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# A Review on Oral Dissolving Film

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**ABSTRACT**

Efforts to assure efficacy, safety, and patient acceptance have likely increased over the past few decades as a result of the trend toward novel drug delivery technologies. Recent trends are changing toward designing and developing novel drug delivery systems for already existing medications because the research and development of new chemical entity is difficult, expensive and time-consuming procedure. Orally fast dissolving film is a type of drug delivery device that, when placed in the mouth, quickly dissolves or disintegrates without the need for water. In a relatively recent dosage form called an oral fast dissolving film, hydrophilic polymers are used to create a thin film that quickly dissolves or disintegrates on the tongue or in the buccal cavity. It serves as a different platform for compounds with intense first-pass metabolism. Solvent casting, Semisolid casting, Hot melt extrusion, Solid dispersion extrusion and Rolling are the methods used to prepare oral dissolving films. The current assessment provides a description of various preparation method and quality control procedures for the oral fast-dissolving films.

**KEYWORDS:** Fast dissolving film, Oral strips, Tensile strength, etc.

## I. INTRODUCTION

Because they are more adaptable and comfortable, fast dissolving oral films (FDOFs) are the most sophisticated oral solid dose form. As opposed to fast-dissolving tablets, it improves API efficacy by dissolving in the oral cavity in under a minute after coming into touch with less saliva, requiring no chewing, and no water for administration [1,2].

The fast-dissolving oral film consists of a very thin strip that is simply applied to the patient's tongue or any other oral mucosal tissue. Upon becoming wet from secretion, the film quickly hydrates and clings to the area. Once released for oromucosal and intragastric absorption, it swiftly disintegrates and dissolves [3,4].

A novel drug delivery technology for oral medication is fast-dissolving film. For the treatment of a variety of ailments and diseases, about 90% of medications are given to the body orally since this is thought to be the most efficient, convenient and safest drug delivery technique with the highest patient compliance [5,6].

The ODFs are quickly dissolving thin films with a thickness of five to twenty centimeter where the material has matrix-victimization shape of Structure. Using an alternate excipient such as plasticizers, colourants, sweeteners, taste agents for masking, etc. Pharmaceuticals active ingredients may total up to 15 mg. The transitional glass temperature of polymers rises as a result of softener's increased working strength, propagation and durability of films [7].

For patients who have trouble swallowing pills or capsules, using fast-dissolving films for oral delivery was an innovative method. The issue of ingesting solid dose forms is a challenge for geriatric, juvenile, and dysphasic individuals who have a variety of medical problems. One research revealed that 26% of 1576 individuals had trouble swallowing pills [8].

The selection of the polymer and additional excipients such as the superdisintegrant as well as the optimization of the polymer and super-disintegrant concentrations are key factors in formulating a rapid dissolving film. The primary requirements for fast-dissolving films are rapid disintegration on the tongue and a quick commencement of action. Several pharmacological types including NSAIDs, expectorants, antihistaminic, antiulcer, antiasthmatics and antitussives can be made into mouth-dispersing films [9,10].

## II. ADVANTAGES [11-13]

1. Accessibility of a bigger surface area that causes materials to dissolve and disintegrate in the oral cavity within seconds.
2. Quick Dissolving In comparison to FDT, film is flexible, making it less fragile and requiring no specific packaging for protection during shipping and storage.
3. The dysphasic patients are more satisfied because they no longer need to drink water.
4. When opposed to FDT, there is no risk of choking.
5. Additionally, the film dosage form's wide surface area enables rapid salivation, quick disintegration, direct absorption and systemic circulation without first-pass hepatic metabolism, which increases bioavailability.
6. The dose form can be taken whenever and wherever the user pleases.

## III. DISADVANTAGES [14-16]

1. It is not possible to deliver medications that are unstable at buccal pH or that irritate the mucosa by this route.
2. Only administer a drug with a low dosage required.
3. Most medications have a bitter taste, hence taste masking is necessary.
4. Special packaging is required since ODFs must be protected from water and are delicate.
5. A technical difficulty is dose consistency.
6. Oral film's pricey packaging.

