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ORAL THIN FILM: A REVIEW

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ABSTRACT
The goal of this study is to administer the medicine at a faster pace, with a faster start of effect and better bioavailability. The most common method of medicine delivery is through the mouth. As an alternative to tablets, capsules, and syrups, fast-dissolving drug delivery devices were created. Patients who have difficulty swallowing tablets or hard gelatine capsules, such as children and the elderly, benefit from oral thin films. Oral thin film is a relatively recent dosage form in which a polymer-based thin film is created and disintegrates or dissolves quickly on the tongue or in the buccal cavity. It's a platform for molecules that go through a lot of first-order processing.

KEYWORDS:

INTRODUCTION
Oral film technology was first developed in the late 1970s to help geriatric and paediatric patients overcome swallowing difficulties caused by tablets and capsules, but it is now popular in the pharmaceutical industry due to its lower fragility than other oral dosage forms, dosage accuracy, rapid release, and ease of administration. 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. The oral route of medication administration is the most flavourful because of its cost-effectiveness and convenience of administration, which leads to high patient compliance in the paediatric and geriatric populations, but it is not the most flavourful way of drug administration.[1] The oral route of drug administration has long been one of the most convenient and well-accepted methods of drug delivery, with the intraoral route being the most popular due to its ease of use and quick beginning of action. Intraoral dosage forms have evolved as an alternative to traditional tablets, capsules, and liquid preparations. Due to improved patient compliance and ease of administration, quick dissolving dosage forms have gotten a lot of attention. Orally disintegrating tablets (ODTs), the only dosage form of this type authorised by the FDA and mentioned in the orange book, are among the quick-dissolving dosage forms. The European Pharmacopoeia is a collection of pharmacopoeias from around the world.[2] Fast dissolving buccal films provide ease of administration for patients who are mentally ill, disabled and uncooperative; requires no water; have quick disintegration and dissolution of the dosage form. They can be unobstructed and can be designed to leave minimal or no residue in the mouth after administration and also provides a pleasant mouth feel. This delivery system has no risk of choking. It allows high drug loading and has the ability to provide advantages of liquid medication in the form of solid preparation. Fast dissolving films are adaptable and amenable to existing processing and packaging machinery, cost effective and have excellent cohesion. Fast dissolving films can be formulated in various shapes and sizes.[3] The most sophisticated forms of oral solid dosage form are fast dissolving oral films (FDOFs), oral wafers, oral strips (OS), sublingual strips, or oral thin films (OTF). It increases API efficacy by dissolving in the oral cavity in less than a minute after contact with saliva, without the need for chewing and without the use of water. Because of the high blood flow and permeability of the oral mucosa, which is 4-1000 times that of the skin, it allows for fast absorption and bioavailability of medications. FDOFs are helpful in a variety of situations, including paediatrics, geriatrics, bedridden patients, emetic patients, diarrhoea, allergic reactions, and coughing for people who suffer from these conditions. The films produced should be sufficiently tough to prevent damage during transportation or during handling. The inert ingredients used in ODF are usually water-soluble in nature while the drug could be either water soluble or lipid soluble in nature. Because the most basic and significant part of the ODFs is the film forming polymer (which forms the basis for the ODFs), And plasticizer is the most important and essential ingredient of ODFs. A minimum of 40-50 percent w/w of polymer and up to 20 percent of plasticizer (overall weight, polymer) will typically be present based on the overall weight of dried ODFs. Orally disintegrating films (ODFs), mouth

