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A REVIEW ON ORAL THIN FAST DISSOLVING FILM

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ABSTRACT

Because of its ease and flexibility, mouth dissolving film is one of the most advanced oral solid dose forms available. Mouth dissolving films are oral solid dose forms that, when placed in the mouth without water or chewing, dissolve and disintegrate in about a minute. The drug can avoid the first pass metabolism with this dose form, so Medication bioavailability could be increased. Oral fast dissolving film may enhance the rate at which activity begins and decrease the dose and get rid of the choking dread. When creating mouth-dissolving movies, both the visual and performance attributes such as plasticized hydrocolloids and solvent-laminated API flavour masking agents because it provides excellent thickness uniformity, beautifully glossy films, and superior physical qualities. Oral fast dissolving films are assessed based on a number of factors, including thickness and physical characteristics like folding endurance, dissolution and disintegration duration. This paper provides an overview of formulation methods, assessment criteria, summary of mouth dissolving film packaging and some of the marketed goods that are now available. (1)

Keywords: Technology; Thickness; Quick relief; Mouth Dissolving Film

INTRODUCTION

Oral film technology was initially developed in the late 1970s to help paediatric and elderly patients who had trouble swallowing tablets and capsules. Today, it is popular in the pharmaceutical industry because it is less fragile than other oral dosage forms. One of the most popular methods for administering medication is orally since it is more affordable, convenient, and easy to administer, all of which increase patient compliance. A novel medication delivery method for oral administration of medications is the oral fast dissolving film. Since oral drug delivery is thought to be the most patient compliant, convenient, safe, and cost-effective way of drug delivery, almost 90% of medications used to treat various disorders and diseases are given to the body through this route. [(2)] The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of of ingestion, pain avoidance, versatility and most importantly patient compliance. The most popular dosage forms are tablets and capsules. In last two decades, due to enhanced demand of patient compliance a vast research took place in this area. There are around 350 drug delivery systems developed in accordance with patient compliance. Geriatric patients may have difficulty in swallowing and chewing the tablets resulting in patient noncompliance and ineffective therapy. To overcome these problems mouth dissolving tablets are a very good option. They disintegrate and get dissolved faster in saliva without the usage of water. As a result it explains good patient compliance. The demand for this fast and mouth dissolving technology was approximately 16.50 billion US dollars in the year 1996 but now it is expected to grow about 80 billion U S dollars every year. [(3)]

Oral fast dissolving films, a new drug delivery system for the oral delivery of the drugs, was developed 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 oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. [(4)]

Owing to large surface area of the film formulation, there is greater disintegration and dissolution in the oral cavity. As the drug is absorbed through buccal mucosa, first pass metabolism is avoided thus enhancing the bioavailability. Films prove to be advantageous in case of dysphagic patient. As compared to orally disintegrating tablets the films are less fragile and hence provide ease of transportation. [(5)]

Special features of Oral Fast Dissolving Film [(6)]

- Thin elegant films
- Various sizes
- Unobstructive
- Mucoadhesion
- Quick dissolving

- Fast disintegrating

Ideal Requirements of Oral Fast Dissolving Film [7]

The ideal requirements for ODF are summarized below :

• ODF should be thin and flexible, but stable to guarantee a robust manufacturing and packaging process and ease of handling and administration.

•The films should be transportable, not tacky and keep a plane form without rolling up.

• Ease of administration for patients who are mentally ill disabled and uncooperative.

• They should provide an acceptable taste and a pleasant mouth-feel.

• Disintegration time should be as short as possible.

• They should exhibit low sensitivity to environmental conditions such as temperature and humidity.

• They should have ability to provide advantages of liquid medication in the form of solid preparation.

• Surface of the FDF should be smooth and uniform.

- They should remain physically and chemically stable throughout its shelf life.
- Cost effective and ease of commercial production.
- The drug should have pleasant taste
- The drug to be incorporated should have low dose upto 40 mg
- The drugs with smaller and moderate molecular weight are preferable
- The drug should have good stability and solubility in water as well as saliva
- It should be partially ionized at the PH of oral cavity
- It should have the ability to permeate oral mucosal tissue

Advantages of Oral Fast Dissolving Film [8,9]

- ❖ Simple transportation.
- ❖ Ease of swallowing for elderly and young patients.

