FAST DISSOLVING ORAL FILM: AN APPROACH TO ENHANCE PATIENT COMPLIANCE

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ABSTRACT

The tendency toward novel drug delivery technologies over the past few decades has undoubtedly intensified efforts to guarantee efficacy, safety, and patient acceptance. Recent trends have shifted toward creating and manufacturing creative drug delivery methods for already existing medications because discovering and producing new chemical agents is a difficult, expensive, and time-consuming procedure. A type of medication delivery device known as an orally fast dissolving film dissolves or disintegrates in the oral cavity after being deposited there in a matter of seconds without the need for water. The most cutting-edge oral solid dose form is a film that dissolves in the mouth, thanks to its adaptability and user-friendliness. Mouth dissolving films are oral solid dose forms that, when placed in the mouth without any water or chewing, instantly break down and dissolve. This dosage form allows the medication to bypass the first pass metabolism so bioavailability of medication may be improved. Mouth dissolving film has potential to improve onset of action lower the dosing and eliminate the fear of chocking.

KEYWORDS: Fast dissolving film, Buccal cavity, bioavailability

INTRODUCTION [1-5]

Fast-dissolving buccal film drug delivery systems are quickly becoming regarded as an essential new method of drug administration. They are typically applied to pharmaceutical and dietary supplement goods. It is the most cutting-edge drug delivery technology available and offers a very practical way to take prescription drugs and dietary supplements. MDFs can also be utilised when a speedy beginning of action is necessary for a medicine, such as when a local anaesthetic is needed for toothaches, oral ulcers, cold sores, or teething [3-5]. As an alternative to fast dissolving tablets, fast dissolving films are made using hydrophilic polymers that quickly dissolve/disintegrate in the mouth within a few seconds without water and remove the danger of choking. Mainly the fast dissolving film can be considered as an ultra thin strip of postage stamp size with an active pharmaceutical ingredient and other excipients. Most fast dissolving films are having taste masked active ingredients. These masked active ingredients are swallowed by the saliva of patients along with the soluble and insoluble excipients.

SPECIAL FEATURES OF FAST DISSOLVING FILMS [6, 7]

- Thin elegant film
- Unconstructive
- Available in various size and shapes
- Fast disintegration
- Rapid release
- Give a pleasant mouth feel.
- Have an acceptable taste.
- Should not leave residues in mouth.

ADVANTAGES [8-10]

- Availability of larger surface area that leads to quick disintegration and dissolution in the oral cavity within a matter of seconds.
- Fast Dissolving Film is flexible so they are not as fragile so does not need any kind of special package for protection during transportation and storage as compared to FDT.
- No need of water has led to better suitability amongst the dysphasic patients.
- No fear of chocking as compared to FDT.
- The large surface area available in the film dosage form allows rapid wet by saliva then quickly disintegrates and dissolve and absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism and an increase the bioavailability.
- Bypassing hepatic first pass effect leads to reduction in dose which can lead to reduction in side effects associated with the molecule.
- The dosage form can be consumed at any place and any time as per convenience of the individual.
- Precision in administered dose.

DISADVANTAGES [11-12]

- Dose uniformity is a technical challenge.
- Hygroscopic in nature.
- High doses cannot be incorporated (<40 mg/4cm2piece)
- Require special packaging for products stability and safety.

FORMULATION ASPECTS FOR FAST DISSOLVING FILMS: [13-19]

The complex use of aesthetic and functional qualities, such as flavour masking, quick dissolution, physical appearance, mouth feel, etc., is required in the formulation of FDFs. From a regulatory standpoint, every excipient used to create oral strips must be GRAS-listed and permitted for use in pharmaceutical dosage forms intended for oral administration.

A) Drug Class

This technology may be used to deliver a wide range of APIs. High dose medications are hard to include in films, nevertheless, because the size of the dosage form has a limit. For oral thin film, like in the case of quickly dissolving tablets, a less bitter, powerful, and highly lipophilic medication should be chosen.

