to their mechanical strength & stiffness, which depends on the type and amount of polymer we used to formulate the films, the polymers can be used alone or in combination to improve hydrophilicity, flexibility, mouth – feel and solubility characteristics of fast dissolving films. 45% w/w of the concentration of the polymer is used to develop an orally fast dissolving strip. But it can be increased up to 60-65% w/w to attain the desired characteristics. The physicochemical properties of the polymers chosen for film formulation are critical in defining the cast thin film oral dosage form's disintegration time. [21]

Table 3: Examples of natural and synthetic polymers

Group	Class	Example
Natural	***carbohydrate***	Sodium starch glycolate, pullalan, pectin sodium alginate, malt dextrin.
	Proteins	Gelatine
	Resin	Polymerized rosin(novel film former)
Synthetic	***Cellulose derivatives***	Hydroxyl propyl methyl cellulose (E3, E5, E15, K3, K15, K50) Methylcellulose (A3, A6, A15), Carboxyl methylcellulose secskol-30, sodium Carboxymethyl cellulose, Microcrystalline cellulose, croscarmellose sodium (CCS).
	Vinyl polymer	K-90, K-30 polyvinyl pyrrolidone, polyvinyl alcohol, and polyethylene oxide

Ideal properties of film forming polymers:

- It must be nontoxic and non-irritant.
- Should be free from leachable impurities.
- It should not retard disintegration time of film.
- Tasteless.
- It should have a high wetting and spreading ability.
- It should be readily available.
- It should have sufficient peel, shear, and tensile strength.
- It should be easily available and reasonably priced.
- The shelf life should be reasonable.
- It should not aid in causing secondary infections in dental areas or oral mucosa. [22]

Plasticizer

Plasticizer is an important ingredient used in the formulation of orally dissolving films. It helps to increase the flexibility of the polymer and reducing the friability of the film. By lowering the polymer's glass transition temperature, it increases film forming characteristics dramatically. By the addition of the plasticizers, the mechanical and tensile strength of the film will be improved. Plasticizers will be chosen based on their compatibility with the medication, polymer, and the type of solvent used in the film casting process. Plasticizers are commonly used in concentrations ranging from 0 to 20% by weight of dry polymer. Inappropriate usage of plasticizer, on the other hand, might result in the strip's film breaking, splitting, and peeling. It has also been observed that the use of certain plasticizers might influence the drug's absorption rate. Commonly used plasticizer in the formulation of films are: Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil. [23, 24]

Surfactant

Surfactants are used to increase the solubility and wetting property of the film that will provide a quick dissolution and release the active medicament quickly within a minute. It is preferable to use poloxamer 407, sodium lauryl sulphate, benzalkonium chloride, polysorbate, etc. Among these poloxamer 407 is the most important surfactant used as solubilizing, wetting and dispersing agent. [25, 26]

Sweetening agent

Sweeteners are used in the pharmaceutical products to mask the bitter taste of the drug. Both the natural and artificial sweeteners are used in the formulation of films. Natural sweeteners such as sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose, as well as artificial sweeteners such as galactose, glucose, mannose, fructose, xylose, ribose, dextrose, maltose, sucrose, sugar, sorbitol, xylitol, mannitol, and soluble saccharin salts, saccharin, cyclamate salts, acesulfame-K, Aspartame, Neotame etc. The use of natural sugars in this preparation is restrained in diabetic patients. For that reason, artificial sweeteners are the most popular in pharmaceutical preparations and foods. In orally dissolving strips, aspartame and saccharin are used as artificial sweeteners. [27, 28]

Saliva stimulating agent

Saliva stimulating drugs are used to increase saliva production, which aids in the quick disintegration of orally dissolving strips. Salivary stimulants can be used alone or in conjunction with other medications to achieve the best results. Ascorbic acid, malic acid, citric acid, tartaric acid, and lactic acid are some of the most often utilized saliva stimulating substances. [28]

Flavoring agents

Flavoring agents are generally added to the formulation to give the flavor and make the formulation attractive towards pediatric patients. The different flavor can be used such as essential oils or water-soluble extract of menthol, intense mint (peppermint, sweet mint, spear mint), wintergreen, cinnamon, clove, sour fruit flavor (lemon), fruit essence (apple, raspberry, cherry, pineapple), etc. [29, 30]

METHOD OF PREPARATION

The methods for the preparation of orally fast dissolving films are;

