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Oral Film : A Boon to Bioavailability Enhancement.

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Abstract

Oral fast disintegrating films (OFDF) is an emerging technology brings out "formulations taken without water" with quick onset of action and improved patient compliance as well as Bioavailability. Oral films provide better drug utilization in by-passing the first pass metabolism, enhance drug bioavailability, mask the bitter taste of the drug and do not need water to swallow. OFDF formulations are suitable for cough, cold remedies, sore throat, allergenic conditions, nausea, pain and CNS disorders. Multivitamins, caffeine strips, snoring aid and sleeping aids are also applicable for incorporation in the oral films. The major constraints of OFDF are limited drug aqueous solubility, poor permeability and its high dose. Present article overview the advancement in the oral dosage forms, application, formulation consideration, method of preparation, evaluation, and patented technologies of oral fast disintegrating films.

Keywords : Oral fast disintegrating films , fast dissolving oral film .

INTRODUCTION

Oral route is most preferred route by medical practitioners and manufacturer due to highest acceptability of patients. About 60% of all dosage forms available are the oral solid dosage form. The lower bioavailability, long onset time and dysphagia patients turned the manufacturer to the Parenterals and liquid orals.[1]

Definition

A fast dissolving oral film (FDOF) is defined as "**an ultra-thin film** containing active ingredient that dissolves or disintegrates in the saliva at a remarkably fast rate, within few seconds without the aid of water or chewing".[2]
Fast dissolving oral films (FDOFs) are the most advanced form of oral solid dosage form due to more flexibility. It improves the efficacy of APIs by dissolving within minute in oral cavity after the contact with saliva without chewing and no need of water for administration. It gives quick absorption and instant bioavailability of drugs due to high blood flow and permeability of oral mucosa is 4-1000 times greater than that of skin. [3] FDOFs are useful in patients such as paediatric, geriatrics, bedridden, emetic patients, diarrhoea, sudden episode of allergic attacks, or coughing FDOFs are prepared using hydrophilic polymer that rapidly dissolves on the buccal cavity, delivering the drug to the systemic circulation via buccal mucosa.[4]

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. [5]

The concept of oral dissolving film:

- This system has a thin-film. When placed on tongue, immediately it dissolves within few seconds(sec) therefore avoids first- pass metabolism, hence increase bioavailability of drug.
- Accessibility of larger SA leading quick disintegration &dissolution in mouth.
- FDFs dissolves in mouth as a cotton candy.[6]

Classification of oral films

There are 3 types of oral films, they are:
1. Flash release/Fast dissolving films (placed on the tongue)
2.Mucoadhesive melt away films (gingival or buccal region)
3.Mucoadhesive sustained release films (adhere to the buccal mucosa) [7]

Oral Thin Films:
It is also called as oral wafers. Form the past few years the oral thin films are evolved in confection and oral care markets in the form of breath strips

Advantages of orally FDFs:

- ODFs can be administered without water, anywhere& anytime.
- Larger superficial area (LSA) films aid in rapid disintegration as well as in dissolution of the bodies oral cavity.
- Promoting mouth-freshening property. [8]

Disadvantages :

- Drugs that are required in high doses made difficult formulate into thin films. For instance, Rifampin (600mg), Ethambutol(1000mg).
- Thermal process of drying affect drug & polymer stability.
- Require packing(special) for products stability & safety. [9]