Clinical Advantages:

- Improved oral absorption
- Improved bioavailability due to less amount of degradation of drug.

Medical Advantages:

- Overcomes unacceptable taste of drugs by masking bitter taste of drugs with taste masking agents.
- Improved patient compliance, especially patients suffering from dysphasia and pediatric and geriatric population.

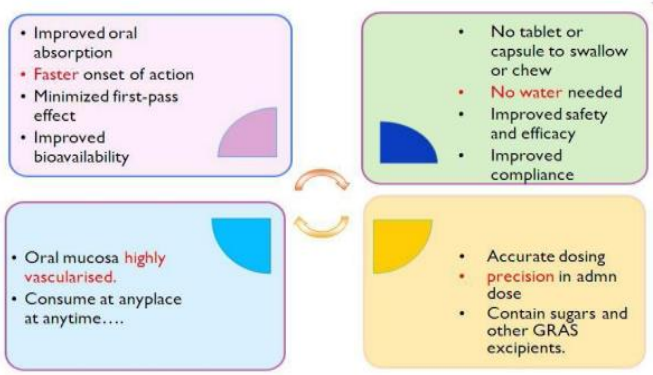

Fig 1: Advantages of OFDF

Comparison Between Orally Fast Dissolving Films and Oral Disintegrating Tablet.

Orally Fast Dissolving Films	Orally Disintegrating Tablets
1. Larger surface area gives greater dissolution.	1. Less surface area gives less dissolution than ofdf.
2. These are flexible and durable.	2. These are brittle and less durable.
3. Only low dose can be incorporated.	3. High dose can be incorporated.
4. Ofdf thicknes are 50 to 500 µm.	4. Odt thickness as like convention tablet.
5. Patient compliance is more.	5. Patient compliance is less than odf.

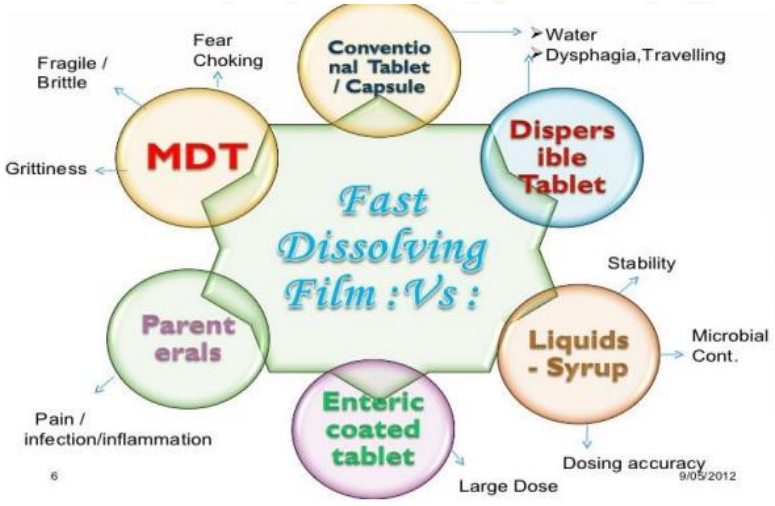

Fig 2 : Comparison of fast dissolving oral film over other dosage forms.