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

Solvent casting method

Water soluble polymers and plasticizers are dissolved in a suitably volatile solvent such as ethanol or distilled water to produce a clear viscous solution in this process. The solution is then agitated for 2 hours in a magnetic stirrer before being set aside. API and other ingredients are dissolved in aqueous solvent separately. Then both the solutions are mixed thoroughly stirring at 700-1,000 rpm. The entrapped air is removed by vacuum. The resulting solution is casted into a suitable Petri dish and dried in an oven at 50◦C for 24 hrs. which is then cut into pieces of the desired size and shape. [31, 32]

Semi-solid casting method

When acid insoluble polymers like cellulose acetate phthalate and cellulose acetate butyrate are used in the film, this approach is usually flavored. The water soluble polymers are initially dissolved in water in this procedure. The resulting solution is mixed with a second acid insoluble polymer solution. Both solutions are thoroughly combined. Following the mixing of the two solutions, a suitable amount of plasticizer is added to the final solution to get the gel's mass. Finally, heat-controlled drums are used to cast the gel mass onto the films or ribbons. The film should be between 0.015 and 0.05 inches thick. In a 1:4 ratio with the film-forming polymer, the acid insoluble polymer should be utilized. [34]

Hot- melt extrusion method

Extrusion of a combination combining medication, polymer, and excipients at a high temperature to generate a homogeneous mass that is subsequently casted to form smooth films is known as hot melt extrusion. This is a solvent free process. However, because of the high temperature used during extrusion, this procedure has a severe limitation in the processing of thermo labile compounds. [35, 36]

Solid dispersion extrusion method

A suitable liquid solvent is used to dissolve the medication. To make a solid dispersion, the resulting solution is mixed with a pre-melted appropriate polymer. Finally obtained solid dispersion is shaped into the strips by using dyes of different size and shapes. [37]

Rolling method

The drug solution and the film-forming polymer solution are completely mixed in the rolling process, and the resulting solution or suspension is rolled. Rheological considerations should be taken into account while creating the solution or suspension. The film is cut into suitable shapes and sizes after being cured on rollers. [38]

EVALUATION PARAMETERS

Organoleptic evaluation

The film should exhibit appropriate organoleptic qualities such as colour, flavor, and taste as it disintegrates in the oral cavity. Because they are given to youngsters, an oral thin film should have a pleasing colour and be consistent. The flavors in the formulation should have a pleasant odour and cover the taste of the polymer, medication, and other excipients. Patients' acceptance is influenced by their sense of taste. For the physical examination, specially designed taste panels are employed. The electronic tongue approach, which is based on the potentiometric titration method, is also utilized. [39]

Thickness test

Thickness of film is directly related to accuracy of dose distribution in the film. It is measured with a micrometer Screw gauge or calibrated digital Vernier calipers at five distinct critical spots, with the mean value indicating the film's ultimate thickness. The thickness of the film should be in the range of 5-200µm. [39]

Dryness/ tack test

The tendency with which a strip sticks to an accessory (a piece of paper) that has been pushed into contact with the strip is referred to as tack.About eight stages of film drying process have been identified and they are set-to-touch, dust-free, tack-free, dry-to-touch, dry-hard, dry-through (dry to handle), dry to recoat and dry print free. Various instruments are also available for this study. [40]

Tensile strength

Tensile strength is the maximum stress applied to a point of film at which the strip specimen breaks. A film should have good tensile strength. Load failure refers to the weight at which the film breaks. Tensile strength is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below: [2]

$$\% \text{ Tensile strength} = \frac{\text{(Load at failure)}}{\text{(Strip thickness} \times \text{Strip width)}} \times 100$$

Percentage elongation

When a strip sample is stressed, it stretches, which is referred to as strain. Strain is defined as the distortion of a strip divided by the sample's initial dimension. In general, when the plasticizer concentration increases, strip elongation increases. The Hounsfield universal testing machine is used to measure it.It is calculated by the formula: [41]

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip}}{\text{Initial length of strip}} \times 100$$

Tear resistance

Tear resistance is the resistance or tear strength of the strip that is how long a strip can withstand the effect of tearing when some load or force is applied on the film specimen. Tear resistance of strip is a complex function of its ultimate strength to rupture. Mainly a very low rate of loading 51 mm/min is employed and is designed to measure the force required to tear the specimen is recorded as the tear resistance value in Newton's or pound-force. [42, 43]

Young's Modulus

It is also called elastic modulus. It is used to measure the stiffness of the strip. It is calculated by the ratio of applied stress over the stain in the region of elastic deformation.