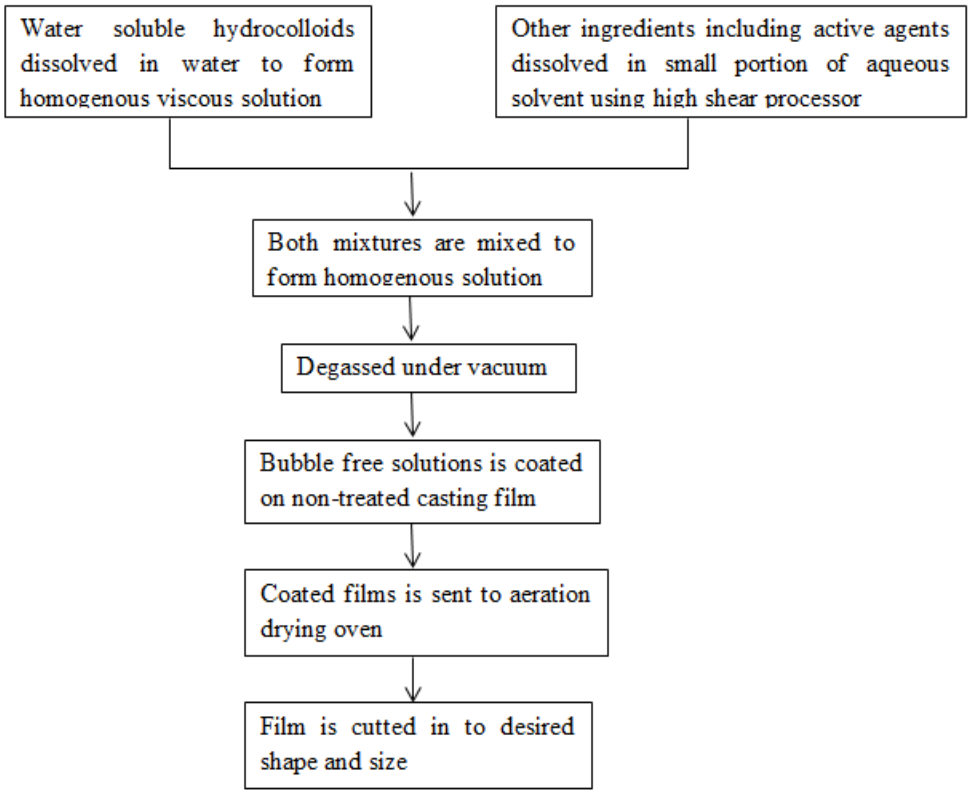
Table1: Comparison between fast dissolving tablets and fast dissolving films

Fast Dissolving Film	Fast Dissolving Tablet
FDFs are Orally Dissolving Films	FDTs are Oral Disintegrating Tablets
Greater dissolute due to the large surface area	Lesser dissolution due to less surface area
Better durable action than oral disintegrating tablets	Less durable as compared with oral films
Low dose can only be incorporated in formulation	High dose can be incorporated in formulated
More patient compliance	Less patient compliance than films
No risk of chocking	It has a fear of chocking
FDFs are of thickness 0.015-0.5inches	FDTs are of same size of convention tablet

Technologies used in manufacture of FDFs:

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

1. **Solvent Casting Method: [10]**



2.Semi solid casting

In this process solution of the polymer of the water-soluble film former is suitably mixed with the acid & allowed it to treat for sonication [11]

3. Hot- Melt Extrusion

In hotmelt extrusion method, initially drug is diverse with movers present solid form. Secondly, extruder that have radiators melts mixer & lastly this shaped into films by dies. [12]

4. Solid-Dispersion Extrusion

Solid dispersions are formulated by dispersion of 1 or more activeingredients in inert carrier. The method constitutes of extrusion of immiscible components with drug followed by preparation of solid dispersions (SD. Finally, these are shaped into films by means of dies. [13]

5. Rolling-Method

Rolling of a solution/suspension comprising drugs onto a carrier constitutes rolling method.[14]

Characterization of Oral Film:

Physical characterization of Film can be carried out by visual inspection for characteristics such as colour, thickness, brittleness, peeling ability, transparency, surface smoothness, tack property and film forming capacity.[15]

1 Peeling ability is measured as the easy or difficulty in separating the film from the release liner.[16]

2 Transparency is checked by placing the film against an illuminated background & viewing carefully to find any opacity.[17]

3 Film-forming (FF) capacity is the ability of the film forming polymer to form an efficient film, thin enough and also with sufficient drug loading ability. Film forming capacity may be rated as poor, average, good and excellent based on the overall examination.[18]

***4. In vitro* quality control tests**

Large Film of 63.64cm2 was cut into even square pieces of 4cm2(2cmX2cm) each and evaluated to verify following parameters.[19]

