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Mouth Dissolving Film: An Innovative and Effective Drug Delivery System

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Abstract:
Due to their versatility and user-friendliness, orodispersible films are the most advanced oral solid dosage forms. The orodispersible film is an oral solid dosage form that dissolves and breaks down quickly after being placed in the mouth without water or chewing. By using this dosage form, the drug can bypass first-pass metabolism, thereby increasing its bioavailability. Orodispersible films have the ability to reduce dosage, accelerate onset of action and eliminate choking issues.
API By using the solvent casting and semisolid casting techniques, taste-masking agents are laminated. The solvent casting method is chosen over other methods because it provides excellent thickness uniformity and films prepared with fine glossy look and better physical properties. The evaluation of mouth dissolving films takes into account a number of factors, including thickness, physical characteristics such folding durability, disintegration, and dissolution time. This review provides information on formulation methods. and evaluation parameters of mouth dissolving films.

Keywords: Bioavailability, fast disintegration, onset of action, oro-dispersible film, solvent casting,

INTRODUCTION:

Due to its simplicity, lack of intrusiveness, adaptability, patient compliance, and acceptability, the oral route of drug administration is one of the most popular. For pediatric, geriatric, nauseous, and non-compliant patients, numerous substitutes for the oral route of drug administration have been presented over time using modern novel technologies. The development of technology has led to the creation of bioadhesive mucosal dosage forms, such as adhesive tablets, gels, and patches.[1,2]

These systems were created in the late 1970s as an alternative to traditional dosage forms such as tablets and quick dissolving capsules for older and younger patients who had difficulty in ingesting this dosage forms. The average size of MDF is generally comparable to a postage stamp.[3]

MDF has attracted considerable attention in the pharmaceutical field due to its unique properties and rapid disintegration time of only seconds to minute. They also have no expensive freeze drying, high mechanical strengthand reduced chocking problems.

Due to its pharmacological effects, such as antitussive, antiepileptic, antiasthamatic and expectorant, MDF can be combined with various drugs.[4]

MOUTH DISSOLVING FILMS (MDF)-

By using word soluble polymers (usually hydrocolloids, but also bioadhesive polymers), the dosage form can quickly hydrate, adhere, and dissolve to release the drug when placed on the tongue or in the mouth [5,6].The terms fast dissolving film, orodispersible film, orally disintegrating film, and fast dissolving film are also used to describe them.[7] For active substance that must react the human mucosa, such as drugs and breath freshness, MDF can be a useful and efficient delivery mechanism.[8] For the drug to enter the blood stream, it can be administered intragastrically, orally, or sublingually[9].When MDF is ingested , it allows rapid sublingual absorption of the drug, which ultimately results in a rapid onset of therapeutic activity.MDF must dissolve or disintegrate fast in the buccal cavity, therefore choosing the right excipients and components for its formulation is essential. The formulation may also contain other chemicals, such as flavours, plasticizers, surfactants, colourants, sweetening agents, saliva-stimulating agents, pharmacological agents, antibacterial agents, nutraceutical substances, and other excipients, depending on how it will be used [10].

Composition of Mouth Dissolving film-

The active ingredientis enclosed in a film with an area of 2 to 8 cm

Which dissolves in the mouth. The unique water soluble polymer matrix disintegrates quickly in water or saliva. A maximum of 40 mg of the drug can be taken in a single dose. Oral dissolving film ingredients include:

a) Active Pharmaceutical Agents:

Any class of pharmaceutically active chemical substances that can be administered orally or buccally can be considered a pharmacologically active substance. Various categories of drugs such as antiemetic, neuroleptics, cardiovascular agents, analgesics, antiallergic, antiepileptic, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents and drugs used for erectile dysfunction, antialzheimers, expectorants and anitussive [11-17].

Here are the desirable characteristics of a drug to choose from:

- The drug should have pleasant taste.
- The drug should be used in small amounts, usually less than 40mg.

