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Overview "A Novel Approach of Fast Dissolving Films and Their Patients"

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Abstract: Recently, fast-dissolving drug delivery systems have started gaining fame and acceptance as new drug delivery systems, which aim to enhance safety and efficacy of a drug molecule by formulating it into a conventional oral dosage formfor administration and to achieve better patient compliance. Some companies introduced more robust forms of fast-dissolving drug delivery the film is placed on the top or the floor of the tongue. When put on the tongue, this film dissolves instantaneously, releasing the drug which dissolves in the saliva. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such case is enhancing drug bioavailability, No risk of chocking, Provide good mouth feel. Fast dissolving drug delivery system to overcome this problemdifficulty in swallowing tablets/capsules etc. This review article overview the advancement in the oral dosage forms, application, formulation consideration, method of preparation, evaluation, marketed product and patented technologies of oral fast disintegrating films.

Key words: Fast Dissolving Film · Low Dose · High Solubility · High Permeability · Patient Compliance

INTRODUCTION

Oral route is the most preferred route of administration for systemic effect. About 60% of all the formulations are solid dosage form. Tablet is the most preferred dosage form due to ease of transportation, manufacturing and more patient compliance [1]. Generally geriatric, pediatric and bedridden patient experience difficulties in swallowing the conventional oral dosage form. To overcome this problem a novel formulation was developed i.e. oral fast dissolving films.

Fast dissolving films (FDF), a type of oral drug delivery system for the oral delivery of the drug, was developed based on the technology of the transdermal patch. This delivery system consists of a thin film, which is simply placed on the patient's tongue or mucosal tissue, instantly wet by saliva; the film rapidly dissolves**.** Then it rapidly disintegrates and dissolves to release the medication for oralmucosal absorption [2, 3]. This fast dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to themoistoral environment.

FDF is prepared using hydrophilic polymer that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via buccal mucosa [4].

The fast dissolving drug delivery system are specially designed for the drugs which have extensive first pass metabolism and have low dose, for the enhancement of bioavailability [5].

Definition of FDF: Fast dissolving films are most advance form of solid dosage form due to its flexibility. It improve efficacy of Active pharmaceutical ingredient (API) dissolving in the short duration oral cavity after the contact with less amount of saliva as compared to dissolving tablet.

Fig. 1: Fast dissolving oral film

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Special feature[6]:

- Available in various size and shape
- Thin elegant film
- Un-obstructive
- Fast disintegration or dissolution
- Rapid release

Advantage [3-8]:

- No risk of chocking
- Convenient dosing or accurate dosing
- No need of water to swallow or chew
- Small size for improved patient compliance
- Rapid onset of action
- Ease of handling and transportation
- Improve bioavailability for certain therapeutic ingredient.
- Enhanced stability
- Taste masking

Disadvantages:

- 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 products stability and safety
- High dose cannot be incorporated into the oral film.

Development of Oral Solid Dosage Form: Various stages of development of the of oral solid dosage formulation [1].

Overview of Oral Mucosa: The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Belowthis lies a basement membrane, a lamina propria followedby the submucosa as the innermost layer. The epitheliumis similar to stratified squamous epithelia found in the restof the body in that it has a mitotically active basal celllayer, advancing through a number of differentiatingintermediate layers to the superficial layers, where cellsare shed from the surface of the epithelium [8].

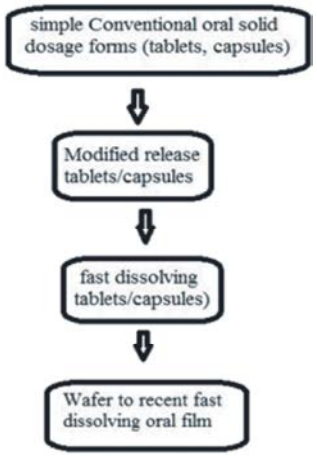

Fig. 2: Development of oral solid Dosage form

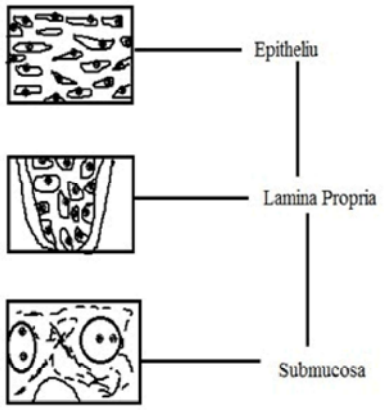

Fig. 3: Various layers of oral mucosa

Comparison Between Fast Dissolving Films (Fdf) and Fast Dissolving Tablets [9]

