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Review Article

A Review On : Fast Dissolving Oral Thin Film

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ABSTRACT

Oral 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.

INTRODUCTION

Oral disintegrating/dissolving films or strips can be defined as follows: "These are drug delivery systems that they are quickly releasing the drug by dissolving or adhering in the mucosa with saliva within a few seconds due to it contains water-soluble polymers when it placed in the mouth cavity or on the tongue". 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 because of some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed

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by surface form and taste. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water1- 4 .

1.1 Special features of oral thin films

- Thin elegant.
- Available in various size and shapes.
- Un-obstructive.
- Excellent mucoadhesion.
- Fast disintegration and rapid release

1.1.3. Ideal properties of oral thin films

- It should have an acceptable taste with pleasing mouth feel.
- It should be less friable and have good mechanical strength to withstand the post manufacturing handling.
- The drug should have good stability and solubility in water as well as in saliva.
- It should leave least or no residue in mouth.
- It should quickly dissolve to release drug instantaneously in mouth.
- It should be compatible with the other ingredients.

1.1.4. Advantages of oral thin films.

- No need of water to swallow or chew.
- Rapid onset of action.
- Ease of handling and transportation.
- Improve bioavailability for certain therapeutic ingredient.
- Enhanced stability.
- Taste masking.
- No risk of chocking.
- Convenient dosing or accurate dosing.

1.1.5. Disadvantages of oral thin films

- It is hygroscopic in nature so it must be kept in dry places.
- It also shows the fragile, granule property.
- They require special packing for the products stability and safety.

depending on whether the active ingredients are soluble or insoluble drugs, with the dose capability

- High dose cannot be incorporated into the oral film.

1.1.6. Advantages of fast dissolving films

- No risk of chocking.
- Convenient dosing or accurate dosing.
- No need of water to swallow or chew.
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- Improve bioavailability for certain therapeutic ingredient.
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1.1.7. Disadvantages of fast dissolving films

- It is hygroscopic in nature so it must be kept in dry places.
- It also shows the fragile, granule property.
- They require special packing for the products stability and safety.
- High dose cannot be incorporated into the oral film

1.3.1 CLASSIFICATION OF FAST DISSOLVING TECHNOLOGY

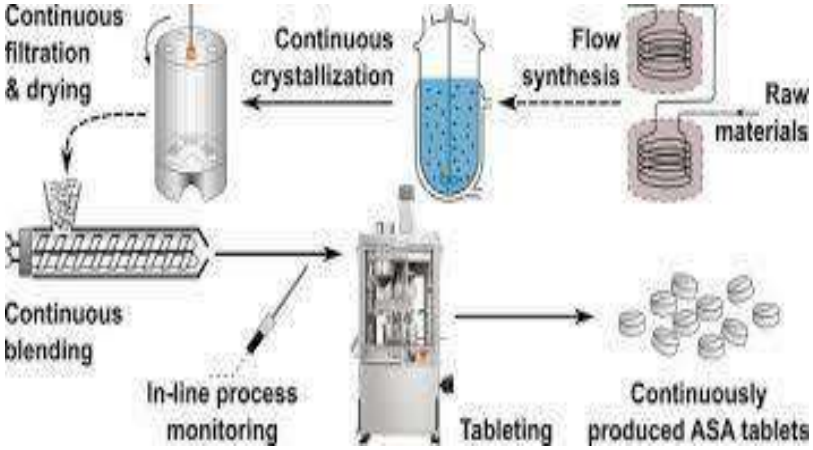
1. **Lyophilized systems**
2. **Compressed tablet-based systems,**
3. **Thin film strips.**

1.Oral fast dissolving films .

1. **Lyophilized systems**

This system has been by far the most successful among them in terms of sales value, sales volume and number of worldwide product approvals. The technology around these systems involves taking a suspension or solution of drug with other structural excipients and, through the use of a mold or blister pack, forming tablet-shaped units. The units or tablets are then frozen and lyophilized in the pack porosity, which allows rapid water or saliva penetration and very rapid disintegration. Dose handling capability for these systems differs

being slightly lower for the former than for some tablet-based systems. The units are capable of incorporating a range of taste-masked materials and have more rapid disintegration than tablet-based systems



2. Compressed tablet-based systems

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 in to the core of the tablet.

