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A Review on Mouth Dissolving Film

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Abstract : Mouth dissolving film becomes a novel approach to oral drug delivery system as it provides convenience and ease of use over other dosage forms such as orally disintegrating tablets buccal tablets and sublingual tablets, so mouth dissolving films are gaining the interest of large number of pharmaceutical industries. The transdermal patch technology was used to create a mouth dissolving film. Mouth dissolving films are thin solid dosage forms that dissolve in the oral cavity in a matter of seconds without chewing or drinking water. Due to the highly vascularized oral mucosa, medicines can be absorbed directly and enter the systemic circulation without first-pass hepatic processing. This advantage can be leveraged to develop products with enhanced oral bioavailability of compounds subject to the first pass effect. These films demonstrate how to easily deliver medication to pediatric, geriatric, and immobile patients. The mouth dissolving film has the ability to shorten the time to action, lower dosage, and increase drug efficacy and safety. An superb film should have a high level of stability, flavor, and handling.

Keywords- Mouth dissolving film, Solubility, Polymer, Novel drug delivery system, Permeation

INTRODUCTION

Oral route is a most convenient route of drug administration & most common dosage form taken by oral route are tablets, capsule but main problem associated with them is difficulty in taking this large solid forms especially in the case of geriatric & pediatric patients, mentally ill patients , developmentally disabled patients who are uncooperative [2].Another main problem with this conventional oral route dosage form for administration is low bioavailability due to very high first pass metabolism[9], less absorption due to interaction with the food present in the stomach and forming insoluble complexes from which drug unable to diffuse out, less absorption due to efflux pump (P-glycoprotein) this limit the ability of many drug to reach the therapeutic level by oral route sometimes there is possibility that abrupt release of the drug from solid dosage form due to less binding force or unable to release due to fail to disintegrate because of very high compression force[1].

Many drugs having amide, ester linkage (Peptide drugs) are prone to hydrolysis (breaking of ester & amide bonds) in the GIT by esterases, hydrolases, amidases and loss of therapeutic activity and being peptide drugs they have very high molecular weight therefore impossible to be absorb by passive diffusion the most common route of absorption due to this they being taken in systemic circulation by active transport process. Active transport has its own disadvantage of being a saturable process.

This Novel drug delivery system was introduced as substitute to Conventional dosage form for drugs having difficulty in formulation as conventional dosage form & for patient showing difficulty in swallowing medicine [3].

This NDDS solve the problem of drug which having poor bioavailability due to either slow dissolution or low permeation [3]. Both problems are solved by this as drug is fastly disintegrate into its original particles & going very fastly into solution form & will fastly absorbed from the buccal mucosa.

Mouth dissolving films contain active pharmaceutical ingredient either in dissolved or dispersed form, the way to take this dosage form is placing the films on the tongue where it disintegrate & dissolved and gets absorbed. It is one of the best suitable dosage form to substitute the conventional oral dosage forms [11].

Hydrophilic polymers are used to create fast-dissolving oral films, which quickly disintegrate on the tongue or buccal cavity and release the medicine into the bloodstream when they come into contact with liquid. An innovative replacement for the conventional pills, capsules, and liquids frequently seen in prescription and over-the-counter drugs is the fast-dissolving oral film. Thin-film strips are primarily intended for oral administration, with the user placing the strip on or under the tongue (sublingual) or along the interior of the mouth. They are similar in size, shape, and thickness to postage stamps (buccal).These drug delivery methods enable the medication to skip the first pass metabolism, increasing the bioavailability of the drug. The key difficulties in the current investigation where taste masking and increasing the drug's aqueous solubility because all drugs that reach the oral cavity, whether through swallowing, sublingual absorption, or oral inhalation, should have a pleasant taste. The taste of the active pharmaceutical ingredients (APIs) in various dose forms has been noted as one of the main obstacles preventing patients from following a prescribed treatment schedule. One

of the key determinants of the market penetration and economic success of oral formulations, particularly in pediatric medicine, is taste. It plays a significant role in the development of oral medications with regard to patient acceptability and compliance [8].