Fast Dissolving Film	Fast Dissolving Tablet
Large surface area gives greater dissolution.	Less surface area gives less dissolution than FDF.
Fast dissolving films are flexible and durable.	Fast dissolving tablet are brittle and less durable than FDF.
Only low dose can be incorporated in formulation	High dose can also be incorporated in formulation
Fast dissolving films are of thickness 0.015-.05 inches.	Fast dissolving tablet are of same size of convention tablet
Patient compliance is more	Patient compliance is less than FDF

Formulation Consideration: The area of drug loaded FDF should be between 1-20cm^2. The drug can be loaded up to a single dose of 30mg.

All excipientused in the fast dissolving film should be generally regarded as safe (GRAS-listed) and authorized for use in oral strip. Formulation considerations have been reported as important factors which affected mechanicalproperties of the films .[11].

A typical composition contain following

S. No.	INGREDIENTS	AMOUNT (w/w)
1.	Drug	1-30%
2.	Film forming polymer	40-50%
3.	Plasticizer	0-20%
4.	Saliva stimulating agent	2-6%
5.	Sweetening agent	3-6%
6.	Flavoring agent	q.s.
7.	Surfactant	q.s.
8.	Colors, Filler	q.s.

Active Pharmaceutical Ingredient: A distinctive composition of the film contains 1-30%w/w of the active pharmaceutical ingredient. Always uselow dose active pharmaceutical ingredients used because high dose of drug are difficult to incorporate in fast dissolving film micronized API is useful become it enhance the texture of film and provide improved dissolution and uniformity in the fast dissolving film. A number of drugs can be used as fast dissolving oral film [1, 2, 12].

Below List of few drug that can be incorporated in fast dissolving film [9, 13]

Drug	Dose	Therapeutic action
Azatidine Maleate	1mg	Anti histaminic
Nicotine	2mg	Smoking cessation
Loperamide	2mg	Anti diarroheal
Ondensetron	2.5mg	Anti emetic
Triplodine hydrochloride	2.5mg	Anti histaminic
Zolmitritpan	2.5mg	Anti migraine
Salbutamol	4mg	Anti histaminic
Chlorpheniramine Maleate	4mg	Anti allergic
Cetrizine	5-10mg	Anti histaminic
Acrivastine	8mg	Anti histaminic
Loratidine	10mg	Anti histaminic
Omiprazole	10-20mg	Proton pump inhibitor
Famotidine	10mg	Antacid
Ketoprofen	12.5mg	Analgesic
Dicyclomine hydrochloride	25mg	Muscle relaxant
Diphenhydramine hydrochloride	25mg	Anti allergic
Sumatriptan succinate	35-70mg	Anti migraine

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. These polymers are mostly attracted considerable attention by medical and neutraceuticals industry. 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 [14].

Ideal Property of Film Forming Polymer:

- It should be non-toxic and non irritant.
- Polymer must be hydrophilic.
- It should have excellent film forming capacity.
- It should have good wetting and spread ability property.
- Polymer should be readily available & should not be very expensive.
- Polymer should have low molecular weight.
- It should have sufficient shelf-life.
- Polymer must be tasteless, colorless.
- It should not cause any secondary infection in oral mucosa.
- It should exhibit adequate peel, shear and tensile strengths.

