



Oral Thin Films: A Multi – Faceted Drug Delivery System

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ABSTRACT

The most popular route of administration is oral route because of low cost and better patient compliance. Tablets and capsules are the most popular dosage forms taken through oral route, but many pediatric & geriatric patients find it difficult to swallow and do not take their medicines as prescribed. To overcome these difficulties, several fast-dissolving oral thin film drug delivery systems are developed. This is convenient and straightforward to use compared to other delivery types like orally disintegrating tablets. When thin film is kept on tongue, it disintegrates and dissolves in very less time without intake of water so it is easy to swallow and most convenient for patients. This review will give the overview of advantages & disadvantages of oral thin film technology, ideal characteristics of drug to be selected, manufacturing processes, novel technologies, polymers used & evaluation of oral thin films.

Keywords: Oral thin film, Novel drug delivery system, Polymers, Plasticizers.

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Other applications of oral thin films include the preparation of caffeine strips, multivitamins, sleeping aid and snoring aid etc.⁵

METHODS

Oral thin film technology

Oral thin films are flat sheets that are administered into the mouth. They are composed of very thin polymeric strips, incorporating an active pharmaceutical ingredient and are intended to disintegrate in the oral cavity within seconds. This is useful as the drug can give rapid onset of action through the oral mucosa.²

Advantages

- i. Oral Thin Films have enhance the bioavailability of the drug which leads to quicker action.
- ii. Unlike in the case of conventional dosage forms drugs in oral thin films bypasses the first pass action and hence the amount of drug required to be loaded is reduced.
- iii. Compared to liquid dosage form oral thin films have greater stability.
- iv. As the drug is loaded into an abuse resistant matrix oral thin films do not require special packaging.
- v. As compared to tablets Oral thin films are less friable.
- vi. Research has proven that, oral thin films have lesser side-effects.
- vii. Oral thin films have faster dissolution & disintegration due to higher surface area of oral cavity.
- viii. Easily portable

INTRODUCTION

Among different modes of administration, the oral route is the most preferred route for patients. Research in the field of oral drug delivery has led to the evolution of dosage forms from simple conventional tablets/capsules to modified release tablets/capsules to disintegrating tablets and recently development of fast dissolving oral thin films (OTF).¹ Oral thin films are flat sheets which are administered into the oral cavity. They are composed of very thin polymeric strips, incorporating an active pharmaceutical ingredient and are intended to disintegrate in the oral cavity within seconds. This dosage form is useful as the drug can give rapid onset of action through the oral mucosa.² The European Pharmacopoeia defines them as “orodisperse” tablets, which are to be placed within the mouth where they disperse rapidly before swallowing. For the systemic drug delivery of active pharmaceutical ingredients (API) fast dissolving films are well proven & worldwide accepted technology.¹

An oral thin film are manufactured as an outsized sheet then cut into individual dosage unit for packaging. Oral thin films are used for local action in mouth such as local anaesthetic for toothaches, oral ulcer, cold sores or teething etc. Many drugs like cough remedies, antiasthmatics, antihistaminic, erectile dysfunction drugs, sore throat, gastrointestinal disorders, nausea, pain and CNS drugs can be incorporated in this dosage form.



ix. Can be used to give drugs in a non-invasive manner for e.g., Delivery of Opioids through the Sublingual or buccal route to reduce the need of invasive means like parenteral injections.²²

Clinical Advantages

- As oral thin films are given by oral route their administration is easy as it employs the oral route.
- In paediatric and geriatric patients the risk of choking or suffocation is reduced.
- Oral Thin Films are a better alternative for patients with nausea.
- Oral Thin Films do not required to be swallowed with water.

Market Advantages

- This novel drug delivery system presents pharmaceutical companies with patents on the verge of expiration to increase their revenue cycles.
- OTFs dissuade the misuse, tampering and abuse related to some prescribed drugs because the film is loaded with an exact amount of drug.
- The oral thin films market is currently in its embryonic stages and limited only to certain over the counter drugs available within the American, Japanese and EU Markets. Thus, researches and corporations have a great scope in formulating drugs that haven't been previously formulated into OTFs and developing newer and cheaper technologies.

iv. In India, per Indian demographics for 2017 roughly 13.39% of the population are senior citizens while 45.7% are children. Thus, Indian investors have a good consumer range and this technology is inchoate in our country

