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Fast Dissolving of Sublingual Film of Poorly Soluble Drugs

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ABSTRACT: Sublingual route is a useful when rapid onset of action is desired with better patient compliance. The portion of drug absorbed through the sublingual blood vessels bypasses the hepatic first pass metabolism processes giving acceptable bioavailability. Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology, which aim to enhance safety and efficacy of a drug molecule to achieve better patient compliance. Many patients find it difficult to swallow tablets and hard gelatin capsules particularly pediatric and geriatric patients and do not take their medicines as prescribed. Difficulty in swallowing or dysphasia is seen to afflict nearly 35% of the general population. In some cases, such as motion sickness, sudden episode of allergic attack or coughing and an unavailability of water, the swallowing of tablet or capsules may become difficult in such situation fast dissolving drug delivery system is useful.

KEY WORDS: Sublingual film, rapid dissolving, water soluble polymers, patient compliance.

I. INTRODUTION

The fast-dissolving Drug Delivery Systems was an advancement that came into existence in the early 1970 s as an alternative to tablets, capsules, and syrups. Fast dissolving films have become a novel approach to oral drug delivery system as it provides convenience The and ease of use over other dosage forms such as orally disintegrating tablets, buccal tablets and sublingual tablets, so mouth dissolving films are gaining the interest of large number of pharmaceutical industries. Most of the drugs are taken orally in the form of tablets, capsules, etc. by all patients including adult, pediatric and geriatric patients. But these dosage forms have to face many problems such as

- Need of water for their disintegration.
- Choking problems
- Poor patient compliance
- Unpleasant taste and odour
- Difficult to administer in children, aged people, mental patients, in unconscious states etc.

To overcome these difficulties, several fast-dissolving drug delivery systems are developed. The concept of sublingual films has been introduced to overcome the problems associated with conventional oral dosage forms and improve bioavailability there by optimization of therapy. Fast dissolving films are most advance form of solid dosage form due to flexibility. It improves efficacy of active pharmaceutical ingredient [API] dissolving in short duration oral cavity after film with an area of 5-20 sq.cm containing an active pharmaceutical ingredient. various sizes and shapes, un-obstructive, mucoadhesion, fast disintegration, quick dissolving, rapid release etc. It provides the direct entry into the systemic circulation there by avoiding the hepatic first pass Effect and ease of administration and also it gives quick on set of action. This delivery system consists of a thin film, is simply place below the tongue, instantly wet by saliva; the film rapidly dissolves. Then it rapidly disintegrates and dissolves to release the medication for systemic absorption This fast-dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist sublingual environment. FDFs are useful in patients such as paediatric, geriatrics, bedridden,

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emetic patients, diarrhoea, sudden episode of allergic, attacks, or coughing for those who have an active lifestyle [1][2]

II. FAST DISSOLVING FILMS

Fast-dissolving drug delivery systems have been developed as an alternative to conventional dosage form as an oral means of drug delivery in case of chronic conditions. Now a day's fast dissolving films are preferred over conventional tablets and capsules for masking the taste of bitter drugs to increase the patient compliance. Fast dissolving films consist of a very thin oral strip which dissolves in less than one minute when placed on the tongue. Dissolvable oral thin films are in the market since past few years in the form of breath strips and are widely accepted by consumers for delivering vitamins, vaccines and other drug products. The various manufacturing techniques for the preparation of films have also been detailed in the review. The present review details most of the patents on such fast-dissolving films in recent years. A brief study has been made on various parameters which are used to evaluate such films. In case of chronic disorders these fast-dissolving films are better for delivering drugs and obtaining faster therapeutic blood levels and superior in comparison to other oral conventional dosage forms. The ultimate goal of any drug delivery system is the successful delivery of the drug to the body; however, patient compliance must not be overlooked. Fast dissolving drug delivery systems, such as, Mouth Dissolving Films (MDF), offer a convenient way of dosing medications, not only to special population groups with swallowing difficulties such as children and the elderly, but also to the general population. MDF are the novel dosage forms that disintegrate and dissolve within the oral cavity. Intra-oral absorption permits rapid onset of action and helps by-pass first-pass effects, thereby reducing the unit dose required to produce desired therapeutic effect. The present review provides an overview of various polymers that can be employed in the manufacture of MDF and highlights the effect of polymers and plasticizers on various physico-mechanical properties of MDF. It further gives a brief account of formulation of MDF and problems faced during its manufacture.[3]