Advantages of mouth dissolving film [18]

- Oral films are flexible and therefore less fragile in comparison to ODTs because of their larger surface area and flexibility.
- As a result, handling and storage by consumers and during transportation are both simple.
- Accuracy in dosage administration.
- No choking hazard.
- Drugs that cannot be crushed or injected by patients can be administered to patients with the aid of a mouth-displacing film medication administration system.
- Increased patient adherence.
- Better acceptance among patients with dysphagia has resulted from the ease of swallowing and the lack of a requirement for water.
- Dosage forms can be taken whenever and wherever it is most convenient for the user.
- By passes first pass metabolism and hence enhanced bioavailability [13].
- Appropriate dosage form for all age group.

Disadvantages of mouth dissolving film [18]

- High dose can't be incorporated into the strip.
- Special equipment requires for packaging.
- Dose uniformity is a technical challenge.
- Moisture / Temperature sensitive.

Special Features of mouth dissolving film

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

Ideal characteristics of drug candidate

- Pleasant taste
- Low Dose
- Low Molecular weight
- Good stability & solubility
- Unionized at PH of oral cavity
- Ability to permeate oral mucosal tissue
- High permeability

General composition of MDF

Sr. No.	Ingredient	Quantity (w/w)
1	Drug	1-25%
2	Water soluble polymer	40-50%
3	Plasticizer	0-20%
4	Saliva stimulating agent	2-6%
5	Sweetening agent	3-5%
6	Flavouring agent	q. s
7	Surfactant	q. s
8	Colours	q. s
9	Fillers	q. s

Table: 1 General composition of MDF

Formulation aspect for mouth dissolving film

1. Drug Category- 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.

Various categories of drugs such as antiemetic neuroleptics, cardiovascular agents, analgesics, antiallergic, antiepileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction, antialzheimers, expectorents, etc [4,6].

2. Film Forming Polymer- Water-soluble polymers are employed as film formers because they give the films with fast disintegration, nice mouth feel, and mechanical strength[12]. The resilience of the strip is determined by the type of polymer used and the amount used in the formulations. For the manufacture of films, a range of polymers are available, the most popular of which are pullulan, gelatin, and hypromellose. Pullulan, gelatin, guar gum, xanthan gum, hydroxypropyl methyl cellulose (HPMC), modified starches, PVPK30, PVA, and other water-soluble polymers are examples. Among these, Pullulan and HPMC are the finest polymers for FDF preparation. Pullulan is a neutral glucan (similar to Amylose, Dextran, and Cellulose), with a chemical structure that varies depending on the carbon source, generating microbe (several strains of Aureobasidium pullulans), and fermentation circumstances. 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:

- ✓ Polymers should not be poisonous, irritating, or bitter.
- ✓ Polymers ought to be odourless.
- ✓ There should be no leachable contaminants in it.
- ✓ It should be affordable and easily accessible.
- ✓ It shouldn't present a barrier throughout the disintegration process.
- ✓ It should have good spreading and wetting characteristics.
- ✓ It must have enough peel, shear, and tensile strength.
- ✓ It should have a long enough shelf life and not lead to secondary infections in the mouth.

3. 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 [5].

4. Sweetening agents-Sweeteners are now a crucial component of both food and medicinal items that are meant to dissolve or disintegrate in the mouth. Both natural and artificial sweeteners are used to increase the mouth-feel of mouth-dissolving formulations.

(1) Water soluble natural sweeteners, such as xylose, ribose, glucose, sucrose, maltose, and stevioside, are some acceptable sweeteners.
(2) Artificial sweeteners that dissolve in water, such as acesulfame-K and sodium or calcium salts of saccharin.
(3) Aspartame, a dipeptide-based sweetener

5. Cooling agents-Cooling agents such as monomethyl succinate can be used to increase the taste intensity and mouth-feel of the product. In addition to tastes, cooling agents such as WS3, WS23, and Utracoll II can be utilised.

6. Flavouring agents-Individual perception of flavour varies depending on ethnicity and taste preferences. Flavouring agents can be chosen from synthetic flavour oils, oleo resin extracts, and extracts produced from various portions of plants such as leaves, fruits, and flowers. The amount of flavour required to cover the taste is determined by the flavour type and strength.