Disadvantages

- A significant manufacturing difficulty that confronts manufactures is that the drying time required for the OTFs. Since thermolabile drugs prohibit the utilization of hot air ovens and high temperatures, it takes each day for the films to dry at room temperature thereby reducing the production rate.
- As the films are highly hygroscopic and tend to lose stability in environments having high relative humidity.
- In oral thin films it is difficult to achieve uniformity of dosage.
- Drugs which are unstable at the buccal pH or irritate the mouth mucosa cannot be formulated into thin films.
- The co-administration of multiple drugs remains to be a challenge because the dissolution time is affected.³
- Drug with small dose requirement can only be administered.⁵
- Taste masking is required for bitter taste drugs.
- Special packaging is required for OTFs, so as to protect it from water.¹

Oral thin film marketed products

Sr no.	Category of drug	Name of drug	Marketed name	Manufacturer	Strength	Reference
1.	5-HT agonist	Zolmitriptan	Zolmitriptan rapidfilm	Labtec	2.5mg, 5mg	[6]
2.	Antiemetic (5HT ₃ receptor blocker)	Ondansetron	Setofilm	Labtec Gmb H	4mg, 8mg	[13]
3.			Zuplenz	Galena Biopharma	4mg, 8mg	[12]
4.			Zofran	GSK	8mg	[6]
5.			Schedule IV drug	Phentamine citrate	Onsolis	Midpharma, Bio Delivery Sciences International
6.	Mouth Freshner	Cool mint	Listerine cool mint pocket paks	Pfizer, Inc.	–	[12]
7.	Antihistamines H ₁ Antagonist	Diphenhydramine HCL	Benadryl	Pfizer	12.5, 25 mg	[12]
8.			Triaminic	Novartis	12.5mg	[12]
9.	Homogalaturonan	Methanol/ Pectin	Orajel	Del	2mg/30mg	[12]
10.	Antitussives	Dextromethorphan HBR	Theraflu	Novartis	15mg	[12]
11.	Nasal decongestants	Phenylephrine	Sudafed PE	Wolters Kluwer Health, Inc.	10mg	[12]
12.	Local anesthetic	Benzocaine/metha nol	Chloraseptic	Prestige	3mg/3mg	[12]



13.	Cough suppressant	Methanol	Suppress	Innozen, Inc.	2.5mg	[12]
14.	GIT agent	Simethicone	Gas-X	Novartis	62.5mg	[12]
15.	Nasal decongestants	Phenylephrine HCl	Nasal decongestant	Pfizer	10mg	[12]
16.	Benzodiazepines	Clonazepam	Klonopin Wafers	Solvay Pharmaceuticals	0.125 mg, 0.25mg, 0.5 mg, 1mg, 2mg	[12]
17.	CNS stimulant	Amphetamine	KP106	MonoSol Rx and KemPharm	5mg	[6]
18.	Stimulants	Caffeine	Caffeine films	Dow chemical company	50mg	[1]

Ideal characteristics of a drug to be selected for oral thin film

- The drug should be pleasant in taste.
- The drug having dose up to 40 mg is selected.
- The drugs having smaller or moderate molecular weight are preferred.
- The drugs having better stability and solubility in water & saliva are selected.
- It should not completely ionized at the pH of oral cavity.
- The drugs should permeate through the oral mucosal membrane.¹
- Not require water to swallow, but it should dissolve or disintegrate in the mouth in few seconds.
- Drugs having pleasant mouth feel are selected.
- The drug should be compatible with flavour masking.
- Drugs should exhibit low sensitivity to environmental conditions such as temperature and humidity.

After oral administration the drug should leave minimum or no residue in the mouth.²



Figure 1: Special features of Oral thin film

Manufacturing Methods

Conventional approaches

To manufacture the fast dissolving oral films, following methods are generally used:-

1. Solvent casting method
2. Hot melt extrusion
3. Semi-solid casting
4. Rolling method
5. Solid dispersion extrusion

Solvent casting method

The current most preferred manufacturing process for fabrication of oral thin films is the solvent casting method. In this method, both water-soluble polymer and plasticizer are dissolved in distilled water. The solution is stirred up for 2 hour with the help of magnetic stirrer and kept aside to remove all the air bubbles entrapped. Meanwhile, the excipients and API are dissolved and stirred well for 30 minutes, after the completion of stirring both the solutions are mixed together. Finally, the solution is cast on a flat surface suitable for shaping a film. The film is dried and carefully removed.¹ The same technique of solvent casting was adopted in fabrication of an abuse deterrent and microemulsion-based sublingual film of buprenorphine hydrochloride for breakthrough pain management.²¹