The one exception to this approach for tablets is bio vails fuisz technology. It uses the proprietary shear form system to produce drug-loaded candy floss, which is then used for tableting with other excipients. These systems can theoretically accommodate relatively high doses of drug material, including taste-masked coated particles. The potential disadvantage is that they take longer to disintegrate than the thin-film or

3. Oral fast dissolving films .

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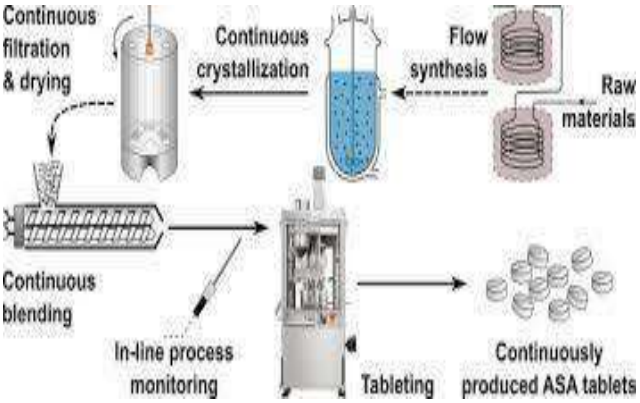

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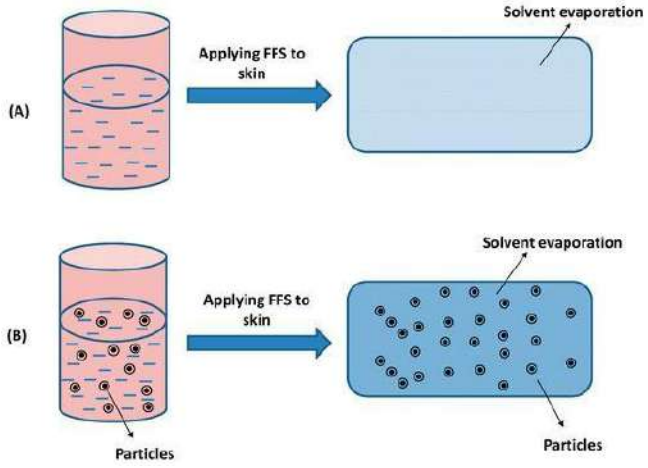
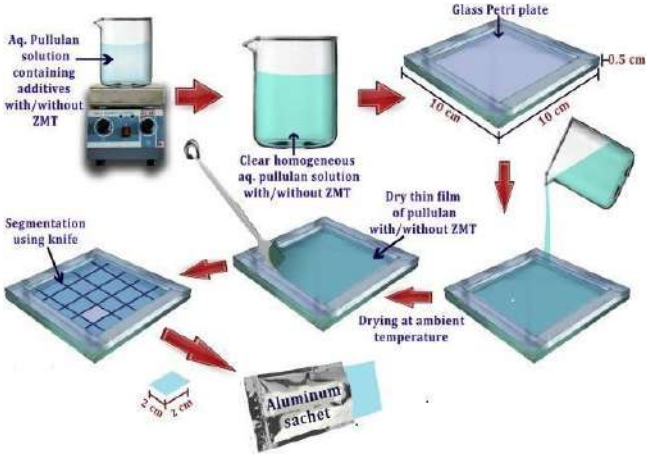


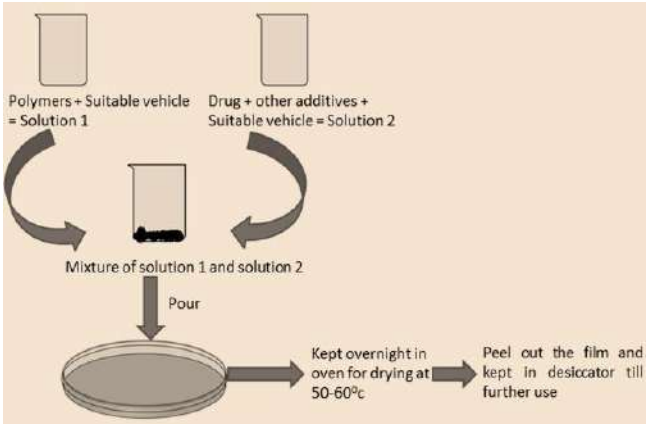
6. Thin films (OTF)

