International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 5(3): May-June 2015

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Review Article……!!!

Received: 03-06-2015; Revised: 08-06-2015; Accepted: 09-06-2015

A SHORT REVIEW: AN INNOVATIVE DRUG DELIVERY SYSTEM OF FAST DISSOLVING ORAL FILMS

Pranjali K Halnor*, Sheetal B Gondkar, Ravindranath B Saudagar

KCT'S R.G. Sapkal College of Pharmacy, Anjaneri, Nashik-422 213, Maharashtra, India.

Keywords:

Fast dissolving drug delivery, oral thin film, polymers, solvent casting technique

For Correspondence:

Pranjali K Halnor

KCT'S R.G. Sapkal College of Pharmacy, Anjaneri, Nashik-422 213, Maharashtra, India.

E-mail:

pkhalnor@gmail.com

ABSTRACT

Fast-dissolving drug-delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience difficulties swallowing traditional oral solid dosage forms. The oral thin-film technology is still in the beginning stages and has bright future ahead because it fulfill all the need of patients. Eventually, film formulations having drug/s will be commercially launched using the oral film technology. Fast-dissolving oral thin film is a solid dosage form, which disintegrate or dissolve within 1 min when placed in the mouth without drinking of water or chewing. Oral film includes various ingredients for its formulation which includes polymers, active pharmaceutical ingredient, film stabilizing agents, sweeteners, flavors, colors, saliva stimulating agents, preservatives, surfactants etc. but the first and far most a very essential ingredient which helps in film formation is a Polymer. Fast dissolving Film is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via dissolution when contact with liquid is made. Water-soluble polymers are used as film formers for fast dissolving films. The water-soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the films. Fast-dissolving oral thin film offer fast, accurate dosing in a safe, efficacious format that is convenient and portable, without the need for water or measuring devices.

INTRODUCTION

Mouth dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed based on the technology of the transdermal patch. The delivery system consists of a very thin oral strip, which is simply placed on the patient's 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 and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. Despite of so much of advancements in various delivery system developed for administration of various drugs through different routes such as oral, parental, transdermal and nasal etc., the oral route is considered as the preferred route of administration which includes painless, ease of administration, patient friendly and so on. Several new technologies had been developed for oral delivery is being available to address to improve the patient compliance. Fast dissolving drug delivery system (FDDS) is gaining popularity in pharmaceutical companies as they are new drug delivery technique in order to provide the patient with medicine without obstacles in swallowing. FDDS include tablets and films. Fast dissolving tablets are designed in such a way that they disintegrate and then swallowed without the need of water as compared to other conventional dosage form. [8]

Ideal Characteristics of Fast Dissolving Drug Delivery System[12]

- It should have an acceptable taste.
- It should give a pleasing mouth feel.
- It should be less friable and have good mechanical strength to withstand the post
- Manufacturing handling.
- It should be stable in environmental conditions.
- Subsequent to oral administration, it should leave least or no residue in mouth.
- It should quickly dissolve to release drug
- Instantaneously in mouth.
- It should be compatible with the other ingredients.

Special features of mouth dissolving films5

• Thin elegant film

• Available in various size and shapes

• Un-obstructive

• Excellent Muco-adhesion

• Fast disintegration

Advantages of oral dissolving film (ODF) over fast dissolving tablet (FDT) [29, 35]

- Accessibility of larger surface area that leads to quickly disintegrate and dissolution in the oral cavity within seconds.
- ODF is flexible so they are not as fragile and need not any kind of special package for
- Protection during transportation and storage as compared to FDT.
- No need of water has led to better satisfactoriness amongst the dysphasic patients.
- No fear of chocking as compared to FDT.
- The large surface area available in the film dosage form allows rapid wettive by saliva then quickly disintegrates and dissolve and absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism and on increase the bioavailability
- The dosage form can be consumed at any place and any time as per convenience of the
- The first pass effect can be avoided, so a reduction in the dose which can lead to reduction in side effects associated with the molecule
- Patients suffering from dysphagia, repeated emesis, hypertension, heart attack, asthma,
- Motion sickness, paralysis and mental disorders prefer this dosage form as they are not capable to swallow large quantities of water.