III. OVERVIEW OF THE ORAL CAVITY:

The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer. The oral mucosa in general is intermediate between that of the epidermis and intestinal mucosa in terms of permeability. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. There are considerable differences in permeability between different regions of the oral cavity diverse structures and functions of the different oral mucosa.[4]

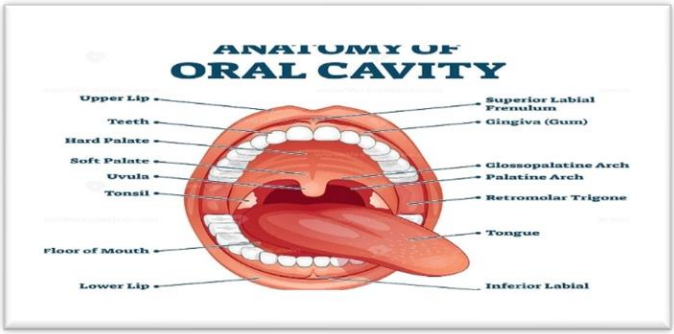

Fig 1 Anatomy of oral cavity

IV. SUBLINGUAL GLANDS

Salivary glands are present in the floor of the mouth underneath the tongue. They are also known as sublingual glands. They produce mucin in turn produces saliva. The fluid which is produced by the glands gets mix with the food, so the food gets easily chewed. The absorption is transfer of the drug from its site of administration into systemic circulation, so it can be said that absorption is directly proportional layer thickness. The absorption of the drug follows in this way Sublingual > Buccal > Gingival >Palatal. Due to high permeability

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and rich blood supply, the sublingual route can produce rapid onset of action so the drug with short delivery period can be delivered and dose regimen is frequently permeability.[5]

V. IDEAL CHARACTRISTICS FOR A DRUG TO INTO SUBLINGUAL FILM

- The drug should have pleasant taste.
- The drug that is incorporated should have low dose up to 40mg.
- The drug with smaller and moderate molecular weight is preferable
- The drug should have good stability and solubility in water as well as in saliva.
- It should be have partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

VI. ADVANTAGES OF SUBLINGUAL FILM:

- Convenient dosing or accurate dosing.
- No need of water to swallow or chew.
- Rapid onset of action.
- Easy of handling & transportation.
- Enhanced stability.
- Taste masking.
- Administered without water, anywhere, any time
- Due to larger surface area, provides rapid disintegration and dissolution in the oral cavity
- Dose accuracy.
- Acidic environment of stomach can be avoided
- Site specific action and local action.
- Flexible and portable in nature so provides ease in transportation during consumer handling and storage.
- Suitable for geriatric and pediatric patients, who experience difficulties in swallowing, mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake or are nauseated.
- Beneficial in motion sickness, acute pain, allergic attack or coughing, where rapid onset of action is required.
- Stable for longer duration of time, since the drug remains in solid dosage form till it is consumed.
- The oral or buccal mucosa being highly vascularized, drugs get absorbed directly and enter the circulation without undergoing first-pass hepatic metabolism.
- The sublingual and buccal delivery of a drug via film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament
- Provide new business opportunity like product differentiation, product promotion and patent extension [6]

VII. DISADVANTAGES

- High dose cannot be incorporated, expensive packaging is required, dose uniformity is a technical
- Since sublingual administration of drugs interferes with eating, drinking, and talking, this route generally considered unsuitable for prolonged administration.
- Although this site is not well suited to sustained delivery systems.
- Sublingual medication cannot be used when a patient is unconscious or uncooperative.
- The patient should not smoke while taking sublingual medication, because smoking causes vasoconstriction of the blood vessels. This will decrease of the medication.[7]

VIII. FORMULATION OF FAST DISSOLVING [11][12][13][14]

Mouth dissolving film is a thin film with an area of 5-20 cm2 containing an active ingredient. The immediate dissolution, in water or saliva respectively, is reached through a special matrix from water soluble polymers. A typical composition contains the following:

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S. No.	Composition of strip	Quantity
1.	Active pharmaceutical agent	1-25%
2.	Film forming polymer	40-50%
3.	Plasticizer	0-20%
4.	Saliva stimulating agent	2-6%
5.	Sweetening agent	3-6%
6.	Flavoring agent	10%
7.	Colouring agent	1%

Table No:1 composition of fast dissolving sublingual films

A. Active pharmaceutical agent:

The drugs selected for oral films should possess good stability in saliva and water with low dose. The film should consist of 1-25% w/w of the drug. Small dose molecules are the best candidates to be incorporated in Oral fast dissolving film. Multivitamins up to 10% w/w of dry film weight was incorporated in the films with dissolution time of less than 60 seconds. It is always useful to have micronized API which will improve the texture of the film and also for better dissolution and uniformity in the Oral fast dissolving film.

