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ISSN: 0975-7538
Review Article

Fast dissolving film: A review

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ABSTRACT

Fast-dissolving drug-delivery systems (FDDS) 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. Over the past three decades, fast disintegrating tablets (FDTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. FDTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue. But in this, there are still some chances of chocking. So Oral dissolving film Technology (ODFTS) are another FDDS 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. Itcan be administrated in the buccal cavity for a shorter period of time in Secs and gives better therapeutic action. OFDFs are very similar to postage stamp in their shape, size and thickness. These films have a potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action. This type of technology offer a convenient way of dosing medication, not to special population groups like pediatric, geriatric, bedridden patients, mentally ill patients, but also to the general population.

Keywords: Mouth dissolving films; Oral dispersible films; Oral disintegrating films

INTRODUCTION

Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, but oral drug delivery systems still need some advancements to be made (Anderson, O.et al.,1995) because of their some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphasic patients(Joseph, F.S. et al., 2005) associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms (Habib,W. et al.,2000). So, fast-dissolving drug-delivery systems came into existence in the late 1970's as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid-dosage forms (Liang, C.A. et al., 2001). These systems consist of the solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water. Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to oral disintegrating tablet (ODT) to wafer to the recent development of oral fast dissolving films (Goel, H.et al., 2008; Bhowmik, D. et al., 2009). Fast dissolving films is 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 oralmucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. The drug is released from the dosage form upon disintegration and dissolution. The disintegration and dissolving times are prolonged as the film thickness increases as shown in the Figure 1 (International Corporation, 2010).

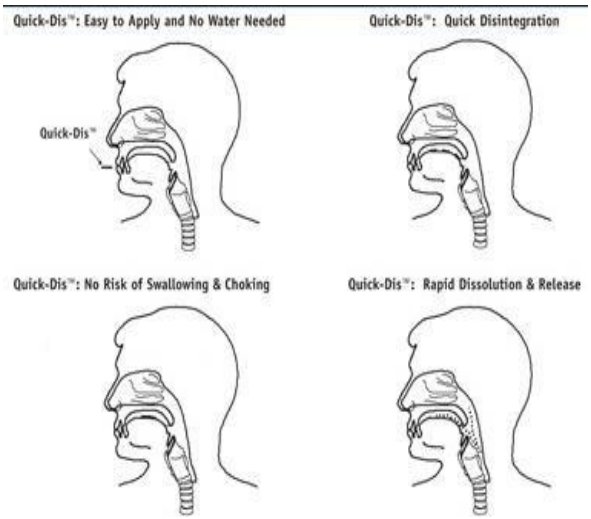

Figure 1: Fast dissolving films based on technology

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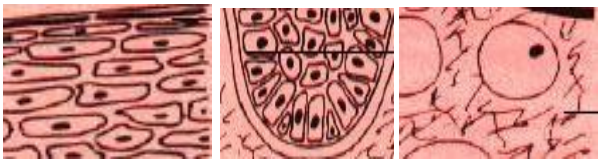
Contact: +91-8447267245
Received on: 27-06-2012
Revised on: 29-07-2012
Accepted on: 03-08-2012

Structural features of oral mucosa

The oral mucosa is composed of an outermost layer of stratified squamous epithelium, below this layer of a basement membrane, a lamina propria followed by the sub mucosa as the innermost layer. (Figure 2) Three different types of oral mucosa can be identified. i.e. masticatory, lining and specialized mucosa (Borsadia, BB. et al., 2010). It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. Even during disease, blood flow through human oral mucosa is believed to be sufficiently fast as not to be rate-limiting in drug absorption (Kumar, D. et al., 2010).