Disadvantages[29]

- The disadvantage of OTF is that high dose cannot be incorporated into the strip. Hence researchers have proven that the concentration level of active can be improved up to 50 percent; per dose weight. Novartis Consumer Health's Gas-X® thin strip has aloading of 62.5 mg of simethicone per strip 7
- Expensive packaging of oral film

Table 1: Classification of oral thin films

Type /property	Flash release wafer	Muco-adhesive wafer(melt-away)	Muco-adhesive sustained release wafer
Area (cm^2)	2-8	2-7	2-4
Thickness(µm)	20-70	50-100	50-500
Structure	Film: single layer	single or multilayer system	Multilayer system
Excipients	Hydrophilic polymers	Hydrophilic or suspension	Low/non-soluble polymers
Drug phase	Solid, solution, suspension	Solid,solution or suspension	Suspension or solid,solution
Application	Tounge (upper palate)	Gingival or buccal region	Gingival or other region in oral cavity
Dissolution	Maximum 60 seconds	Disintegration in a few minutes, forming gel	Maximum 8-10 hr

Formulation Aspects for Fast Dissolving Films [28]

1) Drug Category

2) Film Forming Polymers

3) Plasticizers

4) Sweetening Agents

5) Saliva Stimulating Agents

6) Cooling Agent

7) Flavoring Agent

8) Coloring Agent

9) Surfactants

10) Stabilizing and thickening agents

1.Drug Category: [12, 13]

This technology has the potential for delivery of variety of APIs. However since the size of the dosage form haslimitation, high dose drugs are difficult to be incorporated in films. Several classes of drugs can be formulated as fast dissolving films including antiulcer, anti-asthmatics, antitussives, expectorants, anti-histaminic, NSAID'S etc.

2. Film Forming Polymers[18]:

Water-soluble polymers are used as film formers as they provide rapid disintegration, good mouth-feel, and mechanical strength to the films. The robustness of the strip depends on the type of polymer and its amount in the formulations. Water-soluble polymers film, adheres to the buccal mucosa and rapidly delivers medication into the systemic circulation. A variety of polymers are available for preparation of films of which pullulan, gelatin and hypromellose are most commonly used. At least 45%w/w of polymer should generally be present based on

the total weight of dry film. Examples of water-soluble polymers include: Pullulan, Gelatin, guar gum, Xanthium gum, Hydroxyl propyl methyl cellulose, Modified starches, Hydroxyl ethyl cellulose etc.

3. Plasticizers[35]:

Plasticizer is a vital ingredient of the oral films. The selection of plasticizer depends upon its compatibility with the polymer and also the type of solvent employed in the casting of film. It helps to improve the flexibility of the film and reduces the brittleness of the film. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. Typically the plasticizers are used in the concentration of 1 20%w/w of dry polymerweight. Examples include: Glycerol, Propylene glycol, Low molecular weight polyethyleneglycols, Citrate derivatives like triacetin, acetyl citrate, and Phthalate derivatives like dimethyl, diethyl, dibutyl derivatives and Castor oil etc.

4. Sweetening agents[27]:

Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Suitable sweeteners include:

(a) Water soluble natural sweetener: xylose, ribose, glucose, sucrose, maltose, steviosideetc.

(b) Water soluble artificial sweetener: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc.

(c) Dipeptide based sweetener: aspartame

5. Saliva stimulating agent[31]: The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster dissolution of the film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them.

6. Cooling agents[34]: Cooling agents like monomethyl succinate can be added to improve the flavor strength and to enhance the mouth-feel effect of the product. Other cooling agents like WS3, WS23 and Utracoll II canalso be used in conjunction with flavors.

7. Flavoring agents[34]: Perception for the flavor changes from individual to individual depending on the ethnicity and liking. It was observed that age plays a significant role in the

taste fondness. Flavoring agents can be selected from synthetic flavor oils, oleo resins, extract derived from various parts of the plantslike leaves, fruits and flowers. Peppermint oil, cinnamon oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence type. The amount of flavor needed to mask the taste depends on the flavor type and its strength.

