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A COMPREHENSIVE REVIEW ON ORODISPERSIBLE FILM ON DRUG DELIVERY

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ABSTRACT
Buccal delivery is considered to be an imperativesubstitute to the peroral route for the systemic administration of drugs, as it considered the most appropriate, easy, safest route of administration. Oral mucosa has rich vasculization, offers better permeability to many drugs and it act as an excellent site for the absorption of drugs. Orodispersible film is used as a novel approach, which when placed in the oral cavity disintegrate or dissolve within a few seconds without the intake of water and directly reaches to the systemic circulation. Oral film technology fulfills all the requirements of potential solid dosage form**.** It is an alternative platform for molecules that undergoes high first pass metabolism. A wide variety of drugs such as cardiovascular drugs, analgesics, antihistamines, antiasthmatics, neuroleptics etc. can be formulated as Orodispersible film. There are various techniques are accessible including solvent casting, semisolid casting, hot melt extrusion, solid dispersion extrusion to fabricate the oral dispersible films at the buccal cavity. The present article overview the characteristic features, formulation components, methods of preparation, and evaluation, marketed products and future prospects of orodispersible films.

Key Words: Orodispersible film, Buccal delivery, Fast dissolving, Oral soluble film

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INTRODUCTION
Oral route is the most preferred and acceptable route due to ease of ingestion, pain avoidance, versatility and most importantly, the patient compliance. Nearly 70% of the formulation is solid dosage forms. Almost 90% of the drugs are administered to the body via oral route for the treatment of various disorders and diseases as it regarded as the safest, most convenient and most economical method of drug delivery[1]. The drug is either dissolved or swallowed, which then enters into the systemic circulation to produce the desired effect. Despite great advancement in drug administration of a drug for systemic effect because of self-medication, ease of administration and avoidance of pain compared to parenteral route.[2]

FAST DISSOLVING DRUG DELIVERY SYSTEMS
Fast dissolving drug delivery system is a new generation delivery system also known as fast dissolving/disintegrating film for the oral delivery of the drugs which came into existence in the late 1970's as an alternative to tablets, capsules, syrups and other formulations for pediatric and geriatric patients who experience difficulties in swallowing traditional solid dosage forms which combines both the advantages of conventional tablet and of liquid formulation. FDDS is easy to administer and provides better patient compliance in the elderly, pediatric, mentally retarded, nauseated and uncooperative patients. This delivery system consists of the solid dosage forms that dissolve

quickly i.e. within a matter of seconds in the oral cavity without administration of water. The delivery system consists of a very thin oral strip which is simply placed on the patients tongue or any other oral mucosal tissue and instantly gets wetted by saliva. The film rapidly hydrates onto the site of application. It is then rapidly dissolves and disintegrates to release the medication for oro-mucosal absorption. Fast dissolving oral thin films are widely accepted by patients and also to the caregiver for their ease-of-delivery, portability and accurate dosing.[3]The robustness of the film depends upon the type and amount of polymer used and general dissolution time for orally dissolving film is 5-20 min. as per pharmacopoeia. They also provide quick onset of action within few seconds as the oro-mucosal absorption of the drug occurs directly from the site of administration to the systemic circulation avoiding the first-pass metabolism to produce the desired effect.[4]

ORODISPERSIBLE FILMS

Orodispersible film (Fast dissolving oral film), a novel drug delivery system for the oral delivery of the drugs is an ultra-thin film prepared using hydrophilic polymers that rapidly dissolves on the top or the floor of the tongue or buccal cavity.

It is an ultra-thin strip (50-150 microns thick) of postage stamp size with an active agent and other excipients developed on the basis of transdermal patch technology (Fig.1). The delivery system consists of a very thin oral strip, which is simply placed on the patients tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates in a matter of seconds and dissolves to release medication for oromucosal absorption.

Mouth dissolving films for oral delivery of drugs, was developed based on the technology of transdermal patch. The oral films quickly dissolve in the oral cavity, and the active ingredient can be absorbed into the blood-stream via the oral mucosa. The active ingredient, once absorbed by the oral mucosa, thus bypasses the liver's first pass effect, which improves bioavailability.