B. Film forming polymer:

The polymers can be used alone or in combination to obtain the desired strip properties. Both natural as well as synthetic polymers can be used in the formulation of oral films. In order to prepare a film formulation that is water-soluble, excipients or polymer must be water soluble with low molecular weight and excellent film forming capacity. The polymer employed should be non-toxic, nonirritant and devoid of leachable impurities. It should have good wetting and spread ability property. The polymer should exhibit sufficient peel, shear and tensile strengths. At least 45% w/w of polymer should generally be present based on the total weight of dry film. The various natural as well as synthetic polymers to make fast dissolving films include cellulose or cellulose derivatives, pullulan, gelatin, Hypromellose, hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol, sodium alginate, xanthan gum, tragacanth gum and guar gum. Pullulan is a natural polymer obtained from nonanimal original and does not require chemical modification.

C. Plasticizers:

It helps to improve the flexibility of the strip and reduces the brittleness of the strip. Plasticizer significantly improves the strip properties by reducing the glass transition temperature of the polymer. Glycerol, propylene glycol, low molecular weight propylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some commonly used plasticizer excipients. Typically, the plasticizers are used in the concentration of 0-20% w/w of the dry polymer weight.

D. Saliva stimulating agent:[8]

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strip formulations. These agents are used alone or in combination between 2-6% w/w of the strip. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants.

E. Sweetening agents:[9][10]

Sweeteners have become the important part of pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The classical source of sweetener is sucrose, dextrose, fructose, glucose, liquid glucose and isomaltose. Polyhydric alcohols such as sorbitol, mannitol and isomalt can be used in combination as they additionally provide good mouth feel and cooling sensation. The artificial sweeteners like Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-k, sucralose, alitame and neotame which fall under the second-generation artificial sweeteners. Generally, sweeteners are used in the concentration of 3 to 6 %w/w either alone or in combination.

F. Flavouring agents:

Preferably up to 10%w/w flavors are added in the Fastdissolving film formulations The acceptance of the oral disintegrating or dissolving formulation by an individual is largely depends on the initial flavor quality

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which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min. The geriatric population like mint or orange flavors while younger generation like flavors like fruit punch, raspberry etc. Flavoring agents can be selected from the synthetic flavor oils, oleo resins, extracts derived from various parts of plants like leaves, fruits and flowers. Any flavors can be added such as essential oils or water-soluble extracts of menthol, intense mints such as peppermint, sweetmint, spearmint, wintergreen, cinnamon, clove, sour fruit flavor such as lemon, orange or sweet confectionary. Flavors such as vanillin, chocolate or fruit essence like apple, raspberry, cherry, pineapple.

G. Coloring agents:

A full range of colors is available including FD&C colors, EU colors, natural coloring agents and natural juice concentrates, pigments such as titanium dioxide, silicon dioxide and zinc oxide and custom pantone matched colors.

IX. MANUFACTURING METHODS[16][17][18]

Following processes can be used to manufacture fast dissolving films:

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

A. Solvent casting method

In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plates, dried and cut in to uniform dimensions.

Figure 1

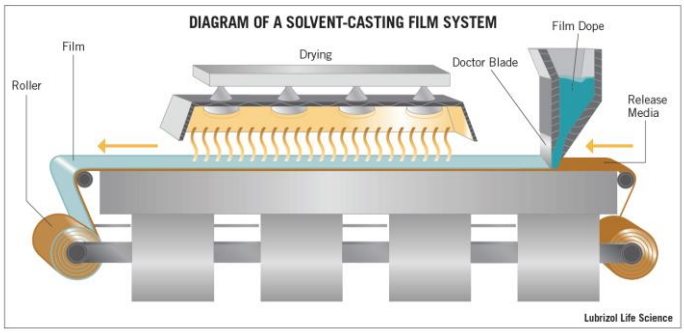

Fig 2 Solvent casting film system

B. Semisolid casting method

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 was 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

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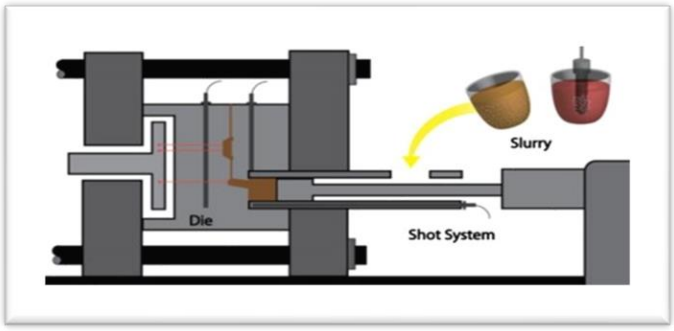

Fig 3 Semisolid casting film system

C. Hot melt extrusion method

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 16.

