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Fast Dissolving Oral Films a Novel Oral Drug Delivery System: An Overview

Preeti Kulkarni[1], Devendra Nirwan[2], Rohit Pacharane[3]

[1, 2, 3]Department of Pharmaceutical Quality Assurance, Gahlot College of Pharmacy Navi Mumbai 400709, Maharashtra, India
[1]*preeti.qara[at]gmail.com*
[2]*devendranirwan1995[at]gmail.com*
[3]*rohit.pacharane[at]gmail.com*

Abstract: ***The oral route is most popular route because of the low cost of therapy and ease of administration lead to patient compliance. As increase in new drug moiety is quite expensive, so the main aim is to develop a new drug delivery system with the same drug as it produce its maximum therapeutic effect over conventional tablets. Fast dissolving oral films are gaining interest as a substitute of fast dissolving tablets over conventional tablets. Fast dissolving oral films are oral solid dosage form, designed to dissolve within few seconds as they come in contact with wet environment of the oral cavity. They quickly disintegrate and dissolve, and there is no need of water for their administration, making them suitable for paediatrics and geriatric patients. This review article overviews the advancement in the oral dosage form, advantages, disadvantages, application, method of preparation, and evaluation of fast dissolving oral dosage form.***

Keywords: Fast dissolving films, Oral dosages form

1. Introduction

Oral route of drug administration is the most common and popular route of drug delivery. About 60% of all dosage forms available in market are oral solid dosage forms, but effectiveness of certain drugs gets reduced when administered through the per-oral route. The problems associated with oral route of administration are first pass metabolism, drug degradation in variable pH condition o gastrointestinal tract, inadequate absorption and slow onset of action. [1] The film is prepared by using polymer and dissolves in the mouth within a few minutes, it was developed in the late in 1970 as an alternative of capsules, tablets and syrups for that patients who have difficulties in swallowing and chewing.[1,2]

Criteria for selecting a suitable drug candidate:

- Drug should have pleasant taste.
- Therapeutic dose of the drug should not be greater than 40mg.
- Drug should have good solubility in water and saliva.
- It should be stable in water.
- Drug should be partially unionized at oral cavity pH.
- Drug should have small molecular size and low molecular weight.
- Drug molecule should have the capability to permeate oral mucosa. [2,3]

Advantages of Fast Dissolving Films Oral Film:

- Available in different size and shape.
- Muco adhesion is excellent.
- Fast releasing and disintegration within minutes in the mouth.
- Water not requires to swallowing.
- It is thin and elegant.
- It is compatible with taste masking.
- It leaves less or no residue in the mouth.
- It is Useful in case of rapid onset of action required such as sudden episodes of allergic attack or coughing, in motion sickness, bronchitis or asthma.
- Improved patient compliance. [2,3]

Disadvantages of Fast Dissolving Films

- Drugs whose therapeutic dose is greater than 40mg cannot be incorporated in the film.
- Packaging of films is difficult and it requires special equipment's.
- Challenge of maintaining dose uniformity in films.
- Technical limitation of maintaining uniform thickness of film while manufacturing on large scale. [3,4]

Ideal properties of Fast Dissolving Films

- Films should have good mechanical strength and should be less fragile.
- Should have acceptable pleasant taste.
- Film should quickly dissolve and release the drug instantly.
- After oral administration film should leave very small or no residue in mouth.
- Should disintegrate fast even without water. [4,5]

Methods of Preparation

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

Solvent Casting

In this method water soluble polymers are dissolved in water and the drug along with other ingredients is dissolved in suitable solvent. Then both the solutions are mixed, stirred, finally casted in to the petri plate and dried.

Advantages
- Better film clarity and thickness uniformity than extrusion method.
- Fine gloss on film and lack of die lines.
- Films with more flexible and better physical properties are produced by this method.