Currently, both natural & synthetic polymers are used for the preparation of fast dissolving film. Now a day's various natural & synthetic polymers are available in preparation of fast dissolving film [1, 2, 6]

Polymers used in preparation of fast dissolving film [15]

S.No.	Natural polymer	Synthetic polymer
1	Pullulan	Hydroxypropylmethyl cellulose
2	Starch gelatin	Polyvinyl pyrrolidone
3	Pectin	Polyvinyl alcohol
4	Sodium alginate	Carboxy methyl cellulose
5	Maltodextrin	Poly ethylene oxide
6	Polymerized rosin	Kollicoat
7	Lycoat NG 73	Hydroxypropyl cellulose
8	Xanthan	Hydroxyl ethyl cellulose

Various Propertiesoffew Films Forming Polymer Are Listed below [2, 11]

S. No.	Hydroxy propyl methyl cellulose	Gelatin	Pullulan	Kollicoat	Starch and modified starch
Molecular weight	10,000-1,500,000	15,000-250,000	8000-2,000,000	About 45000	50,000-1,60,000
Solubility	Soluble in cold water, insoluble in chloroform, ethanol.	Soluble in glycerin, acid and alkali -Swell in water.	It is soluble in hot as well as in cold water.	≥50% in water	Starch is insoluble in cold water and ethanol. It swells in water by about 5 to 10% at 37°c.
Film forming ability	It has film forming capacity (2-20%w/w concentration).	Very good film forming ability	It has high adhesion and film forming ability	Its provides good film forming properties	Modified starch have a property to form fast dissolving film
Melting point	190-200ºC	_	107°C	_	250ºC
pH	5-8	3.8-6.0	5-7	6.7	_

Plasticizers: Plasticizer is a very important ingredient of oral strip formulation. It helps to improve the flexibility and reduce the brittleness of the fast dissolving film and by addition of Plasticizers, tensile strength and elongation can be improved. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of oral strip [1, 16].

Sweetening Agent: -Sweeteners have become the essential part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Both natural and artificial sweeteners are used in the formulation to improve the palatability of the fast dissolving film. Generally sweeteners are used in the formulation in concentration of 3-6%w/w, either alone or in combination [2, 17].

Saliva Stimulating Agent: The rationale of employing saliva stimulating agents is to increase the rate of production of saliva that would be aid in the faster disintegration of the fast dissolving film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants, like- citric acid, malic acid, lactic acid, ascorbic acid etc. These are used alone or in combination between concentration 2 to 6%w/w of the film Sweeteners also act & as saliva stimulating agent [3, 6, 18].

Surfactant: Surfactant are used as a solubilizing or wetting or dispersing agent so that the film gets dissolve within seconds and release the active agent instantly. Several number of surfactantare used in oral strip. One of the most important surfactant is poloxamer 407 that is used as solubilizing, wetting and dispersing agent [11, 19].

Flavoring Agent: Selection of flavor is depending on which type of drug is to be incorporated in the formulation. The recognition of the oral disintegrating/ dissolving formulation by an individual depend on the initial flavor quality which is observed in the first few seconds after the product has been consumed and the after taste of formulation lasts for at least 10 min. The amount of flavor required to mask the taste depend on the flavor type and its strength. Flavoring agent is used in the formulation in concentration of 10%w/w [12, 20].

Coloring Agent: FD & C approved coloring agent is incorporated in fast dissolving film. Generally coloring agent is not exceeding concentration a level of 1%w/w in fast dissolving film. mainly titanium dioxide is used in the formulation [1, 2, 21].

Type of agent used for preparation of fast dissolving film [2, 11, 22, 23]

Plasticizers	Sweeting agent	Saliva stimulantingagent	Surfactant	flavoring agent	Coloring agent
Glycerol	Sorbitol	Citric acid	Polaxamer 407	Pippermint oil	Titanium dioxide
Propylene glycol	Sucrose	Malic acid	Sodium laurylesufate	Cinnamon oil	Sunset yellow
Polyethylene glycol 400,200,600	Cyclamate	Lactic acid	Tweens	Menthol	
	Erosin red				
Dimethyl, Dicetyl, dibutyle Phthalate	Aspartmate	Ascorbic acid	Spans		
	Orange oil				
	Melochite green				
Triacetrin	Neotame	Tatric acid	Benzalkonium chloride	Lemon oil	
Castor oil	Saccharin			Chloroform water	
Citrate ether	Mannitol				
Try ethyle citrate	Acesulfame–K				

Methods of Preparation of FDF: There are following methods which can be used for preparation of fast dissolving film such as:

- Solvent casting method
- Semisolid casting method
- Hot melt extrusion
- Solid dispersion extrusion
- Rolling method [4, 6, 9].