dissolving films (MDFs), melt in-mouth films, quick dissolving and rapid disintegrating films, oral-dispersible films, melt in-mouth films are all synonyms for FDFs. A variety of polymers are available for preparation. This includes both natural and manufactured polymers. To produce the desired film qualities, the polymers can be used alone or in combination. The film created should be durable enough to withstand handling and shipping. The thickness of the films is determined by the polymer type and quantity used in the formulation. Fast dissolving film is formulated by using hydrophilic polymers that dissolve quickly on the oral or buccal cavity, transmitting the drug through dissolution to the systemic circulation when contact with liquid is made. For fast dissolving films, water-soluble polymers are used as film formers. The water-soluble polymers fulfil the films ' rapid disintegration, good mouth sensation and mechanical properties.[4] Due to their unique properties and advantages, such as the availability of a larger surface area that leads to rapid disintegration and dissolution in the oral cavity, the absence of water, accurate dosing, rapid onset of action, ease of transportability, ease of handling, pleasant taste, and improved patient compliance, fast dissolving drug delivery systems have gained great importance in the pharmaceutical industry. There are a variety of fast-dissolving over the counter (OTC) and prescription (Rx) medicines on the market, the majority of which were introduced in the last three to four years. The number of new chemical entities under research using a fast-dissolving drug delivery method has also increased significantly.[5]

Concept of oral dissolving film

- This delivery system is composed of a thin film.
- After keeping it on the top of the tongue, the film dissolves within seconds, promoting first pass metabolism as estimated to tablet and other immediate release oral solid dosage forms, and may enhance the bioavailability of drug.
- ODF dissolves in the mouth like cotton candy.[6]

Trans mucosal routes of drug delivery involve the delivery of the drug through the mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavity. Amongst these oral cavities is a novel site for drug delivery. The oral mucosa has been investigated in several studies as a means to give both local and systemic amounts of drug. Drug delivery across the oral mucosa, can be divided into three different types.

1. sublingual delivery: consisting of administration through the membrane of the ventral surface of the tongue and the floor of the mouth.
2. Buccal delivery: consisting of administration through the buccal mucosa, mainly composed of the lining and directly delivering the drug to the systemic circulation.
3. Local delivery: consisting of administration through all area other than the former two regions.

These sites differ anatomically in their permeability to drugs, rate of drug delivery, and ability to maintain a delivery system for the time required for drug release out of the delivery apparatus and into the mucosa.

Structure of Oral Mucosa

Oral mucosa contains following three layers of cells

i. **Stratified squamous epithelium** - It's the outermost layer of the oral cavity. Basement membrane is the interface between connective tissue and epithelium.

ii**. Lamina propria** - It's a connective tissue present below basement membrane

iii. **Sub mucous membrane** - It is the innermost layer of the oral cavity.

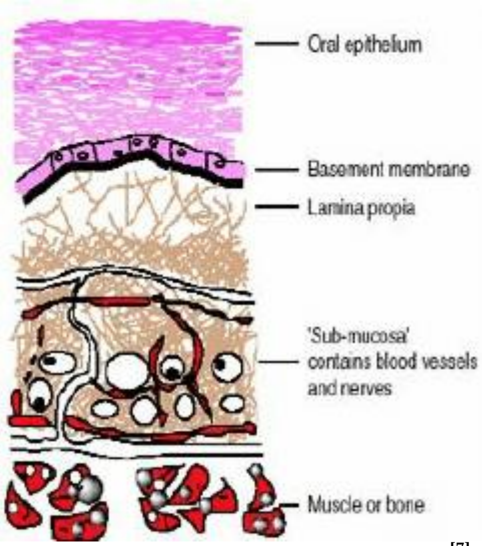

Fig- 1. Structure of the human oral mucosa.[7]

Advantage

- Improved patient compliance which allows patients to easily swallow the dosage form for systemic absorption through rapid dissolution or disintegration in the oral cavity.
- Improved patient convenience to carry and administer dosage forms especially when traveling.

- Rapid absorption and onset of action of rapid disintegrating/dissolving dosage forms.
- Avoidance of first pass effect which improves bioavailability.
- Improved stability compared to liquid dosage form.
- No water requirement.
- No risk of choking. Enhanced stability.
- Ease of administration.
- Bypass of the GIT improves its bioavailability
- Good mouth feels.
- Rapid onset of action in case of mouth sickness and allergies.
- Controlled release of drugs facilitates the rate and extent of absorption.
- Does not interfere with normal function like talking, drinking etc.
- Delivery of those API is possible which are at high risk of degradation in the gastrointestinal tract.