## IV. IDEAL CHARACTERISTICS OF FAST DISSOLVING FILM [17]

Following are the ideal characteristics of ODFs:

- It must be lightweight, versatile and simple to use.
- The films must be transportable, non-clingy and maintain a plane structure without going up.
- Directing should be easy.
- The film should have a great mouthfeel and a pleasing taste.
- The breaking down time should be as quick as is reasonable given the conditions.
- The film's surface should be even and smooth.
- Throughout the duration of its use life, it must continue to be really and synthetically stable.
- It should be less susceptible to environmental factors, such as humidity and temperature.
- Unit film size shouldn't be excessively large.

## V. FORMULATION OF FAST DISSOLVING FILM

1.Active Pharmaceutical Ingredient

1-25% of the drug by weight is present in a typical formation of the film. Fast-dissolving films can deliver a variety of pharmaceutically active substances. Oral fast-dissolving films are best suited for incorporating small dosage compounds. Multivitamins were absorbed in the films with a disintegration time of less than 60 seconds up to 10% dry film weight [18-21]. The dose of the drug should be in mgs (less than 20 mg/day) for an effective formulation [22]. Numerous medications such as antihistamines, anti-diarrheal medications, antidepressants, vasodilators, anti-asthmatic medications and antiemetics can be used in oral dissolving films [23]. The water solubility and permeability of the drug should be adequate(belongs to BCS class 1)[24] .

Table 1: List of few drug that can be incorporated in fast dissolving film [25,26]

| Sr. No | Drug | Dose(mg) | Therapeutic Use |
|---|---|---|---|
| 1 | Azatadine Maleate | 1 | Anti-histaminic |
| 2 | Nicotine | 2 | Smoking cessation |
| 3 | Loperamide | 2 | Anti-diarrhoeal |
| 4 | Ondansetron | 2.5 | Anti-emetic |
| 5 | Triprolidine hydrochloride | 2.5 | Anti-histaminic |
| 6 | Zolmitriptan | 2.5 | Anti-migrane |
| 7 | Salbutamol | 4 | Anti-histaminic |
| 8 | Chlorpheniramine Maleate | 4 | Anti-allergic |
| 9 | Cetirizine | 5-10 | Anti-histaminic |
| 10 | Acrivastine | 8 | Anti-histaminic |
| 11 | Loratadine | 10 | Anti-histaminic |
| 12 | Omeprazole | 10-20 | Proton pump inhibitor |
| 13 | Famotidine | 10 | Antacid |
| 14 | Ketoprofen | 12.5 | Analgesic |
| 15 | Dicyclomine hydrochloride | 25 | Muscle relaxant |
| 16 | Diphenhydramine hydrochloride | 25 | Anti-allergic |
| 17 | Sumatriptan succinate | 35-70 | Anti-migrane |

2. Film forming polymers

In order to prepare films, primarily water soluble polymer is used [27]. Because the tensile strength of oral films depends on the type and total quantity of polymer used, choosing the right polymer is one of the most important and significant factors for their effective production. The primary component of the fast dissolving oral film is polymers. The quantity of polymer incorporated into the oral strip affects how robust the film is. On the basis of the total weight of the dried film, 45% w/w of polymer is often utilized [28]. By increasing the molecular weight of the polymer film bases, the disintegration rate of the polymers is decreased [29]. Natural and synthetic polymers are the two types of polymers employed. Pullulan, gelatin, guar gum, and xanthan gum are examples of natural polymers. Hydrogenated propyl methyl cellulose (HPMC), PVPK30, PVA, modified starches and other synthetic polymers[27].

