International Standard Serial Number (ISSN): 2319-8141
International Journal of Universal Pharmacy and Bio Sciences 7(2): March-April- 2018
INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES
*IMPACT FACTOR 4.018****
*ICV 6.16****
Pharmaceutical Sciences **REVIEW ARTICLE ……!!!**

FAST DISSOLVING FILM: A NOVEL APPROCH TO ORAL DRUG DELIVERY SYSTEM

Riya B Kothari* Dr.K.R.Patel, Dr A.D.Patel
Shri B. M. Shah College of Pharmaceutical Education and Research, 252 Dhansura Road, Modasa, Dist. Aravalli – 383315.

KEYWORDS:

Fast dissolving film , Film forming polymer , Oral drug delivery system , solvent casting method.

For Correspondence:
Riya B Kothari*
Address:
Shri B. M. Shah College of Pharmaceutical Education and Research, 252 Dhansura Road, Modasa, Dist. Aravalli – 383315.

ABSTRACT

Fast dissolving fim is a type of drug delivery system , which is dissolved within 1 min when placedinto mouth without water and chewing. The fast dissolving drug delivery system is suitable for the drugs which undergo high first pass metabolism. It is used for improving bioavailability with reducing dosing frequency to mouth plasma peak levels which is turn minimum adverse effect. Fast dissolving film are formulated using hydrophilic polymers.which is rapidly dissolved on Buccal cavity and tongue . It is manufactured using solvent casting method ,solid dispersion method, rolling method,extrusion method. Fast dissolving films are evaluated for tensile strength, thickness, folding endurances, dissolution. OFDFs are very similar to postage stamp in their shape, size and thickness.

INTRODUCTION:

Oral route is the most commonly used and acceptable drug delivery route among all other delivery routes. Orally disintegrating tablets are available in the market which disintegrates in one to two minutes, whereas FDF are capable to disintegrate within few seconds. FDF consists of a thin film, which is placed on the patient‟s tongue or mucosal tissue, film gets wet by saliva and dissolves rapidly. FDF is useful in paediatric and geriatric patients as they have difficulty in swallowing conventional oral dosage forms resulting in poor patient compliance. To eliminate the drawbacks of fast dissolving tablet a fast dissolving film can be placed. Fast dissolving films are very similar to ultra-thin strip of postage stamp in their shape, size and thickness.

In the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing oral solid dosage forms formulate the fast dissolving tablets by using superdisintigrants and hydrophilic ingredients which has the higher bioavailability, quick action and most patient compliance.

Technology Catalysts forecasts the market for drug products in oral thin film formulations to be valued at $500million in 2007 and could reach $2 billion. FDOF formulations are suitable for cough, cold remedies, sore throat, allergenic conditions, nausea, pain and CNS disorders. Multivitamins, caffeine strips, snoring aid and sleeping aids are also applicable for incorporation in the oral films.

Special features of Fast Dissolving Films

- Thin elegant film
- Fast disintegrating
- Unobstractive
- Various size and shapes
- Have an acceptable taste.
- Good mouth feel.
- Should not leave residue in mouth.
- Rapid release

Advantages:

1 Convenient dosing or accurate.
2 No special set up required for the industry
3 Minimum size for improved patient compliance.
4 Minimal side effects.
5 No risk of chocking.
6 Patent life extension
7 Ease of handling and transportation.
8 No need of water to swallow or chew.
9 Improve bioavailability for certain therapeutic ingredient.
10 Enhanced stability.
11 Lower doses.
12 Rapid onset of action
13 The drug enters the systemic circulation with reduced hepatic fires pass effect.
14 Site specific and local action.
15 Non-invasive.
16 It provides dose removal possibility in emergency situation.
17 Destructive acidic environment

Disadvantages:

1 High dose cannot be incorporated into the oral film.
2 It shows the fragile, granule property.
3 It is hygroscopic in nature so it must be kept in dry places.
4 They require special packaging for the products safety and stability .

COMPOSITION OF THE SYSTEM

- Active pharmaceutical ingredient
- Film forming polymers
- Plasticizer
- Sweetening agent

- Saliva stimulating agent
- Flavoring agent
- Coloring agent

Active pharmaceutical ingredient

Active pharmaceutical substance can be from any class of pharmaceutically active substances that can be administered orally or through the buccal mucosa. E.g antiulcers, antitussive, antihistaminic, antiasthmatics antiepileptic, expectorants, antianginal etc.