Depending on the selected film type, the active ingredient's release may also be delayed. In this case it is absorbed after swallowing via the gastrointestinal tract. The fast passage of dissolved dosage form to the stomach provides a better opportunity for the medication to be absorbed through the membrane of the buccal cavity, Pharynx and Esophagus for improved bioavailability and quick onset of drug action. Oral films are paper – thin polymer films used as carriers for pharmaceutical agents. The innovative dosage form is taken orally but does not require water or swallowing.[5, 6]

Figure 1. Orodispersible films

a. Special Features of ODF

- Thinand elegant films.
- Available in various sizes and shapes.
- Excellent mucoadhesive capture.
- Fast disintegration and dissolution.
- Rapid drug release.
- Can be administered without water.[1,7]

b. Advantages of ODF

- Easy transportation.
- Ease of swallowing for geriatrics and paediatrics.
- Convenient and accurate dosing.
- No need of water for administration.
- Convenient for dysphasic patients having difficulty in swallowing tablets and capsules.
- Rapid onset of action with increased BA due to bypassing hepatic first pass effect and stability.
- No risk of chocking.
- Good mouth feel property helps to change the perception of medication as the bitter pill particularly in paediatric patients.
- Stability for longer duration of time, the drug remain in solid dosage forms till it is consumed than the compression to the stability on liquid dosage forms.

- Flexible and portable in nature, so they provide ease of transportation, during consumers handling and storage.
- As compared liquid formulation, precision in the administered dose I ensured from each strip of the weavers.
- Taste masking.
- They has the potential to improve the onset of action, lower the design and enhance the efficacy and safety profile of the medicament.
- Provide new business opportunity like product differentiation, product proportion patent extension.[1,7]

c. Disadvantages of ODF

- High doses cannot be incorporated.
- Dose uniformity is a technical challenge.
- It is hygroscopic in nature, so it must be kept in dry places.
- It also shows the fragile, granule property.
- They require special packaging for the product stability and safety.
- The drug, which is unstable give buccal pH cannot be administered.[1,7]

d. Types of ODF

There are three types of ODF[3]

a. Flash release wafers
b. Mucoadhesive melt-away wafers
c. Mucoadhesive sustained-release wafers

The characteristic features of these films are summarized in Table-1.

Table-1 Properties of different types of oral films

Property	Mucoadhesive sustained release	Mucoadhesive melting film	Flash release
Structure	Multilayer	Single/multilayer	Single layer
Area (cm^2)	2-8	2-7	2-8
Thickness	50-250	50-500	20-70
Drug phase	Solid solution/Suspension	Suspended drug particles or solid solution	Solid solution
Excipients	Non-soluble/low polymers	Hydrophilic, soluble polymer	Highly hydrophilic soluble polymers

FORMULATION AND DESIGN OF ODF

ODF is a mouth dissolving film is a thin wafer with an area of 5-20 cm^2 containing an active ingredient. The instant dissolution, in water or saliva correspondingly, is reached through a special matrix from water-soluble polymers. Drugs can be incorporated up to a single dose of 15mg. Formulation considerations (polymer, sweetener, plasticizer etc.) have been reported as important factors affecting mechanical properties of the wafers, such as changing the glass transition temperature to lower temperature.[8,9]The general composition of an oral dispersible film is shown in Table-2.

Table-2 Composition of oral dispersible film

Sl. No.	Category	Percentage Amount (%)
1	Drug(API)	1-30%
2	Polymer	40-50%
3	Plasticizer	0-20%
4	Surfactant	q.s
5	Saliva stimulating agent	2-6%
6	Sweetening agent	3-6%
7	Flavouring agent	0-10%

8	Colouring agent	q.s
9	Stabilizing /Thickening agent	0-5%

a. Drugs: Different type of API can be successfully incorporated in the oral strip technology. Micronized API can improve the texture of the film and also dissolution and uniformity of the oral fast dissolving film. Different molecule can be incorporated into the delivery system. Taste of bitter drug need to be masked for that cyclodextrins or resins can be used; they prevent the direct contact of API with the saliva. It include cough/cold remedies(antitussive, expectorants), anxiety drugs, CVS agent, sore throat, erective dysfunction drugs, antihistamines, antiasthamatics, GI disorders, nausea, pain and CNS (antiparkinson's disease).