7. Colouring agents-When some of the formulation ingredients or medications are insoluble or suspended, pigments such as titanium dioxide or FD&C approved colouring ants are added (not exceeding concentration levels of 1%w/w) in oral strips.

8. Surfactants-Surfactants are utilised as solubilizing, wetting, or dispersing agents, causing the film to dissolve in seconds and the active substance to be released immediately. Surfactants help improve the solubility of medications that are poorly soluble in fast dissolving buccal films. Polaxamer 407, sodium lauryl sulphate, benzalkonium chloride, benzthonium chloride, tweens and spans, and so on are examples.

Chemicals & Methods

Drug -	API
Water soluble polymer -	HPMC E3, E5 & E15 & K3, Methyl cellulose A-3, A-6 & A-15, Carboxymethylcellulosemcekol 30, polyvinylpyrollidone K-90, Pectin, gelatin, sodium alginate, hydroxypropylcellulose, Polyvinylalcohol, maltodextrin.
Plasticizers -	Glycerol, dibutyl phthalate, polyethylene glycol, etc.
Surfactant-	Sodium lauryl sulphate, benzalkonum chloride, Tween, etc.
Sweetning agents-	Saccharin, cyclamate & aspartame

Saliva stimulating agents- Citric acid, malic acid, lactic acid, ascorbic acid.
Fillers, Colors, Flavors- FD & C colors, US FDA approved flavors.

Methods

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

1. Solid dispersion extrusion:-

This method involves dissolving the drug in suitable liquid solvent & putting this solution into thee melt of suitable film forming polymer at appropriate Temp. without removing the liquid solvent and at the end this solid dispersion are passed through dies to shape them in form of film.
Caution- Liquid solvent showed not to be miscible with melt of polymer.

2. Hot melt extrusion:-

Mixture of Drug & Polymer is prepared placing this mixture in hopper & conveyed and melted & extruded, die gives shape to the melt in required form. Advantage of this is involve low Temp. & short residence time but in this method organic solvent can't be used.

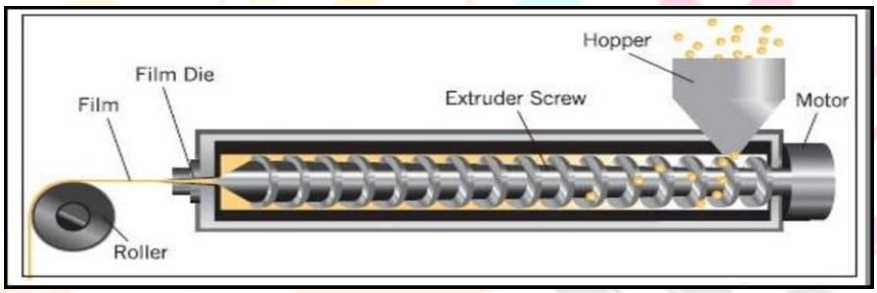

Figure1. Hot Melt Extrusion

3. Solvent casting method:-

In this method firstly the solution of film forming polymer, plasticizer & other excipient is being prepared in the volatile solvent like ethanol or water and then drug is dissolved or dispersed in the above solution. Then casted in petri plate and passed through drying equipment to remove the volatile solvent. The formed film is removed and cut into strips and packed. Heat sensitive drug film can be prepared by this method.