Disadvantages of OTF

- Packing requires special equipment. So, it is difficult to pack.
- Not suitable for drugs which irritate and are unstable at buccal ph.
- Only a small dose of the drug can be administered.
- Hygroscopic in nature. So, longer preservation is difficult.
- Drugs which are absorbed only by passive diffusion can be administered by this route.
- Restriction of eating and drinking for some time after consumption of oral film.
- Methods for preparation are expensive as compared to oral dissolving tablets.[8]

Special Orally dissolving strips

- Film should be thin and elegant.
- Available in various sizes and shapes.
- Un obstructive.
- It should adhere to the oral cavity easily.
- Should process fast disintegration without water.
- Rapid release.[9]

Classification of oral thin films

Table No – 1 classification of oral thin film.

`Property/ subtype	Flash release water	Mucoadhesive melt away wafer	Mucoadhesive sustained release wafer
Area (cm^2)	2-8	2-7	2-4
Thickness	20-70	50-500	50-250
Structure	Film; single layer	Single or multilayer system	Multi-layer system
Excipients	Soluble, highly hydrophilic polymer	Soluble, hydrophilic polymer	Low /insoluble polymer
Drug phase	Solid solution	Solid solution or suspended drug particle	Suspension and solid solution
Application	Tongue (upper palate)	Gingival or buccal region	Gingival, (other region in the oral cavity)
Dissolution	Maximum 60 seconds	Disintegration in few minutes forming gel	Maximum 8-10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

[10]

MOUTH DISSOLVING FILMS (MDF)

A film or strip can be defined as a dosage form that ploys a water-dissolving polymer (generally a hydrocolloid, which may be a bio adhesive polymer), which allows the dosage form to quickly hydrate, adhere, and dissolve to re-lease the drug when placed on the tongue or in the oral cavity. They are also known as fast-dispersing, mouth dissolving, orally disintegrating, fast-melting, Quick dissolving films. MDF can provide a convenient and effective vehicle for delivering active ingredients such as pharmaceutical compounds and breath freshening agents, to the mucosa of humans and animals. It allows the drug to be delivered to the blood stream either intragastrically, buccal or sublingually. As soon as MDF are taken, rapid absorption of drugs, through the sublingual route is possible, which finally leads to quick onset of drug action. The proper selection of incorporated excipients/ ingredients for formulating MDF is very important as MDF has to disintegrate and/or dissolve quickly into the oral cavity. Besides water-dissolving polymer, the formulation may include other components depending on its intended use viz. pharmaceutical agents, antimicrobial agents, nutraceutical ingredients, plasticizers, surfactants, colorants, sweetening agents, saliva stimulating agents, flavours, flavour enhancers and other excipients. A typical composition contains the following excipients:

Drug 1 - 25 %
Water-soluble polymers 40 - 50 %
Plasticizers 0 - 20 %
Fillers, colour, flavour etc. 0 - 40 %

As polymers and plasticizers form the main body of MDF, therefore, their properties greatly affect the characteristics of MDF.[11]

Manufacturing method

1. Solvent casting

This is the most widely used method for manufacturing of fast dissolving oral thin film Steps

a) Water soluble polymers are dissolved in water
b) Other excipients and APIs are dissolved in aqueous solution under high shear
c) Both the mixtures are combined to give viscous homogenous solution
d) The solution is deaerated and transferred to the casting station where solution is cast into film on a release liner of thickness 30-120 cm
e) Casted film is dried in oven
f) Dried films are cut into desired shape
g) Film product is investigated for desired qualities
h) Final inspection is done
i) Product is sent for packaging

The preferred finished film thickness is 12-100 µm

Process parameter

a) Mixing temperature: 20- 90o C
b) Agitation time: 40-120 minutes
c) Rotating speed: 1000-2000 RPM
d) Flow rate while deforming: 80 litres/hour
e) Passage time during casting: 2-8 minutes
f) Drying temperature: 50-130o C

Fig- 2 solvent casting.[12]

2. Semisolid casting methods Step

Solution of water soluble film forming polymer is prepared It is poured into the solution of acid insoluble polymers in the ratio of 1:4 (e.g. cellulose acetate phthalate, cellulose acetate butyrate) A gel mass is obtained by the addition of relevant amount of plasticizer It is casted into the films or ribbons by using heat controlled drums. The thickness of the film should be about 0.015-0.05 inches