- Drugs with lower and more moderate molecular weights should be recommended.
- Drugs must be reliable and soluble in water and saliva.
- It should bind slightly when it reaches the pH of your mouth.
- It must be able to penetrate the tissue of the oral mucosa.

b) Water soluble polymers:

Water soluble polymers provide films with rapid disintegration, pleasant mouth feel and mechanical properties.By increasing the molecular weight of the polymer film base, the rate at which the polymer disi ntegrates is reduced. [18-20]

c) Plasticizers:

It was noted that the formulation factors had a significant impact on the mechanical properties of the film (by using plasticizer).The mechanical characteristics like elongation and tensile strength to the films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties.[21]

d) Saliva stimulating agent:

More saliva production helps in the rapid disintegration of the fast dissolving film formulations. Therefore, acids from food preparations should be included in formulations as salivary stimulants.[22]

e) Flavoring agents:

The flavoring agents can be chosen from synthetic aromatic oils, oleoresins, extracts of plant parts such as leaves, fruits and flowers. Flavors available alone or in combination.Any flavor can be added including menthol extracts or water soluble essential oils, strong mints like peppermint, sweetmint, wintergreen, cinnamon, and cloves, fruit flavors like lemon and orange, or sweet candies like vanillin and vanilla, chocolate or fruit essence like apple, raspberry, cherry and pineapple. The amount of perfume needed tp mask the taste depends on the type of perfume and its strength.[23]

f) Sweetening agents:

Sweeteners have become the important part of pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The classical sources of sweetener are sucrose, dextrose, fructose, glucose, liquid glucose. The artificial sweeteners have gained more popularity in pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which comes under the second generation artificial sweeteners. [24-25]

g) Surfectants:

Surfactants act as solubilizers, wetting agents or dispersants in formulations, allowing films to dissolve qu ickly and release active ingredients.Some of the commonly used surfactants are sodium lauryl sulfate, benzalkonium chloride, tweens etc.[26]

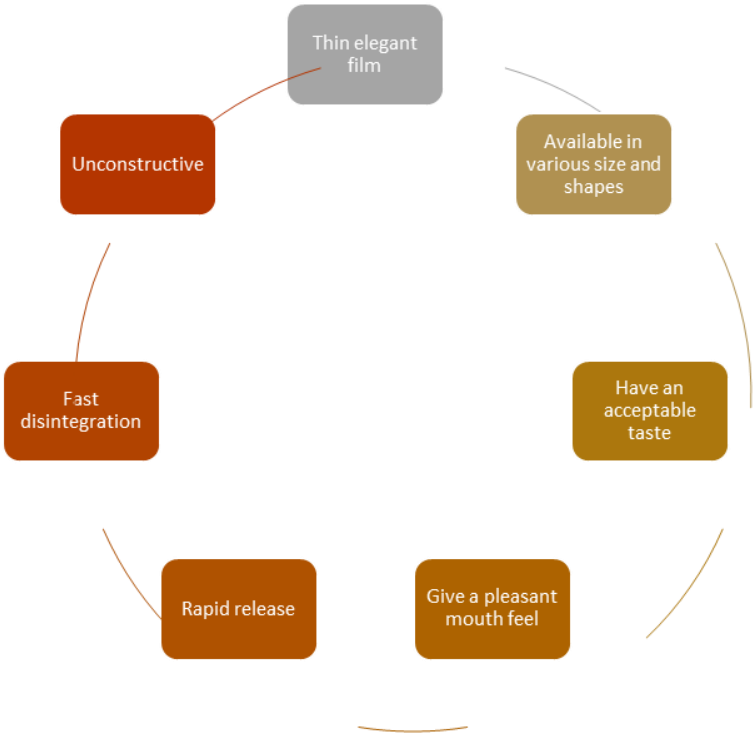

Figure 1:-Special qualities of Mouth Dissolving Films

Table 1: Typical composition of a MDF[26]

Ingredient	Quantity	Use (Examples)
Drug	5-30 %w/w	Drug should be in low dose
Water soluble polymer	45% w/w	Film forming capability (Methyl cellulose A3, A6, A15, Polyvinylalcohol, Maltodextrin Polyvinyl pyrollidon K-90, HPMC E3, E5, E6, E15, K3,Pectin, gelatin, Sodium alginate, Hydroxy propyl cellulose, Pullulan,)
Plastisizers	0-20 %w/w	Increases the flexibility and reduces the brittleness of film (Glycerol, Polyethylene gycol, Dibutylpthallate,triethyl citrate)
Surfactant	Q.S.	Used as solubilizing and wetting agents (Tween 80,Sodium lauryl sulphate)
Sweetning agent	3-6 %w/w	Increasing the palatability of the film (Aspartame, Saccharin,Cyclamate,Alitame and Neotame, Acesulfame-K)
Saliva Stimulating agent	2-6 %w/w	Increases saliva stimulation to facilitate film rupture (Citric acid, Malic acid)
Colors, Flavors	Up to 1% w/w	Silicon dioxide (pigment) is used as coloring agents. Fruity flavors like cocoa, apple, raspberry are widely used.