The ideal characteristics of a drug to be selected:

1 The drug should have pleasant taste.
2 The ideal characteristics of a drug to be selected
3 The drugs with smaller and moderate molecular weight are preferable.
4 The drug to be incorporated should have low dose less than 40mg.
5 The drug should have stability and solubility in water as well as in saliva.

Film forming polymers

Water-soluble polymers are used as film former polymer. water soluble Polymer provides a quick disintegration, good mouth feel, and mechanical strength to the films. Different polymer like pullulan, gelatin and hypromellose are most commonly used in the preparation of film. And other different water soluble polymer like HPMC E-3 and K-3, Methyl cellulose A-3, A-6 and A-15, carboxmethylcellulosecekol 30, Polyvinylpyrollidone PVP K-90, Pectin, Sodium Alginate, Hdroxypropylcellulose, Polyvinyl alcohol, Maltodextrins and EUDRAGITRD10,Polymerized rosin is a novel film forming polymer. A stirp robustness depends on the type of polymer and its amount in the formulations. The disintegration rate of the polymers is decreased by increasing the molecular weight of polymer film bases.

Plasticizers

Plasticizer is a important 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. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. It helps to improve the flexibility of the film and reduces the brittleness of the

film. the plasticizers are used in the film. Examples include: Propylene glycol, polyethylene glycols.

Sweetening agents

Sweeteners are the essential part of the food products as well as pharmaceutical products. In case of oral dosage form the sweet taste in formulation is more important especially for pediatric population. Thus, to improve the pleasing of the mouth dissolving formulations Natural sweeteners as well as artificial sweeteners are used. the sweeteners which are Suitable in fast dissolving film formulation are given below:

(a) Water soluble natural sweetener: ribose, xylose , glucose, sucrose, maltose, stevioside etc. (b) Water soluble artificial sweetener: sodium or calcium saccharin salts, cyclamate salts.

(c) Dipeptide based sweetener: aspartame.

Saliva stimulating agent

The saliva stimulating agents are used to increase the rate of production of saliva that is helpful in the faster dissolution of the film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. Examples: Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid etc. Among these citric acid is most preferred saliva stimulating agent in the formulation

Flavoring agent

Flavoring agents can be selected from the synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Any flavor added like or fruit essence like apple , raspberry, cherry, pineapple. essential oils or water soluble extracts of menthol, intense mints such as peppermint, sweetmint, cinnamon, wintergreen, spearmint, clove, sour fruit flavor such as lemon , orange or sweet confectionary flavors such as vanillin, chocolate. The amount of flavour needed to mask the taste depends on the flavour type and its strength.

Coloring agent

Titanium dioxide or FD&C approved colouring agents are incorporated in FDF formulation when some of the formulation ingredients or drugs are present in insoluble or suspension form.

METHODS OF MANUFACTURE OF FAST DISSOLVING FILMS

One of the following processes may be used to manufacture the oral films:

1 Solvent casting
2 Hot-melt extrusion
3 Semisolid casting
4 Solid dispersion extrusion
5 Rolling.

1 Solvent casting method

In this method, firstly at the speed of 1,000 rpm the water soluble polymers are dissolved in water and heated up to 60ºC. All the other excipients such as colors, flavouring agent, sweetening agent are dissolved separately. Finally, both the solutions obtained are mixed thoroughly with stirring at the speed of 1,000 rpm. The API dissolved in suitable solvent is incorporated in the above obtained solution. By using vacuum the entrapped air is removed. The resulting solution is cast as a film and allowed to dry and then it is cut into pieces of the desired size.

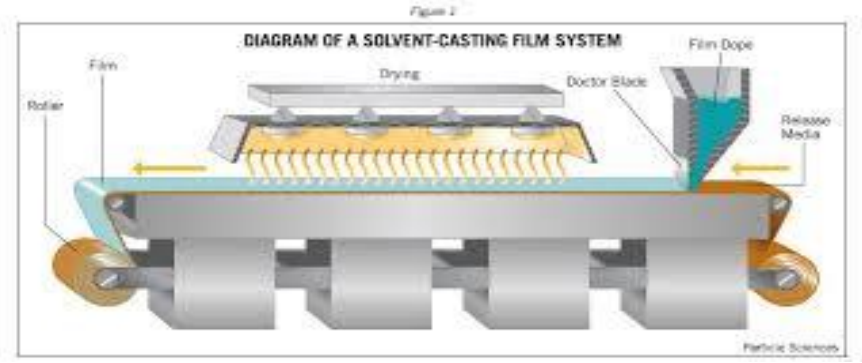
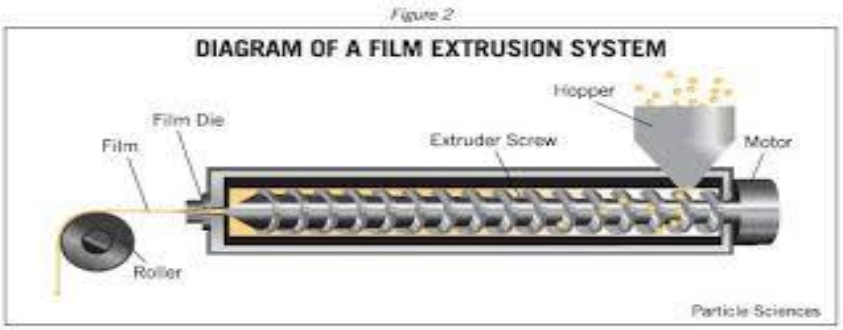