3. Hot melt extrusion

Steps

a) The mass is prepared under controlled temperature and steering speed by mixing API with excipients
b) Mixture is melted in the extruder
c) The film is coated and dried in a drying tunnel
d) Then splitting is done
e) The films are punched, pouched and sealed

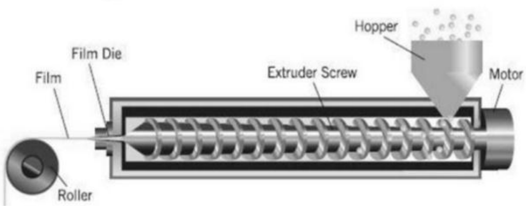

Fig- 3 Hot melt extraction.[13]

Process parameters

a) Screw speed: 15 rpm
b) Processing temperature: 650-1150o C
c) Extrude temperature: 650o C
d) Final film thickness: 200 µm

4. rolling method

Initially a pre-mix is prepared by film forming polymers, polar solvent and other additives except a drug.
Add the required amount of drug to the pre-mix.
The drug is blended with pre-mix to obtain a uniform matrix.
The mixture obtained is fed into the roller.
Film is formed and carried away by a support roller.
Wet film is then dried using controlled bottom drying.
Film is cut into desired size and shape.[14]

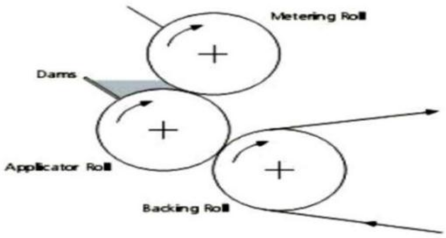

Fig- 4 rolling method.[14]

Various technologies used in oral film formulation

XGel

X Gel Film Technology developed by Bio Progress is causing a revolution in the product offerings and manufacturing methods now available to the pharmaceutical industry.

Soluleaves

This is applied to flavour-release products such as mouth fresheners, confectionery and vitamin products. SOLULEAVES technology can be used to deliver active ingredients to oral cavity efficiently and in a pleasant and easily portable form

Wafe rtab

Wafer tab is a patented delivery system that uses a unique process to prepare drug loaded thin films which can be used in topical or oral application. Active ingredients are incorporated into the film after casting.

Foam burst

FOAMBURST is a new patent granted in September 2004 which is for capsules made of foamed film. Gas is blown into the film during production, resulting in a film with a honeycomb structure. The voids in the film may be gas-filled, empty or filled with other materials to produce specific taste-burst characteristics or to deliver active drugs. The light honeycomb structure results in capsules that dissolve rapidly, causing a melt-in-the-mouth sensation.

Micap

Micap plc signed an option agreement in 2004 to combine its expertise in micro encapsulation technology with the Bio Progress water-soluble films. The developments will be aimed at providing new delivery mechanisms for the global market for smoking cessation product.[15]

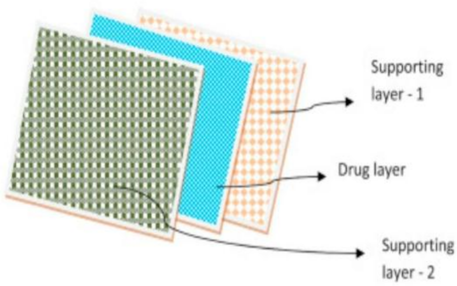

Fig 5 multi layered of oral thin film.[16]

Active pharmaceutical ingredient

A typical formation of the film contains 1-25% w/w of the drug. Variety of active pharmaceutical ingredients can be delivered through fast dissolving films. Small dose molecules are the best candidates to be incorporated in oral fast dissolving films. Multivitamins up to 10% w/w of dry film weight were absorbed in the films with dissolution time of less than 60 seconds. It is always useful to have micronized active pharmaceutical ingredients which will improve the texture of the film and also for better dissolution and uniformity in the oral fast dissolving films. Many active pharmaceutical ingredients, which are potential candidates for oral fast dissolving film technology, have bitter taste. This makes the formulation uneatable especially for paediatric preparations. Thus before incorporating the active pharmaceutical ingredients in the oral fast dissolving films, the taste needs to be masked. Various methods can be used to improve the edible of the formulation. Among the techniques employed, the simplest method involves the mixing and co-processing of bitter tasting active pharmaceutical ingredients with excipients with pleasurable taste.[17]