The ideal characteristics of a drug to be selected are;

a. Drug should have pleasant taste.

b. Incorporated drug should have low dose (upto 40mg).

c. Possess smaller and moderate molecular weight.

d. Good stability and solubility in water as well as in saliva.

e. Partially unionizes at the pH of oral cavity.

f. Ability to penetrate oral mucosl tissue.

A typical composition of the film contains 1-25 % w/w of the drug. Variety of APIs can be delivered through fast dissolving films. Small dose molecules are the best candidate to be incorporated in OFDFs. Multivitamins upto 10% w/w of dry film weight was incorporated in the with dissolution time of less than 60 s.[10]

b. Film Forming Polymers: Polymers are the most important ingredient of the oral fast dissolving film. Robustness of the film depends on the amount of polymer added in the oral strip. Generally 45 % w/w of polymer is used which is based on total weight of dry film. Mainly Hydrophilic polymers are used in the oral strip as they rapidly disintegrate in the oral cavity as they come in contact with saliva[11].

Ideal Property of Film Forming Polymer:

- Non-toxic and non-irritant.
- Must be hydrophilic.
- Should have excellent film forming capacity.
- Should have good wetting and spreadability property.
- It should have good mouth feel property.
- It should have good shelf life.
- It should be non-bitter.
- It should be devoid of leachable impurities.
- It should be inexpensive and readily available.
- It should not be an obstacle in the disintegration time.
- It should exhibit sufficient peel, shear and tensile strength.
- It should not cause secondary infection in the oral cavity[12,13].

The different types of polymers employed in the formulation of ODF is shown is table-3.

Table-3 Types of polymers employed in the formulation of ODF

Group	Class	Examples
Natural	Carbohydrates	Pullulan, Pectin, Sodium alginate, Maltodextrin, Sodium starch glycolate
	Proteins	Gelatine
	Resin	Polymerized resin
Synthetic	Cellulose derivatives	HPMC (E3, E5, E15,K3, K15, K50), Methyl cellulose (A3, A6, A16), carboxy methyl cellulose secekol- 30, Sodium carboxy methyl cellulose, Microcrystalline cellulose, Croscarmellose sodium
	Vinyl polymer	Poly vinyl pyrrolidine (K-90, K- 30), Poly vinyl alcohol, Poly ethylene oxide
	Acrylic Polymer	Eudragit (RD- 100, 9, 10, 11, 12 and RL-100)

c. Plasticizer: Plasticizers are the important excipient of the oral film. It improves the flexibility and a mechanical property of the film like tensile strength and elongation and reduce the brittleness of the film. It significantly improves the strip properties by reducing the glass transition temperature of the polymer. It should be selected so that it must be compatible with the drug. It can improve the flow and enhances the strength of polymer. They are used in concentration of 0-20%w/w of dry polymer weight. The plasticizers used involves Glycerol, Propylene glycol, Polyethylene glycol, dimethyl, dibutyl, diethyl phthalate, tributyl, triethyl, acetyl citrate, triacetin and castor oil.

d. Sweetening agents: Sweeteners are used for the taste masking of bitter drugs so that the drugs are palatable. The sweet taste in formulation is important in case of paediatric formulation. They are used alone or in combination between the concentrations of 3-6%w/w. Natural as well as artificial sweeteners are used in the preparation of oral films. Xylose, ribose, glucose, sucrose, maltose, steviosides, dextrose, fructose, liquid glucose and isomaltose are used as natural sweeteners. Fructose is sweeter than sorbitol and mannitol and is widely used sweetener. Artificial sweeteners used are sodium or calcium saccharine salts, cyclamate salts, acesulfame potassium etc. Acesulfame potassium and sucralose have more than 200 and 600 times sweet. Neotame and altitame have more than 2000-8000 times sweetening power as compared to sucrose.

e. Saliva stimulating agents: The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in fast disintegration of the rapid dissolving film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid,lacticacid,ascorbic acid and tartaric acid are some examples. These are used alone or in combination between 2-6%w/w of weight of the film.

f. Flavouring agents: The flavours enhance the acceptance of the formulation and enhance the elegance properties of the film. They must be non-toxic, soluble, stable and compatible with the excipients. The quantity of flavouring agent required to mask the taste depends on the flavour type and its strength. They can be used alone or in combination. The generally used flavouring agents for different classes of drugs is shown in Table-4.