Hot melt extrusion

This method is commonly used for the preparation of granules, extended-release tablets, transdermal and transmucosal drug delivery system. Processing of films by this system, involves shaping a polymer into a movie via the heating process instead of through the normal solvent casting technique. The equipment used for hot melt extrusion consists of extruder, downstream auxiliary equipment and monitoring tools. Extruder is composed of a feeding hopper barrel, screw, die, screw-driving unit and heating/cooling device. Producing thin films for transdermal/transmucosal drug delivery and wound care are via film casting using aqueous or organic solvents.³

Semisolid casting

In this method, water-insoluble polymer is used. A solution of insoluble polymer is prepared in ammonia and in sodium hydroxide. The two solutions are mixed with an appropriate amount of plasticizer to form a gel-like solution. This gel-like solution is applied to thermoregulated drums to form thin films or ribbons. 1:4 is the ratio maintained between the amounts of acid insoluble polymer to the film forming polymer. Various acid insoluble polymers are cellulose acetate phthalate, cellulose acetate butyrate, etc.³

Rolling Method

In this method, the drug is rolled with solvents & a carrier. A solution or suspension with film forming polymer is prepared and subjected to a roller. The solution or

suspension should have specific rheological consideration.¹ Solvents mainly used in this method are the water and mixture of water and alcohol. By the means of high shear processor, API and other excipients are dissolved in small portion of aqueous solvent. Water-soluble hydrocolloids are dissolved in water to form a smooth, viscous solution.. The resulting solution or suspension is used to make the film with the help of rollers.²

A specific amount of solution is fed into pan through second metering pump. The metering roller determined thickness of film. The film is finally formed on substrate and carries away by the support roller. The wet film is dried by using controlled bottom drying. Finally, the obtained film is cut in to the desired shapes and sizes.⁵

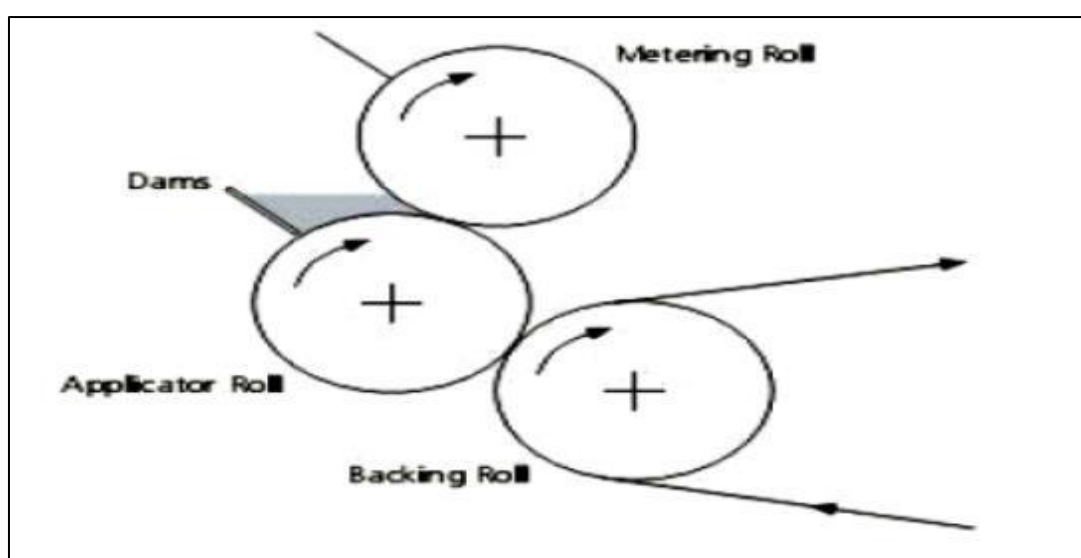


Figure 2: Rolling Method⁵

Solid dispersion extrusion

It involves the dispersion of two or more active ingredients in an inert carrier in the presence of amorphous hydrophilic polymers in solid state. The drug or API is firstly dissolved in a suitable liquid solvent and then this solution is incorporated in melt of PEG below 70°C. The selected solvent or drug could not be miscible in melted PEG. Solid dispersions are then shaped into films by means of dies.⁵