FIGURE 1: SOLVENT CASTING METHOD

2 Hotmelt extrusion

Hot metal extrusion method is commonly used to prepare granules, transdermal, sustained release tablets, and transmucosal drug delivery systems. Melt extrusion was used as a manufacturing tool in the pharmaceutical industry



3 Semi solid casting

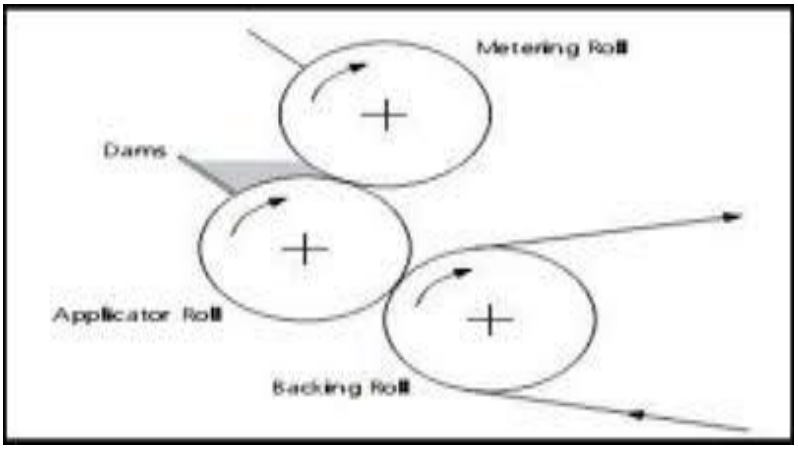
When film ingredient involves acid insoluble polymer at that time this method is mostly preferred. In this method, the water soluble polymers are dissolved in water. The obtained solution is added to the acid insoluble polymer solution which is separately formed. Both the solutions are mixed properly. To this mixture of two solutions, appropriate amount of plasticizer are added to the obtained final solution so that gel mass can be obtained. Finally with the help heat controlled drums the gel mass are casted onto the films or ribbons. The thickness of the film should be about 0.015-0.05 h. The ratio of the acid insoluble polymer to film forming polymer should be 1:4. cellulose acetate phthalate and cellulose acetate butyrate Are the examples of acid insoluble polymers.

4. 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. Then solution is incorporated into the melt of polyethylene glycol, obtainable below 70 ◦ C Finally the solid dispersions are shaped into the films by means of dies.

5. Rolling method

The rolling method involves thorough mixing of both the drug solution and film forming polymer solution. Finally, the resultant solution or suspension is subjected to the roller. The solution or suspension should have specific rheological consideration. The film is dried on rollers and cut into desired shapes and sizes.



EVALUATION PARAMETERS OF FAST DISSOLVING FILMS

1 Tensile Strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks 14. It is calculated by the applied load at rupture divided by the cross- sectional area of the strip as given in the equation below:

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

2 % Elongation

The percent elongation is measured when the film snaps as sufficient force applied so as to exceed the elastic limit. Percentage elongation can be obtained by following equation:

It is calculated as

$$\text{Percentage elongation} = \frac{\text{Increase in length X 100}}{\text{Original length}}$$

3 Disintegration test

Disintegrating time is defined as the time (second) at which a film breaks when brought into the contact with water or saliva. The disintegration time is the time when a film starts to break or disintegrate. Thickness and mass play a role in determining the dissolvable films physical properties. Disintegration test is done by Disintegration apparatus.

4 Folding endurance

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

5 In vitro drug release

Dissolution studies of films were performed by USP XXIII type II apparatus in 6.8 phosphate buffer and 0.1N HCl . The temperature (37±0.5°C) and the rotation speed was 50 rpm. The samples were withdrawn at various time intervals and analyzed spectrophotometrically.