Solvent Casting Method: In this method, the water soluble polymers are dissolved in suitable solvent and the drug along with other excipients is dissolved in suitable solvent. Then both solutions are mixed and stirred and finally casted into the Petri plate and dried.

Polymer dissolved in solvent + Drug & excipient dissolved in suitable

To form solution ⇓ solvent

Both solution are mixed with rapid stirring

⇓

Homogenous solution is then spread on flat surface

Dried

⇓

Film formed [9, 24]

Advantage:

- Great uniformity of thickness & great clarity than extrusion.
- Films have fine gloss & freedom from defect such a die lines.
- Films have more flexibility & better physical properties.

Disadvantage:

- The polymer must be soluble in a volatile solvent or water.
- The stable solution with reasonable minimum solid content & viscosity should be formed.

Semisolid Casting Method:

Solution of water soluble film forming polymer is prepared

⇓

Resulting solution is added to a solution of acid insoluble polymer (*E.g.* cellulose acetate phthalate, cellulose acetate butyrate)

⇓

Appropriate amount of plasticizer is added to obtained gel mass

⇓

Gel mass is casted into the films or ribbons using heat controlled drums

⇓

The thickness of the film should be about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4 [17, 18].

Solid Dispersion Extrusion: The term solid dispersions refer to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers.

⇓

Drug is dissolved in a suitable liquid solvent

⇓

Incorporated solution into the melt of polyethylene glycol, below 70ºC

⇓

Solid dispersions are shaped into the films by means of dies[16, 25]

Hot Melt Extrusion:

The drug is mixed with carriers in solid form

⇓

Extruder having heaters melts the mixture

⇓

Finally the melted mixture is shaped in films by the dies [1, 14, 15].

Advantages:

- Fewer operation units
- Better content uniformity
- An anhydrous process

Rolling Method: A suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and gives desired shape and size [2, 10, 25].

Quality Control Test For Fast Dissolving Film

Morphology Study: The morphological study of oral strip is done by the scanning electron microscopy (SEM) at a definite magnification. Study refers the differences between upper and lower side of the films. It also helps in determination of thedistribution of API [26].

Weight Variations: Weight variation is measured by individually weighting randomly selected 10 films. The average weight should not differ significantly from the average weight [27].

Thickness: The thickness of film is determined by micrometer screw gauge at 5 different points of the film i.e. central and the four corners and means thickness is calculated. For measurement of Uniformity of thickness, 5 film are randomly selected and thickness is measured on location of each formulation Maximum variation in the thickness of the films should be less than 5% and mean±S. Dis calculated [6, 28].

Surface pH: The surfacepH of oral strip is calculated in order to examine the risk of any adverse effect *in vivo.* Since acidic or alkaline pH may cause irritation in the oral mucosa, it is determine to maintain the surface pH as close to neutral aspossible. The surface pH of oral strip isdetermined by combined pH electrode [10, 29].

Dryness Test/Track Tests: About eight stage of film drying process have been identified and they are set-to-touch, dust free, track free, dry to touch, dry hard, dry through, dry-to-recoat and dry print free. The details of evaluation of this parameter can be checked tack is the tenacity with which the film adheres to accessory which contact with the strip [1, 30].

Tensile Strength: Tensile strength of film is determinedby applying the maximum stress to a point tillthe oral film breaks. It is calculated by the applied load at rupture divided by the cross section area of the oral film as given in the equation below [3, 31].

$$\text{Tensile strength} = \frac{\text{Load at break}}{\text{Strip break} \times \text{Strip Width}}$$

Percentage Elongation: Percentage elongation is determined by noting the distance travelled by pointer before breaking of the film on the graph paper. Generally elongation of oral strip increase as the plasticizer content increases [2, 32].

$$\% \text{ Elongation} = \frac{L \times 100}{L^{\circ}}$$

L = Incerese in the length of film,
L° = Initial length of film

Folding Endurance: Folding endurance is measured by manualrepeated foldingof film at same place till it broke. The number of time the film is folded without breakingis known as the folding endurance value [1, 33].