Novel technologies

Printing technologies

Novel technologies such as 3D printing could be used for manufacturing polymeric thin films. It could potentially be a platform for producing the dosage forms beneficial to the individual patient. This could possibly help in creating customized medicine for each patient. The printing technologies are gaining popularity because of its flexibility

and cost-effectiveness.⁸ The examples include the use of off-the-shelf consumer inkjet printers in which drug-loaded inks are deposited to yield accurately dosed units of pharmaceutical ingredients. The inkjet printing was used for printing of active pharmaceutical ingredient on different substrate, whereas the flexographic printing was employed to coat the drug loaded substrate with a polymeric thin film.⁸

Regardless of the various types of printing technique used, all of them contribute to producing a film with more homogeneous distribution and accurate dosage of the drug throughout the films.⁸ To summarize, printing a drug on dosage form is the latest intervention for film preparation and it has become a powerful tool to manufacture dosage form with excellent uniformity, speed-ability, and stability.⁸

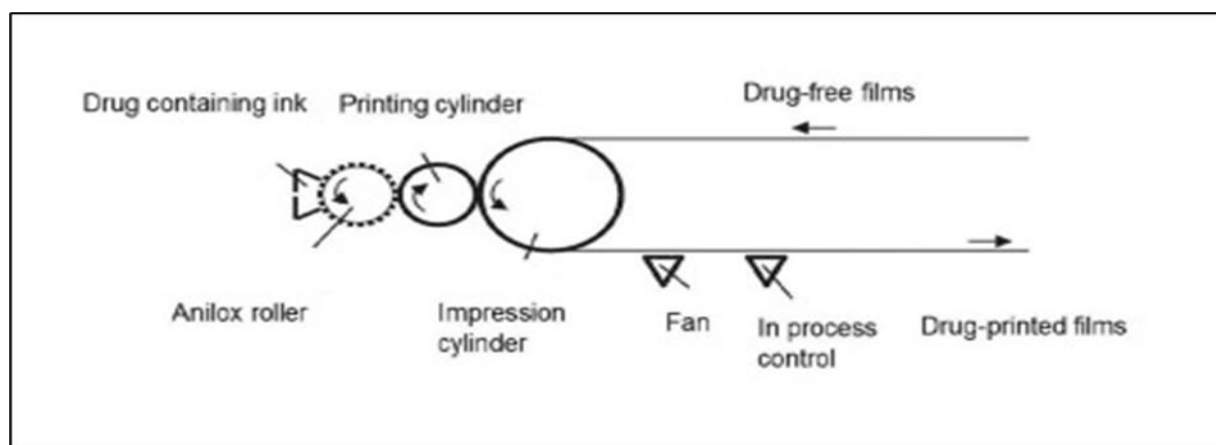


Figure 3: Schematic overview of flexography technology for the preparation of films⁸

XGel

For healthcare and pharmaceutical products, XGel™ film provides unique product benefits. It is made without the use of animals, has religious approval, and is ideal for vegetarians. The film is devoid of GMOs, and continuous production processing allows for a cost-effective and competitive manufacturing platform. Taste masking, colouring, layering, and enteric qualities are all possible with XGel™ films, which also have the ability to contain active pharmaceutical ingredients. XGel™ film systems are frequently used to encapsulate any oral dose form and must be soluble in both cold and hot water. XGel™ film is made up of a variety of water-soluble polymers that have been precisely tailored for the application.¹⁰

Soluleaves

This technology is employed to supply a variety of oral delivery films that may incorporate active ingredients, colours, and flavours. Soluleaves™ films are often designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients, and flavours. For pharmaceutical uses, this method of administration is particularly useful for paediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. The delivery system are often used for the cough/cold, gastrointestinal and pain therapeutic areas also as delivering nutritional products. Soluleaves™ films can also be made to attach to mucous membranes and release the active component over a 15-minute period.¹⁰

