An Updated Review on Mouth Dissolving Film

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I. INTRODUCTION

The oral route of administration is the preferred route of administration because of its ease of administration, non-invasiveness, adaptability, palatability, and acceptability. Many replacements for the oral route of drug administration have been presented for paediatrics, geriatrics, nauseated, and non-compliance patients using current innovative technologies.Bioadhesive mucosal dosage forms such as adhesive tablets, gels, and patches have been developed as a result of technological innovations. Among the many dose forms, the use of polymeric films to administer medication into the buccal cavity has recently shown tremendous promise.After disintegration and/or dispersion, orally disintegrating films (ODFs) swiftly gets hydrated by absorbing saliva and releasing the active pharmaceutical ingredient from the pharmaceutical formulations.Orally disintegrating films are a type of formulation that is frequently made with hydrophilic polymers to allow for quick dissolving when exposed to saliva.Orally dispersing drug delivery technologies include oral disintegrating films (ODFs) and oral disintegrating tablets (ODTs).These methods were created in the late 1970s as an alternative for conventional dose forms, such as rapid disintegrating tablets and capsules, for elderly people and small children patients who had trouble swallowing traditional dosage forms.A standard ODF is approximately the size of a postage stamp [1].In the marketplaces, the launch of ODT was tightly linked to patient education regarding proper administration, with instructions such as "do not chew/do not ingest."Despite these guidelines, events involving swallowing and chewing were recorded frequently.ODFs, on the other hand, freed the people from such calamities.The administration of ODFs offers a number of benefits, some of which are listed below:

1. Convenient transportation.
2. Swallowing comfort for geriatrics and children.
3. Dosing is convenient and precise.
4. Water is not required for administration.
5. Suitable for dysphasic people who have trouble ingesting tablets and capsules.
6. Enhanced absorption and rapid beginning of action due to bypassing the hepatic initial pass effect.

The quality attributes of ODFs21a include cheap lyophilization, high mechanical strength, quick disintegration, and reduced choking risks. Because of its unique features and quick dissolution rate spanning from seconds to one minute, ODFs21a has become extremely important in the pharmaceutical business.The architecture of ODF allows for the incorporation of a wide range of medications for their pharmacological effects, such as antitussives, anti-epileptics, anti-asthmatics, expectorants, and so on. Extreme humidity and temperature [2].

SPECIAL FEATURES OF MOUTH DISSOLVING FILMS

1. A delicately thin film.
2. Unconstructive.
3. Available in different size and shapes.
4. Rapid decomposition.
5. Quick release.
6. Make the mouth feel good.
7. Have a good sense of taste.
8. No remnants should be left in the mouth.

DISADVANTAGES

1. Dose homogeneity is a difficult technical problem to solve.
2. It has a hygroscopic character.
3. It is impossible to absorb high doses. (<40 mg/4cm2 piece).
4. Special packing is required for products safety and stability.

COMPOSITION OF MOUTH DISSOLVING FILM [3]:

Composition	Concentration
Drug	1-25%
Water soluble polymer	40-50%
Plasticizers	0-20%
Fillers, colours, flavours	0-40%

FORMULATION ASPECTS FOR MOUTH DISSOLVING FILMS:

Active Pharmaceutical Ingredient:

Antihistamines, anti-diarrheals, anti-depressants, vasodilators, anti-asthmatics, anti-emetic medicines, and so on can all be added into ODFs. Dimenhydrinate could also be used to disguise the flavour of ODFs. Salbutamol sulphate, rizatriptan benzoate, verapamil ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, and other medicines are commonly found in ODFs.

Film Forming Polymer:

Water-soluble polymers are utilised as film formers because they allow the films to disintegrate quickly, have a pleasing mouth feel, and have mechanical properties. The type of polymers used and the amount utilised in the formulations determine the strip's hardness. Pullulan, gelatin, and hypromellose are the most often utilised polymers for film production. Examples of water soluble polymers are, Gelatin, xanthan gum, guar gum, Hydroxyl propyl methyl cellulose (HPMC), Pullulan,Modified starches, PVPK30, PVA etc. HPMC E3/E5/E6/E15.

The polymeric materials used in the oral film should have the following properties:

1. Polymer should be safe, irritant-free, and tasteless.
2. Polymer must have no flavour.
3. It should be free of contaminates that can be leached.
4. It should be at low-cost and easily accessible.
5. It should not be a hindrance during the dissolution process.
6. It must have a high level of wetness and spreadability.
7. It must have adequate peeling, shearing, and tensile strength.
8. It must not induce secondary infection in the mouth and must have a long lifespan. [4]

Plasticizers:

Generally, adding plasticizer to formulations improves mechanical qualities like as tensile strength and % extension. Plasticizer concentrations typically vary from 0% to 20% weighted average.PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, and other plasticizers are typical examples.

Sweetening Agent:

Sweeteners have now become a common component of food items that are intended to be disintegrated or dispersed in the mouth.To increase the compliance of the oral disintegrating formulation, organic and inorganic sweeteners are employed. Sweeteners that are suited include:

1. Natural sweeteners that are hydrophilic, such as xylose, ribose, glucose, sucrose, maltose, and stevioside.
2. Synthetic sweetener that dissolves in water: sodium or calcium saccharin salts, acesulfame-K, etc.
3. Aspartame is a dipeptide-based sweetener.