Epithelium Lamina Propria Submucosa

Figure 2: Different layers of oral mucosa (Shojaei, A., 1998)

Oral mucosal dosage form: There are various types of Oral Mucosal dosage forms which use the oral mucosa as a drug delivery site such as – fast dissolving tablets, oro dissolving films, fast caps, buccoadheshive film and tablets, chewing gums etc. The brief Introduction of each dosage form is given as below:

(a) Fast Dissolving Tablet (FDT): FDTs can be prepared by various techniques like direct compression, sublimation, melt granulation, moulding, volatilization and freeze drying. Some of patented technologies are zydis, orasolve, durasolv, flash dose, wowtab, flash tab etc. The solubility of drug was increased by various methods to make a fast dissolving tablet like solid dispersion technique, by cogranulation with beta – cyclodextrin.

(b) Fast Dissolving Films: However, the fear of taking solid tablets and the risk of choking for certain patient population still exist despite their short dissolution/disintegration time. So one such approach for this is rapidly dissolving film. It consists of a very thin oral strip, which releases the active ingredient immediately after uptake into the oral cavity. Rapid film combines all the advantages of tablets (precise dosage, easy application) with those of liquid dosage forms (easy swallowing, rapid bioavailability). Methods of preparing Fast dissolving film can be hot melt extrusion, solid dispersion extrusion, rolling, semisolid casting, and solvent casting.

(c) Fast Caps: A new type of fast dissolving drug delivery system based on gelatin capsules was developed. In contrast to conventional hard capsules, the fast caps consist of gelation of low bloom strength and various additives to improve the mechanical and dissolution properties of the capsule shell. The advantage of these fast disintegrating capsules are high drug loading, possible solid and liquid filling, no compression of coated taste-masked or extended release drug particles/pellets, good mechanical properties, simple manufacturing, mechanical stability and requirement of special packaging.

(d) Buccoadheshive Film and Tablets

Recent years have seen an increasing interest in the development of novel muco- adhesive buccal dosage forms. Water soluble drugs are considered difficult to deliver in the form of sustained or controlled release preparations due to their susceptibility to “dose dumping phenomena “. Attempts have been made to regulate their release process by use of mucoadhesive polymers in order to achieve a once- a- day dose treatment.

(e) Medicated Chewing Gums: Medicated chewing gum is an attractive alternative for drug delivery system with several advantages including convenience for administration, individually controlled release of active substance and effective buccal drug administration for the treatment of local oral disease and systemic action. Mainly chewing gum is used to promising controlled release drug delivery system. Medicated chewing gums are currently available for pain relief, smoking cessation, travel illness and freshening of breath (Kumar, D. et al., 2010).

Classification of fast dissolving technology:

For ease of description, fast-dissolve technologies can be divided in to three broad groups:

Lyophilized systems,

Compressed tablet-based systems,

Thin film strips.

The lyophilized systems

The technology around these systems involves taking a suspension or solution of drug with other structural excipients and, through the use of a mould or blister pack, forming tablet-shaped units. The units or tablets are then frozen and lyophilized in the pack or mould. The resulting units have a very high porosity, which allows rapid water or saliva penetration and very rapid disintegration.

Compressed tablet-based systems

This system is produced using standard tablet technology by direct compression of excipients. Depending on the method of manufacture, the tablet technologies have different levels of hardness and Friability. The speed of disintegration for fast-dissolve tablets compared with a standard tablet is achieved by formulating using water soluble excipients, or super-disintegrant or effervescent components, to allow rapid Penetration of water into the core of the tablet.

Table 1: Difference between oral dissolving films and oral disintegrating tablets

Orally Dissolving Films (ODF\OS)	Oral Disintegrating Tablets (ODT\FDT)
1. Larger surface area gives greater dissolution	1. Less surface area gives less dissolution than odf
2. ODF are flexible and durable	2. ODT are brittle and less durable than odf
3. only Low dose can incorporated in formulation	3. High dose can incorporated in Formulation
4. ODF thickness are 50 to 500 mm	4. ODT thickness as like convention tablet
5. Patient compliance more	5. Patient compliance is less than Odf
6. No risk of chocking	6. It has a fear of chocking
7. Easy to carry and handle	7. Difficult to carry and handle (Bhavan B. et al., 2011).