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

Young's modulus and tensile strength are two properties of films that are connected to hardness and brittleness. With minimal elongation, a hard and brittle film has a greater tensile strength and Young's modulus. [44]

Folding endurance

Folding endurance is assessed manually by folding a film at the same location over and over until it breaks. The folding endurance value is the number of times the film can be folded without breaking. Mechanical strength is improved by a film with a greater folding endurance rating. Films' mechanical strength and folding resistance are tightly connected. Because plasticizer concentration affects mechanical strength, it's clear that it also affects folding endurance indirectly. [45]

Drug content uniformity

The homogeneity of an oral strip's content is determined in order to estimate API content in a single strip. Any of the standard test procedures established in the standard pharmacopoeia for the drug can be used. It's determined by analyzing the drug content of each image. The drug content of the material should be between 85 and 115 percent. [46]

Weight Variation

Weight variation of the strip is evaluated by weighing the individual weight of every strip and then the average weight is calculated. The average weight of the strip is then subtracted from the individual strip of the film. A large number of weight variations indicate non-uniform drug content. [47]

In- Vitro disintegration test

The disintegration period of a film is determined using disintegration machinery stated in authoritative pharmacopoeias. The disintegration time is usually a function of the film composition, since it changes with the formulation, and it typically spans from 5 to 30 seconds. This test is commonly performed using the USP disintegration device. For estimating the disintegration period of orally rapid dissolving films, there are no established recommendations available. [47] There are two ways for calculating film disintegration time:

Slide Frame Method:

A drop of distilled water is dropped across the film that has been clamped into slide frames in a petri dish. The time it takes for the film to disintegrate is recorded.

Petri Plate Method:

The strip is placed on the 2 ml of distilled water in a Petri plate. The time at which the strip is dissolved completely in distilled water is measured. [36]

***In- Vitro* dissolution test**

In-vitro dissolution, drug release of the strip is determined by standard USP dissolution apparatus Type I (Basket) and type II (paddle). Sink conditions should be maintained during dissolution. Film might float over the medium during this operation, making it impossible to execute the test accurately. Because this problem is more likely to arise with the paddle approach, the basket equipment is most commonly used. 6.8 pH phosphate buffer (300 mL) and 0.1 N HCl were employed as media (900 ml). The temperature is normally kept around 37 ± 0.5 C, and the rotation speed is set at 50 rpm. At pre-determined intervals, samples of dissolved medication are collected and evaluated using a UV-spectrophotometer. [2]

Surface pH

Surface pH of film may cause irritation to the oral mucosa. The pH of the film's surface has to be checked. The film's surface pH should be neutral, or near to it, i.e. 7. This may be accomplished with a mixed pH electrode. The pH is determined by putting the electrode in contact with the film and recording the pH measurement. A 1.5 percent w/v agar gel is produced and the prepared films are put on to determine the surface pH. pH paper is used to determine the pH of the surface. It is put on the film's surface, and the pH paper's colour changes to indicate the film's surface pH. [49]

Permeation studies

Modified Franz diffusion cell and porcine buccal mucosa can be utilized to investigate permeability. A donor compartment and a receptor compartment make up this cell. Mucosa is positioned between the two chambers (size of the mucosa should be the same size as that of the head of receptor compartment). After

that, the receptor compartment is filled with buffer (pH 6.8) and kept at 37 degrees Celsius.1 mL simulated saliva fluid (pH 6.8) should be placed in the donor compartment. A magnetic bead stirrer at a speed of 50 rpm is utilized to keep the thermodynamics stable. The film should be wet and kept in touch with the mucosal surface using a few drops of simulated saliva. At regular intervals, samples are removed and replaced with an equal amount of fresh media. The proportion of drug penetration may be estimated using appropriate analytical techniques. [50]

Contact angle

At room temperature, a goniometer can be used to complete this task. Double-distilled water should be utilized for this purpose. On the surface of a dry film, a drop of double distilled water is deposited. Within 10 seconds of deposition, images of water droplets are captured by a digital camera. For calculating contact angle, these digital images are processed with image 1.28 V software. [51]

Transparency

In transparency test, the strip is cut into a rectangle shape and then placed into the internal side of the UV spectrophotometer cell. The strip is determined at 600 nm transmittance. The transparency of the strip is calculated by the following formula:

$$\text{Transparency} = \frac{(logT600)}{b} = -€c$$

T600 is the transmittance at 600 nanometers, b is the film thickness in millimeters, and c is the concentration. [52]

Scanning Electron Microscopy

Scanning electron microscopy (SEM) is a useful tool for examining the surface morphology of films containing various excipients and drugs. A film sample was obtained and put in a sample holder, and several photomicrographs were made at 1000 magnification utilizing the tungsten filament as an electron source. [53]