1 Weight Variation

Weight variation test determines weight difference among films in one batch of a formulation. The weight of films was determined by a digital weighing balance with a precision of 1mg. this examination was performed on three films, out of six films that constitute one batch of 56 each formulation and Mean +SD was calculated. It was measured in milligram (mg). [20] The nominal weight for each film and polymer depends on film forming capacity and adherence to release liner.[21]

2 Thickness

The thickness of a film is Least Measure related directly to disintegration time. Thickness of films was evaluated using a Vernier callipers(digital) with a precision of 0.0010mm i.e. 10µm.ideally films can have thickness up to 10µm. [22]

3 Folding endurance study:

Folding endurance is measure of mechanical strength of a film. Folding endurance study is carried out to ensure the film reminds intact during transportation and handling without breaking off. It was 57 measured manually. A strip was repeatedly folded at the same place till it broke. [23] The number of times the film could be folded at the same place without breaking gave the value of the folding endurance. It was measured as number of counts. [24]

4 Surface pH study

Surface pH is measure of pH on surface on film. This was performed by placing a large enough water drops on surface of film then bulb of pH electrode is brought in contact with surface of water drop.it was performed using a well calibrated pH meter. [25]

5 Content uniformity

Assay/ Drug content are the amount of drug present in a unit film of a batch. Drug content determination helps to know the drug distribution into each small film. [26] Thus, content uniformity can be known. Assay is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. [27]

$$\% \text{ Drug content} = \frac{\text{Concentration} \times \text{Dilution Factor} \times \text{Bath Volume} \times 100}{1000}$$

It was measured in percentage.

6 Tensile strength:

The resistance of a material to a force tending to tear it separately, measured as maximum tension such material can withstand with-out tearing. [28] It can be calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

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

Its units are g/cm2.

7 Percentage elongation:

The percentage increase in the length of a film (L2), when it is pulled under standard conditions of stress just before the point of break is known percentage elongation. The initial length of a film is L1. It is measured in terms of percentage. [29]

$$\text{Percent elongation} = \frac{(L2-L1) \times 100}{L1 \times \text{area of cross section}}$$

However, for films cross-sectional area is very negligible hence, it can be omitted during calculation.

***8 In Vitro*-Disintegration Time**

No official guidelines are available for oral fast disintegrating film strips. This may be used as a qualitative guideline for quality control test or at development stage. [30] The disintegration time of 30sec or less for oral disintegrating tablets described in CDER guide lines can be applied to films. Pharmacopoeial disintegrating test apparatus may be used for this study. Typical disintegration time for strips is (5-30) sec. the medium of study was phosphate buffer pH 6.8. There are two methods of performing this test. [31]

(i) Slide-frame method

In slide frame method one drop of distilled water is dropped by a pipetted onto the film and the film is clamped into slide frames and placed planar on a petri dish. The time until the film dissolves and causes a hole within the film is measured as disintegration time. [32]

(ii) Petri dish system

In petri dish method 2mL of distilled water was placed in 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 slide frame method, the film is test carried out by petri dish method where the film was kept in a petri dish with medium of disintegration. The point of appearance of cracks and segregation of the film was considered as the disintegration time. [33]

The disintegration time of a film was measured in seconds.

***9 in Vitro*-Dissolution Study**

Dissolution testing was performed using the standard rotating basket apparatus (apparatus I) described in the USP. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. [34] For this study 300mL of medium was employed. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed. Hence, basket apparatus is used. The medium of study was phosphate buffer pH 6.8. The parameters of study are:

Apparatus : USP Basket-type apparatus
Agitation speed : 50rpm
Medium : 300mL freshly prepared (pH 6.8) phosphate buffer
Temperature : 37+0.5°C
Sampling interval : 1,2,4,6,8,10 minutes

The samples of 5mL were withdrawn at predetermined time intervals and replaced with fresh medium. The sample concentrations were assayed spectrophotometrically. The cumulative percentage drug release was calculated. [35]

Conclusion:

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 paediatric and geriatric) as well as industrial acceptability. Oral films can replace the over-the-counter (OTC) drugs, generic and name brand is a good tool for product life cycle management . This technology is a good tool for product life cycle management for increasing the patent life of existing products as well as Bioavailability Enhancement.

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