SELECTION OF POLYMER

The physical and mechanical properties of the MDF depend on the characteristics of film-forming polymer, which forms 20 to 75% (w/w) of total dry wt. of the MDF. The selection of polymers, therefore, is one of the most important and critical parameters for the successful development of the formulation. The polymers used should have good hydrophilicity, rapid disintegration, good mouth feel, and suitable mechanical properties. Along with its good solubility, the polymer should have sufficient mechanical, physicochemical and permeability properties. In order to remain intact against the internal and external stresses developed during storage and especially when exposed to environmental conditions, a film should have high mechanical strength with sufficient elongation and elasticity properties.[18]

Film forming polymers

Water-soluble polymers are used as film formers since they achieve rapid disintegration, good mouth feel and mechanical properties to the films. In order to obtain the desired film properties like hydrophilicity, flexibility, mouth feel and solubility, polymers can be used alone or in combination with others. By increasing the molecular weight of polymer film bases, the rate of disintegration of polymers decreases.

The polymers employed in oral thin films should be:
- Non-toxic and non-irritant
-Devoid of leachable impurities
-Good wetting and spread ability property
- sufficient peel, shear and tensile strengths.
-Readily available
- Inexpensive
- Water soluble with low molecular weight
- Excellent film forming capacity
- Should have a good shelf life.

Plasticizer

Plasticizers It is an important ingredient of oral thin films. The plasticizers help to improve the mechanical properties of film such as tensile strength and elongation to the film. It also reduces the brittleness of the film. It may improve the flow and enhance the strength of the polymer. The proper selection of the plasticizers is very important. It should be compatible with the drug, polymers as well as with the other excipients. The improper selection may cause cracking, splitting and peeling of the film. The commonly used plasticizers are glycerol, propylene glycol, polyethylene glycol, dimethyl, dibutyl, diethyl phthalate, tributyl, triethyl, acetyl citrate, triacetin and castor oil.

Saliva stimulating agent

The purpose of using saliva stimulating agents is to increase the rate of production of saliva so that the oral film disintegrates and dissolves faster in the oral cavity. It can be used alone or in combination in the range of 2-6%. Commonly used saliva stimulating agents are citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid. Among these, citric acid is the preferred one.

Sweetening agents

sweeteners are used to mask the bitter taste of certain drugs. Both natural and artificial sweeteners can be used alone or in combination. shows various natural and artificial sweeteners used in fast dissolving oral thin films.
Artificial Sweetener
E.g.: Saccharin, saccharin sodium, aspartame
Nutritive: Sucrose, fructose and glucose
Polyols: Mannitol, Sorbitol, xylitol, erythritol, maltitol.
Non-Nutritive: Aspartame, sucralose, neotame and saccharine.
Novel sweeteners: Trehalose, tagatose.[19]

Flavouring agent

They impart flavour to the formulation. It can be selected from synthetic flavour oils, oleoresins, and extract derived from various parts of the plants like leaves, fruits and flowers. It can be used alone or in combination. The amount of flavour required to mask the taste depends on the flavour type and its strength.

Example- Oils -peppermint oil, cinnamon oil, spearmint oil, nutmeg oil
Fruit flavours- Apple, raspberry, cherry, strawberry, pineapple
Salt -Butterscotch, maple, apricot, peach, vanilla, mint, anise
Bitter- Wild cherry, walnut, chocolate, mint, anise
Sweet -Vanilla, fruit, berry
Sour -Citrus flavour, root beer, raspberry.[20]

Surfactant

They are generally used to increase the solubility, wettability and dispersibility of the film so that the film gets dissolved within seconds and releases the drug fastly. Commonly used surfactants are sodium lauryl sulphate; surfactants are poloxamer 407, benzalkonium chloride, benzethonium chloride, tweens etc.