Wafertab

Wafertab™ may be a drug delivery system that comes with pharmaceutical actives into an ingestible filmstrip. When the strip comes into contact with saliva in the mouth, the system allows quick breakdown and release of actives. The Wafertab™ filmstrip are often flavoured for additionally improved taste masking. The active ingredient is carefully dosed and integrated into the body of a prefabricated XGel™ film, avoiding needless heat and moisture exposure and potentially improving product stability. Wafertab™ are often prepared in a variety of shapes and sizes and is a perfect method for delivery of medicines,

which require fast release or to be used by patients who have difficulty in swallowing.¹⁰

Foamburst

It's a variation of the Soluleaves™ technology in which a noble gas is injected into the film during the manufacturing process. This results in a honeycombed film that dissipates quickly, providing a completely unique tongue feel. Foamburst™ has attracted interest from food and confectionary manufacturers as a way of carrying and releasing flavours.¹⁰

Evaluation of Oral thin films

Thickness

A micrometre screw gauge or a calibrated digital vernier calliper is used to determine the thickness of the film. The film thickness should be in the range of 5-200 m. The thickness of the film should be assessed at five separate points (four corners and one in the middle), and uniformity in the thickness of the film is critical since it is directly related to the accuracy of dose distribution in the film.¹⁰

Dryness test/Tack test

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 are the eight phases of the film drying process that have been recognised. Although these tests are generally designed to evaluate paint films, the majority of the investigations may be meticulously altered to assess pharmaceutical OTF. The tenacity with which the strip sticks to an accessory (a piece of paper) that has been pressed into contact with the strip is referred to as tack.⁶

Tensile strength

The greatest stress applied to a point where the strip specimen breaks is known as tensile strength. It's computed by dividing the applied load at rupture by the film's cross-sectional area, as shown below.¹

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Film thickness} \times \text{film width}}$$

Percent elongation

Strain occurs when tension is given to a film ($2 \times 2 \text{ cm}^2$) sample, which causes it to stretch. Strain is the deformation of a strip prior to it breaking due to stress. The Hounsfield universal testing machine is used to measure it. Strip elongation increases in general when the plasticizer content rises. It is calculated by the formula.¹⁰

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

Young's modulus

Young's modulus, sometimes known as elastic modulus, is a measure of strip stiffness. In the zone of elastic deformation, it is expressed as the ratio of applied stress to strain:

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

With little elongation, hard and brittle strips show high tensile strength and Young's modulus. Typical young's modulus value for film is $0.30 \pm 0.07 \text{ Mpa}$.¹

Tear resistance

The rip resistance of plastic film or sheeting is a complex function of its ultimate rupture resistance. The tear resistance value in newton (or pounds force)¹ is the maximal stress or force necessary to tear the specimen (which is usually determined around the commencement of tearing). The load is mostly applied at a low rate of 51 mm/min .¹⁰

Folding endurance

To test folding endurance, a strip of film is cut and folded repeatedly at the same location until it breaks. The value of folding endurance is determined by the number of times the film could be folded at the same location without breaking. Typical folding endurance for film is between 100-150.¹

Swelling index

The examinations of the film's swelling index are carried out in simulated salivary fluid. The film sample is weighed and placed in a stainless-steel wire sieve that has been pre-weighed. In a mortar, the mesh containing the film is submerged in 50 ml of simulated salivary medium. At each interval, the weight of the film is measured until it reaches a consistent weight. The following formula is used to determine the degree of swelling:

$$\text{SI} = \frac{\text{wt} - \text{wo}}{\text{wo}}$$

Where,

SI = swelling index

Wt = the film's weight at time "t"

and Wo = weight of the film at $t = 0$ [1]

Surface pH test

Because the surface pH of a fast-dissolving strip can have negative effects on the oral mucosa, it's important to check the pH of the film. The pH of the film's surface should be 7 or close to neutral. A mixed pH electrode can be used for this purpose. OTF was slightly wetted with water, and the pH was determined by placing an electrode on the surface of the oral film. This research should be carried out on at least six films of each formulation, with the mean and standard deviation calculated. Another approach for determining the surface pH is to place the films on a 1.5 percent w/v agar gel, then place the pH paper on the film, and the change in colour of the pH paper gives the surface pH of the film.¹⁰