Table-4 Preferred flavours as peer the taste of the drug

Drug	Preferred Flavour
Antibiotics	Cherry, maple, pineapple, orange, raspberry, banana, vanilla, butter scotch, coconut-custard, cinnamon, strawberry, vanilla
Antihistamines	Apricot,cherry,cinnamon,grape,honey-lime,peach-orange,peach-rum,raspberry,wild cherry
Barbiturates	Banana-pineapple, banana-vanilla, cinnaon-peppermint, orange, peach-orange, grenadine-strawberry.
Decongestants & Expectorants	Anise, apricot, butterscotch, cherry, coconut custard, custard-mint-strawberry, grenadine peach, strawberry-lemon, gooseberry, orange lemon, coriander, pineapple, raspberry
Electrolyte solutions	Cherry, grape, lemon-lime, raspberry, wild cherry syrup, grenadine-strawberry, lime, port-wine, cherry-wine, wild-strawberry.
Salt taste drugs	Butterscotch, maple
Bitter taste drugs	Wild cherry, walnut, chocolate-mint, licorice
Sweet taste drugs	Fruit berry, vanilla

g. Colouring agents: Colouring agents impart colour to the formulation. They are selected according to the flavour. FD&C approved colouring agents are incorporated in the oral film. The colouring agents should not exceed concentration levels of 1% w/w.

h. Surfactants: Surfactants are used as solubilising or

wetting or dispersing agents so that the film is getting dissolved within seconds and release active agent immediately. Commonly employed substances are polaxamer 407, benzethonium chloride, tweens, sodium lauryl sulphate, benzalkonium chloride. The most commonly used one is polaxamer 407 and it is used as wetting, solubilizing and dispersing agent.[1, 14, 15]

MANUFACTURING METHODS

There are five methods which are used alone or in a combination with the following process for the manufacture of the fast dissolving oral films.

a. Solvent casting: The oral thin film is preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution. The API and other agents are dissolved in smaller amounts of solution and combined with the bulk by using high shear processor. Vacuum is used to remove the air entrapped. The solution then formed is then cast as a film and pour the solution in a glass mould and allow the solution to dry in an oven at 45-50 ^{0}C which is the cut into pieces of the desired size.

b. Semisolid casting: This method is preferred when acid insoluble polymers are used in the preparation of oral fast dissolving films. In this method, first of all a solution of water soluble film forming polymer is prepared. Then resulting solution is added to a solution of acid insoluble polymer. Then approximate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted into the films or ribbon by using heat controlled drums. The thickness of film is about 0.015 - 0.05 inches. The ratio of acid insoluble polymers to film forming polymer should be 1:4.

c. Hot melt extrusion: In this method the polymers which have low molecular weight and low viscosity are preferred. Drug is mixed with the carrier in the solid form so that granular material is formed. These granules are then dried and then introduced into the extruder. The speed of the screw should be around 15rpm so that the granules reside inside the extruder for about 3-4min.The processing temperatures should be 80 ^{0}C (zonel), 115℃ (zone2), 100C (zone3), and 65 ^{0}C (zone 4). The extrudate (T=65℃) then pressed into a cylindrical calender to obtain a film.

d. Solid dispersion extrusion: In this method immiscible components are taken and they are then extruding with drugs. Solid dispersion is then prepared and by means of dies the solid dispersion is shaped into films.

e. Rolling method: In this method firstly solution or suspension of drug is prepared which have certain rheological consideration. Either water or mixture of water and alcohol is mainly used as solvent. Suspension or solution containing drug is rolled on the carrier. Films are dried on the rollers and cut into desirable shapes and sizes.[5,8,14,,16]

EVALUATION OF ODF

a. Mechanical properties

i. Thickness: A thickness of film should be measured with the help of micrometer screw gauge or calibrated digital verniercallipers. Film should be measured at five points. i.e. from the centre and from all the four corners and then mean thickness is calculated. It is necessary to determine the uniformity of thickness as it is directly related to accuracy of dose in the film.[17]

ii.Dryness/Tack test: Dryness is the property to measure the solvent or water content present in the film whereas the tack is the tendency with which the film adheres to any piece of paper which is pressed into contact with the strip. Eight stages of film drying process have been recognized. i.e. set-to-touch, dust-free, tack-free, dry-to-touch, dry-hard, dry-through, dry-to-recoat and dry print free. Now Instruments are also available to study.[17,18]

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

Tensile strength = Load at failure x 100 /strip thickness x strip width[18].

iv. Percent Elongation: When stress is applied, a film sample stretches and this is referred to as strain. Strain is basically the deformation of film divided by original dimension of the sample. Generally elongation of film increases as the plasticizer content increases.