Disadvantages
- Polymers to be used should be soluble in volatile solvents.
- Formation of a stable solution with considerable minimum solid content and viscosity is required, which is difficult to attain
- Homogenous film preparation with proper drug release from casting support must be attain. [6,7]

Semi Solid Casting
This method is mostly preferred when film ingredient involves acid insoluble polymer. In this firstly, 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. After mixing the two solutions, appropriate amount of plasticizer is added to the obtained final solution so that gel's mass can be obtained. At last, the gel mass is casted onto the films or ribbons using heat-controlled drums.The thickness of the film should be about 0.015-0.05". The ratio of the acid insoluble polymer to film forming polymer should be 1:4. Examples of acid insoluble polymers are cellulose acetate phthalate and cellulose acetate butyrate. [7, 8]

Hot Melt Extrusion
This method involves shaping polymer into film through heating process. Firstly, the drug - polymer mixture is filled in hopper and is conveyed, mixed & melted by the extruder. A die gives shape to the melt in required form. This method involves lower temperature and short residence time (< 2 min.) for the drug polymer mixture. Organic solvents are not used in this method and it can operate continuously with minimum product wastage. Operating parameters can be controlled efficiently by this method.

Advantages
- Less processing steps.
- No need of solvent or water.
- Less energy is required compared to high shear methods.
- Uniform dispersion of fine particles due to intense mixing and agitation.
- No importance of drug compressibility properties.

Disadvantages
- Number of polymers is limited.
- Polymer flow properties are essential to processing.
- Drug/polymer stability problem as it is a thermal process. [8,9]

Solid Dispersion Extrusion
Method involves the solid dispersion of drug incorporated in melted polymer solution so that drug can be loaded. The drug is dissolved in suitable liquid solvent and obtained solution is added to the melt of suitable polymer, obtainable below 70°C without removing the liquid solvent to obtain the solid dispersion. Finally the obtained solid dispersions are shaped into films by means of dyes.

Advantages
- Low shear method
- Uniform dispersion of fine particles
- Less processing steps. [9,10]

Rolling
Solvents mainly used in this method are water and mixture of water and alcohol. By the means of high shear processor, active agent and other ingredients are dissolved in small portion of aqueous solvent. Water-soluble hydrocolloids are dissolved in water to form homogenous viscous solution. Then the resultant solution or suspension containing drug is rolled on a carrier. Finally, the obtained film is cut in to desired shapes and sizes. [10, 11]

2. Evaluation Parameters

- Organoleptic Evaluation
- Thickness
- Folding Endurance
- Surface pH
- Tensile Strength
- Young's Modulus
- Tear Resistance
- Contact Angle
- Transparency
- Drug Content Uniformity
- In-vitro Disintegration Study
- In-vivo Dissolution Studies

Organoleptic Evaluation:
Organoleptic properties like colour, odour and taste play important role in acceptance of formulation by patients. Colour of the formulation should be acceptable; it provides means of identification or differentiation for different pharmaceutical products. Colour of the film should be uniform. Odour of the film should not be unpleasant. Odour presence can also indicate stability problem. Presence odour may be characteristic of drug. Taste is the most important factor in acceptance of the formulation by patients. Some companies judge the taste of the formulation prepared using different flavors; they use a taste panel to choose the formulation with best acceptable flavour and flavour level. So FDOF prepared should have good acceptable organoleptic properties.

Thickness
As the thickness of film is directly concern with drug content uniformity, it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital vernier calipers at different strategic locations.

Folding Endurance
To determine folding endurance, a strip of film is cut and repeatedly folded at the same place till it broke. The number of times the film could be folded at the same place without

breaking gives the value of folding endurance. Typical folding endurance for film is between 100-150.

Surface pH

Surface pH of film can cause irritation to the oral mucosa when placed in mouth if its pH is too acidic or alkaline, so it's important to determine surface pH of the film. Surface pH of the film should be neutral i.e. 7 or should be close to 7. A combined pH electrode can be used to determine surface pH. The film is made slightly wet with water, the electrode is brought in contact with film, and the pH reading is noted. This test is applied on at least 6 films and the average is taken which is the final value of surface pH. There is one more method to determine the surface pH; in this, the film is left for swelling on surface of agar plate. Agar plate is prepared by dissolving 2% w/v agar in warm phosphate buffer solution of pH - 6.8 with continuous stirring and the final solution is poured in petri dish and left to solidify at room temp. The surface pH can be measured using pH paper, pH paper is placed on surface of swollen film and change is colour gives the value of surface pH of the film. The average of three readings should be taken.