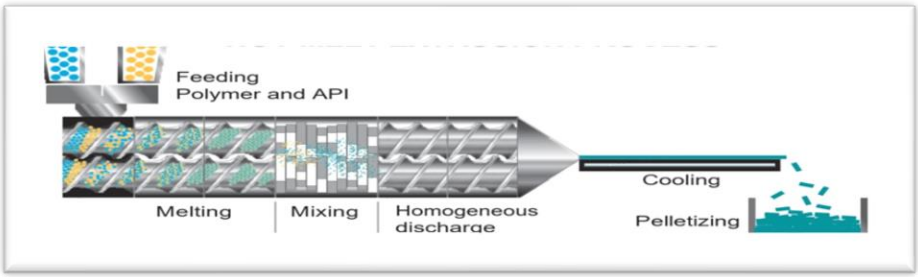

Fig 4 Hot melt extrusion system

D. Solid dispersion extrusion method

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.

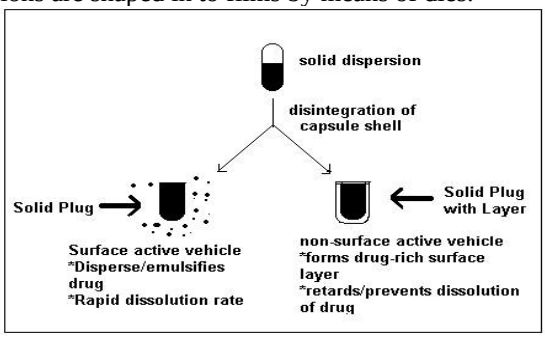

Fig 5 Solid dispersion extrusion process

E. Rolling method

In rolling method, a solution or 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 cutted in to desired.

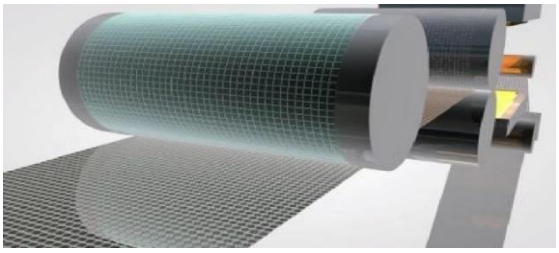

Fig 6 Rolling method

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X. EVALUTION [19][20][21][22][23]

A. Organoleptic evaluation:

Colour is a vital means of identification for many pharmaceutical products and is also important for consumer acceptance. The colour of the product must be uniform within a dosage form. Odour is also important for consumer acceptance of oral dosage forms and can provide an indication of the quality of oral films as the presence of an odour in a batch could indicate a stability problem. Taste is also essential factor for the consumer acceptance. Taste preference is subjective and the control of taste in the production of oral soluble films is based on the presence or absence of a specified taste 18.

B. Drug content uniformity test:

The test for the content uniformity is carried out taking a sample film of size 2×2 sq cm which is placed in a beaker containing 10 ml of a suitable medium. The contents are stirred in a cyclo-mixer to dissolve the film which is then transferred to a volumetric flask (10ml). The absorbance of the solution is measured against the corresponding blank solution at particular wavelength using a standard assay method described for the particular API mentioned in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%.

C. 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 the folding endurance value. This gives an indication of the brittleness of the film. 4.4 Surface pH: Film is placed on a petri dish and moistened with 0.5 ml of distilled water. Kept for 30 seconds. The pH is noted after bringing the electrode of the pH meter in contact with the surface of film. Final result is determined by taking the mean of 3 readings.

D. Thickness test:

Thickness of the film is measured using Micrometer Screw Gauge at different locations. Final result is determined by taking the mean of 6 readings. Thickness of the film ranges from 1-10 mm 20.

E. Disintegration test:

Disintegration of orally fast dissolving films requires USP disintegration apparatus. The disintegration time limit of 30 seconds or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Disintegration time vary depending on the formulation but typically the disintegration ranges from 5 to 30 seconds. IAlthough, no official guidance is available for oral fast disintegrating films strips.