Percent elongation = L x 100/L_0

L = Increase in length of film

Lo = Initial length of film[18]

v. Young's Modulus: Young's modulus or elastic modulus is the measure of stiffness of film. It is represented as the ratio of applied stress over strain in the region of elastic deformation as follows:

Young's Modulus = Slope x 100/Film thickness x cross head speed.

Hard and brittle film demonstrates a high tensile strength and Young's modulus with small elongation.[17,18]

vi. Tear resistance: The maximum stress or force (that is generally found near the onset of tearing) required to tear the film is recorded as the tear resistance value in Newton.[18]

vii. Folding Endurance: Folding endurance is determined by repeated folding of the film at the same place till the fill breaks. The number of times the film is folded without breaking is computed as the folding endurance value.[18]

b. Organoleptic Evaluation

This is essential step in case of most oral formulation due to more residence time in the oral cavity. The product should possess the desired features of sweetness and flavour which is acceptable to large mass of population. For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeial methods are being used for this purpose. Experiments using electronic tongue measurements have also been reported to distinguish between the sweetness levels in taste masking formulation.[19]

c. Swelling Test

Simulated saliva solution is used to conduct the swelling property study. Firstly weigh all the samples of film and placed on the preweighed 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: $\alpha = (w_t - w_o) / w_o$

where, w_t = weight of film at time t

w_o = weight of film at time zero[18]

d. Surface pH Test

Surface pH of the film was determined by placing the film on the surface of 1.5%w/v agar gel followed by placing pH paper (pH range1-11) on films. The change in colour of pH paper observed and reported.[20]

e.Contact Angle

Contact angle are measured by Goniometer at room temperature. Take a dry film and place a drop of distilled water on the surface of the dry film. Images of water droplet were recorded with in 10 sec of deposition by means of digital camera. The contact angle was measured on both side of drop and average is taken.[20]

f. Transparency

The transparency of the films can be determined using a simple UV spectrophotometer. Cut the film in the rectangular shape and placed inside the spectrophotometer cell. The transparency of the film at 600nm can be calculated as follows:

Transparency = $(\log T_{600}) / b = -\text{Ɛ}C$

where, T_{600} = transmittance at 600nm.

b = film thickness (mm)

C= concentration.

g. Assay/Content Uniformity

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85 -115%.[21]

h. Disintegration Test

The disintegration time limit is 90 s or less, although no official guidelines is available for oral strips. Pharmacopoeial disintegrating test apparatus may be used for the study. Typical disintegration time for oral strip is 5-30 s.[22]

i. *In vitro* Dissolution test

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.[22]

j. Stability study

Stability study of fast dissolving films is carried out for all the batches according to ICH guidelines. After predetermined intervals, the films are evaluated for the drug content, disintegration time and physical appearance.[1, 23]

PACKAGING OF ODF

Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast dissolving dosage forms. A variety of packaging options are available for fast dissolving films. Single packaging in mandatory for films, which are pharmaceutical products; an aluminium pouch is the most commonly used packaging format. APR-Labtec has developed the Rapid card, a proprietary and patented packaging system, which is specially designed for rapid films. The rapid card has same size as a credit card and holds three raid films on each side. Every dose can be taken out individually.