❖ Advantages[27]:

The advantages of Mouth dissolving films are-

1) Administered without water, anywhere, any time.
2) Due to its large surface area, it quickly dissolves and disintegrates in the oral cavity.
3) Dose accuracy.
4) The stomach's acidic environment can be avoided.
5) Site-specific action and local action.
6) Flexible and portable so provides ease in transportation during consumer handling and storage.
7) For anyone young or old, who has difficulty swallowing, who has a mental or developmental disability, who is refractory to treatment, who has fluid limitations or who is not feeling well.
8) Beneficial in motion sickness, acute pain, allergic attack, or coughing, where the rapid onset of action is required.

❖ Disadvantages[28] :

1) Dose consistency is a technical issue.
2) High doses cannot be incorporated and expensive packaging is required.
3) Thin, pleasing film available in a variety of sizes and shapes
4) Tastes great, feels great on the tongue .
5) Quick release
6) Dissolves quickly
7) Non-constructive

METHOD OF PREPRATION:-

A. Solvent casting method:

In this process, the excipients are dissolved in water, a water soluble polymer is added, and then the drug is added. The mixture was then stirred to obtain a homogeneous solution. After pouring into the petri dish, the liquid is dried.[23,25]

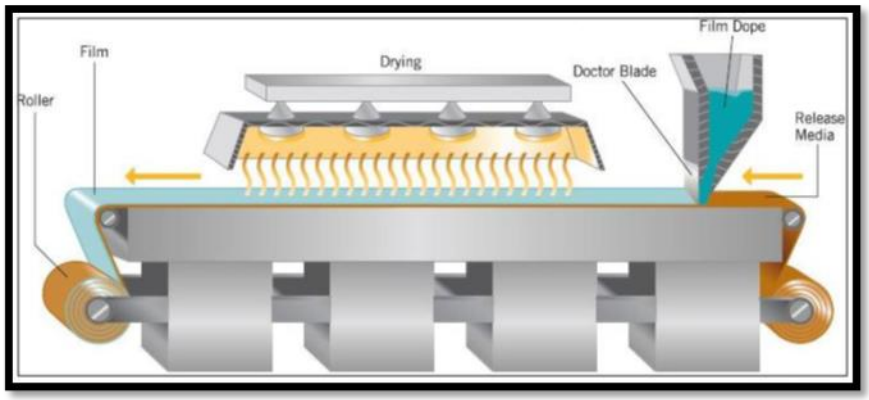

Figure 2: Solvent casting

B. Semi-solid casting:

In this process, a homogeneous viscous solution of an acid insoluble polymer is mixed with a solution of a film forming polymer (such as cellulose acetate butyrate). It is suitable for films that have not undergone any post- sonication treatment. The film should have a thickness of between 0.015 and 0.05 inches after drying. The ratio of the film- forming polymer to the acid-insoluble polymer should be 1:4.[23,25]

3. Hot melt extrusion:

In hot melt extrusion, drug and carrier are first mixed in solid form.This is used to form the melt into a fim after the liquid has melted using the extruder heater.Hot extrusion has several advantages, including – Fewer operation units Better content uniformity, An anhydrous processing.

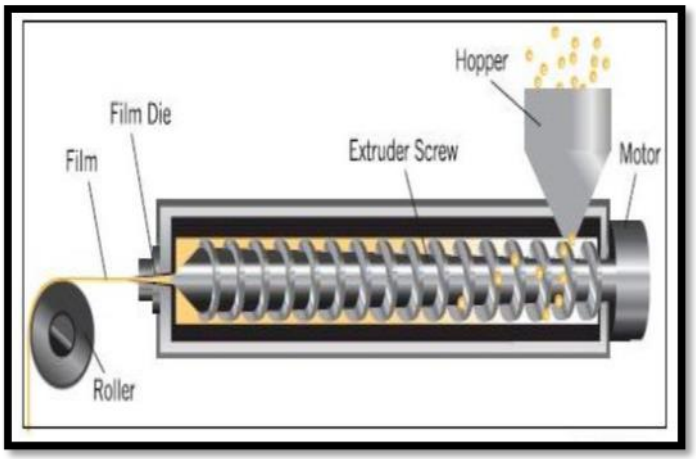

Figure 3:- Hot Melt Extrusion

4) 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.[29,30]