Figure 1

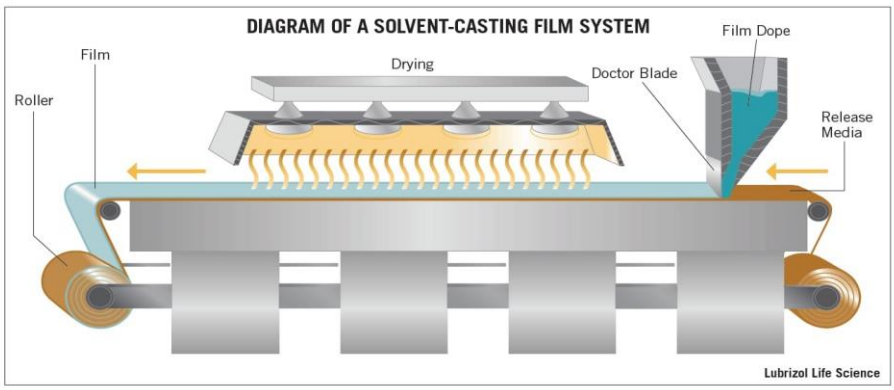

Figure2. Solvent Casting

4. Semisolid Casting:-

This method use when acid insoluble polymer are used. In this method using water film forming polymer solution is prepared and this solution is poured in the solution of acid insoluble polymer prepared in sodium or ammonium hydroxide then add the plasticizer to form get mass. Plasticizers will affect the property of gel mass formed this gel mass is then casted into film or ribbens using heat controlled rollers / drums.

5. Rolling method:-

The rolling method involves rolling a drug containing solution or suspension on a carrier. Mostly water and combination of water and alcohol are used as the solvent. On the rollers, the film is cured before being cut into the necessary shapes and dimensions. In a little amount of aqueous solvent, other components and the active substance are dissolved, a processor with high shear. A homogeneous, viscous solution is created when water soluble hydrocolloids are dissolved in water.

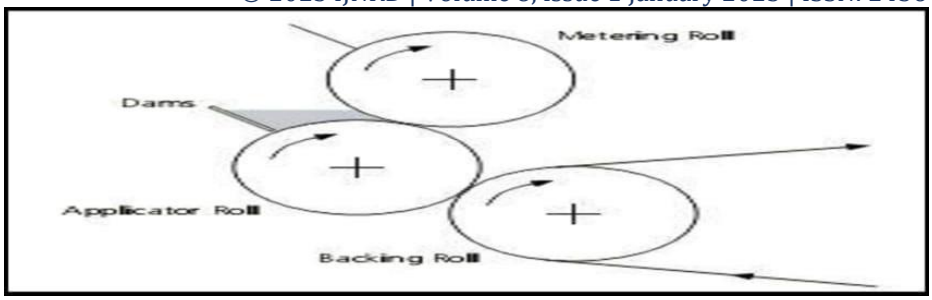

Figure3. Rolling Method

Evaluation parameters

1. Thickness
2. Organoleptic tests
3. Surface pH test
4. Folding endurance
5. Transparency
6. Disintegration test

1. Thickness

Because the thickness of the film is directly related to drug content uniformity, it is vital to ensure uniformity in the thickness of the film. At various important places, it can be measured with a micrometre screw gauge or calibrated digital Vernier Calipers [10]

2. Organoleptic tests

Special controlled human taste panels are employed for psychophysical evaluation of the product. For this goal, in-vitro approaches utilising taste sensors, specially developed apparatus, and drug release via modified pharmacopoeial procedures are being used. These in-vitro taste assessment apparatus approaches are ideal for high-throughput taste testing of oral medicinal formulations.

3. Surface pH test

The surface pH of a fast dissolving film was evaluated to investigate the likelihood of any in vivo adverse effects. Because an acidic or alkaline pH might irritate the oral mucosa, the surface pH was set to be as close to neutral as possible. For this, a mixed pH electrode was employed. The pH was determined by putting the electrode into contact with the surface of the oral film, which had been previously soaked with water [16].

4. Folding endurance

Folding endurance is measured by repeatedly folding the strip at the same location until the strip breaks. The folding endurance value is calculated by counting the number of times the film can be folded without breaking [14].

5. Transparency

A basic UV spectrophotometer can be used to determine the transparency of the films. Cut the film samples into rectangles and lay them on the spectrophotometer cell's interior side. The transmittance of films at 600 nm is determined. The films' transparency was determined as follows:

Transparency = (logT600)/b = - €c

Where, T600 is the transmittance at 600 nm, b is the film thickness in millimetres, and c is the concentration.

6. Disintegration test

Orally fast dissolving films must be disintegrated using US disintegration equipment.

Fast dissolving oral strips are subject to the same disintegration time limit of 30 seconds or less for orally disintegrating tablets as indicated in Centre for Drug Evaluation and Research (CDER) guidance. Depending on the formulation, disintegration times can vary, although they commonly range from 5 to 30 seconds. However, there is no formal advice for oral fast-dissolving film strips.

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