The material selected must have the following characteristics:

- They must protect the preparation from environmental conditions.
- They must be FDA approved.
- They must meet applicable tamper-resistant requirement
- They must be non-toxic.
- They must not be reactive with the product.
- They must not impart to the product tastes or odors.[24]

CURRENT STATUS OF ODF

a. Current Research in ODF

i.Chauhan I *et al.,* (2019) were formulated fast dissolving oral film of zolmitriptan using solvent casting method. Various placebo films were prepared using varied combinations of hydrophilic polymers by trial and error method. HPMC E-15,PVP K-30,Lycoat RS 720 was chosen for film formation in different proportions. Glycerol was used as plasticizer and citric acid was used as saliva stimulating agent. This formulation was enhanced the BA of drug and produced quick action for migraine patients.[25]

ii. RajniBala and Shailesh Sharma (2018) were formulated fast dissolving oral films of aprepitant for the prevention and treatment of chemotherapy induced nausea and vomiting. The ODF was prepared using solvent casting method and optimized employing central composite design considering two independent variables film forming polymer (pullulan) and PEG 400. The FDF of antiemetic drug aprepitant showed significant improvement in pharmacokinetic parameters (AUC, Cmax, tmax, AUMC & MRT) and in BA as compared with marketed product and also minimum disintegration time, highest dissolution rate and satisfactory physicochemical properties.[26]

iii. Jabir S A and Sulaiman T H (2018) were formulated fast dissolving oral film of lafutidine by solvent casting method using HPMC E5,PVA and SCMC as film forming polymers. PEG 400, Propylene glycol and Glycerin were used as plasticizer to enhance film forming properties of polymer. Tween 80 and poloxamer 407 were used as a surfactant, Citric acid as saliva stimulating agent and croscarmellose as a super disintegrant. The films were found to be satisfactory when evaluated for both physical and mechanical characterizations. HPMC E5 showed the shortest *in vitro* disintegration time accompanied with acceptable mechanical properties and dissolution behaviour. PEG 400 was the best plasticizer and it showed improvement in the mechanical and physical characteristics of lafutidine ODF.[27]

iv. Sarangi D K.et al., (2017) were formulated fast dissolving oral film of losartan potassium. It was prepared using different polymers like PVA, PVP, HPMC, carpool, pectin and tragacanth by solvent casting method. The physical appearance and folding endurance properties were found to be good. The drug content showed uniform mixing of drug & in vitro drug release showed 78-96% drug release within 5 minutes. The ODF of losartan potassium produced rapid action and it improved BA and enhanced the absorption by avoiding first pass effect.[28]

v. He Zhang *et al.,* (2015) were formulated fast disintegrating films of levothyroxine by solvent evaporation method using HPMC, Croscarmellose sodium (CCS) as superdisintegrant, and Propylene glycol(PG) as a plasticizer. The minimum disintegrating time was 15 seconds and maximum drug release in one hour was 97.56%.[29]

vi. Senthilkumar K and Vijaya C (2014) were formulated mouth dissolving film of etoricoxib for the management of pain by solvent casting method by using etoricoxib-BCD along with HPMC as film forming polymer. The ODF showed enhanced dissolution properties and acceptable taste masking was achieved by forming inclusion complex with

betacyclodextrin in 1:1g ratio. It shows adequate mechanical strength and desired rapid disintegration which on administration will result in rapid therapeutic action.[30]

vii. Buchi N. Nalluri*et al.*, (2013) were formulated fast dissolving oral film of sumatriptan succinate by wet film applicator technique .Film former, HPMC along with film modifier/solubilizing agents, PVP K30 and sodium lauryl sulphate were used to formulate ODF. The film with 13% (w/w) of HPMC E5 showed better dissolution properties. The formulation showed good mechanical properties like tensile strength, folding endurance and % elongation and dissolution properties. The film prepared using HPMC E5 and PVP K30 showed the highest dissolution rate, suitable *in vitro* disintegration time and satisfactory physico-chemical properties.[31]

viii. Sumedha Bansal *et al*., (2013) were formulated fast dissolving oral film of losartan potassium for the treatment of hypertension, by using polymers such as PVA and MD(maltodextrin) in different concentrations. Propylene glycol was used as plasticizer. The formulation showed satisfactory drug content, *ex vivo* permeation, effective *in vitro* drug release, disintegration time of 24s and satisfactory stability.[32]