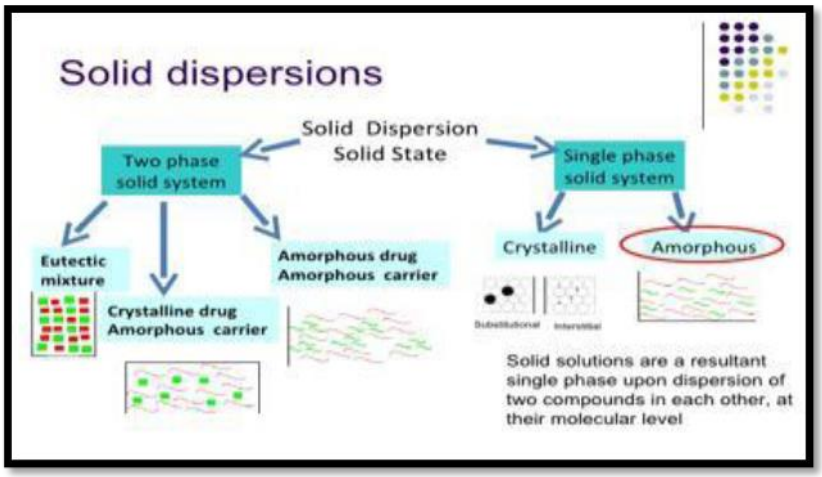

Figure 4:- Solid dispersion method

5) Rolling Method:-

The rolling method involves rolling a solution or suspension containing a drug onto a carrier.

Most solvents consist of water and alcohol water mixtures. After the film has dried on the drum, it is cut into the desired shape and size. In a small amount of aqueous solvent, dissolve the other ingredients, including the active ingredient, using a high shear processor.

Water soluble hydrocolloids are dissolved in it to produce a homogeneous viscous solution.

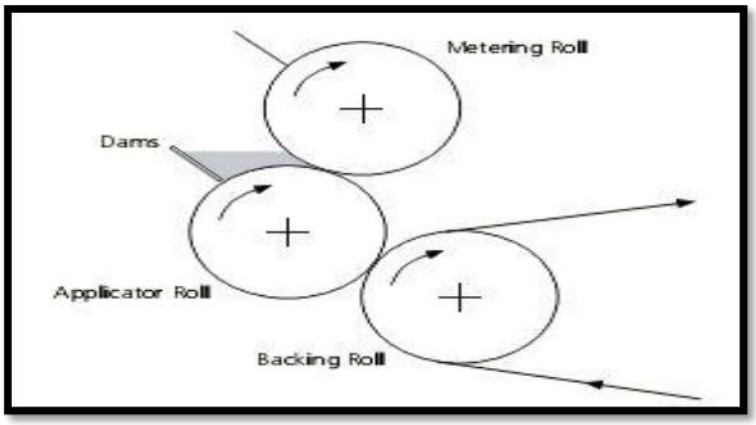

Figure 5:- Rolling method

EVALUATION PARAMETERS:

1)Thickness test:

Thickness of a film is determined by using calibrated digital micrometer and then subsequently mean average is calculated. Generally, three readings from all the batches are determined and average is calculated. Weight variation of a film is calculated in triplicate by cutting the film and determining weight of each film. Uniformity in thickness is important to as certain as it is directly proportional to dose accuracy of the film.[31]

2)Tack test:

When the film is coated onto the strip it adheres to the attachment with some tackiness.This test also determines the dryness.[32]

3)Tensile strength:

Tensile strength is describe as maximum stress applied at which the film breaks. Basically, this test is performed to measure the mechanical strength of films. It can be calculated from applied load at rupture divided by the strip cross-sectional area given in the equation below. [32,33]

Tensile strength = Load at breakage/ Strip thickness × Strip Width

4) Percentage Elongation:

The tensile stress on the sample film causes the film to deform, thereby elongating or stretching the sample. Predict the ductility of polymers using a texture analyzer.It is calculated by formula:

% Elongation = Increase in length ×100 / Original length

5)Folding Endurance:

A part of the film is repeatedly cut and folded in the same place until it breaks to measure the resistance to folding. Folding endurance is determined by the number of times the film is folded into the same position without breaking. The typical folding endurance of the film is between 100 and 150[34].