Colouring agent

pigment like silicon dioxide, titanium oxide or FD and C approved colouring agent most commonly used. their concentration level should not exceed 1%.[21]

Table No -2 Type of agents used for preparation of oral dissolving film.[22]

Plasticizer	Sweetening agent	Flavouring	Colouring	Saliva stimulating agent	surfactant
Acetyl Triethyl citrate	Mannitol, sorbitol	Lemon	Natural colouring agent	Citric acid	Polaxamer 407
PEG	Xylitiol, polyols	Peppermint	titanium oxide	Lactic acid	Benzalkoniumchlorid
Propylene Glycol	Aspartame	vanillin	Zinc oxide	Ascorbic acid	tweens
Glycerine	Saccharin,cyclamate	menthol		Tartaric acid	Spans

Evaluation Parameters

1. Mechanical Properties

· **Thickness test**

Thickness specifies the dose of drug perfection in the film. It is measured by a micrometre screw gauge or calibrated digital Vernier callipers at five unlike strategic locations and the mean value is calculated which indicates the final thickness of the film. The width of the film should be in the range of 5 - 200 µm.

· **Dryness test**

About eight stages of the film drying process have been identified and they 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. Although these tests are essentially used for paint films most of the studies can be change intricately to evaluate pharmaceutical OFDF. The details of estimation of these parameters can be checked elsewhere and are beyond the scope of this review. Tack is the determination with which the strip adheres to an accessory (a piece of paper) that has been pressed into contact with the strip. Instruments are also available for this study.

· **Tensile strength**

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

Tensile Strength = load of breakage/ strip thickness × strip width

· **Percent elongation**

When stress is appeal, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip split by original dimension of the sample. Generally, elongation of strip increases as the plasticizer content increases30.

% Elongation = Increase in length ×100/original length

· **Young's modulus**

It is the estimate of film stiffness. It is found as balance of applied stress to the strain in the elastic deformation region. It is given by the following formula

Young's modulus = (Slope/strip thickness *cross head speed)/ 100

It can also be written as:

Young's modulus = force at corresponding strain/ cross-sectional area*corresponding strain

Hardness and brittleness are attributing to the films which are related with Young's modulus and tensile strength. A hard and brittle film represents a higher value of tensile strength and Young's modulus with small elongation.

· **Tear resistance**

Tear resistance of plastic film is a complex function of its ideal resistance to rupture. Basically a very short rate of loading 51 mm (2 in)/min is employed and is designed to measure the force to begin tearing. The maximum force required to tear the The specimen is recorded as the tear resistance value in Newton.

· **Folding endurance**

Folding endurance is set by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is evaluating is folding endurance value.

2. Transparency

The transparency of the films can be decided using a simple UV spectrophotometer. Cut the film samples into rectangles and place them on the inner side of the spectrophotometer cell.

The direct transmittance of films at 600 nm. The transparency of the films was calculated as follows:

Transparency = (logT600)/b = - €c

Where

T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration

3. Contact angle

It allows the information about wetting behaviour, disintegration time and dissolution of oral film. This can be executed with the help of a goniometer at room temperature. For this cause, double distilled water should be used. A dry film is taken and a drop of double distilled water is sitting on the surface of the dry film. Images of water droplets are taken by a conveyor of digital cameras within 10 s of deposition. Digital pictures should be analysed by image software for angle determination.

4. Scanning electron microscopy

Scanning electron microscopy is a prime method to study the surface morphology of the film between different excipients and drug. A film sample is taken and placed in sample holder and at ×1000 magnification and various photomicrographs were taken using the tungsten filament as source of electron.