Primary concerns / Formulation aspects of Oral Fast dissolving films

Selection of the API: It is very important part of the process. The selection of API depends on the potency of API, dose, as well as therapeutic efficacy. Most suitable API for ODF includes anti-allergic, antihistaminic, anti-parkinson, sleeping aids and analgesic drugs are preferred selection. It is possible to provide a range of active pharmacological substances. High-dose medications are challenging to include in the movie due to a

restriction on the size of the dosage form. Ideal dynamic voice for oral films pharmaceutical ingredients (APIs) should ideally be strong, highly lipophilic, and less bitter. About 5% w/w to 30% w/w of the dry film is made up of the drug, and up to 10% w/w of the dry film can be made up of multivitamins. Both children and many adults dislike active pharmacological substances that have a bitter taste and/or irritate the mouth and throat. (10)

Film-forming polymer : The water-soluble polymers give the films quick disintegration, a pleasant mouthfeel, and mechanical qualities. Brand-new polymers utilized in medicine delivery. By increasing the molecular weight of the polymer film bases, the disintegration rate of the polymers is slowed down. HPMC E-3 and K-3, Methylcellulose A-3, A- 6 and A-15, Pullulan. Carboxymethyl Cellulose Cekol 30, Polyvinylpyrrolidone PVP K-90, Pectin, Gelatin, Sodium alginate, Hydroxypropyl cellulose, Polyvinyl alcohol, Maltodextrins, and Eudragit-RD10 are some of the water soluble polymers. (11)

Plasticizers: It has been found that formulation factors (plasticizers, etc.) have a significant impact on the mechanical properties of films. The use of plasticizers has also enhanced the mechanical characteristics of the films, such as tensile strength and elongation. These attributes could be impacted by variations in their concentration. Plasticizers like glycerol, di-butylphthallate, and polyethylene glycols are frequently utilized. (12)

Surface active agents: Surfactants are employed as solubilizing, wetting, or dispersion agents to breakdown films quickly and release active ingredients right away. Among the frequently utilized are tweens, sodium lauryl sulfate, benzalkonium chloride, and bezthonium chloride. Poloxamer 407, a surfactant utilized as a solubilizing, wetting, and dispersion agent, is one of the most significant surfactants. (12)

Flavouring agents: You can add any taste, including strong mint, acidic citrus, or sweet confectionary flavours. (12)

Color: There is a wide variety of colors to choose from, including FD&C, EU, Natural and custom colors that match pantones. (12)

Saliva Stimulating agents: To improve the disintegration and provide a quick release, several saliva-stimulating chemicals may also be included. Citric acid, tartaric acid, malic acid, ascorbic acid, and succinic acid are a few of these agents. (12)

Sweetening agents: The goal of the sweeteners is for them to melt or dissolve in the mouth. All sweeteners, artificial and natural, are employed in the preparation of ODFs. There seems to be two hundred metallic elements in sweetening sweeter than sugar by three to five hundred times. Rumor has it that sweeteners and aromatic compounds together have no effect on the film's elasticity. (12)

METHODS OF PREPARATIONS FOR THE FILM

There are several methods employed for the manufacturing of such dosage forms such as casting, spraying, and extrusion. Method of preparation of fast-dissolving films fast-dissolving films can be prepared by:

a. Solvent casting method

b. Semisolid casting method

c. Hot melt extrusion

d. Solid dispersion extrusion

e. Rolling method.

Solvent Casting Method

It is very old film making method. In this method the drug is either dissolved or suspended in a solution containing polymers, plasticizers and other excipients which are dissolved in a volatile solvent, like ethanol or water. It is referred as film dope, it is then casted in petri plate and passed through drying equipment like oven to remove all the volatile solvents. Then the dried film is die cut into strips and packed in sealed atmospherically resistant pouches. This method is suitable for films containing heat sensitive drug/API as the temperature needed to remove the volatile solvents is comparatively low than hot melt extrusion method