2. Commercially Available ODF[2]

Table-5 gives information on various marketed orodispersible films**.**

Table-5 List of commercially available ODF

Product	**Active drug**	**Dose strength (mg)**	**Application**	**Company**
Triaminic	Dextromethorphan HBr	5/7.5	Seasonal allergy	Novartis
Triaminic	Diphenhydramine HCl	10/20	Long acting cough	Novartis
Theraflu	Dextromethorphan HBr	62.5	Long acting cough	Novartis
Gas- X	Simethicone	10	Anti Gas	Novartis
Sudafed PE	Phenylephrine HCl	12.5	Decongestant	Pfizer
Benadryl	Diphenhydramine HCl	3/3	Anti histaminic	Pfizer
Chlorseptic	Benzocaine: Menthol	-	Chloraseptic relief strips	Prestige
Suppress	Dextromethorphan	2.5	cough	Innozen
Suppress	Menthol	2/30	Cough	Innozen
Orazel	Menthol/ Pectin	-	Cough and cold	Del
Listerine	Cool mint	-	Antiseptic mouth wash	Pfizer
Little colds	Pectin	-	Sore throat	Prestige brands
Eclipse	Sugar free mints	-	Chewing gum, Breath mint	Wringley's
Donepzil	DonepzilHCl	5/10	Alzheimer's	Labtec GmbH
Ondansetron	Ondansetron	4/8	Anti emetic	Labtec GmbH

FUTURE PROSPECTS

In the pharmaceutical industry, great advancements have been made in oral drug delivery technologies. The market has come a long way from the conventional tablets/capsules to modern-day fast disintegrating and rapidly acting tablets/films. Various limitations such as lower bioavailability of oral solid drugs, the inconvenience of administering injections, inaccurate dosing by liquid formulations are keystone which has turned the focus of pharmaceutical companies to develop novel oral dosage forms that eliminate these limitations. Fast dissolving oral thin films are designed to meet most of these challenges. The concept isn't new and several over the counter oral thin films are readily available. Good acceptance from the users and an increasing demand of over the counter oral film products has led to the development of prescription drugs into oral thin films. [7, 15]

This emerging area is gaining attention from both established and start-up pharmaceutical firms. Companies are utilizing their oral thin film technologies to develop different types of oral thin films (e.g. oral dispersible, sublingual, buccal). In addition to the drugs, several hormones and vaccines are also being formulated into oral thin films with the aim of providing improved patient compliance. Some of the key players in this area include MonoSol Rx, Applied Pharma Research/Labtec GmbH, BioDelivery Sciences and NAL Pharma. Many companies are collaborating with these technology providers and utilizing oral thin films as a lifecycle management tool for their branded drugs that have lost patent in other dosage forms. [9, 22]

There are not many prescriptions for oral thin films currently available in the market; however, the pipeline holds a wider promise. Despite the uncertainties related to the development, approval and penetration rate, the market is likely to witness stable growth in the coming decade. According to the clinical and regulatory aspects in the US Food and Drug Administration (US FDA), if the product is bioequivalent to that of the existing oral product the drug, an Abbreviated New Drug Application (ANDA) route is followed. There are no clinical studies associated with this generic approval processes (section 505 (j) of the Food, Drug, and Cosmetic Act). The example of such case would be a comparative bioequivalence between an orally disintegrating tablet (ODT) formulation and orally dissolving film (ODF) product.[15]

However, developed oral film product may exhibit different pharmacokinetic profile compared to the existing marketed product. The ODF is categorized as "new dosage form" and the section 505 (b) (2) approval processes needs to be followed. In this case, a new clinical study would be required. The advantage of new clinical study is that it would award 3 years of marketing exclusivity to the product. Preclinical toxicity studies are not required if the molecule is the same as that of the approved product. Safety, tolerability, and efficacy features are to be demonstrated in such trials. Oral mucosa-irritation testing is carried out in both animal models and humans. The future looks very promising for the film technology in the time to come as new technologies are rapidly introduced to prepare thin films.[4, 8, 11]

CONCLUSION

Oral route always remains the primary drug delivery route because of ease of administration with beneficial release characteristics and better patient compliance. Orodispersible films are the novel revolutionary approach in oral drug delivery systems for all the population groups especially geriatric, pediatric and patients with swallowing difficulties. They are also of great importance during emergency cases such as allergic reactions and asthmatic attacks whenever immediate onset of action is desired. In future, this system will be most acceptable and prescribed due to its great potential of delivering the drug systemically as well as locally with improved patient compliance, rapid onset of action, decreased dosing frequency by avoiding first pass metabolism, improved bioavailability. Based on the present review, it can be concluded that delivery of drug into an elegant, stable and effective orodispersible film may bridges the gap between solid and liquid dosage forms.

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