Table 2: Types of wafers and their properties (Verena G. et al., 2009)

Property/Sub Type	Flash release water	Mucoadhesive melt-away wafer	Mucoadhesive sustained release wafer
Area (cm2)	2-8	2-7	2-4
Thickness (µm)	20-70	50-500	50-250
Structure	Film: single layer	Single or multilayer System	Multilayer system
Excipients	Soluble, highly hydrophilic polymers	Soluble, hydrophilic Polymers	Low/Non-soluble Polymers
Drug phase	Solid solution	Solid solution or suspended drug particles	Suspension and/or solid Solution
Application	Tongue(upper palate)	Gingival or buccal Region	Gingival, (other region in the oral cavity)
Dissolution	Maximum 60 seconds	Disintegration in a few minutes, forming gel	Maximum 8-10 hours
Site of action	Systemic or local	Systemic or local	Systemic or local

Oral Thin Films (OTF)

Dissolvable oral thin films (OTFs) or oral strip (OS) 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. This technique is derived on the basis of transdermal technology (Vondrak, B. et al., 2008). This film can reportedly incorporate soluble, insoluble or taste-masked drug substances. The film is manufactured as a large sheet and then cut into individual dosage units for packaging in a range of pharmaceutically acceptable formats (Drug delivery.com).

Classification of Oral Film

There are three different subtypes

(1) Flash release,

(2) Mucoadhesive melt-away wafer,

(3) Mucoadhesive sustained-release wafers.

These three types of oral films are differentiated from each other in following table 2.

Technology behind the mouth dissolving film

The Peroral application is an effective and inexpensive way for drugs that can be absorbed in the gastrointestinal tract. However, in some case the application of tablets or solution is a problem: A tablet has to disintegrate in the gastrointestinal tract in order to dissolve the drug. The Process extends the absorption of drug to some extent, which is undesirable in some diseases, like pain, vomiting. That problem was solved in the past by the application of the drug in the form of drop or syrup. However, the regimen of the amount of drop or the use of metering spoon needs and it is not precise. Furthermore not all drugs are stable in aqueous – alcoholic solution. Children very often fight against oral medicine; they may spit out tablet or not consume the entire dose. Mouth dissolving Films have all the advantages of tablets (precise dosage, easy application) with those of liquid dosage forms (easy swallowing, rapid bioavailability).The film dissolves immediately after application in the mouth and release the drug. The system ensures an excellent patient compliance even in cases of nausea. Children cannot spit the drug out because the film adheres to the upper gum after dissolution. Therefore, safe application is increased in children. As a single dose application, the precision of the dose can be ensured, which is not the case with drops or syrups. The Mouth Dissolving Film Technology also has clear advantages over Oral Dissolving Tablets (ODT). ODTs are sometimes difficult to carry, store and handle (fragility and friability);Many ODTs are produced using the expensive lyophilization process; MDFs/OTFs can be packed using various options, such as pouches, blister cards dispensers and Rapid Card (Borsadia, B. et al., 2003).

Special features of Fast dissolving films

- Thin elegant film
- Available in various size and shapes

Table 3: Some of the promising drug candidate for fast dissolving film

Drug	Action	Dose (mg)
Salbutamol	Anti asthmatic	4
Levocetrizine	Antihistaminic	75
Chlorohexidine	Antiseptic	12
Ondensteron	Anti emetic	2.5
Caffeine	CNS stimulant	2.5 mg
Diphenhydramine HCl	Antihistaminic	2.5 mg - 5 mg

Table 4: Examples of fast dissolving films which are formulated by solvent casting method in literature

S.No	Drug	Polymers	Plasticizers	Sweeteners
1	Ondansetron	Polyvinylalcohal, polyvinyl pyrrolidone, Carboopol 934P	Propylene glycol or PEG 400	Mannitol or sodium saccharin
2	Maltodextrin	Polyvinylalcohal	Glycerol	Glycerine
3.	Salbutamol	HPMC	Glycerol	Aspartame

- Unobstructive
- Excellent mucoadhesion
- Fast disintegration
- Rapid release (Suresh, B. et al., 2006).