3. Plasticizers

It is a key component of oral thin films [30]. Plasticizer is crucial in ensuring that film is flexible. Flexibility, tensile strength and elongation are essential for formulation purposes; therefore, by adding a plasticizer, we may get all of these properties in the film[31]. It should work well with polymers, the drug and other excipients [29]. By lowering the polymer's glass transition temperature, plasticizer greatly enhances the characteristics of the strip. The usage of plasticizer improves the flow of polymer and increases the polymer's strength [32,33]. Some of the frequently used plasticizer excipients are castor oil, glycerol, propylene glycol, low molecular weight polyethylene glycols, citrate derivatives like tributyl, triethyl, acetyl citrate. Phthalate derivatives like dimethyl, diethyl, and dibutyl phthalate. But inappropriate plasticizer use can cause the film to fracture, split and peel off the strip [34-36]. The amount of plasticizer in the formulation of the film also depends on its concentration; for example, turbidity in the film results from having too much plasticizer [31].

4. Sweetening agent

For the purpose of giving the formulation a sweetening effect, sweetener is added. Some medications have an extremely bitter taste, thus in those cases we add sweetener [61]. Sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose are the traditional sources of sweetener [37]. To make the mouth-dissolving formulations more palatable, both natural and artificial sweeteners are utilized.

a) Xylose, ribose, glucose, sucrose, maltose and other naturally occurring water-soluble sweeteners are suitable sweeteners.

b) artificial sweeteners that dissolve in water such as acesulfame-K, cyclamate salts, sodium or calcium saccharin salts, etc.

c)Aspartame, a sweetener with a dipeptide base.

d)Thaumatin I and II, protein-based sweeteners.

As they additionally provide nice mouth-feel and a cooling effect, polyhydric alcohols like sorbitol, mannitol and maltitol can be used in combination [38]. Oral strips containing valdecoxib were made using aspartame [39]. Maltodextrin was used as a sweetener for the oral piroxicam strip [40]. Typically, sweeteners are used alone or in combination at a concentration of 3 to 6%w/w [41]

5. Saliva stimulating agents

In order to accelerate the breakdown of the formulations of fast dissolving films, these agents are used to increase saliva production rates. The majority of the time, acids that are employed in food preparation can be used as salivary stimulants [42]. Citric acid, tartaric acid, ascorbic acid, lactic acid and malic acid are the most frequently used saliva stimulants [61]. Between 2 and 6% w/w of the film's weight, these agents are used alone or in combination [43].

6. Surfactants

Surfactants are used as a solubilizing, wetting or dispersing agent to dissolve the film quickly and release the active ingredient [42]. The following substances are frequently used: tweens, sodium lauryl sulphate, benzethonium chloride, poloxamer 407, etc. Poloxamer 407 is one of those most frequently utilized surfactants [44].

7. Flavouring agents

It is necessary for the flavours employed in the formulation to be stable, soluble, non-toxic and should be compatible with the excipients [46]. Depending on the type and strength of the flavour, a certain amount of flavour is required to mask the taste. Flavoring agents can be chosen from synthetic flavour oils, oleo resins and extracts made from different plant components, such as leaves, fruits and flowers. Flavors can be utilized either alone or in combination [47].

8. Colouring agent

The film is coloured with a colouring agent [48]. Natural colours , FD&C-approved colours, pigments like titanium dioxide, etc. are the often used colouring compounds. A 1%w/w maximum concentration for the colouring agents is recommended [49]. Oxide is most frequently utilized in ODFs and different pharmaceuticals [50].

## VI. METHOD OF PREPARATION

Different methods for achieving fast dissolving film formulation by the following:

A] Casting and drying

1. Solvent Casting

The water-soluble components are broken down to create a viscous clear solution. Smaller volumes of the solution are used to dissolve the API and other substances before mixing them with the bulk. The aqueous viscous solution is then given this combination. A vacuum is used to extract the trapped air. The finished mixture is cast into a film, allowed to dry and then it is cut into the required number of pieces [51].