Contact angle

Contact angle measurement predicts the wetting behaviour, disintegration time, and dissolution of oral film. These measurements are performed with help of goniometer and the measurements should be done at room temperature. Double distilled water should be used to determine the contact angle. On the surface of the dry film, a drop of double distilled water is applied. A digital camera is used to capture images of water droplets within 10 seconds of their deposition. Digital pictures can be analysed by image 1.28v software (NIH, USA) for angle determination.¹⁰

Transparency

A basic UV spectrophotometer can be used to determine the transparency of the films. Cut the film samples into rectangles and set them on the spectrophotometer's interior side. Then, at 600 nm, determine the transmittance of the films. The films' transparency was determined as follows:

$$\text{Transparency} = \frac{(\log T_{600})}{b} = -\epsilon c$$

Where,

T_{600} is the transmittance at 600 nm

b is the film thickness (mm)

c is concentration¹

Content uniformity

Each film is filtered after being dissolved in a suitable solvent for content uniformity, and the drug content in each film is determined using the appropriate quantification method. It is expected that the relative standard deviation % is not more than 6%.¹¹

Moisture content

The produced film was first weighed and then put in cadmium chloride desiccators. After 3 days the film was reweighed to obtain the percentage of moisture loss.¹



$$\% \text{ Moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Disintegration test

When a film comes into contact with water or saliva, the disintegrating time (seconds) is measured. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for film is 5-30 s.¹

a. Slide frame method

A pipette was used to drop one drop of distilled water on the oral films. Then the films were clipped into slide frames and placed on a petri dish surface.¹ The time it took for the film to dissolve and a hole to appear within it was measured.

b. Petri dish methods

2 ml of distilled water was placed in a petri dish and one film was placed on the surface of the water and the time measured until the oral film dissolves completely was recorded.¹

In vitro dissolution studies

Under standardised conditions of liquid/solid interface, temperature, and solvent concentration, dissolution is defined as the amount of drug material that enters the solution per unit time. For dissolution testing, any of the pharmacopoeia's standard basket or paddle apparatus can be utilised. The dissolution medium will be chosen based on the sink circumstances and the greatest dose of API. The temperature of the dissolving media should be kept at 37.0°C and the rotational speed at 50. The paddle apparatus has the problem of causing oral films to float over the dissolving media when used.¹⁰

Organoleptic evaluation

Most of the people accept products with sweet taste. Special controlled human taste panels are used for product evaluation. For this purpose, in-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are used.⁵

Stability study

The International Conference on Harmonization (ICH) guidelines should be followed when conducting a stability study. The prepared formulation was wrapped in a unique fashion. Firstly, it was wrapped in a butter paper then above it an aluminium foil was wrapped and the packing should be placed in an aluminium pouch and make it heat sealed. Storage temperatures for formulations should be 30°C/60 percent relative humidity (RH) and 40°C/75 percent RH, respectively. The films were examined for drug content, disintegration time, and physical appearance after 3 months.¹⁰

Stickiness Determination

It is evaluated by texture method usually used for measurement of the tack of pressure sensitive adhesives.⁶

Determination of % yield

The following formula [10] can be used to compute the percentage yield of buccal patches:

$$\% \text{ yield} = \frac{\text{Mass of the buccal patches obtained}}{\text{Total weight of drug and polymer}} \times 100$$

Scanning electron microscopy

To study the surface morphology of film, scanning electron microscopy is used. The film sample should be placed in a sample holder, and various photomicrographs with tungsten filament as an electron source can be taken at 1000 magnification.¹⁰

FT-IR

FT-IR (ATR) spectrophotometer is used to detect unwanted interactions between formulation components and the pure API.¹¹

XRD

The X-ray diffraction analysis helps to determine the crystal or amorphous nature of the drugs incorporated in the films. Thus it helps to check whether any polymorphic changes have occurred in the drug containing film, during the various stages of manufacturing.¹¹

DSC

The DSC analysis is used to show that the medicine is compatible with other auxiliary chemicals. The reference and sample are brought to the same temperature, and the sample's interactions are investigated based on the heat exchange.⁷ A portion of the OTF sample is sliced, placed in the alumina pan, and analysed at a specific flow rate of atmospheric nitrogen (mL/min).¹¹

Polymers used in formulation of Oral thin films

Polymers are the foundation of film formulations, and a variety of polymers are available for thin film production. For achieving desired film properties polymers can be used alone or in combination of other polymers.