Oral films, also called oral wafers in the related literature, are a group of flat films which are administered into the oral cavity. Although oral film systems, the third class, have been in existence for a number of years, they have recently become the new area of interest in fast- dissolve pharmaceutical drug delivery. 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.



6. oral fast dissolving films .

The solvent casting method is a process that involves the solubilization of a Pharmaceutics of polymer and plasticizer, the spreading of the solution on a substrate, and solvent removal, which causes the molecular orientation of the polymer chains and the intercalation of plasticizer



1.4.1 Classification of oral film

There are three different sub types,

1. Flash release.

2. Mucoadhesive melt-away films.

3. Mucoadhesive sustained-release films.

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

Oral films formulation components

Formulation of oral film involves the intricate application of aesthetic and performance haracteristics such as taste masking, fast dissolving, physical appearance, mouth-feel etc.

The excipients used in formulation of oral film are given below as per their categories. From the regulatory perspectives, all excipients used in the formulation of oral film should be generally regarded as safe (i.e. Gras-listed) and should be approved for use in oral pharmaceutical dosage forms.

Films forming polymers

A variety of polymers are available for preparation of oral films. The polymers can be used alone or in combination to obtain the desired film 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 depen dson the type of polymer and the amount in the formulation19. On the other hand, fast dissolving. Films dosage form should have the property to disintegrate in seconds when placed in mouth and deliver the drug to the oral cavity instantaneously

Plasticizers

Plasticizer is a vital ingredient of the oral film formulation. It helps to improve the flexibility of the strip and reduces the brittleness of the strip. Plasticizer plays important role to improve the properties of strip by lowering down the glass transition temperature of the polymer. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of film. Flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer

Choice of drug candidate2

- Suitable drug candidate for FDF should possess:
- No bitter taste.
- Stability in water and saliva.
- Dose should be low.

Sweetening agent

Sweeteners have become the essential part of the formulation intended to be disintegrated or dissolved in the oral cavity. Both natural sweeteners as well as artificial sweeteners are used in the formulation of fast dissolving films. Generally, sweeteners are used in the formulation in concentration of 3-6%w/w, either in combination. Polyhydric alcohols such as sorbitol, mannitol and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation.

Saliva stimulating agent

The rationale of employing saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving film formulations. Generally, acids which are used in the preparation of food can be utilized as salivary stimulants, like citric acid, malic acid, lactic acid, ascorbic acid etc. These agents are used alone or in combination between 2 to 6%w/w of weight of the film. Sweeteners also act as saliva stimulating agent.

Flavouring agent

Selection of flavour is depending on which type of drug is to be incorporated in the formulation. The acceptance of the oral disintegrating/ dissolving formulation by an individual depend on the initial flavour quality which is observed in the first few seconds after the product has been consumed and the after taste of formulation lasts for at least 10 min. The amount of flavour required to mask the taste depend on the flavour type and its strength. Flavouring agent is used in the formulation in concentration of 10%w/w.