Advantages [52]

- Superior than extrusion in terms of thickness homogeneity and clarity.
- An oral thin-film batch produced by liquid casting typically has a relative standard deviation (RSD) of around 2% when subjected to uniformity testing.
- The film is free of defects like die lines and has a nice shine.
- Films are more flexible and have higher physical qualities.
- Although different thicknesses are conceivable to suit API loading and dissolving requirements, 12-100 mm is often the optimum finished film thickness.

2. Semisolid Casting Method [53,54]

A water soluble film-forming polymer solution is prepared and introduced into the acid-insoluble polymer solution in 1:4 ratio. The right amount of plasticizer is incorporated to create a gel mass. It is casted utilizing heat-controlled drums into the films or ribbons. The film's diameter should be between 0.015 and 0.05 inches.

B] Extrusion

1. Hot melt extrusion

Polymer is shaped using the hot melt extrusion method. The high temperature is allowed in this approach for polymer substances and medicinal molecules [27]. Essentially, the drug and carrier are combined in solid form when using the hot melt extrusion process. The material is then put into the extruder as dry granules. To process the granules for three to four minutes inside the extruder barrel, the short speed should be set at 15 rpm. $80^0$C (zone 1), $115^0$C (zone 2), $100^0$C (zone 3) and $65^o$C should be the processing temperatures (zone 4). The extrudate ($T = 65^0$C) was subsequently compressed into a cylindrical calendar to produce a film. Hot melt extrusion offers a few conveniences [55]. By using hot-melt extrusion technique, maltodextrin can be employed to produce fast-dissolving films with a significant drug loading capacity [56,15].

2. Solid Dispersion Extrusion

When one or more active chemicals are dispersed in an inert carrier in a solid form and amorphous hydrophilic polymers are present, this is referred to as a solid dispersion. In a suitable liquid solvent, the drug is dissolved. Then the solution is added to the melt of polyethylene glycol, which can be obtained below 70 °C. In the end, dies are used to mould the solid dispersions into films [57]. A more solid extrusion approach has been used to cast films that include domperidone solid dispersion produced with beta-cyclodextrin, PEG 400 and HPMC E15[58].

3. Rolling method

This approach involves rolling a drug-containing solution or suspension on a carrier. Water and an alcohol-water mixture make up the majority of the solvent. The film is cut into the desired shapes and sizes after it has dried on the rollers [59]. There should be a variety of rheological characteristics in the drum's rolling [60].

Evaluation of fast dissolving film

1. Thickness of the film

Five different spots on the film sample should be measured for thickness (the centre and four corners) and the mean thickness should be determined [61,29]. The perfect drug dosage is specified by the film's thickness[62]. The width of the film will range from 5 to 200 m [63]. At various key locations, it can be measured with a micrometer screw gauge or calibrated digital Vernier Calipers [29]. The individual film was positioned between the screw gauge's two anvils and the sliding knob was rotated until the film was adjusted. It was noted the digital reading that was displayed [64]. The dissolving rate is determined by the thickness of the film; if the film is thin, the dissolution rate will be higher and vice versa [65].

2. Visual Inspection [66]

The administration of the film depends in large extent on the patient's acceptance of the dosage form. The primary inspection criteria are clarity, transparency and oiliness. If it was found satisfactory, additional evaluations were conducted. The formed films were scrapped if they weren't satisfactory.

3. Tensile Strength

The maximum stress at which a strip specimen breaks is known as the tensile strength [67]. A film's toughness can be determined by its tensile strength [68]. The mechanical properties of film are assessed using this test. Basically, the amount of polymer employed in the formulation determines the tensile strength [69].

Tensile Strength = load at failure/strip thickness × strip width*100 [70]

4. Dryness or tack test

This test is done to see whether a film can stick to a piece of paper that has been placed between strips [71]. Tack refers to the tenacity with which the strip attaches to a supplement (a piece of paper) that the strip has been forced into touch with it. Instruments for this investigation are also accessible [62,67]. The dry-to-pieces, dry-to-coat,

dry heavy, visible, dust-flow, dry-three and dry-print-free phases of film drying are established. The film drying techniques consist of about eight phases.