8. Coloring agents[34]: Pigments such as titanium dioxide or FD&C approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in OS when some of the formulation ingredients or drugsare present in insoluble or suspension form.

9. Surfactants[35]: Surfactants are used as solubilizing or wetting or dispersing agents so that the film gets dissolved within seconds and release active agent immediately. Surfactants also improve the solubility of poorly soluble drugs in fast dissolving buccal films. Some of the commonly used are polaxamer 407, sodiumlauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc.

10. Stabilizing and thickening agents[26]:

The stabilizing and thickening agents are employed to improve the viscosity and consistency of dispersion or solution of the strip preparation solution or suspension before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivatives can be used in the concentration up to 5%w/w as thickening agents and stabilizing agents.

Methods of Manufacturing Fast Dissolving Films [34]

Following are the methods of manufacturing for fast dissolving films. One or combinationof the following process can be used to manufacture the fast dissolving films –

i. Solvent casting method

ii. Semisolid casting method

iii. Hot melt extrusion

iv. Solid dispersion extrusion

v. Rolling method

Generally the solvent casting method is employed for manufacture of strips.

1) Solvent Casting Technique

Fast dissolving films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and

finally casted in to the Petri plate and dried, which is then cut into pieces of the desired size. The properties of the API play a critical role in the selection of a suitable solvent. Water-soluble hydrocolloids used to prepare RDFs include: hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose (HPC), pullulan, sodium alginate, pectin, carboxy methyl cellulose (CMC), polyvinyl alcohol (PVA). Solvents used for the preparation of solution or suspension should ideally be selected from ICH Class 3 solvent list. Specific types of equipment such as rollers are required for pouring the solution on an inert base. The clearance between the roller and the substrate determines the required thickness of the film. The final step, drying the film, removes the solvent and helps to obtain the finished product. Usually, glass, plastic, or Teflon plates are used as an inert base for film casting. When the manufacturing technology is transferred from laboratory scale to production scale, several problems can be encountered. These problems can include the casting of the film, obtaining uniform thickness of the film,and proper drying of the sample. The selection of the proper type of dryer is needed in the final step of drying.Once the films are dried, cutting, stripping, and packaging is done. Suitable size and shapes of films can be cut. The commonly available sizes of films are 3 x 2 cm2 and 2 x 2 cm2

Advantages:

- Better uniformity of thickness and better clarity than extrusion.
- Film has fine gloss and freedom from defects such as die lines.
- Film has more flexibility and better physical properties.
- The preferred finished film thickness is typically 12-100 μm, although various thicknesses are possible to meet API loading and dissolution needs.

Disadvantages:

- The polymer must be soluble in a volatile solvent or water.

2) Semisolid casting

In semisolid casting method, firstly a solution of water soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. Cellulose acetate phthalate, cellulose acetate butyrate), which can be prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

3) Hot melt extrusion

Hot melt extrusion is commonly used to prepare granules, sustained-release tablets, and transdermal and transmucosal drug-delivery systems. In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies. Usually, when designing RDFs, polymers with low molecular weight or viscosity, such as HPMC E5 or pullulan PI.20, are preferred. A combination of various grades of polymers may also be used to achieve desired physical properties. Mixing polymers of high and low viscosity produces a film with good mechanical strength and high drug solubility in the film. The manufacturing process for the wafers in the pharmaceutical industry is divided into different steps.

Generally, the mass is prepared first under the control of temperature and steering speed. Afterwards, the wafers are coated and dried in a drying tunnel, once again the temperature, air circulation and line speed are controlled. Then follows a slitting and in the last step the wafers are punched, pouched and sealed. Other ways of manufacturing oral wafers are spraying process or extrusion, in particular hot-melt extrusion

Advantages:

- Without use of any solvent or water.
- Fewer processing steps.
- Compressibility properties of the API may not be of importance.
- Better alternative for poorly soluble drugs.
- More uniform dispersion because of intense mixing and agitation.
- Less energy compared with high shear methods.