5. Swelling Test

Simulated saliva solution is used to conduct the swelling property study. Firstly weigh all the samples of film and place them on the reweighed stainless steel wire mesh. 15ml of the saliva solution is added in the plastic container and the mesh containing film sample is submerged into it. Increase in weight of film was observed until a constant weight was observed. The degree of swelling was calculated using parameters:

α = wt.-wo/wo

Wt. = weight of film at time t

Wo = weight of film at time zero.[23]

6. In vitro disintegration test

It is the time at which the film breaks or disintegrates when brought in contact with water or saliva. This test is carried out by placing the film in the phosphate buffer. United State Pharmacopoeia (USP) disintegration apparatus can be also used to study the disintegration time. The disintegration time should be in the range of 5-30 sec.

7. **In-vitro dissolution test**

Amount of drug substance that goes into the solution per unit time under standard conditions of temp, solvent concentration and liquid/solid interface is called dissolution. A standard basket or paddle apparatus described in any of the pharmacopoeia can be used for dissolution testing. When paddle type dissolution is used, it's difficult to perform dissolution study of oral film as they can float over the dissolution medium. Selection of the dissolution media depends on the sink conditions and the highest dose of drug. During dissolution study, the temperature of the medium should be maintained at 37 ± 0.5 ^{0} C and rpm at 50.

8. Stability studies

Stability testing of the prepared formulation is mainly ready to check whether it is a stable product or not. It is also used for the determination of effect of temperature and humidity on the stability of the drug for the actual storage, initially the formulation is wrapped in a butter paper followed by aluminium foil wrapping over it, then this is loaded in an aluminium pouch and heat sealed. Formulation should be stored at 45oC / 75 % RH for 3 months. Through the time of stability studies, triplicate samples are taken at three sampling intervals i.e. 0, 1 and 3 month and films should be evaluated for physical change and drug content.[24]

9. Disintegration time and mouth dissolving time

Oral thin films are formulated so that they disintegrate very rapidly allowing the drug to release in seconds. Presence of disintegrate in the formulation caused a marked effect 5. batch films disintegrate in 33 seconds whereas 8 films disintegrate in 57 secs. Increase in polymer. concentration caused to increase in the disintegration time of the formulation.[25]

Packing

Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the fast dissolving dosage forms. Single packaging is mandatory. An aluminium pouch is the most commonly used packaging material. APR-Labtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for the Rapid films. The Rapid card has the same size as a credit card and holds three films on each side. Every dose can be taken out individually. The material selected must have the following characteristics

1. It must not be reactive with the product
2. It must protect the preparation from environmental conditions
3. It must be FDA approved
4. It must be tamper-resistant
5. It must be non-toxic.

Packaging-materials

Foil, paper or plastic pouches The flexible pouch can provide sufficient tamper resistance and high degree of environmental protection. A flexible pouch is formed during the product filling by either vertical or horizontal forming, filling, or sealing equipment. The pouches can be single pouches or aluminium pouches.

Singlpouch

Fast dissolving oral pouches. Single pouch thin film drug delivery pouch is a peel able pouch for fast dissolving soluble films with high barrier properties. The pouch is transparent for product display. Using a two structure combination allows for one side to be clear and the other to use cost-effective foil lamination. The foil lamination has essentially zero rate of transmission for both gas and moisture. The single dose pouch provides both product and dosage protection. Aluminium pouch is the most commonly used pouch.

Blister card with multiple units

The blister container consists of two components

a) Blister, which is the formed cavity that holds the product

b) Lid stock, which seals the blister.

The blister package is formed by heat softening a sheet of thermoplastic resin and then vacuums drawing the softened sheet of plastic into a contoured mold. After cooling, the sheet is released from the mould. Then it proceeds to the filling station of the packaging machine.

The previously formed semi rigid blister is filled with the product and lidded with the heat sealable backing material. Generally, the lid stock is made up of aluminium foil. The material used to form the cavity is plastic, which can be designed to protect the dosage form from moisture. Barrier Films Many drug preparations are extremely sensitive to moisture and therefore require high barrier films. Several materials may be used to provide moisture protection such as polychlorotrifluoroethylene film, polypropylene. Polypropylene does not stress crack under any conditions. It is an excellent barrier to gas and vapor. But the drawback is lack of clarity.[26]

The Introduction of ODT in the market was accompanied by educating the mass about the proper way to administer the product like giving instructions "do not swallow" or "do not chew". The process of manipulating the ODT in oral or buccal cavity was also important. However, since the OST derived products were readily popular in the market in the form of breath-freshening strips, no further efforts were needed to re-instruct the populace about the technique of administration of this dosage form. OST was already popular amongst the people in the early 2000 year with the introduction and widespread use of Listerine pocket strips, a new launch in the mouthwash and many of the products.[27]

Applications of Oral Films in Drug Delivery

· Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of OTFs could become a preferential delivery method for therapies in which rapid absorption is desired, including those used to manage pain, allergies, sleep difficulties, and central nervous system disorders.

