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Review Article

AN OVERVIEW ON FAST DISSOLVING FILMS

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Fast-dissolving oral film is an emerging technology with rapid onset of action and improved patient compliance. These oral films are solid dosage forms, which disintegrate or dissolve within 1 min when placed in the mouth without drinking water or chewing. These formulations are suitable for cold, allergic rhinitis, asthma attacks, CNS disorders where rapid onset of action is required for faster relief. The portion of drug absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes giving acceptable bioavailability. The fast dissolving oral films are formulated using polymers, plasticizers, flavors, colors and sweeteners, and manufactured by using solvent casting method, rolling method, extrusion method and solid dispersion method. Films are evaluated for various attributes such as thickness, disintegrations, dissolution, tensile strength and folding endurance

Keywords: Fast-dissolving oral film, solvent casting method, bioavailability and extrusion method.

INTRODUCTION

Fast dissolving drug delivery systems were first developed in the 1970s as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who experience difficulties swallowing traditional oral fast dispersing dosage form is known as fast dissolve, rapid dissolve, rapid melt and quick disintegrating tablets. By definition a solid dosage form typically the size of a postage stamp that dissolves or disintegrates quickly in the oral cavity resulting in solution or suspension without the need for the administration of water is known as an oral fast dispersing dosage form. FDF is prepared using hydrophilic polymer that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic circulation via buccal mucosa. The fast dissolving drug delivery system are specially designed for the drugs which have extensive first pass metabolism and have low dose, for the enhancement of bioavailability.¹

Definition of FDF: Fast dissolving films are most advance form of solid dosage form due to its flexibility. It improve efficacy of Active pharmaceutical ingredient (API) dissolving in the short duration oral cavity after the contact with less amount of saliva as compared to dissolving tablet.²

Special features of oral thin films:

- Available in various size and shape
- Thin elegant film
- Un-obstructive
- Fast disintegration or dissolution
- Rapid release³

Ideal Characteristics of a suitable drug candidate

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose upto 40mg.
- The drugs with smaller and moderate molecular weight are preferable.



- The drug should have good stability and solubility in water as well as in saliva.
- The should be partially unionized at the pH oral cavity.
- It should have the ability to permeate oral mucosal tissue.⁴

Advantage:

- No risk of choking
- Convenient dosing or accurate dosing
- No need of water to swallow or chew
- Small size for improved patient compliance
- Rapid onset of action
- Ease of handling and transportation
- Improve bioavailability for certain therapeutic ingredient.
- Enhanced stability
- Taste masking⁵

FORMULATION OF FAST DISSOLVING FILMS

Active Pharmaceutical Ingredient: A distinctive composition of the film contains 1-30%w/w of the active pharmaceutical ingredient. Always use low dose active pharmaceutical ingredients used because high dose of drug are difficult to incorporate in fast dissolving film micronized API is useful because it enhance the texture of film and provide improved dissolution and uniformity in the fast dissolving film. A number of drugs can be used as fast dissolving oral film.^{6,7}

Film Forming Polymers: Polymers are the most important ingredient of the oral fast dissolving film. Robustness of the film depends on the amount of polymer added in the oral strip. These polymers are mostly attracted considerable attention by medical

and nutraceuticals industry. Generally 45% w/w of polymer is used which is based on total weight of dry film. Mainly hydrophilic polymers are used in the oral strip as they rapidly disintegrate in the oral cavity as they come in contact with saliva.⁸

Ideal Properties of Film Forming Polymer:

- It should be non-toxic and non irritant.
- Polymer must be hydrophilic.
- It should have excellent film forming capacity.
- It should have good wetting and spread ability property.
- Polymer should be readily available & should not be very expensive.
- Polymer should have low molecular weight.
- It should have sufficient shelf-life.
- Polymer must be tasteless, colorless.
- It should not cause any secondary infection in oral mucosa.
- It should exhibit adequate peel, shear and tensile strengths.⁹

Currently, both natural & synthetic polymers are used for the preparation of fast dissolving film.