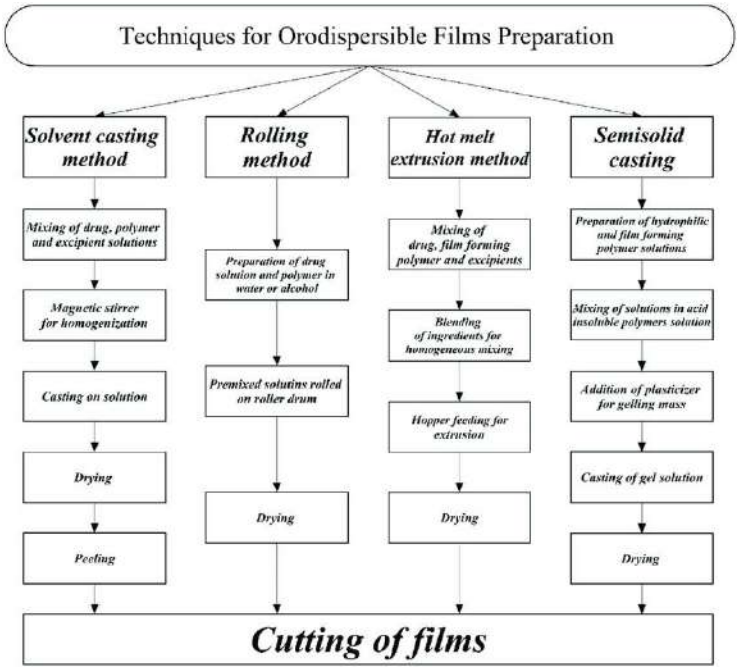
Colouring agent

FD and C approved colouring agent is incorporated in fast dissolving film. Generally colouring agent is not exceeding concentration a level of 1%w/w in fast dissolving film. Mainly titanium dioxide is used in the formulation35.

4.2 Manufacturing methods

Various approaches to manufacturing of rapid dissolving film are classified as follow:

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



4.3 Evaluation of fast dissolving oral films

Organoleptic evaluations

Formulated films were evaluated for organoleptic evaluations like color, odor and taste.

- **Physical appearance and surface texture**

Physical appearance was checked by visual inspection and surface texture was evaluated by touch or feel of the film.

- **Weight uniformity**

The cast film was cut at different places and the weight of each film was checked with the help of an electronic balance and the average weight was calculated.

- **Folding endurance**

Folding endurance was determined by repeatedly folding the film at the same position until it breaks. The number of times the films can be folded without breaking is termed as the folding endurance value.

- **Tensile strength**

Tensile strength is the maximum stress applied to a point at which the film specimen breaks. This test is basically performed to measure the mechanical strength of the films. It can be calculated from applied load at cleavage divided by the film cross sectional area given in the equation below: Tensile strength =(load at failure / strip thickness ×strip width) × 100

- **Percent elongation**
  - When stress is applied, a film sample stretches, and this is referred to as a strain. Strain is basically the deformation of film divided by the original dimension of the sample.
  - Percentage elongation=increase in length×100 /original.
- **Thickness of films**
  - The thickness of a film is determined by using a digital screw gauge at different decisive location (at least 5 locations). Therefore, it is essential to determine uniformity in the thickness of the film

- which is directly related to the accuracy of the dose in the film formulation.

- **Disintegration time**
  - 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 for the fast dissolving oral films.
  - Disintegrating time will vary depending on the formulation but generally the disintegration ranges from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films.
- **Surface pH**

The surface pH of the films was determined in order to investigate the possibility of any side effects in vivo by placing the film on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on films. The change in the colour of pH paper was observed and reported.

- **Drug content**

The film can be tested for drug content uni formityby UV visible spectrophotometric method. Films of each formulation can be placed in different 100ml volumetric flask and can be dissolved using the pH buffer and volume was made up to 100ml. After 30min, 5ml of sample can withdraw and transferred into a 10ml volumetric flask and the volume was made up to mark. The absorbance of resulting solution measured against blank in UV spectrophotometer. The percentage drug content was determined using the standard graph. The mean and standard deviation were calculated.

- **In-vitro drug release**

Standard official basket or paddle apparatus is used for conducting dissolution studies on films. Sink conditions should be maintained during dissolution. Sometimes while performing this process, film floats over the medium making it difficult to perform the test properly. This problem is more likely to occur in case of paddle method thus the basket apparatus is mostly preferred. Media used are 6.8 pH phosphate buffer (300ml) and 0.1 N HCl (900ml). Temperature is maintained at 37 ± 0.5 _C and rotation speed of 50 rpm is usually adjusted. Samples of drug dissolved are collected at predetermined intervals and are analyzed by using UV spectrophotometer.

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