The ideal characteristics of a drug to be selected:

- The medication should taste good.
- The substance that will be added should only have a low dose of up to 40 mg.
- It is advisable to use medications with a low to moderate molecular weight.
- The medication should be stable and easily soluble in both saliva and water.
- It should be able to penetrate oral mucosal tissue and be partially unionised at the pH of the oral cavity.

Antiemetic neuroleptics, cardiovascular drugs, analgesics, antiallergy, antiepileptics, sedatives, hypnotics, diuretics, anti-parkinsonian drugs, anti-bacterial pharmaceuticals, and medications for erectile dysfunction, anti- Alzheimer's, expectorants, etc.

B) Film Forming Polymers

Due to their quick disintegration, pleasant tongue feel, and mechanical strength, water-soluble polymers are utilised as film formers. The resilience of strip depends on the type of polymer and its amount in the formulations. The most popular polymers for making films are pullulan, gelatin, and hypromellose, which are all available. Pullulan, Gelatin, Guar, Xanthan, Hydroxypropyl Methylcellulose (HPMC), Modified Starches, PVPK30, PVA, and others are examples of polymers that are water soluble.

The ideal polymers for the preparation of FDF are Pullulan and HPMC among them. Like Amylose, Dextran, and Cellulose, pullulan is a neutral glucan whose chemical composition is somewhat influenced by the carbon source, producing microorganisms (such as various strains of Aureobasidium pullulans), and fermentation conditions. HPMC is propylene glycol ether of methylcellulose. The low viscosity grades of HPMC are use for the preparation of MDF like HPMC E3/E5/E6/E15.

Ideal properties of the polymers used in the oral film:

1. Polymers should not be poisonous, irritating, or bitter.
2. Polymers should not have any flavour, and
3. They shouldn't include any leachable contaminants.
4. It should be affordable and easily accessible.
5. It shouldn't present a barrier throughout the disintegration process.
6. It should have good spreading and wetting characteristics.
7. It shouldn't result in a secondary infection in the oral cavity and should have a long enough shelf life.
8. It should have adequate peel, shear, and tensile strength.

C) Plasticizers

A key component of the mouth-dissolving films is plasticizer. The choice of plasticizer is based on how well it works with the polymer and the kind of solvent used in the casting of the film. It aids in enhancing the film's elasticity and lessens the brittleness of the film. By lowering the polymer's glass transition temperature, plasticizer greatly enhances the characteristics of the strip. The concentration of plasticizers employed typically ranges from 1 to 20% by weight of dried polymer. The plasticizer must be highly flammable. Examples include triacetin acetyl citrate, glycerol, propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives such as dimethyl, diethyl, and dibutyl derivatives, and others.

D) Sweetening agents

Sweeteners are now a crucial component of both food and medicinal items that are meant to dissolve or disintegrate in the mouth. Artificial and natural sweeteners are both utilised to increase the mouth-feel of mouth-dissolving formulations. Suitable sweeteners comprise:

(1) Natural sweeteners that dissolve in water, such as xylose, ribose, glucose, sucrose, maltose, etc.

(2) Artificial sweeteners that dissolve in water, such as acesulfame-K and sodium or calcium salts of saccharin.

(3) Aspartame, a dipeptide-based sweetener

E) Cooling agents

Monomethyl succinate and other cooling agents can be added to products to increase mouthfeel and flavour intensity. You can combine flavours with additional cooling agents like WS3, WS23, and Utracoll II.

F) Flavoring substances

Individuals' perceptions of flavours vary depending on their ethnicity and preferences. Flavoring agents can be chosen from synthetic flavour oils and extracts of oleo resins from different plant components, such as leaves, fruits, and flowers. The type and strength of the flavour determine how much flavour is required to cover up the taste.

G) Coloring agents

Pigments such as titanium dioxide or FD&C approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in oral strips when some of the formulation ingredients or drugs are present in insoluble or suspension form.