6 **Stability study**

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

7 Surface pH of film

Surface pH of the films was determined by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the colour of pH paper was observed.

8 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 percent.

PATENTED TECHNOLOGIES:

1. **ZYDIS TECHNOLOGY**:

Scherer has patented the Zydis technology. Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material .A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but

instead peel the film back to release the tablet. In addition, it utilizes microencapsulation with specialized polymers or complexation with ion exchange resins to mask the bitter tasting drug.

2. **WOWTAB TECHNOLOGY**

The Wowtab fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years. Wowtab technology is patented by Yamanouchi Pharmaceutical Co. The WOW in Wowtab signifies the tablet is to be given "With Out Water". It is recently been introduced into the U.S. The Wowtab technology makes use of sugar and sugar-like (e.g., mannitol) excipients. This process is a blend of low mouldability saccharides (rapid dissolution) and high mouldability saccharides (good binding property).The two different types of saccharides are mixed to attain a tablet formulation with ample hardness and fast dissolution rate. Due to its significant hardness, the Wowtab formulation is slightly more stable to the environment than the Zydis or OraSolv .

3. ORASOLV TECHNOLOGY

The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder.OraSolv is Cima's first fast-dissolving/disintegrating dosage form. The OraSolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence The taste masking associated with the OraSolv formulation is two-fold. The unpleasant flavor of a drug is not merely counteracted by sweeteners or flavors; both coating the drug powder and effervescence are means of taste masking in OraSolv. This technology is frequently used to develop over-the-counter formulations. The major disadvantage of the OraSolv formulations is its mechanical strength because the Orasolve tablets are only lightly compressed. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing.

4. FLASH DOSE TECHNOLOGY

Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick-dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, Flash Dose. The

Flash Dose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shearform. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed onto the tongue. Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly

5. DURASOLV TECHNOLOGY

DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to OraSolv, DuraSolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting.DuraSolv is so durable that it can be packaged in either traditional blister packaging or vials. DuraSolv tablets are prepared by using conventional tabletting equipment and have good rigidity(friability less than that 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. One disadvantage of DuraSolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses.The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound.

6. **FLASH DOSE TECHNOLOGY:**

Flash dose technology has been patented by Fuisz Technologies Ltd. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self-binding shear form matrix termed as “floss”. Shear form matrices are prepared by flash heat processing.

7. **QUICK –DIS TECHNOLOGY**

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market. The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm’s proprietary patented technology12 and is a

thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption.

8. **PHARMABRUST TECHNOLOGY**

Pharmaburst technology is being patented by SPI pharma. The tablet manufactured by this process involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds.

PACKAGING OF FAST DISSOLVING FILM

A variety of packaging options are available for fast dissolving films. Single packaging is compulsory 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. In the pharmaceutical industry it is essential that the package selected adequately preserve the integrity of the product. Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast dissolving dosage forms. 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.

Aluminum pouch

The pouch is transparent for product display. Using a 2 structure combination allows for one side to be clear and the other to use a cost-effective foil lamination. Soluble film drug delivery pouch is a peelable pouch for “quick dissolve” soluble films with high barrier properties. The foil lamination has essentially zero transmission of both gas and moisture. The package provides a flexible thin film alternative for nutriceutical and pharmaceutical applications. The single dose pouch provides both product and dosage protection. Aluminum pouch is the most commonly used pouch.

Foil, paper or plastic pouches

A flexible pouch is usually formed during the product filling operation by either vertical or horizontal forming, filling, or sealing equipment. The pouches can be single pouches or aluminum pouches . The flexible pouch is a packaging concept capable of providing not only a

package that is temper- resistance, but also by the proper selection of material, a package with a high degree of environmental protection.

Barrier Films

Many drug preparations are sensitive to moisture and therefore require high barrier films. Several materials may be used to provide moisture protection such as Polychlorotrifluoroethylene (PCTFE) film, Polypropylene. Polypropylene does not stress crack under any conditions. It is an excellent gas and vapour barrier. Lack of clarity is still a drawback.

Blister card with multiple units

The blister container consists of two components: the blister, which is the formed cavity that holds the product, and the lid stock, which is the material that seals to the blister. The blister package is formed by heat – softening a sheet of thermoplastic resin and vaccum- drawing the softened sheet of plastic into a contoured mold. After cooling the sheet is released from the mold and proceeds to the filling station of the packaging machine. The semi –rigid blister previously formed is filled with the product and lidded with the heat sealable backing material. The film selection should be based upon the degree of protection required. Generally the lid stock is made of aluminum foil. The material used to form the cavity is typically a plastic, which can be designed to protect the dosage form from moisture.