Disadvantages:

- Thermal degradation due to use of high temperature
- Flow properties of the polymer are essential to processing
- Limited number of available polymers
- All excipients must be devoid of water or any other volatile solvent
- Thermal process so drug/polymer stability problem
- Flow properties of the polymer are essential to processing
- Limited number of available polymers

5) Solid dispersion extrusion

The term solid dispersion refers to the dispersion of one or more APIs in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers using methods such as HME. In this method, immiscible components are extruded with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

6) Rolling Method

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water or a mixture of water and alcohol. The film is dried on the rollers and cutted into desired shapes and sizes.

Various Technologies Used in Oral Film Formulation[25]

1. **X-Gel:** X-Gel film Technology developed by Bio-Progress is causing a revolution in the product offerings and manufacturing methods now available to the pharmaceutical industry.
2. **Soluleaves:** This is applied to flavor-release products such as mouth fresheners, confectionery and vitamin products. SOLULEAVES technology can be used to deliver active ingredients to oral cavity efficiently and in a pleasant and easily portable form.
3. **Wafertab:** WAFERTAB is a patented delivery system that uses a unique process to prepare drug-loaded thin films which can be used in topical or oral application. Active ingredients are incorporated into the film after casting.
4. **Foamburst:** FOAMBURST is a new patent granted in September 2004 which is for capsules made of foamed film. Gas is blown into the film during production, resulting in a film with a honeycombed structure. The voids in the film may be gas-filled, empty or filled with other materials to produce specific taste-burst characteristics or to deliver active drugs. The light honeycombed structure results in capsules that dissolve rapidly, causing a melt-in-the mouth sensation.
5. **Micap:** Micap is an option agreement in 2004 to combine its expertise in micro encapsulation technology with the BioProgress water-soluble films. The developments will be aimed at providing new delivery mechanisms for the $1.4bn global market for smoking cessation products (SCPs).

Evaluations parameters[28]:

1) Mechanical properties

Mechanical properties of films are evaluated Instron using a TA.XT2 texture analyzer equipment equipped with a 5kg load cell. Films are held between two clamps positioned

between 3cm. During measurement the strips were pulled at rate of 2mm/sec. The force and elongation were measured when film breaks. Three mechanical properties namely tensile strength, elastic modulus and % elongation are calculated.

a) Tensile strength

Tensile strength is calculated by formula

force at break/ initial cross/sectional area of film in mm2

b) Elastic modulus

Elastic modulus is calculated by formula

Elastic modulus =force at corresponding strain /Cross sectional area (mm2) Corresponding strain

c) % Elongation

It is calculated as =Increase in length/Original length×100

d) Folding endurance

Folding endurance is determined by folding the films of uniform cross sectional area and thickness until it breaks.

2) Morphology study

The morphology of the films is studied using scanning electron microscopy (SEM), at a definite magnification

3) Swelling property

Film swelling studies is conducted using simulated saliva solution. Each film sample is weighed and placed in a pre-weighed stainless steel wire mesh. The mesh containing film sample is submerged into 15ml medium in a plastic container. Increase in the weightof the film was determined at preset time interval until a constant weight was observed20.The degree of swelling was calculated using parameters **wt-w0/wo, wt** is weight of film at time t, and **wo**is weight of film at time zero.

4) Contact angle

Contact angle measurements are performed at room temperature with a goniometer (AB Lorentzen and Wettre, Germany). A drop of double distilled water was placed on the surface of the dry film. Images of the water droplet were recorded within 10 seconds of deposition by means of digital camera. Digital pictures were analyzed by image 1.28v software (NIH, USA)for angle determination. A minimum of five measurements, taken at different positions of the film, was carried out. The contact angle was measured on both sides of the drop and averaged.

5) *In vitro* disintegration time

In vitro disintegration time is determined visually in a glass dish of 25ml distilled water with swirling every 10 sec. The disintegration time is the time when the film starts to break or disintegrates10.

6) In vitro dissolution studies

The *in vitro* dissolution study is carried out in-simulated saliva solution pH 6.4 phosphate buffer using USP paddle apparatus at 37±0.5°C. Samples are withdrawn at regular time interval interval and analyzed by UV-Visible spectrophotometer.