Tear Resistance: The maximum force required to tear the film is recorded as the tear resistance Value. It is expressed in Newton or (pounds –force) [2, 34, 35].

Transparency: The measurement of the oral film transparency can be determined byusing a simple UV spectrophotometer. Cut the film sample into rectangles and placed on the internal side of the spectrophotometer cell. Now determine the transmittance of the film at 600 nm. The transparency of film was calculated as follows [1, 35, 36].

$$\text{Transparency} = (\log T600)/b = - \in C$$

where
T_{600} = Transmittance,
b = Film thickness
C = Concentration

Young's Modulus: Young's modulus is used to determine the stiffness of oral film. It is represented as the ratio of applied stress over strain in the region of elastic deformation. It is calculated as follows: [2, 4, 36, 37, 38].

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

Assay/drug Content and Content Uniformity: Assay, drug content and drug content uniformity is determined by any standard assay method which is described for the particular API in any standard pharmacopoeia. Limit of content uniformity is 85-115% [40, 41].

Disintegration Time: The disintegration time limit is of 30sec or less for orally disintegrating tablets, asdescribed in CDER guideline and can be applied to fast dissolving oral film. No official guideline is available for oral fast dissolvingfilms. Pharmacopoeial disintegrating test apparatusmay be used for this study. Typical disintegration time for film is 5-30 sec. [42, 43, 44].

***In-vitro* Dissolution Test:** *In-vitro* Dissolution study can be performed using the paddle or basket apparatusas describedin the pharmacopoeia. The volume of dissolution medium will essentially be selectedas per as the sink condition and highest dose of the API. Mainly paddle type dissolution apparatus is used for the dissolution test of oral strip because sometimes the dissolution test can be difficult due to the tendency of the strip to float onto the dissolution medium [45, 46, 47].

Stability Testing: Stability measurement is done by storing the of oral strip were stored under controlled conditions of 25ºC/60%RH as well as 40°C/75% over a period of 12 months in stability chamber according to the ICH guideline [48, 49].

During storage period various evaluating parameter like thickness, morphological properties, tensile strength, water content and dissolution behavior are checked [50, 51, 52].

Patented Product of Fast Dissolving Film [10] List of some marketed products available as mouth dissolving film

Product	Manufacturer/Distributor	API	Use
Listerine	Pfizer	Cool mint	Mouth freshenars
Triaminic	Novartis	Dextromethorphan HBr	
Suppress®	InnoZen®, Inc	Menthol	Cough suppressants
Chloraseptic	Prestige	Benzocaine Menthol	
Gas-X	Novartis	Simethicone	Anti Flatuating
Theraflu	Novartis	Dextromethorphan HBr	Anti allergic
Ondansetron ODF	Setofilm	BioalliancePharma	Anticancer
Ondansetron ODF	Zuplenz(R)	Monosol Rx	Anticancer
Donepezil film	Donepezil Rapidfilm	Labtec	Alzheimer's disease
Sudafed PE	Wolters Kluwer Health Inc.	Phenyleprine	Relieving Congestion
Klonopin Wafer	Solvay Pharmceuticals	Clonazepam	Treatment of anxiety

Impact in industry: Rotavirus vaccine is prepared in United States by Johns Hopkins University in 2006. Rotavirus vaccine is a room temperature stable quick-dissolving oral thin film delivery system for vaccines that will make vaccinations almost as simple as freshening your breath. This delivery system exhibits many advantages not available in current products. The first of this kind of oral strips were developed by the major pharmaceutical company Pfizer who named it as Listerine® pocket packs™ and were used for mouth freshening [2, 6].