Advantages of Oral Thin Film

This dosage form enjoys some distinct advantages over other oral formulations such as-

1. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity.

2. Since the films are flexible they are not as fragile as most of the ODTs. Hence, there is ease of transportation and during consumer handling and Storage.

3. As compared to drops or syrup formulations, precision in the administered dose is ensured from each of the strips.

4. OTFs offer fast accurate dosing in a safe, efficacious format that is Convenient and portable, without the need for water or measuring devices

5. The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing First-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect.

6. Since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in side effects associated with the Molecule.

7. Patients suffering from dysphagia, repeated emesis, motion sickness, and mental disorders prefer this dosage form as they are unable to swallow large Quantity of water.

8. OTFs are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of seconds for the rapid release of one or more APIs (Zhang, H. et al., 2002).

Disadvantage of Oral Strip

- High doses cannot be incorporated.
- Dose uniformity is a technical challenge (Bhavn, B.et al., 2011).
- It is hygroscopic in nature so it must be kept in dry places.
- They require special packaging for the products stability and safety.
- It also shows the fragile, effervesces granule property.

Mechanism of action

The delivery system is simply placed on a patient's tongue or any oromucosal tissue. Instantly wet by saliva due to presence of hydrophilic polymer and other excipients, the film rapidly hydrates and dissolves to release the medication for oromucosal absorption (Siddiqi, M. et al., 2011).

Ideal characteristics for fast dissolving film

- Require no water for oral Administration.
- Dissolve / disperse/ disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel and taste masking.
- Less friable and have sufficient hardness.
- Leave minimal or no residue in mouth after administration.
- Manufacturing using conventional manufacturing method.
- Utilizes cost effective production Method (Bradoo, R. et al., 2005).

The ideal characterstics of a drug to be selected

- No bitter taste
- Dose lower than 20mg

Table 5: List of marketed preparation of fast dissolving film (Arya A et al., 2010)

S. No.	Product	Mfg. By
1.	Dextromethorphan HBr (cough suppressant), Diphenhydramine Citrate (cough and cold), Breath Strips	MonoSolRx
2.	Doneprezil rapid dissolving films, Ondansatron rapid dissolving Films	Labtec Pharma
3.	Life-saving rotavirus vaccine to infants	Johns Hopkins
4.	Methylcobalamin fast dissolving films, Diphemhydramine HCl fast dissolving films, Dextromethorphan fast dissolving films, Folic Acid 1mg fast dissolving films, Caffeine fast dissolving films	Hughes medical Corporation

- Small to moderate molecular weight
- Good stability in water and saliva
- Partially non ionized at the oral cavities pH
- Ability to diffuse and partition into the epithelium of the upper GIT (logp>1, or Preferably>2)
- Ability to permeate oral mucosal tissue (William, R. et al., 2005).

Composition of the Formulation

Active pharmaceutical agents	1-25%
Water soluble film forming polymer	40-50%
Plasticizers	0-20%
Sweetening agent	3 to 6 %w/w
Saliva stimulating agent	2 to 6%w/w)
Fillers, colors, flavors etc	0-10%

(Kaur. Et al., 2012).

Oral strip formulation components

Formulation considerations

Formulation of oral Strip (OS) involves the intricate application of aesthetic and performance characteristics such as taste masking, fast dissolving, physical appearance, mouth-feel etc. The Excipients used in formulation of OS are given below as per their categories. From the regulatory perspectives, all excipients used in the formulation of OS should be generally regarded as Safe (i.e. GRAS-listed) and should be approved for use in oral pharmaceutical dosage forms.