· Topical applications: The use of dissolvable films may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications.

· Gastro retentive dosage systems: Dissolvable films are being considered in dosage forms for which water-soluble and poorly soluble molecules of various molecular weights are contained in a film format. Dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially be used to treat gastrointestinal disorders.

· Diagnostic devices: Dissolvable films may be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic device.[28]

LIMITATIONS

Like any delivery system, OTFs have their own set of limitations. The incorporation of water-insoluble drugs into OTFs is still in its infancy. Tablets and capsules can carry components to help a drug dissolve. In contrast, OTFs are a more streamlined drug delivery system and rely primarily on polymers to increase a drug's solubility. To expand the capabilities of OTF technology, scientists are exploring promising new particle engineering techniques to find new ways to increase solubility of water-insoluble drugs in OTFs. Another constraint of OTFs is that they are capable of only carrying a relatively small drug load of about 10 to 20 mgs. Additionally, the larger surface area of an OTF renders it more sensitive to humidity and temperature. Fortunately, special packaging can preserve OTFs in a range of conditions.

One final testing challenge is that the standard, non-biological methods don't adequately capture the film's or drug's behaviour in vivo. Water or bio relevant media used in testing does not perfectly mimic the oral cavity's saliva and does not accurately simulate the mechanical stress from the tongue and palate. Dissolution testing procedures need to reflect the varied amounts of saliva present in each patient's mouth. As the ability to incorporate more poorly soluble micro- and Nano-particles into OTFs grows, many dissolution tests have been found to be inadequate. While USP IV, which uses a flow-through cell dissolution apparatus, currently has superior discriminating power in this arena, additional methods may further expand our ability to test insoluble drugs carried by OTF.[29]

Future scope and development

The formulation of a drug into various films has been popular in recent years. Several undesirable drawbacks associated with conventional dosage forms such as inconvenience of administration, lower bioavailability and patient non-compliance have pushed the development of novel polymeric thin films as a drug delivery platform. This drug delivery platform is being under surveillance from both start-up and established pharmaceutical companies. The companies strive to design a wide range of thin films for oral, buccal, sublingual, ocular and transdermal routes. Therefore, as an alternative to conventional dosage forms, polymeric thin films are expected to stand out as a dosage form to overcome the limitations posed by existing dosage forms. The film dosage form encounters several challenges during the phases of formulation development and manufacture. Such issues should be addressed to optimize the overall formulation even after transferring to large-scale manufacturing. The future looks very promising for the film technology in the time to come as new technologies are rapidly introduced to prepare thin films.[30]

CONCLUSION

OTFs have emerged as a revolutionary trend, and most pharmaceutical companies in this field continue their research and development activities to adapt their drugs in various categories to this technology. This technology is an innovative drug delivery system for all patient groups who have swallowing problems, especially paediatric and geriatric patients. It also offers many advantages over the other dosage forms, such as improved bioavailability and faster effects. It is one of the most important dosage forms that can be used orally in cases of emergency and when an immediate-onset effect occurs. the active pharmaceutical ingredients in the single formulation using multilayer films laminated together. An inactive film layer separating the incompatible active pharmaceutical ingredients can be introduced in between. Active pharmaceutical ingredients with significant trans mucosal flux rates can be incorporated into thin films for dissolving slowly into buccal or sublingual regions. Drugs coated with controlled release polymers can also be incorporate. Therefore, it can be concluded that OTFs with excellent patient compliance and many advantages have innovative futuristic opportunities.

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