F. Dissolution test:

Dissolution studies of films is performed by using USP type II apparatus in 6.8 phosphate buffer (900ml) and 0.1N HCl (900ml). The temperature (37±0.5°C) and the rotation speed is 50 rpm. 5ml samples is withdrawn at various time intervals and analyzed spectrophotometrically.

G. Elongation test:

Kinston Universal Testing Instrument is used. Films are pulled by 2 clamps at a rate of 100 mm/min. Force and elongation is measured when film breaks. 4.9 Tensile strength test: It is the maximum stress applied to a point at which the strip specimen breaks. It is performed to check the strength and elasticity of the film by using tensile tester. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below.

$$\%elongation = \frac{increase\ in\ length}{original\ length} \times 100$$

H. Tensile strength test:

It is the maximum stress applied to a point at which the strip specimen breaks. It is performed to check the strength and elasticity of the film by using tensile tester. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below.

$$tensile\ strength = \frac{load\ at\ failure}{strip\ thickness \times strip\ width} \times 100$$

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XI. APPLICATIONS [24]

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of FDFs could become a preferential delivery method for therapies in which rapid absorption is desired, including those used to manage pain, allergies, sleep difficulties, and central nervous system disorders. Dissolvable FDFs evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products.

A. Topical applications: The use of dissolvable films may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications

B. Gastro retentive dosage system:

Dissolvable films are being considered in dosage forms for which water soluble and poorly soluble molecules of various molecular weights are contained in a film format. Dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially be used to treat gastrointestinal disorders.

C. Diagnostic devices: Dissolvable films may be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic

XII. MARKETEDSUBLINGUALFILMS:

Product Name	Manufacturer	Active Product Ingredient (API)	Dosage form	Use of the Product
Listerine	Pfizer	Cool mint	Film strip	Mouth Freshener
Benadryl	Pfizer	Diphenylhydramine HCL	Film strip	Antiallergic
Orajel	Del	Menthol/Pectin	Film strip	Mouth Ulcer
Theraflu	Novartis	Dextromethorphan HBR	Thin Film strip	Cough suppressant
Theraflu	Novartis	Diphenylhydramine HCl	Thin Film strip	Cough suppressant
Theraflu	Novartis	Phenylephrine HCl/ Dextromethorphan HBR	Thin Film strip	Cough suppressant
Theraflu	Novartis	Phenylephrine HCl/Diphenylhydramine HCl	Thin Film strip	Cough suppressant
Sudafed PE	Wolters Kluwer Health Inc.	Phenylephrine	Film strip	Relieving Congestion
Triaminic	Novartis	Dextromethorphan HBR	Thin Film strip	Antiallergic
Triaminic	Novartis	Diphenylhydramine HCl	Thin Film strip	Antiallergic
Triaminic	Novartis	Phenylephrine HCl/ Dextromethorphan HBR	Thin Film strip	Antiallergic
Triaminic	Novartis	Phenylephrine HCl/Diphenylhydramine HCl	Thin Film strip	Antiallergic
Chloraseptic	Prestige	Benzocaine/menthol	Film strip	Sore throat
Klonopin Wafers	Solvay Pharmaceuticals	Clonazepam	Wafer	Treatment of Anxiety
Suppress	InnoZen Inc.	Menthol	Film	Cough Suppressant
Gas-X	Novartis	Simethicone	Film	Anti Flatuating
Zuplenz	Galena Biopharma	Ondansetron	Film	Nausea and vomiting
Zofran	GSK	Ondansetron	Film	Nausea and vomiting

Table no:2 marketed fast dissolving films

XIII. 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 asthmatic attacks whenever immediate onset of action is desired. Fast dissolving films are intended to be applied in the mouth and it is a very innovative dosage especially to pediatric and geriatric patients. These dosage forms are of great importance in case of emergency conditions such as allergic reactions and asthmatic attacks where immediate onset of action of action is desired. Sublingual absorption is efficient since the percent of drug absorbed by this route is generally higher than that achieved by oral route. Therefore, oral thin films are an accepted technology for systemic delivery of API's.