Strip forming polymers

A variety of polymers are available for preparation of OS. The polymers can be used alone or in combination to obtain the desired strip properties. The film obtained should be tough enough so that there won't be any damage while handling or during transportation. The robustness of the strip depends on the type of polymer and the amount in the formulation (Corniello, C et al., 2006). The various polymers available, pullulan, gelatin and hypromellose are most commonly used for preparation of OS. Pullulan is a natural polymer obtained from nonanimal origin and does not require chemical modification. Modified starches are also used for preparation of OS. Due to low cost of these excipients it is used in combination of pullulan to decrease the overall cost of the product. About 50 to 80 percent w/w of pullulan can be replaced by starch in the production of OS without loss of required properties of Pullulan. Combination of microcrystalline cellulose and maltodextrin has been used to formulate OS.

Plasticizers

Plasticizer is a vital ingredient of the OS formulation. 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 (Banker, G et al., 2006). The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of strip. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer (Sakellariou, P et al., 1995). Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, citrate derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients. Typically the plasticizers are used in the concentration of 0–20 percent; w/w of dry polymer weight (McIndoe, L et al., 2006). However, inappropriate use of plasticizer may lead to film cracking, splitting and peeling of the strip. It is also reported that the use of certain plasticizers may also affect the absorption rate of the drug.

Sweetening agents

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 classical source of sweetener is sucrose (derived from cane or beet in the form of liquid or dry state), dextrose, fructose, glucose, liquid glucose and isomaltose. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, and isomalt can be

used in combination as they additionally provide good mouth-feel and cooling sensation.

Polyhydric alcohols are less carcinogenic and do not have bitter after taste which is a vital aspect in formulating oral preparations. The artificial sweeteners have gained more popularity in food and pharmaceutical preparations. 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. Acesulfame-K and sucralose have more than 200 and 600 time sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Rebiana which is a herbal sweetener, derived from plant *Stevia rebaudiana* (South American plant) has more than 200 -300 time sweetness (Parkash, G et al., 2008).

Saliva stimulating agent

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 dissoving strip 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.

Flavoring agents 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 plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. 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.

Coloring agents

Pigments such as titanium dioxide or FD & C approved coloring agents are incorporated (not exceeding concentration levels of 1 percent; w/w) in OS when some of the formulation ingredients or drugs are present in insoluble or suspension form (Gavaskar, B et al., 2010).

Manufacturing methods for producing fast dissolving film

One (or a combination) of the following processes may be used to manufacture the oral films:

- Solvent casting
- Hot-melt extrusion
- Semisolid casting
- Solid dispersion extrusion
- Rolling.

Solvent Casting

Fast dissolving buccal 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 stirred and finally casted in to the Petri plate and dried (Repka, M et al., 2002).

Water soluble ingredients are dissolved in water and API and other agents are dissolved in suitable solvent to form a clear viscous solution

↓

Both the solutions are mixed

↓

Resulting solution is cast as a film and allowed to dry

↓

film is collected

Hotmelt extrusion

Hot metal extrusion is commonly used to prepare granules, sustained release tablets, transdermal and transmucosal drug delivery systems (Malke, S. et al., 2010). Melt extrusion was used as a manufacturing tool in the pharmaceutical industry as early as 1971.

The drug is mixed with carriers in solid form

↓

Extruder having heaters melts the mixture

↓

Finally the melt is shaped in films by the dies

Advantages of hot melt extrusion are fewer operation units, minimum product wastage, possibility to scale up, an anhydrous process, absence of organic solvents, include shorter temperature and shorter residence time of the drug carrier mix and better content uniformity.

Semisolid casting

In this method solution of water soluble film forming polymer are mixed to solution of acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate, cellulose acetate butyrate). After sonication it is coated on non-treated casting film. The thickness of the film is about 0.381-1.27 cm. The ratio of the acid insoluble polymer to film forming polymer should be 1:4 (Frey., 2006).

Solid dispersion extrusion

The term solid dispersions refer to the dispersion of one or more active ingredients in an inertCarrier in a solid state in the presence of amorphous hydrophilic polymers (Ceballos, A et al., 2005).