5. Folding endurance

It was discovered by repeatedly folding a film with a constant cross-sectional area and thickness until it broke [72]. This test validates the film's tensile strength [73]. The folding endurance value was calculated as the number of folds the film could undergo without breaking [74]. An increase in folding endurance value indicates a film's mechanical strength [75]. As the polymer concentration grew in the formulations, folding endurance values similarly increased [76].

6. Drug content uniformity

To estimate the amount of drugs in each film, the content uniformity is calculated [75]. This is determined by any standard assay method specified for the specific API in any of the standard pharmacopoeia [77,78]. The contents should lie within the range of 85% and 115% with a standard deviation not greater than 6%, in accordance with USP27 [75].

7. Transparency [79,80]

A straightforward UV spectrophotometer can be used to determine the film’s transparency. Film samples should be cut into rectangles and put inside the surface of the spectrophotometer at the films' 600 nm direct transmittance.

8. Disintegration time

It is the time when comes into contact with water, the film starts to disintegrate apart [80,81]. The disintegration time often varies with formulation and ranges from 5 to 30 seconds depending on the film composition. For this test, the USP disintegration apparatus is typically utilized.

9. In-vitro dissolution test

Dissolution studies on films are carried out using standardized approved basket or paddle apparatus. During dissolution, sink conditions must be maintained [51]. Dissolution is the rate at which a drug substance moves into a solution per unit of time given typical temperature, solvent content and liquid/solid interface circumstances. The sink conditions and the drug's maximal dose affect the choice of the dissolving medium. The medium should be kept at a temperature of 37+- 0.5ºC and a rotational speed of 50rpm for the dissolving investigation [80,81]. The 900 ml of buffer solution added to the 6.8 pH phosphate buffer after preparation [82].

10. Surface pH [83]

The surface pH of the film is calculated using buffer. Get a petri dish and put cut film in it. Add 0.5 ml of buffer solution to the film, then measure the pH. A digital pH meter is used.

11. Stability studies

The major purpose of the formulation's stability testing is to determine whether or not the final product is stable. It is also used to determine how temperature and humidity would affect a drug's stability during actual storage. The formulation is initially covered with butter paper, then aluminium foil is placed on top of that and last it is loaded into an aluminium bag and then heat sealed. Formulation should be kept for three months at 45°C and 75% RH. Triplicate samples are obtained during the stability studies at three intervals, namely 0,1 and 3 months and films should be examined for variations in the body and drug content [84-86].

12. Weight Variation Test

Individual films were examined for weight variation. The average weights were calculated after being weighed. Then the typical patch weight is subtracted from the total weight of the patches. A wide range of weights indicates the ineffectiveness of the technique used and is probably not homogeneous in its drug composition [87] .

## VII. CONCLUSION

Fast dissolving film has recently grown in favor as a dosage type and is the most popular and reliable oral dose form that bypass the hepatic system and exhibit greater therapeutic response. The pharmaceutical industry prefers this dosage form owing to patient compliance, particularly in addition to industrial acceptability, these conditions include paediatric and geriatric. They combine the increased durability of a solid dosage form and a liquid's high ability to be applied. Oral films can substitute brand name and generic medications for over-the-counter

medications brand from the market owing to decreased costs and consumer preference. This technology is a useful tool for product development life cycle management to lengthen the patent life of existing goods. Oral dissolving film also have a lot of potential of successfully distributing the therapeutic agent systemically. Several benefits over numerous dosages are seen locally even over the rapidly dissolving pills. This describes the extensive study being done on this technology. This technology is therefore developing quickly, requesting the majority of pharmaceutical corporations to a variety of active consumers.

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