Swelling Index

In a simulated saliva solution, the swelling property of the oral strip is tested. The strip sample is weighed before being put on the already weighted stainless steel wire mesh. The mesh is then placed in a container with 15 cc of media. The formula for calculating the swelling index of a strip is:

$$\text{Swelling Index} = \frac{Wt - Wo}{Wo}$$

Where, *Wt* is the weight of the strip at time *t* and *WO* is the weight of the strip at time zero

Moisture Uptake

The purpose of this test was to determine the films' physical stability and integrity in high-humidity environments. The humidity within the desiccator was maintained at 79.55 percent RH by using film in the desiccator holding a standard solution of aluminium chloride. Films were collected and weighed after three days to determine the percentage moisture absorption of the films.

$$\%\ \text{Moisture uptake} = \frac{(\text{Final weight} - \text{Initial weight})}{(\text{Initial weight})} \times 100$$

Moisture loss

The hygroscopicity of a film is determined by the percent moisture loss. This metric is usually calculated by first determining the film's original weight, then placing the film in a desiccator for three days. Calcium

carbonate is found in desiccator. Strips are removed after three days and weighed again. The following formula is used to calculate moisture loss. [54]

$$\% \text{ Moisture loss} = \frac{(\text{Initial weight} - \text{Final weight})}{(\text{Initial weight})} \times 100$$

Stability studies

According to the ICH guidelines, the stability of Oral strips is maintained under controlled conditions (25°C temperature/60% relative humidity and 40°C temperature/75% relative humidity) for 3 months. During the periods of stability studies the films should be evaluated for physical changes and drug content. [55, 56]

Packaging of orally fast dissolving strips

For storage, protection, and stability of the dosage form, packing considerations are crucial. The following items are included in the packaging for oral thin films: [57]

- Foil, paper or plastic pouches,
- Single pouch or aluminium pouch,
- Blister packaging with multiple units
- Barrier films

Barrier films are most typically employed for medications that are highly sensitive to moisture. Primary packaging comprised of a sealing bag gives ample room for logos, codes, directions, or other information, according to Labtec GmbH's rapid film technique. The films are laminated, and the packing costs are equivalent to that of tablets. [58] The following properties must be present in the packing material:

a) They must safeguard the preparation from the elements.
b) They must be FDA approved.
c) They must meet the applicable tamper-resistant requirement.
d) They must be non-toxic.
e) They must not respond to the product in any way.
f) They must not impart to the product tastes or odour.

Foil, paper or plastic pouches

The flexible pouch is a packaging design capable of offering not only a temperature-resistant container, but also a product with a high degree of environmental protection due to good material selection. During the product filling process, a flexible pouch is normally manufactured using vertical or horizontal forming, filling, or sealing machinery. Single pouches or aluminium pouches can be used. [57]

Single pouches or Aluminium pouches

A soluble-film medication delivery pouch is a peel able pouch for soluble films with good barrier qualities that "rapid dissolve." The bag is transparent to allow the product to be seen. The usage of a two-structure combination enables for one side to be transparent and the other to be laminated with a cost-effective foil. Gas and moisture transfer are virtually non-existent via the foil lamination. For nutraceutical and pharmaceutical applications, the package offers a flexible thin-film option. The single-dose bag safeguards both the substance and the dosage. The most common pouch is made of aluminium. [59]

Blister card with multiple units

The blister container is made up of two parts, which is the created chamber that houses the product, and the lid stock (aluminium), which is the material that seals the blister, are the two components of a blister contain. [57]

Heat softening is used to create the blister packaging, and the following procedures are used:

- A sheet of thermoplastic resin is softened by heating.
- Softened sheet is vacuum dried into a countered mold.
- After cooling, the sheet is removed from the mould.
- Proceed to the packing station of filling machine.
- The product is poured into a previously manufactured semi stiff blister, which is then sealed with heat sealable backing material.

Barrier Films

Because many pharmacological formulations are particularly sensitive to moisture, strong barrier coatings are required. Polychlorotrifluoroethylene (PCTFE) film and Polypropylene are two materials that can be utilized to offer moisture protection.Under all circumstances, polypropylene will not stress fracture. It works well as a gas and vapor barrier. The lack of clarity remains a flaw. [59]

Conclusion

OFDS's have emerged as a novel trend, and most pharmaceutical companies in this field continue their research &development activities to adapt their drugs from various categories to this technology. Oral strips have proved to be an innovative drug delivery system for all groups of patients with the problem of swallowing. It also offers many advantages over the other dosage forms, such as improved bio-availability and faster onset of action. Therefore, it can be concluded that OFDS's with excellent patient compliance and many advantages have innovative futuristic opportunities.

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