Drug is dissolved in a suitable liquid solvent

↓

Then solution is incorporated into the melt of polyethylene glycol, obtainable below70◦C

↓

Finally the solid dispersions are shaped into the films by means of dies.

Precautions while preparing sold dispersions

The selected solvent or dissolved drug may not be miscible with the melt of the polyethylene Glycol and polymorphic form of the drug precipitated in the solid dispersion may get affected by the liquid solvent used.

Rolling method: In rolling method a solution or suspension of drug with film forming polymer is prepared and subjected to the roller. The solution or suspension should have specific rheological consideration. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes (Arya, A et al., 2010).

The various recent advancements in fast dissolving film are given as below:

TECHNOLOGIES

1) SOLULEAVES™ technology is used to produce a range of oral delivery films that can incorporate active ingredients, colours and flavors. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. For pharmaceutical Uses this method of administration is especially useful for paediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, Gastrointestinal, pain therapeutic areas, delivering nutritional products, flavor-release products such as mouth fresheners, confectionery and vitamin products. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes

2) WAFERTAB™

Is a patented drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. Active ingredients are incorporated into the film after Casting. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a pre-manufactured XGEL™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The WAFERTAB™ system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. WAFERTAB™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release or for use by patients who have difficulty swallowing.

3) FOAMBURST™ is a special variant of the SOLULEAVES™ technology. 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 as 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. FOAMBURST™ has attracted interest from food and Confectionary manufacturers as a means of carrying and releasing flavors.

4) XGEL™ film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. XGel film Technology developed by BioProgress is causing a revolution in the product offerings and manufacturing methods now available to the pharmaceutical industry.

5) Micap: Micap plc signed 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). (Meldexinternational.com).

Quality control test for fast dissolving film

i) Thickness

Oral disintegrating film thickness measured by micrometer screw gauge. Films thickness check at five different points for uniform film thickness as well as content uniformity. By using calibrated digital micrometer (CLM1–15QM, Mitutoyo, Kawasaki, Japan) (Yoshifumi M et al., 2010). Three readings from all the batches were taken and mean thickness was evaluated (Shingh, S et al., 2010).

ii) Mechanical properties

A) Tensile strength: Tensile strength means the point at which films is break

$$Tensile\ strength = \frac{Load\ at\ failure}{Film\ thickness \times\ film\ width} \times 100$$

B) Percent elongation: When tension is applied to the film and film strip is starches this is a strain. If elongation of film increase means addition of plasticizer is increase.

$$\%\ Elongation = \frac{Increase\ in\ length}{Original\ length} \times 100$$

C) Folding endurance

Folding endurance is determined by folding a film up to it break at the folding point, attempt required to cut the film is folding endurance value (Mahajan, A et al., 2011).

iii) Swelling property

Swelling property of the oral film is check by using saliva solution. Keep the film on the pre weighed steel mesh one part is place in the 50 ml saliva solution. Weigh the film after specific time up to constant weight of film is come (Arya, A et al., 2010).

Degree swelling property is calculated by following formula (Mahajan, A et al., 2011).

$$SI = wt – wo / wo$$

Where SI is the swelling index,

wt is the weight of the film at time "t", and

wo is the weight of film at t = 0

iv) Contact angle

Contact angle is measured by goniometer (AB Lorentzen and Wettre, Germany) in this method double distilled water drop place on dry film by using goniometer, digital picture is take within 10 second of drop add on film analyzed by imageJ 1.28v software (NIH, USA) for angle determination. Minimum five times at different position check the contact angle film (Arya, A et al., 2010).

v) In vitro disintegration time

Manually check the disintegration byplacing the film in 10 ml water and time required to break or disintegrate the film (Vishwkarma, D. et al., 2011). In vivo disintegration test take the volunteer (n =6) then place the odf in the mouth of volunteer and check the time to disintegrate the film (Renuka.M. et al., 2011).