Fast dissolving products has grown rapidly from sales in 2007 of about $850 million & $2billion in near future according to technology catalysts.[11, 51, 52, 53]

CONCLUSION

Fast dissolving films have gained popularity because of better patient compliance, rapid onset of action, the drug is directly absorbed into systemic circulation. Oral films have several advantages overthe conventional dosage forms. So they are of greatimportance during the emergency conditionlike: allergy, Short term spasm and asthma a wheneverimmediate onset of action is desired.

REFERENCES

1. Siddiquinehal, M.D., G. Garg and P.A. Sharma, 2011. Short review on A novel approach in oral fast dissolving drug delivery system and their patents. Advances in Biological Research, pp: 291-303.
2. Dixit, R.P. and S.P. Puthli, 2009. Oral strip technology: Overview and future potential, Journal of Controlled Release., 139: 94-107.
3. Vollmer, U. and P. Galfetti, 2006. Rapid Film: Oral Thin Films as an Innovative Drug Delivery System and Dosage Form. Drug Development Report, pp: 1-5.
4. Mahajan, A., N. Chhabra and G. Agarwal, 2011. Formulation and Characterization of Fast Dissolving Buccal film: A Review; Der Pharmacia Sinica., 3(1): 152-165.
5. Suresh, B., D. Halloran and L. James, 2006. Quick Dissolving Films: A Novel Approach to Drug Delivery. Drug Development Technology., pp: 1-7.
6. Gavaskar, B., S.V. Kumar, G. Sharan and Y. Madhusudan, 2010. Overview on Fast Dissolving Films. International Journal of Pharmacy and Pharmaceutical Sciences, 3(2): 29-33.
7. Cilurzo, F., P. Paola Minghetti, A. Como and L. Montanari, 2010. MaltodextrinFasmaltodextrin Fast Dissolving Film: A Feasibility Study. AAPS Journal, 11: 4.
8. Singh, P., K. ChauhanIti, M. Verma, Yasir Mohd, A. Khan, Sharma and N. Gupta, 2011. Orally disintegrating tablets : formulation, preparation techniques and evaluation Nagar Journal of Applied Pharmaceutical Science, 1(4): 35-45.
9. Dhere, P.M. and S.L. Patwekar, 2011. Review on preparation and evaluation of oral disintegrating films IJPT, 3(4): 1572-1585.
10. Gauri, S. and G. Kumar, 2012. Fast dissolving drug delivery and its technologies, The pharma Innovation, 1(2): 34-39.
11. Aggarwal, J. and G. Singh, 2011. Fast Dissolving Film: A Noval Approach to oral drug delivery. International Research Journal of Pharmacy, 2: 69-74.
12. Kalyan, S. and M. Bansal, 2012. Recent Trends in the Development of Oral dissolving Film, International Journal of Pharm Tech Research, 4(2): 725-733.
13. Coppens, K.A., M.J. Hall, S.A. Mitchell and M.D. Read, 2005. Hypromellose, Ethyl Cellulose and Polyethylene oxide used in Hot Melt Extrusion. Pharmaceutical Technology, pp: 1-5.