Natural Polymer: Pullulan, Starch Gelatin, pectin, Sodium alginate, Maltodextrin, Polymerized rosin, Xanthan

Synthetic polymers: Hydroxypropylmethyl cellulose, Polyvinylpyrrolidone, Polyvinyl alcohol, Carboxy methyl cellulose, Poly ethylene oxide, Kollicoat, Hydroxypropyl cellulose, Hydroxyl ethyl cellulose.¹⁰

Plasticizers: Plasticizer is a very important ingredient of oral strip formulation. It helps to improve the flexibility and reduce the brittleness of



the fast dissolving film and by addition of Plasticizers, tensile strength and elongation can be improved. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of oral strip. E.g. Glycerol, Propylene glycol, Polyethylene glycol 400,200,600, Castor oil.¹¹

Sweetening Agent: -Sweeteners have become the essential part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Both natural and artificial sweeteners are used in the formulation to improve the palatability of the fast dissolving film. Generally sweeteners are used in the formulation in concentration of 3-6%w/w, either alone or in combination. E.g. Sorbitol, Sucrose, Mannitol, Aspartame.¹²

Saliva Stimulating Agent:Saliva stimulating agents is used to increase the production of saliva that helps to improve the disintegration of sublingual film. Acids which are used in the food preparation can be utilized as saliva stimulating agent like citric acid, lactic acid, malic acid, ascorbic acid etc. Saliva stimulating agent is used alone or in combination between concentration 2 to 6 % w/w.E.g. Citric acid, Malic acid, Lactic acid, Ascorbic acid, Tartaric acid.¹³

Flavoring Agent:In sublingual film formulations up to 10 % w/w flavors are added. The acceptance of the film is depends on the flavor which is observed in few seconds after the administration of film which lasts for about 10 min. The geriatric patient's loves mint or orange flavors while the younger generation

loves flavor like fruit punch, raspberry etc. Flavoring agents can be selected from the synthetic flavor oils, resins and extracts derived from part of plants like fruit, leaves and flowers. Other flavor such as water soluble extracts of menthol, mints such as wintergreen, cinnamon, clove, peppermint, sweet mint and flavors such as chocolate, vanillin etc. E.g. Peppermint oil, Cinnamon oil, Menthol, Lemon oil.¹⁴

Coloring Agents:A FD & C approved coloring agents is used in the sublingual film. Also natural coloring agents, pigments such as silicon dioxide, zinc oxide and titanium oxide are used. E.g. Titanium dioxide, Sunset yellow.¹⁵

Methods of Preparation of Fast Dissolving Films

Generally following methods are used to preparation of fast dissolving films:

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

Solvent Casting Method: In this method, the water soluble polymers are dissolved in suitable solvent and the drug along with other excipients is dissolved in suitable solvent. Then both the solution is mixed in one beaker and stirred on magnetic stirrer to form homogeneous solution. Mixture is finally casted in to the petri plate and dried at appropriate temperature and cut in to uniform dimensions.^{16,17}

Advantage:

- Great uniformity of thickness & great clarity than extrusion.



- Films have more flexibility & better physical properties.¹⁸

Semi solid casting method: If acid insoluble polymers are used in the preparation of sublingual film the semisolid casting method is preferred. In this method the water soluble polymers solution is prepared then this solution is added in solution of acid insoluble polymers. The acid insoluble polymers like cellulose acetate butyrate and cellulose acetate phthalate. The solution of acid insoluble polymer is prepared in ammonium or sodium hydroxide. Then plasticizers is added in that solution, gel mass is obtained. This gel mass is casted in to the films or ribbons using heat controlled drums. The ratio of acid insoluble polymer and film forming polymer should be 1:4.^{19,20}

Hot Melt Extrusion:

In this method the drug mixed with carriers in solid form. Then this dried granular material is introduced in extruder. Speed of screw set at 15 rpm in order to process the granules in the extruder barrel for approximately 3-4 min. Extrudate then pressed in a cylindrical calendar in order to obtain film.²¹

Advantage:

- Better content uniformity
- An anhydrous process²²

Solid Dispersion Extrusion: In solid dispersion extrusion method the components which are immiscible are extrude with drug and then solid dispersions are prepared. Finally by using dies solid dispersions are shaped in to films.²³

Rolling Method: In rolling method drug and film

forming polymer mixed and solution or suspension is prepared. This solution or suspension is subjected to the roller. The suspension or solution should have specific rheological consideration. The solvent is water or the mixture of alcohol and water. The prepared film is dried on the rollers and cutted in to acceptable size and shape.^{24,25}

EVALUATION OF FAST DISSOLVING FILMS

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

Weight Variations: Weight variation is measured by individually weighting randomly selected 10 films. The average weight should not differ significantly from the average weight.¹⁸

Thickness: The thickness of film is determined by micrometer screw gauge at 5 different points of the film i.e. central and the four corners and means thickness is calculated. For measurement of Uniformity of thickness, 5 film are randomly selected and thickness is measured on location of each formulation. Maximum variation in the thickness of the films should be less than 5% and $\text{mean} \pm S$.^{27,28}

Surface pH: The pH of the film can be determine by placing film in the petriplate and add 0.5 ml distilled water drop by drop. Petriplate is kept for 30 sec. After 30 sec the electrode of pH meter is placed on the surface of wetted film and pH is calculated. Three readings of each formulation is



taken and mean is calculated.²⁹

Tensile Strength: Tensile strength of film is determined by applying the maximum stress to a point till the oral film breaks. It is calculated by the applied load at rupture divided by the cross section area of the oral film.^{12,30}

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

Folding Endurance: Folding endurance is determine by cutting the prepared film in 4cm² and repeated folding at same place till the film is break. And the endurance value means the number of times film folded without the breaking.³¹

Percent elongation:

If stress is applied on the film strip, film is stretches and this is referred as strain. Deformation of film divide by original dimension of the sample is called strain. Elongation of film is directly proportional to the Plasticizer.³²

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

Tear Resistance: The maximum force required to tear the film is recorded as the tear resistance Value. It is expressed in Newton or (pounds – force).³³

Transparency: The measurement of the oral film transparency can be determined by using a simple UV spectrophotometer. Cut the film sample into rectangles and placed on the internal side of the spectrophotometer cell. Now determine the transmittance of the film at 600 nm.³⁴

$$\text{Transparency} = (\log T_{600})/b - C$$

Where, T = Transmittance,

b = Film thickness

C = Concentration

Content uniformity: Content uniformity is determined by prepared film 4 cm² dimension is dissolving in 100 ml of stimulated saliva of pH 6.8 for 30 min with shaking. From this, 10ml was diluted to 50 ml with simulated salivary fluid. Absorbance was measured by using UV spectrophotometer. Experiment is carried out three times and average is calculated.¹⁵

Young's Modulus: Young's modulus is used to determine the stiffness of oral film. It is represented as the ratio of applied stress over strain in the region of elastic deformation.³⁰

Disintegration test: Official guidelines are not available for oral fast dissolving film. The disintegration time limit 30 sec or less as compare to orally disintegrating tablets, as described in CDER guideline. Pharmacopeial disintegrating test apparatus is used for disintegration test study. Disintegration time for sublingual film is 5-30 sec.^{23,35}

Dissolution test: USP type II (Paddle apparatus) is used for dissolution study of sublingual film. Dissolution medium is used as 300 ml of simulated salivary fluid. Temperatures of dissolution medium maintain at 37 ± 0.5°C. Samples were withdrawn at every 30 sec, and replace fresh medium place of withdrawn sample. Absorbance of sample is measured in UV spectrophotometer. And the graph is plotted percent drug release vs time.³⁶

Stability Testing: Stability measurement is done



by storing the of oral strip were stored under controlled conditions of 25°C/60%RH as well as 40°C/75% over a period of 12 months in stability chamber according to the ICH guideline. During storage period various evaluating parameter like thickness, morphological properties, tensile strength, water content and dissolution behavior are checked.^{20,37}

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