H) Surfactants

Surfactants are employed as solubilizing, wetting, or dispersion agents to breakdown the film quickly and release the active ingredient. Surfactants also increase the solubility of poorly soluble medications in buccal films that dissolve quickly. For instance, tweens and spans, sodium lauryl sulphate, benzalkonium chloride, benzthonium chloride, and polyloxamer 407.

I) Thickening and stabilising substances

Before casting, the strip preparation solution or suspension is given a boost in viscosity and consistency using stabilising and thickening agents. It is possible to use natural gums such as xanthan gum, locust bean gum, carrageenan, and cellulose derivatives.

METHOD OF PREPARATION [20-25]

There are five methods which are used alone or in a combination with the following process for the manufacture of the fast dissolving oral films

i) Solvent casting

ii) Semisolid casting

iii) Hot melt extrusion

iv) Solid dispersion extrusion

v) Rolling

1. Solvent casting

To create a clear, viscous solution, water-soluble polymers and plasticizers are dissolved in a suitable volatile solvent, such as ethanol or distilled water. The active pharmaceutical component and other ingredients are dissolved in aqueous solvent and blended with the bulk after the solution has been agitated for two hours in a magnetic stirrer. The solution is then cast into a suitable Petri dish and dried in an oven at 50 oC for 24 hours to release the trapped air. The required size and form of the film are cut.

2. Semisolid casting

A water soluble film-forming polymer solution is created. It is put into the acid-insoluble polymer solution in a 1:4 ratio. By adding the appropriate amount of plasticizer, which is cast into the films or ribbons using heat-controlled drums, a gel mass is created. The film should have a diameter of 0.015 to 0.05 inches.

3. Hot melt extrusion

In the hot melt extrusion process, the medication and carrier are virtually combined in solid form. The extruder is then fed with dried, granular material. In order to process the grains inside the extruder barrel for about three to four minutes, the short speed should be set at 15 rpm. Zone 1, Zone 2, Zone 3, and Zone 4 processing temperatures should be 800C, 1150C, 1000C, and 650C, respectively (zone 4). In order to create a film, the extrudate (T = 650C) was then compressed into a cylindrical calendar.

Hot melt extrusion has some advantages

- ✓ Fewer operation units
- ✓ Better content uniformity
- ✓ Anhydrous process

4. Solid dispersion extrusion

This approach disperses one or more active substances in a suspended carrier in a solid state in the presence of amorphous hydrophilic polymers. To create a solution, the active pharmaceutical ingredient is dissolved in a suitable solvent. Without removing the liquid solvent, solution is added to the melt of a suitable polymer (PEG) below 70 °C. Finally, solid dispersion is transformed into films using dies.

5. Rolling

A pre-mix is first created using film-forming polymers, polar solvents, and other additives other than a medication. Add the necessary amount of medication to the pre-mix. To create a stable matrix, the medication is combined with the pre-mix. The resultant slurry is poured into the roller. A support roller forms and removes the film. A controlled bottom drying technique is then used to dry the wet film. The required size and form of the film are cut.

EVALUATION PARAMETERS [26-42]

1. Mechanical Properties [26-38]

- **Thickness test:** Thickness specifies the dose perfection of drug in the film. It is measured by a micrometer screw gauge or calibrated digital Vernier calipers at five unlike strategic locations and the mean value is calculated which indicates the final thickness of the film. The width of the film should be in the range of 5 - 200 µm.
- **Dryness test:** It has been determined that there are roughly eight stages in the drying process of a film: set to touch, dust free, tack free (surface dry), dry to touch, dry hard, dry through (dry to handle), dry to recoat, and dry print free. Although the majority of the studies can be changed extensively to analyse pharmaceutical OFDF, most of the tests are primarily utilised for paint films. The specifics of these parameters' estimation can be found elsewhere and are outside the purview of this review. Tack refers to how firmly a strip sticks to a companion object (such as a piece of paper) after the accessory has been rubbed against the strip. For this investigation, there are also instruments available.
- **Tensile strength:** Tensile strength is the highest stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at break divided by the cross sectional area of the strip as Given in the equation below:

Tensile Strength = load of breakage/ strip thickness × strip width

- **Percent elongation:** A strip sample extends when stress is applied, and this is referred to as strain. Strain is essentially the distortion of a strip split along the sample's original dimension. In general, strip elongation rises as plasticizer content rises30.