vi) In vitro dissolution test

Dissolution studies of films were performed by USP XXIII type II apparatus in 6.8 phosphate buffer (300ml) and 0.1N HCl (900ml). The temperature (37±0.5°C) and the rotation speed was 50 rpm. The samples were withdrawn at various time intervals and analyzed spectrophotometrically (Vishwkarma, D. et al., 2011).

vii) Permeation studies

Permeation studies are done using modified Franz diffusion cell by using porcine buccal mucosa. Buccal mucosa is kept in between the donor and receptor compartment of Franz diffusion cell. In receptor compartment fill buffer kept at 37 °C ± 0.2 °C and maintain the hydrodynamics by using magnetic stirring at 50 rpm. On buccal mucosa the oral disintegrating film is placed before placing mucosa will be moisten by few drop of simulated saliva, in the donor compartment add 1ml of simulated saliva of pH 6.8. Samples withdraw at specific time interval fill with same amount of fluid. Percentage of drug permitted is calculated by taking absorbance by U.V method (Mahajan, A. et al., 2011).

viii) Assay/Drug Content and Content Uniformity:

Assay method determined by specification in different Pharmacopoeia. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115% (Siddiqi, M., 2011).

Ix) Surface morphology

Surface morphology is studied by using environment-scanning-electron microscopy method. In that absence of pore and surface uniformity, striations indicate the good quality of the ODF (Renuka, M. et al., 2011).

x) Taste evaluation

In vivo test evaluation studies going with panel of volunteers and In vitro studies by using the test sensor analyze the sweetness level of test masking agent (Renuka, M. et al., 2011).

Packaging and Storage

A variety of packaging options are available for fast dissolving 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. The material selected must have the following characteristics:

- They must protect the preparation from environmental conditions.
- They must be FDA approved.
- They must meet applicable tamper-resistant requirement.
- They must be non-toxic.
- They must not be reactive with the product.
- They must not impart to the product tastes or odors (Lachmann, L.et al., 1991).

Application of oral strips

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of OTFs 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 oral thin films (OTFs) 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.

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.

Gastro retentive dosage systems: 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 (Barnhart, S et al., 2007). 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.

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 device (Meathrel, B. et al., 2007).

Marketing status and patents

The drug delivery sector of fast dissolve products has grown rapidly from sales in 2002 of about $850 Million to 2005 were estimated sales were around $1.4 billion (IMS Data). [43] The lifestyle and nutraceuticals market was the first to move into thin film format after breath fresheners with a range of Fast dissolving strip products which incorporated actives such as vitamins, herbal extracts and non Herbal extracts. The market for these types of product is in excess of $15bn worldwide. Currently, Worldwide sales of drugs that incorporate a fast dissolve technology are more than $1 billion and Have an annual growth rate of more than 40 percent. This growth is fuelled by the patient demand, And industry estimates show that approximately 88per cent of patients prefer taking medications that Incorporate a fast dissolve any as 40 per cent of all people have difficulty swallowing traditional Tablets (Technology., 2006). Forty-seven OTF products in the pipeline being developed by 12 companies Technology Catalysts forecasts the market for drug products in oral thin film formulations to be valued at $500 million in 2007 and could reach $2 billion by 2010.TCI's report also details the technology programs of 25 companies active in the development of Orally- Disintegrating Tablet technologies and 17 active in the development of Oral Film technologies (Tumuluri, V et al., 2006).

CONCLUSION

The present review conclude that fast dissolving oral film is most acceptable and accurate oral dosage form which bypass the hepatic system and show more therapeutic response. The pharmaceutical companies prefer this dosage form due to both patient compliance (especially pediatric and geriatric) as well as industrial acceptability. . Oral films can replace the over-the-counter (OTC) drugs, generic and name brand from market due to lower cost and consumer‘s preference. This technology is a good tool for product life cycle management for increasing the patent life of existing products.

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