Characteristics of polymers used:-

1. Non-toxic
2. Non-irritant
3. Do not contain any leachable impurities

Water-soluble polymers are used as film formers to create a thin film that disintegrates quickly, has good mechanical strength, and has a pleasant mouth feel. For film preparation, both natural and synthetic polymers are utilised.

For imparting specific properties in thin films different polymers are available. For example, gelatin are available in different molecular weight, and thus the appealing and glossy films could be obtained with the gelatin having a high molecular weight. Pullulan is commonly used to create thin films with good solubility, mechanical strength, and stability over a wide temperature range. Chitosan was



combined with either high methoxy pectin (HMP) or low methoxy pectin (LMP) to produce a thin layer with outstanding mechanical strength. The film forming polymers such as hydroxypropyl cellulose (HPC), methyl cellulose and carboxymethyl cellulose (CMC) produces a thin film with less water vapour barrier due to hydrophilic nature which aids in water retention.

In general polymers are known as excipients, but it is an essential component used in designing and formulating thin films. Therefore it is necessary to understand properties of polymers such as chemistry, rheology and physicochemical properties of polymer for maximizing their use in formulation & designing. The selection of right polymer while developing polymeric film is difficult therefore formulator should consider various points as per requirement. Therefore, it is important to consider the appropriate polymer for producing a thin film with a better performance that assures high therapeutic success.⁷

Effect of Polymers in Oral thin films

Losartan potassium Oral thin films

N. G. Raghavendra Rao, et al., developed fast dissolving oral thin films of losartan potassium in which HPMC polymer was used having viscosity of 15 cps & 50 cps, in a concentration of 1000 mg & 750 mg respectively. With above concentration of polymers, the disintegration time obtained was in range 50-90 sec. Further, with above concentrations of polymers the release pattern of Losartan potassium was about 100% within 30 minutes of *in-vitro* dissolution study.¹²

Fast dissolving oral thin film of Caffeine

Farhana Sultana et al., developed fast dissolving oral thin films of caffeine in which HPMC (15cps), sodium alginate and kollicoat were used in concentration of 1500-2500 mg, 750mg, 750-1250 mg respectively. In these films with above concentration of HPMC the disintegration time obtained was in range 15-45 sec, for sodium alginate the disintegration time obtained was in range 20-35 sec and for kollicoat the disintegration time obtained was in range 15-30 sec. Further using *in-vitro* dissolution study, the release pattern of caffeine was about 100% within 100-300 sec, 150-250 sec and 100-200 sec for HPMC, sodium alginate and kollicoat respectively.¹³ Thus exhibiting faster release of caffeine with lowest concentration of kollicoat polymer.

Fast dissolving drug delivery system of Salbutamol sulphate

N.L Prasanthi et al., developed fast dissolving oral thin films of Salbutamol sulphate in which hydroxy propyl cellulose (HPC), hydroxy propyl methylcellulose (HPMC) & sodium alginate were used in concentration of 0.5-2 mg each respectively. For these films disintegration time obtained was in the range of 1.5-2.5 min, 2-80 min and 25-60 min which indicates the disintegration time is greater with respect to polymer i.e., HPC & sodium alginate is highly variable when HPMC is used as a polymer.¹⁴

Oral thin films of Sumatriptan succinate

Buchi N. Nalluri, et al., developed fast dissolving oral thin films of anti-migraine drug Sumatriptan succinate in which HPMC E5, HPMC E15 and Polyvinylpyrrolidone (PVP) were used in concentration of 650 mg, 650 mg and 2 mg respectively. HPMC was used with and without PVP in the preparation of samples. The disintegration time using petri dish method for HPMC E5 was found to 25-30 sec, for HPMC E15 disintegration time 31-37 sec and for HPMC E5 with PVP the disintegration time was 9-10 sec, thus exhibiting that when HPMC & PVP polymers used in combination the deduction in the disintegration time was observed. Further in *in-vitro* dissolution study, the 100% release of Sumatriptan succinate was obtained in shortest duration of 10 sec when HPMC E5 was used in combination with PVP. Whereas, with single HPMC E5, 100% release was obtained within 40-60 sec and with single HPMC E15, 100% release was obtained within 100-120 sec.¹⁵

Fast dissolving films of Levocetirizine dihydrochloride

Prabhakara Prabhu et al., developed thin films of Levocetirizine dihydrochloride with the purpose of developing a dosage form for a very quick onset of action, which is beneficial in managing severe conditions of allergies. The films of levocetirizine dihydrochloride were prepared by using polymers such as HPMC and PVA, as either single polymer or in combination of two. In films with only HPMC as polymer, the disintegration time was found to be 10-34 sec, whereas in films containing only PVA as a polymer, the disintegration time was 58-106 sec. Whereas when both the polymers were used in combination, disintegration time was found to be 32-130 sec.¹⁶ Thus concluding that when low viscosity HPMC polymer are used, disintegration was obtained in less duration of time.