7) Determination of dissolution rate by conductivity method

In the past 5 years several personal care products formulated in quick release film form have entered the marketplace, of which fast-dissolve breath fresheners were first. The fast dissolve oral films completely dissolve in as little as 1 minute. The majority of oral films on the market today contain ionizable components. This work presents a method for high resolution monitoring of the dissolution of fast dissolving oral films by measuring conductivity of the dissolution medium.

Packaging[23]

A variety of packaging options are available for fastdissolving films. Single packaging is mandatory for films, which are pharmaceutical products; an aluminum 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 the 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.

Marketed Films[4,5,6,8]

Table 2. List of marketed fast dissolving films

Brand name	API	Manufacturer/ Distributor	Use
Triaminic	Dextromethorphan HBr	Novartis	Seasonal allergy
Theraflu	Dextromethorphan HBr	Novartis	Long acting cough
Chloraseptic	Benzocaine: Menthol	Prestige	Chloraseptic Relief Strips
Klonopin Wafers	Clonazepam(0.125mg,0.25mg, 0.5mg, 1mg and 2mg)	Solvay Pharmaceuticals	Treatment of Anxiety
Orazel	Menthol/Pectin	Del	cold relief strips
Listerine	Cool mint	Pfizer	Antiseptic mouthwash
Little Colds	Pectin	Prestige brands	Sore throat strips
Chloraseptic	Benzocaine/menthol (3mg/3mg)	Prestige	Sore throat
Donepzil	Donepzil HCL	Labtec GmbH	Alzheimer's disease
Ondansetron	Ondansetron	Labtec GmbH	Antiemetic, nausea and vomiting

CONCLUSION

Fast dissolving oral films have several advantages over the conventional dosage forms. So they are of great importance during the emergency cases such as allergic reactions and asthmatics attacks whenever immediate onset of action is desired.

REFERENCES

1. Vollmer U, Galfetti P. Rapid film: Oral thin films as an innovative drug delivery System and dosageform.Drug Dev. Report. 2006; 64-67.
2. http:// www.apr.ch.Frey.Film Strips and Pharmaceuticals. Pharma Mfg &PackageSource. 2006:92–93.
3. Vondrak B, Barnhart, Scott. Dissolvable Films: Dissolvable Films for Flex Product Format in Drug Delivery.Pharmatech. 2008; 1-5.
4. .Suresh B, Halloran D, James L. Quick dissolving films: A novel approach to drug delivery.
5. Drug.Dev..tech. 2006;1-7. http://www.drugdeliverytech.com
6. .Mashru R.C, Sutariya BC, Parikh PP. Development and evaluation of fast dissolving films of salbutamol sulphate.Drug dev. Ind Pharm. 2005 ;31:25-34.Doi: 10.1081/DDC-200043947
7. Gohel MC, Sharma R, Soniwala MM. Development of taste masked film of Valdecoxib for oral use.Ind j Pharm Sci. 2007;69:318-320.
8. http://www.hughes-medical.com/products/fast-dissolving-film.htm
9. Cilurzo F, Paola M, Andrea C. Maltodextrin Fast –Dissolving Film: A Feasibility Study. Pharma Films.
10. Milano Italy. http://www.tecnova-srl.it/download/film@EUFEPS051.pdf
11. Chien M J, Tirol G, Chien C, Schmitt R.Film forming polymers in oral films. Poster presented at the 2006
12. Annual Meeting and Exposition of the American Association of Pharmaceutical Scientist Oct. 29–Nov.2AAPS. 2006; 1-5.
13. Cilurzo F, Minghetti P, Como A, Montanari L. Feasibility study of fast-dissolving film containing Piroxicam.The AAPS Journal. - ISSN 1550-7416. - 7:S2 (2005). – pp. W4148-W4148. AAPS Annual Meeting and Exposition, Nashville, 2005
14. Bettini R, Antonello A, Mariana M, Borghetti F. Physiochemical and cell adhesion properties of chitosan films prepared from sugar and phosphate containing Solution's. Eu J Pharm and Bio pharm. 2008;68:74-81.Doi : 10.1061/j.ejpb.2007.03.026
15. Jay jock E, Schmitt R, Chein C. Determination of fast dissolve oral film dissolution rate via conductivity. Dow Chemical Company. 2005; 1-4.
16. Saurabh R, Malviya R, Sharma PK. Trends in Buccal Film: Formulation Characteristics,
17. Recent Studies and Patents. European Journal of Applied Sciences, 2011; 3(3):93-101.
18. Priya Y D, Chaudhary Y A, Murthy T E G K, Seshagiri B. Approaches for taste masking of
19. Bitter drugs: a Review. Journal of Advances in Drug Research, 2011;(2): 58-67.
20. Patel A R, Prajapat D S, Raval J A. Fast Dissolving Films (fdfs) As A Newer Venture In
21. Fast Dissolving Dosage Forms. Int.J.Drug Dev. & Res., 2010; 2(2): 232-246.
22. Mishra R, Amin A. Quick API Delivery. Pharmaceutical Technology Europe, pp. 1-5.
23. Coppens K A, Hall M J, Mitchell S A, Read M D. Hypromellose, Ethyl cellulose and Polyethylene oxide used in hot melt extrusion.Pharmaceutical Technology. September 2005; 1-6.
24. http://www.meldexinternational.com/Development/Enabling_Systems/Orally_Dissolving_Films/SOLULEAVES%e2%84%a2/default.aspx?id=1016
25. Peh K.K, Wong CF. Polymeric film as vehicle for buccal delivery: swelling, Mechanical and Bioadhesive properties.J Pharm Pharm Sci.1999; 2:53-61.
26. Bettini R, Antonello A, Mariana M, Borghetti F. Physiochemical and cell adhesion properties of chitosan films prepared from sugar and phosphate containing solutions. Eu J Pharm and Bio pharm. 2008;68:74-81.Doi : 10.1061/j.ejpb.2007.03.026
27. Kalyan S., Bansal M.**,** Recent trends indevelopment of oral dissolving film, International J. PharmTech., 4(2) Res.2012; 729.