Tensile Strength

Tensile strength is the ability of being stretched. Film should have good tensile strength. To determine film is pulled using pulley system. Weight is gradually increased at one end of the film and the weight at which the film breaks is noted, it is generally called load of failure. It is calculated by using the following formula, which is load, applied at breakage divided by cross section area of the oral film:

Tensile Strength= Load at failure ×100/thickness ×Film width

Young's Modulus

Young's modulus or elastic modulus is measure of the degree of stiffness of the film. Method used for its measurement is similar to that of tensile strength. It measures the resistance offered to deformation and observed by plotting the stress strain curve where slope gives the modulus. Films hard and brittle in nature have high tensile strength and Young's modulus value27. Young's modulus is the ratio of applied stress over strain in region of elastic deformation; mathematically it can be calculated using the following formula:

Young′s Modulus=Slope×100/Strip thickness ×Cross head speed

Tear Resistance

Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. Basically very low rate of loading 51 mm (2 in)/min is employed and is designed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newton's (or pounds-force).

Transparency

To determine transparency of oral film, a simple ultraviolet (UV) spectrophotometer can be used. The film specimen is placed on the internal side of spectrophotometer cell. The transparency of films is calculated as follows:

Transparency = (log T600)/b = −€c

Where T600 is the transmittance at 600 nm and b is the film thickness (mm) and c is concentration.

Drug Content Uniformity

This parameter can be determined by dissolving known weight of film by homogenization in 100 ml of simulated saliva of pH 6.8 for 30 min with continuous shaking. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85-115%.

In-vitro Disintegration Study

Disintegrating time is defined as the time (seconds) at which a film breaks when brought in contact with water or saliva. The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral film. Pharmacopoeias disintegrating test apparatus may be used for this study. Typical disintegration time for film is 5-30 s.

a) **Slide frame method:** one drop of distilled water was dropped by a Pipette onto the oral films. Therefore, the films were clamped into slide frames and were placed planar on a Petri dish. The time until the film dissolved and caused a hole within the film was measured.
b) **Petri dish methods:** 2 mL of distilled water was placed in a Petri dish and one film was added on the surface of the water and the time measured until the oral film was dissolved completely.

In-vitro Dissolution Studies

Amount of drug which gets dissolve and goes in the solution per unit time under standard conditions of temp., solvent concentration and liquid/solid interface is called dissolution. It's difficult to perform dissolution study of oral film as they can float over the dissolution medium when paddle type dissolution apparatus is used, so basket type dissolution apparatus is mostly used. Selection of the dissolution media depends of the sink conditions and the highest dose of drug/API. During dissolution the temperature of the medium should be 37 ± 0.5^0C and speed of rotation of basket or paddle should be 50 RPM. In other method, release of drug is studied on a film of 4cm2 area. In a beaker, film is adhered to side wall of beaker using a cyanoacrylate adhesive and sink condition is provided by placing 50ml phosphate buffer solution (pH - 6.8) in the beaker. The solution in beaker is stirred continuously using magnetic stirrer at 150 RPM. After time intervals of 20, 40, 60, 80, 100 and 120 sec. 3ml of sample is taken and filtered through whattman filter paper and assayed spectrophotometrically to calculate the drug content released at that time. After taking each sample same amount of phosphate buffer is added in the beaker to keep the volume of the medium constant.

3. Conclusion

Fast dissolving oral films are gaining popularity in the field pharmaceutical dosage forms as well as mouth fresheners as their administration is easy .Fast dissolving oral films being

a natural evolution of fast dissolving drug delivery system have prominent advantage over conventional dosage forms and orally disintegrating tablets. Their onset of action also faster than tablets so these can be used in some emergency cases such as asthmatic attacks or allergic reaction. So many of the pharmaceutical companies are launching the technology as these films can be manufactured through non-sophisticated , uncomplicated, equipment and procedures due to these, fast dissolving films have economically feasible development futuristic opportunities.

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