% Elongation = Increase in length ×100/original length

- **Young's modulus:** It is the estimate of film stiffness. It is found as balance of applied stress to the strain in the elastic deformation region. It is determined by the following formula:

Young's modulus = (Slope/strip thickness *cross head speed)/ 100

It can also be written as:

Young's modulus = force at corresponding strain/ cross- sectional area*corresponding strain

Films that have a high Young's modulus and tensile strength are said to be hard and brittle. A tough and fragile film exhibits higher tensile strength and Young's modulus values with minimal elongation.

- **Tear resistance:** A plastic film's tear resistance is a complex function of its ideal rupture resistance. In essence, an extremely quick loading rate of 51 mm (2 in)/min is used, and it is intended to quantify the force needed to start tearing. The tear resistance value is expressed in Newtons and represents the greatest force necessary to rupture the specimen.
- **Folding endurance:** Until the strip breaks, the strip must be folded repeatedly at the same spot to determine folding endurance. The folding endurance value is determined by counting how many times the film can be folded without breaking.

2. Transparency

The transparency of the films can be decide using a simple UV spectrophotometer. Cut the film samples into rectangles and placed on the inner side of the spectrophotometer cell. The direct transmittance of films at 600 nm. The transparency of the films was calculated as follows:

Transparency = (logT600)/b = - €c

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

3. Contact angle

It enables information regarding oral film dissolving, wetting behaviour, and disintegration time. A goniometer at room temperature can be used to test this. Double-distilled water should be utilised for this purpose. A drop of double-distilled water is placed on the surface of a dry film after it has been taken. Within 10 seconds after a water drop's deposition, a digital camera captures an image of it. Image software should be used to analyse digital photos in order to determine the angle.

4. Scanning electron microscopy

An important technique for examining the surface morphology of the film formed between various excipients and drugs is scanning electron microscopy. A sample of film was collected, put in a sample holder, and various photomicrographs were shot using the tungsten filament as an electron source at a magnification of 1000.

5. Test for in vitro disintegration

When conduct comes into contact with water, the film starts to fall apart at that same moment. The film is placed in the phosphate buffer to conduct this test. The disintegration time can also be studied using the United States Pharmacopoeia disintegration device. The disintegration period should be between 5 and 30 seconds.

6. In-vitro dissolution test

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. Dissolution testing can be performed using any of the pharmacopoeia's standard paddle apparatuses. It is challenging to conduct an oral film dissolution study using a paddle-type dissolution device since these films have a tendency to float above the dissolution medium. 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^{o}C and a rotational speed of 50 for the dissolving investigation.

7. Stability studies

The major goal of the formulation's stability testing is to determine whether or not the final product is stable. The formulation is first wrapped with butter paper, then aluminium foil, before being loaded into an aluminium pouch and heated sealed. It is also used to determine the influence of temperature and humidity on the stability of the medicine for the real storage. For three months, formulation should be kept at 45°C and 75% RH. Triplicate samples are taken during the stability studies at three sampling intervals, namely 0, 1, and 3 months, and films should be examined for physical changes and drug content.

CONCLUSION

The most palatable and precise oral dose form is a film that dissolves in the mouth. It avoids hepatic first pass metabolism, which increases the drug's bioavailability and improves therapeutic response. Unlike traditional solid dosage forms (tablets and capsules), there is no risk of choking with the dosage form, and there is no grit in the mouth like there is with ODT. In comparison to traditional oral dosage forms, fast-dissolving oral films have higher patient compliance and may have improved biopharmaceutical characteristics, efficacy, and safety.

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