Mouth dissolving film of Etoricoxib

K. Senthilkumar and C. Vijaya developed thin film of Etoricoxib in which HPMC E15 polymer was used in concentration of 150 mg. In these films with above concentrations of polymers the disintegration time obtained was in range 8-10 sec and about 100% release was obtained within 30 min of *in-vitro* dissolution study.¹⁷ This further confirmed that low viscosity of HPMC polymer is useful to obtain faster dissolution with rapid disintegration.

Oral disintegration thin films of Lovastatin

P. Pragathi et al., developed thin film of lovastatin in which gelatin & PVA polymer was used in the concentration of 4.5 mg & 3.5 mg respectively. In these films with above concentrations of gelatin and PVA the disintegration time obtained was in range 10-72 sec and 7-70 sec, respectively.¹⁸ This exhibited that lower the concentration of PVA, faster disintegration was obtained.

Oral fast-dissolving films of Rupatadine fumarate



A. Roy et al., developed fast dissolving oral thin films of Rupaadine fumarate in which Pullulan, HPMC E 5 and E15 used in concentrations of 300-400 mg, 400-500 mg and 400-500 mg respectively. In these films with above concentration of Pullulan, HPMC E 5 & E15, the disintegration time obtained was in range 30-32 sec, 28-37 sec and 36-38 sec, respectively. Further, with above concentrations of all the polymers release pattern of Rupaadine fumarate was about 100% within 180 sec using *in-vitro* dissolution study.¹⁹

Microemulsion Loaded Sublingual Film of Fentanyl Citrate

D. Mundhey et al., developed thin films of Fentanyl Citrate in which HPMC E5, And HPMC E15 was used in 50mg and 20-50 mg respectively. The disintegration time obtained with 50mg HPMC E 5 with 22.6 mg of HPMC E15 was 20 sec . Further with with the same concentrations the release pattern of fentanyl citrate was about 100% within 5 min using *in-vitro* dissolution study.²⁰

Selection of Polymer

The physical and mechanical properties of the oral thin film depends upon the characteristics of film-forming polymer, which forms about 20 to 75% (w/w) of total dry wt of the oral thin films. As a result, one of the most significant and critical parameters for the formulation's effective development is the choice of polymer. The polymers employed should be hydrophilic, disintegrate quickly, have a pleasant tongue feel, and have appropriate mechanical properties. The polymer should have sufficient mechanical, physicochemical, and permeability qualities in addition to its good solubility. A film must have high mechanical strength with suitable elongation and elasticity qualities in order to withstand internal and external stresses created during storage and, in particular, when exposed to climatic conditions.⁸

CONCLUSION

Films combine the benefits of tablets (precise dosage, ease of application) and liquid dosage forms (easy swallowing, rapid bioavailability). As a result, several pharmaceutical companies are transitioning from tablets to fast-acting oral thin films.

Oral Thin Films are new emerging novel drug delivery system of great importance during the emergency situations whenever immediate onset of action is desired and that allows children, elderly and the general public to take their drugs discreetly wherever and whenever they are needed, therefore filling a gap in the market. This technology provides a solid foundation for developing patent-free products and extending the patent lives of current ones. The use of fast dissolving oral thin films is not restricted to buccal fast dissolving systems, but also includes gastro-retentive, sublingual delivery systems, and other applications. Incorporation of incompatible active medicinal components in a single formulation utilising multilayer films fused together is one of the future applications. In between the incompatible active

pharmacological ingredients, an inactive film layer can be placed. Thin films containing active pharmacological components with high transmucosal flux rates can be inserted into buccal or sublingual regions to dissolve slowly. Drugs coated with controlled release polymers can also be incorporated. This technology is being studied extensively and there is wide scope for further research in this field.

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