6)Swelling Properties:

Film swelling studies were evaluated using simulated saliva. The next step was to use a stainless steel mesh with a predetermined weight of film. The film containing the mesh was then been immersed in the artificial saliva solution. The weight of the film is then increased at regular, pre-set intervals until there is no more weight gain.

The degree of swelling is calculated as final weight (wt) **- initial weight (w0)/initial weight (w0)**

The weight of the film at time t is denoted Wt and its weight at time 0 by W0.

8) Surface pH:

The standard procedure for determining the pH of a film is to place the prepared film in a petridish, allow it to absorb distilled water, and then take a pH reading on the surface of the film by using a pH contact gauge electrode.Determination of surface pH is vital as acidic or basic pH is liable to cause oral mucosal irritation.[34,35]

9) Content uniformity:

Film content is determined using standard test procedures outlined in the pharmacopoeia for each unique substance. The test is performed using an analytical technique using 20 samples. According to the japnese Pharmacopoeia, the acceptance rate of this is less than 15%.According to USP27, the standard deviation of the content should not exceed 6% and should be between 85% and 115%. Content uniformity is used to calculate the drug content of each specific film.[36,37]

9)Disintegration time:

Calculate the disintegration period of the film using a disintegration apparatus listed in a reliable pharmacopoeia. Disintegration times vary from formulation to formulation and range from 5 to 30 seconds depending on film composition. The USP Disintegrator is typically used for this test. There is no set standard for how long it takes an orodispersible film to dissolve. The disintegration time of a film can be determined by one of two methods.[38]

Slide frame method:

Distilled water was dropped onto the film on the Petri dish containing the glass slide. Note the time it takes for the film to dissolve.[39]

Petri dish method:

Place the film on a petri dish filled with 2 ml of distilled water. Dissolution time is the time required for t he film to completely disintegrate.[40]

12) In-vitro dissolution test:

Standard official basket or paddle apparatus is used for conducting dissolution studies on films. Sink conditions should be maintained during dissolution. It can be difficult to test accurately when the film periodically floats on the medium. Since paddle strategies are more prone to this problem, a basket setup is often chosen. Supplement the medium(900 ml) with 300 ml of pH phosphate buffered saline and 0.1 N HCL. The rotation speed of 50rpm was changed frequently and the temperature was maintained at 37 ± 0.5°C.Periodically collect dissolved drug samples and examine them with a UV spectrophotometer. Sol ution testing is often used, but it can suffer from serious accuracy issues and test failures.[41,42]

APPLICATIONS OF MOUTH DISSOLVING FILM-

Topical use:

The soluble films can be used to deliver active ingredients, such as analgesics or antibacterial agents, for t he treatment of wounds and other local diseases.

Gastric Retention Assay Systems:

Soluble films are considered potential dosage forms for drugs with certain molecular weight and low water solubility. The pH of the digestive tract or the enzyme secretions that can be used to treat digestive disorders can cause the membrane to rupture.

Diagnostic devices:

Soluble films can be used to create isolation barriers for the separation of various reagents to provide rapi d response in diagnostic devices, or to load delicate compounds to allow controlled release upon exposure to biological fluids.[43]

CONCLUSIONS:

The oral route is the most commonly used method of delivering therapeutic chemicals through anorally di ssolving membrane due to the low cost of treatment and ease of administration, which improvespatient co mpliance.The mouth dissolving film are barely described and investigated in literature, but seem to be an ideal dosage form for use in young children, especially in elderly and younger patients. They combine the improved durability of solid dosage forms and the good applicability of a liquid.Mouth dissolving oral films has several advantages over the conventional dosage forms. So they are of great importance during the emergency cases such as allergic reactions and attacks whenever immediate onset of action is desired. And more importantly, mouth dissolving films are travel friendly dosage forms where water may not be carried by person or patient. And hence, mouth dissolving film becomes unique, elegant, selective and needful dosage form.

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