14. Arunachalam, A., M. Karthikeyan, S. Ashutoshkumar and K. Kishore, 2010. Fast dissolving drug delivery system: a review, Journal of Global Trends in Pharmaceutical Sciences, 1(1): 92-110.
15. Nagar, P. and Y. Chauhaniti, 2011. AsirMohd, Insights into Polymers: Film Formers in Mouth Dissolving Films, Drug Invention Today, 3(12): 280-289.
16. Frey, 2006. Film strips and pharmaceuticals. Pharmaceutical Manufacturing and Packaging Resourcer, 4: 92-93.
17. Saurabh, R., R. Malviya and P.K. Sarma, 2011. Trend in Buccal Film: Formulation Characteristics, Recent Studies And Patents. European Journal of Applied Sciences, 3(3): 93-101.
18. Vondrak, B., 2008. Barnhart, Scott. Dissolvable Films: A Novel Approach to Drug Delivery. Drug Development Technology, pp: 1-5.
19. Suresh, B.B., H. David and L.O. James, 2003. Quick Dissolving film: A Novel Approach to Drug. Oral Film Technology, 2(3): 1-6.
20. Chien, M.J., G. Tirol, C. Chien and R. Schmitt, 2006. Film Forming Polymers in Oral Films. Poster Presented at the 2006 Annual Meeting and Exposition of the American Association of Pharmaceutical Scientist, AAPS, pp: 1-5.
21. Cilurzo, F., P. Minghetti, A. Como and L. Montanari, 2005. Feasibility Study of Fast Dissolving Containing Piroxicam. AAPS Journal, pp: 50-54.
22. Fulzele SV, P.M. Satturwar and A.K. Dorle, 2002. Polymerised rosin: Novel Film Forming Polymer for Drug Delivery. International Journal of Pharmacy, 249: 175-184.
23. Wale, A. and P.J. Weller, 1994. Handbook of pharmaceutical Excipient. 2nd edition.; 24, 27, 352, 448.
24. Chapdelaine, A.H., D.J. Zyck and M.R. Dzija, 2004. Edible Film Formulations Containing Maltodextrin. US Patent. May25, US Patent, 6740332.
25. Patel, A.R., D.S. Prajapati and J.A. Raval, 2010. Fast dissolving films (fdfs) as a newer venture in fast dissolving dosage forms. International Journal of Drug Development & Research., 2(2): 233-246.
26. Koland, M., V. Sandeep and N. Charyulu, 2010. Fast Dissolving Sublingual Films of Ondansetron hydrochloride: Effect of Additives on *in-vitro* Drug Release and Mucosal Permeation. Journal of Young Pharmacist, 2(3): 216-222.
27. Mahesh, A., N. Shastri and M. Sadanandam, 2010. Development of Tastes Masked Fast Disintegrating Films of LevocetirizineDihydrochloride for Oral Use. Current Drug Delivery, 1(7): 21-27.
28. Kulkarni, A.S., H.A. Deokule, M.S. Mane and D.M. Ghadge, 2010. Exploration of Different Polymers for Use in the Formulation of Oral Fast Dissolving Strips. Journal of Current Pharmaceutical Research, 2(1): 33-35.
29. Kunte, S. and P. Tandale, 2010. Fast Dissolving Strips: A Novel Approach for the Delivery of Verapamil. Journal of Pharmacy and Bioallied Sciences, 2(4): 325-328.
30. Shimoda, H., K. Taniguchi and M. Nishimura, 2009. Preparation of a Fast Dissolving Oral Thin Film Containing Dexamethasone: A Possible Application to Antiemesisduring Cancer Chemotheraphy. European Journal of Pharmaceutics and Biopharmaceutics, 73: 361-365.
31. Patel, R., N. Shardul, J. Patel and A. Baria, 2009. Formulation Development and Evaluation of Mouth Melting film of Ondansetron. Archives of Pharmacal Science & Research, 1: 213-217.
32. Nishimura, M., 2009. *In-vitro* and *In-vivo* characteristics of Prochlorperazine disintegrating film. International Journal of Pharmaceutical Technology, 368: 98-102.
33. Sumitha, C.H., S.N. Karuna, B. Divya, K. Madhavi, V. Kumar, M. Varma and N.N. Charbe, 2009. Taste Masking of Ondansetron Hydrochloride by Polymer Carrier System and Formulation of Rapid –Disintegrating Films. International Journal of Chemistry Research, 68: 90-102.
34. Cilurzo, F., I.E. Cupone, P. Minghetti, S. Buratti and L. Montanari, 2006. Maltodextrin Fast Dissolving Film Containing Nicotin: a feasibility study. APPS Journal, pp: 1-11.
35. Dinge, A. and M. Nagarsenkar, 2008. Formulation and Evaluation of Fast Dissolving Film for Delivery of Triclosan to the Oral Cavity. AAPS Pharmaceutical Science Technology, 9(2): 10.
36. Francesco, C., I.E. Cupone, P. Minghetti, S. Buratti, F. Selmin and G.M. Chiara, 2008. Nicotine Fast Dissolving Films Made of Maltodextrins: A Feasibility Study; European Journal of Pharmaceutics andBiopharmaceutics, 70(3): 895-900.
37. Mashru, R.C., V.B. Sutariya, M.G. Sankalia and P.P. Parikh, 2005. Development and Evaluation of Fast-Dissolving Film of Salbutamol Sulphate. Drug Development Industrial Pharmacy, 1(1): 25-34.
38. Cilurzo, F., P. Minghetti, A. Como and L. Montanari, 2005. Feasibility Study of Fast Dissolving Film Containing Piroxicam. AAPS Journal, 7(1): 52.