CONCLUSION

Fast dissolving films increase the bioavailability of the medication and moreover they are of more patient compliance. Bypassing the hepatic first pass metabolism. Fast dissolving oral films are earning popularity in the field pharmaceutical dosage forms as well as mouth fresheners as their administration is easy. FDOFs can be taken by all type of patients including children and geriatrics. Oral films can replace the over-the counter drug, generic and brand name from market due to lower cost and consumer preference.

REFERENCES

1. Bhura N, Sanghvi K, Patel U,Parmar B, Patel D " A review on fast dissolving film"*Int.J.Pharma.Rea.Bio.Sci* **2012** 3 66-89.

2. Pandya K, Patel K, Patel M, "Fast dissolving film: a novel approach drug delivery system" *Asi.J.Pharma.Sci.Tech* **2013** 3 25-31
3. Pathan A , Gupta N , Jain M, Dubey A, Agrawal A " Fast dissolving oral films: A Review"*Res.Bio.Pharma.Sci* **2015** 4 2319-7536
4. Siddiqui N, Garg G, Sharma P "A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents" *Adv.Bio.Rea* **2011** 5 291-303
5. Bhagyashri M, Vaishali K, Jadhav S "A short review on fast dissolving oral film" *W.J.Pharma.Sci*. **2014** 3 463-475
6. Kumar R, Mercy S " Fast dissolving films: A unique strategy for drug delivery" *Asian J. Pharm. Res.* **2014** 4 47-55
7. Chowdhary Y,Soumya M, "A Review on Fast Dissolving Drug Delivery Systems- A Pioneering Drug Delivery Technology" *Bull. Env. Pharmacol. Life Sci* **2013** 2 64- 75
8. Saini S, Nanda A and Hooda M: Fast dissolving films (FDF): innovative drug delivery system. Pharmacology online **2011** 2 919-928.
9. Dipika Parmar, Upendra Patel. "Orally Fast Dissolving Film as Dominant Dosage for Quick Releases." *Int. J. Pharma. Res. Bio. Sci.* **2012** 1 24-41.
10. Dixit RP, Puthli SP. Oral Strip Technology: Overview and Future Potential. J Cont. Rele**, 2009** 139 94-107.
11. Bhupinder Bhyan, Sarita Jangra, Mandeep Kaur, Harmanpreet Singh. "Orally Fast Dissolving Films: Innovations in Formulation and Technology". *Int. J Pharm. Sci. Rev. & Res* **2011** 9 2-9.
12. Bhyan, B., Jangra, S., Kaur, M., Singh, H., Orally Fast Dissolving Films: Innovations In Formulation And Technology, *Int. J.Pharm. Sci.Re.Res* **2011** 9 50-57.
13. Satam, M., N., Bhuruk, M, D., Pawar, Y., D., Fast Dissolving Oral Thin Film: A Review, *Int. J. Pharm. Bio.Sci* **2013** 4 27-39.
14. Dhere P.M., Patwekar S.L, Review on Preparation and Evaluation of Oral Disintegrating Film. *Int.J.pharm.Tech* **2011** 4 1572-85.

15. Panda B.P, Dey N.S, Rao M.E.B, Development of innovative orally Fast Disintegrating Film Dosage Forms:A Review. *Int. J. Pharma. Sci. Na.* **2012** 5 1666-74.

16. Mitali M Vaidya, Nilesh M Khutle, Parag S Gide, Oral Fast Dissolving Drug Delivery System:A Modern Approach for Patient Compliance. *W.J.Pharma.Res*. **2013** 2 558-77.

17. Swetha Kalyan, Mayank Bansal, Recent Trends in the Development of Oral Dissolving Film. *Int. J.Pharm.Tec. Res*.**2012** 4 725-33.

18. Parul Saini. Anoop Kumar. Pankaj Sharma. Sharad Visht, Fast Disintegrating Oral Films: A Recent Trend of Drug Delivery. *Int.J. Dr. Res* **2012** 4 80-94.

19. Swapnil L. Patil, Paresh R Mahaparale, Madhavi A. Shivnikar, Shradha S. Tiwari, Ketan V. Pawar, Prashant N. Sane, Fast Dissolving Oral Films: An Innovative Drug Delivery system. *Int. J. Res. Rev.Pharm. sci* 2482-496.

20. Dinge A, Nagarsenker M. Formulation And Evaluation Of Fast Dissolving Films For Delivery Of Triclosan To The Oral Cavity. *AAPS Pharm Sci Tech* **2008** 9 34956.