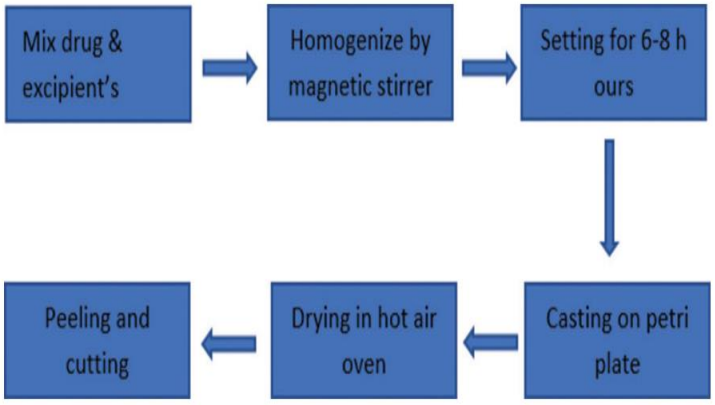

Fig 3 : Solvent Casting Method

Hot Melt Extrusion

Hot melt extrusion is a technique in which a mixture containing drug, polymer and excipients is extruded under high temperature to form a homogenous mass which is then coasted to form smooth films. This is a solvent free process; however, the processing of thermolabile substances is a major drawback of this process.

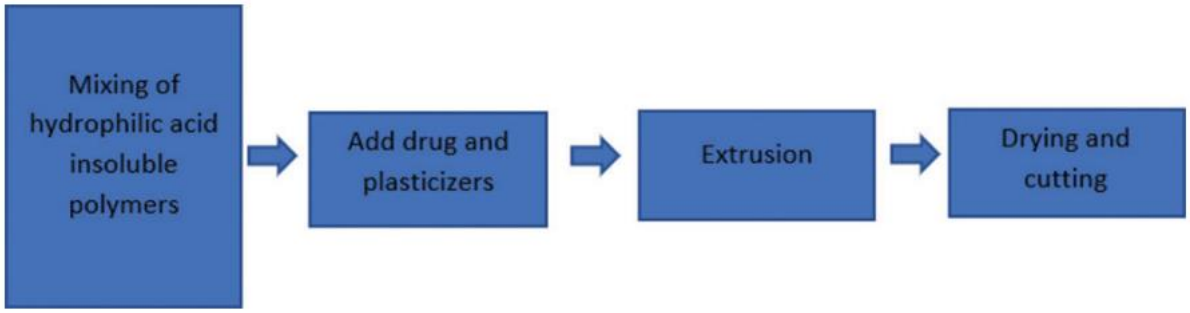

Fig 4 : Hot Melt Extrusion Method

Semi Solid Casting Method

This method is preferably adopted when acid insoluble polymers are to be used in the preparation of the films. Acid insoluble polymers used to prepare films include: cellulose acetate phthalate, cellulose acetate butyrate. Acid insoluble polymer and film forming polymer should be used in the ratio of 1:4. Solution of water-soluble film forming polymer is prepared. Then resulting solution is added to a solution of acid insoluble polymer. After that appropriate amount of plasticizer is added so that gels mass is obtained. Finally, the gel mass is casted into the film or ribbons using heat controlled drums.

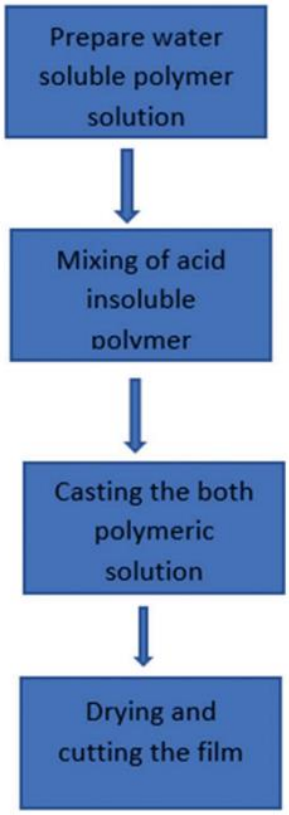

Fig 5 : Semisolid Casting Method

Solid Dispersion Extrusion Method

Solid dispersion of domperidone using beta-cyclodextrin, PEG400 and HPMC E15 was successfully prepared and films were casted using solid dispersion extrusion method.