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REFERENCES

1. Prabhu SC, Parsekar HD, Shetty A, Monteiro SS, Azharuddin M and Shabaraya AR. A Review on Fast Dissolving Sublingual Films for Systemic Drug Delivery. *Int J Pharm &Chem Sci 2014; 3(2): 482-496.*
2. Thakur N, Bansal M, Sharma N, Yadav G and khare P. Overview A Novel Approach of Fast Dissolving Films and Their Patients. *Adv in Bio Res* 2013; 7(2): 50-58.
3. Kumar RK and Mercy SM. Fast Dissolving Film*: A Unique Strategy for Drug Delivery Asian J. Pharm. Res 2014; 4(1): 47- 55.*
4. Rao NR, Reddy SK, Swapna D, Konasree SD and Enugala S. Formulation and evaluation of rapidly dissolving buccal patches. *Int J Pharm & Bio Sci. 2011;1 (3):145-159.*
5. Suresh B, Halloran D, James L. Quick dissolving films: A novel approach to drug delivery. Drug. dev. tech. 2006;
6. Vollmer U and Galfetti P. Rapid film: Oral thin films as an innovative drug delivery System and dosage form. Drug Dev Report. 2006; 64-67.
7. Gavaskar B, Vijayakumar S, Sharma G and Rao YM. Overview on fast dissolving films. *International Journal of Pharmacy and Pharmaceutical Science. 2010; 2(3):29-33.*
8. Gohel MC and Sharma R: Development of taste masked film of valdecoxib for oral use. *Indian Journal of Pharmaceutical Sciences, 2010; 320-323.*
9. Nishimura M, Matsuura K, Sukioka T, Yamashita H, Inagaki N, Sugiyama T and Itoh Y: In-vitro and in-vivo characteristics of prochlorperazine oral disintegrating film. *International Journal of Pharmaceutical Sciences, 2009; 98–102.*
10. Shimoda H and Taniguchi K: Preparation of fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. *European Journal of Pharmaceutics and Biopharmaceutics, 2009; 73: 361-365.*
11. Vaidya MM and Khutle NM, Gide PS. Oral fast dissolving drug delivery system: A modern approach for patient compliance. *World J Pharm Res. 2013;2(3):558-577.*
12. Gowri R, Narayanan N, Revathi S, Prabhavathy P, Preethi Mol G and Rekha G. Melt in mouth films- An effective alternative drug delivery system. *Int J Bio & Pharm Res. 2013;4(9): 645-650.*
13. Satam MN, Bhuruk MD and Pawar YD. Fast dissolving oral thin film- A review. *Int J Universal Pharm & BioSci. 2013;2(4):27-39.*
14. Kumar SV, Gavaskar B, Sharan G and Madhusudhan Rao Y. Overview on fast dissolving films. *Int J Pharm & Pharm Sci. 2010;3(2):29-33.*
15. Cilruzo F and Cupone EI: Fast dissolving films made of maltodextrins. *European Journal of Pharmaceutics and Biopharmaceutics, 2008; 70: 895-900.*
16. Gohel M and Patel M: Formulation design and optimization of mouth dissolving tablet of Nimusulide using vacuum drying technique. AAPS Pharm Sci Tech, 2004; 5: 45- 4.
17. Rathi V, Senthil V, Kammili L and Hans R: A brief review on oral film technology. *International Journal of Research in Ayurveda and Pharmacy*, 2011; 2(4): 1138-1147.
18. Vishwakarma DK, Tripathi AK, Yogesh P and Maddheshiya B: Review article on mouth dissolving film. *Journal of Global Pharma Technology, 2011; 3(1): 1-8.*
19. Malke, M., S. Shidhaye and V.J. Kadam. Formulation and evaluation of Oxacarbazine fast dissolve tablets. -214 *Indian J. Pharmaceutical Sci. 2007, 69(2); 211.*
20. Gohel MC, Sharma R, Stonewall MM. Development of taste masked film of Valdecoxib for oral use. *Ind j Pharm Sci. 2007; 69:318-320.*
21. Singh S, Gangwar S, Garg G, Garg V and Sharma PK. Formulation and evaluation of rapidly disintegrating film of Levocetrizine Hydrochloride. Scholars Research Library Der Pharmacia Lettre. 2010; 2(2): 434-439.
22. Nagar P, Chauhan I and Mohd Yasir. Insights into Polymers: Film Formers in Mouth Dissolving Films. Drug Invention Today. 2011; 3(12): 280- 289.
23. Suresh B, Halloran D and James L. Quick dissolving films: A novel approach to drug delivery. Drug. dev. tech. 2006; 1-7.
24. Rathi V, Senthil V, Kammili L and Hans R. A brief review on oral film technology. *International Journal of Research in Ayurveda and Pharmacy. 2010; 2(4):1138- 1147*