28. Sudhakar Y., Kuotsu K., Bandopadhyay A.K., Buccal bioadhesive drug delivery; a promising option for orally less efficient drugs, Journal of Control Release, 114, 2006 15-40.
29. Patil S.L., mahaparale P.R., Sarda R.R., Screening of the polymers for formulation of fast dissolving film; Inventi Rapid: Pharm Tech, Issue 4, Vol. 2012; 1-3
30. Panchal M.S., Patel H., Formulation and evaluation of mouth dissolving film of Ropinirole HCl using pullulan polymers, International journal Pharm Research allied sci.,1 (3), 2012; 60-72.
31. Dixit R P, Puthli S P. Oral strip technology: Overview and future potential, Journal of Control release, 139, 2009; 94–107.
32. Sharma S., Lewis S., Taste Masking Technologies: A Review, International Journal of Pharmacy and Pharmaceutical Sciences; 2, (2), 2010; 6-7.
33. Morales J.O., McConville J.T., European Journal of Pharmaceutics and Biopharmaceutics 77, 2011; 187–199
34. Bala R., Pawar P., Khanna S., Arora S., Orally dissolving strips: A new approach to oral drug delivery system; International journal of Pharmaceutical investigation, 3, (2), April 2013; 67-
35. Amol Pachade,Urvashi Marakana,Development and evaluation of mucoadhesive films of Acyclovir in oral environment-along with model study on Chlorhexidine, Scholars research library,5(6),2013;60-66.
36. Shaffi Khurana, N.V.Satheesh Madhav,Muco-adhesive drug delivery: mechanism and methods of evaluation: Review , International journal of pharma and Bio sciences, issue1, Vol.2;jan-2011.
37. Sonte sushmita, Sedimbi Revathi , formulation and Evaluation of Mucoadhesive Fast Melt-away wafers using selected polymers; Research journal and pharma tech. ,7(2)feb-2014.
38. D.A. Allemandi, Design of novel antifungal mucoadhesive film Part II. Formulation and in vitro biopharmaceutical evaluation; International journal of Pharmaceutics, 336 (2007); 263-268.