Rolling Method:

In rolling method, a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water or a mixture of water and alcohol. The film is dried on the rollers and cut

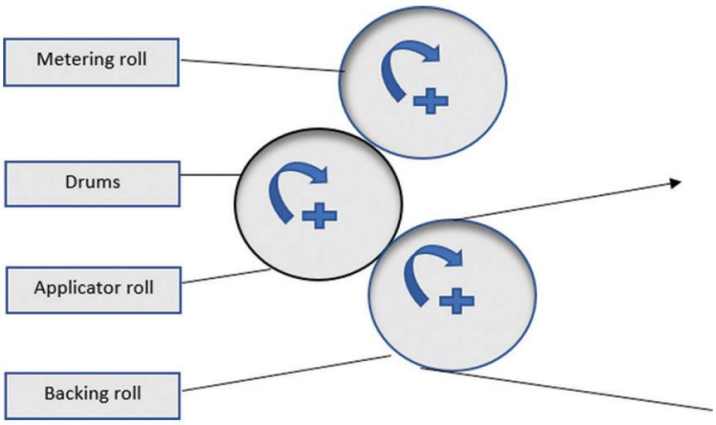

Fig 6 : Rolling Method

EVALUATION OF FAST DISSOLVING FILMS

1 .Appearance, Size, Shape and Thickness:

The formulated films were checked for their appearance, shape and thickness. The thickness of the films was determined at five different places using a digimatic micrometer (Mitutoyo Co., Japan) for each formulation and mean value was calculated. (13)

2 .Weight variation :

The patches were subjected to mass variation study by individually weighing randomly selected patches. The average of five observations of each batch was calculated. Such determinations were carried out for each batch.[13]

3. Folding Endurance :

It was determined by repeatedly folding a small strip of the patch (2×2cm) at the same place till it broke. The number of times a film can be folded at the same place without breaking gave the value of folding endurance. Further, less folding endurance value indicates more brittleness.[13]

4. Tack Test:

Tackiness was evaluated gently by pressing the film between fingertips and results were noted in qualitative terms as tacky or non tacky. [14]

5. Thickness Evaluation:

It is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose distribution in the film. The thickness of the film was measured by calibrated digital Vernier Calipers. The thickness was evaluated at five different locations. [14]

6. pH Evaluation:

The surface pH of the MDFs was determined to investigate the possible side effects due to change in pH in-vivo, since an acidic or alkaline pH may irritate the oral mucosa. The surface pH was determined by using the pH meter. [14]

7. In-vitro Disintegration of Films:

In-vitro Disintegration of Films: In-vitro disintegration time of 2 × 2 cm2 films was determined visually in a petri dish containing 25 ml of phosphate buffer pH 6.8 at 37.0 ± 0.5 °C. The time when the film started to break or disintegrate was recorded, which is the disintegration time of the film

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8. Uniformity of Drug Content :

The drug content of each film was performed by dissolving the film in 100 mL of phosphate buffer pH=6.8 with stirring using a magnetic stirrer for 1 h. This solution was filtered through a 0.45-µm membrane filter and then assayed using a validated HPLC method . The results were presented as the mean of three values . The assay was performed on an HPLC Ultimate 3000 system equipped with a UV detector. [15]

Marketed Films :

Sr.No.	Product	Manufactured By
1.	Donepezil rapid dissolving films, Ondansatron rapid dissolving films	Labtec Pharma
2.	Altoid cinnamon strips, Boots vitamin c strips, Cool shock peppermint strips, Benzocaine films, Caffeine films.	Dow chemical company
3.	Listerine Pocket Paks, Breath Freshening Strips	Pfizer's Warner-Lambert consumer healthcare division
4.	Klonopin Wafers	Solvay Pharmaceuticals
5.	Listerine Cool Mint Pocket Paks	Pfizer, Inc.
6.	Triaminic	Novartis

Table No. 01: List of Marketed Films

CONCLUSION :

OTFs have emerged as a revolutionary trend, and most pharmaceutical companies in this field continue their research and development activities to adapt their drugs in various categories to this technology. This technology is an innovative drug delivery system for all patient groups who have swallowing problems, especially pediatric and geriatric patients. It also offers many advantages over the other dosage forms, such as improved bioavailability and faster effects. It is one of the most important dosage forms that can be used orally in cases of emergency and when an immediate-onset effect is desired. Therefore, it can be concluded that OTFs with excellent patient compliance and many advantages have innovative futuristic opportunities.

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