39. Ghorwade, V.K., A.K. Patil, S.K. Patil, K. Srikonda, R. Kotagiri and P. Patel, 2011. Development and evaluation of fast-dissolving film of Montelukastsodium. WJMPBS, 1(1): 06-12.
40. Bhyan, B. and S. Jangra, 2012. Formulation and evaluation of fast dissolving sublingual films of RizatriptanBenzoate. International Journal of Drug Development & Research, 4(1):
41. Murata, Y., T. Isobe, K. Kofuji, N. Nishida and R. Kamagu chi, 2010. Preparation of Fast Dissolving Films for Oral Dosage from Natural Polysaccharides Materials, 3: 4291-4299.
42. Shelke, P.V., A.S. Dumbare, M.V. Gadhave, S.L. Jadhav, A.A. Sonawane and D.D. Gaikwad, 2012. Formulation and evaluation of rapidly disintegrating film of amlodipine besylate. JDDT, 2(2): 72-75.
43. Brenda Nevidjon, R.N. and F.A.A.N. MSN, 2010. Rekha Chaudhary. MD Controlling Emesis: Evolving Challenges. Novel Strategies, 8(2): 1-10.
44. Mahajan A. Formulation and Evaluation, 2012. Fast dissolving Buccal films of Sertraline. International Journal of Drug Development & Research, 4(1): 220-226.
45. Choudhary, R.D., V.A. Patel, U.K. Chhalotiya, V.H. Patel and J.A. Kundawala, 2012. Natural polysaccharides as film former: a feasibility study for development of rapid dissolving films of ondansetronhydrochloride. Int J. Pharm Pharm Sci., 4(3): 78-85.
46. Javier, O. Morales and T. Jason Mcconville, 2011. Manufacture and characterization of mucoadhesivebuccal films European Journal of Pharmaceutics and Biopharmaceutics., 77: 187-199.
47. Aksungura, P., A. Sungurb, ¨ US. Nalc, A.B. I·skitd, A.C. Squiere and S. Senela, 2004. Chitosan delivery systems for the treatment of oral mucositis: *in vitro* and *in vivo* studies. Journal of Controlled Release., 98: 269-279.
48. Watanabe, S., K. Suemaru, T. Yamaguchi, N. Hidaka and S.M. Akanaka, 2009. Hiroaki Araki Effect of oral mucosal adhesive films containing ginsenoside Rb1 on 5-fluorouracil-induced oral mucositis in hamsters. European Journal of Pharmacology, 616: 281-286.
49. Parmar, D., U. Dr. Patel, Bbhimani, A. Tripathi, D. Daslaniya and G. Patel, 2012. Orally fast dissolving films as dominant dosage Form for quick release. International Journal of Pharmaceutical Research And Bio-science, 1(3): 27-41.
50. Mital S. Panchal, H. Patel, A. Bagada and K.R. Vadalia, 2012. Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers.International Journal of Pharmaceutical Research and Allied Sciences, 1(3): 60-72.
51. Malke M.S. Shidhaye and V.J. Kadam., 2007. Formulation and Evaluation of Oxacarbazine Fast Dissolve Tablet. Indian Journal of Pharmaceutical Science, pp: 64-67.
52. Arya, A., A. Chandra, V. Sharma and K. Pathak, 2010. Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form. International Journal of Chem Tech Research, 2(1): 576-583.
53. Tiwari, G., A. Pathak, R. Goyal, C.S. Jadaun, R. Shivhare and K. Sharma, 2012. Fast dissolving tablets: a novel approach to drug. Delivery World Journal of Pharmaceutical Research, 1(3): 478-499.