Saliva Stimulating Agent:

Salivary boosters are often acidic in nature, aiding the disintegration of ODFs by boosting saliva production in the mouth cavity.Citric acid, malic acid, tartaric acid, ascorbic acid, and lactic acid are some of the most often utilised saliva inducing substances.

Surfactant:

Surfactants are utilised as solubilizing, hydrating, or distributing agents, causing the film to disintegrate in seconds and the active substance to be released immediately. Surfactants also aid the dissolution of less soluble drugs in fast-dissolving buccal films. E.g.: Polaxamer 407, sodium lauryl sulfate (SLS), benzalkonium chloride, benzthonium chloride, tweens and spans etc.

Flavour:

To disguise the bitter or unpleasant taste of the integrated medication, flavours are required. The intensity and character of the flavour determine the amount of flavour.Any US-FDA allowed flavour, such as sweet, sour, or mint, can be utilised. One study found that a combination of mint, licorice, and sucralose effectively masks the bitter taste of diclofenac sodium.To distinguish the effect of various flavouring agents, electronic tongues are used (TMAs).

Colouring Agent:

When some of the formulation ingredients or medications are present in insoluble or suspension form, colours such as titanium dioxide or FD&C authorized colouring additives are incorporated (not exceeding concentration levels of 1% w/w) in oral strips.Flavours are essential to mask the bitter or unpleasant taste of the combined drug. The amount of flavour is determined by the strength and nature of the flavour.

METHOD OF PREPARATION OF FAST DISSOLVING FILM:

The Oral disintegrating film can be made using several of the procedures listed below.:

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

1) Solvent Casting Method:

Solvent casting is the most typical process for creating ODFs with water soluble additives, polymer, and drugs dissolved in de-ionized water; as a result, a saturated solution is achieved by utilizing high shear forces created by a shear processor. To achieve good quality films, the prepared solution is placed onto a petri - dish and the solvent is left to dry by subjecting it to high temperatures. Utilizing varying grades of Lycoat and HPMC, an orodispersible film of tianeptine sodium was effectively created using the solvent casting approach. The film forming polymer is normally dipped in an appropriate solvent overnight in the solvent casting procedure. The type of API that must be included in ODF determines the appropriate solvent based on essential physicochemical parameters of the API, such as melting point, shear sensitivity, and polymorphic form. Before finalising a formulation, the drug's interaction with the solvent as well as other excipients is taken into account. Trapping of air bubbles during formulation can affect the homogeneity of produced films. Deaeration of the mixture is thus accomplished with the aid of a vacuum pump. The solvent casting approach was also used to create an orodispersible film preparation of mosapride. The pouring ability of the solution is a critical factor in the casting process. Pullulan concentrations ranging from 2% to 8% resulting a low viscosity solution, allowing for facile film casting.Anastrozole fast dissolving films were also successfully made using a solvent casting approach involving HPMC (E5) and polyvinyl alcohol (PVA) [6,7].

2) Hot Melt Extrusion:

Projection of a mixture including medication, polymer, and additives at high temperatures to generate a homogeneous mass that is then coasted to form smooth films is known as hot melt extrusion. This is a solvent-free technique; nevertheless, because of the high temperature used during extrusion, processing thermolabile compounds is a major downside.

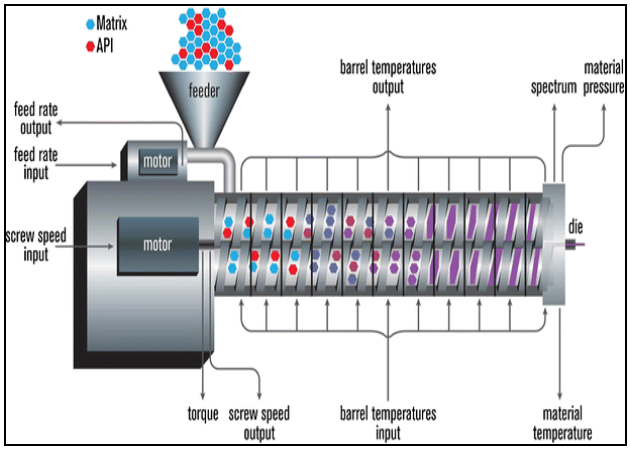
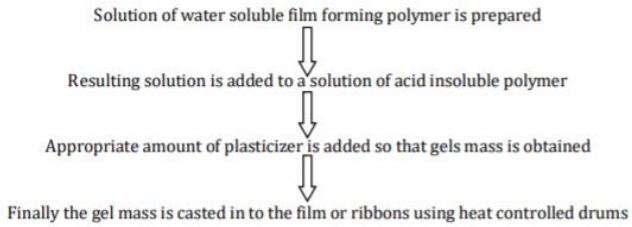


Fig 1 : Hot Melt Extrusion Process

Semi Solid Casting Method:

When acid insoluble polymers are to be employed in the film manufacturing, this approach is preferred. Acid insoluble polymers such as cellulose acetate phthalate and cellulose acetate butyrate are utilised to make films. The ratio of acid insoluble polymer to film forming polymer should be 1:4.



Solid Dispersion Extrusion Method:

Domperidone solid dispersion was effectively synthesised using beta-cyclodextrin,PEG400, and HPMC E15, and films were formed utilising the solid dispersion extrusion method. [9, 10].

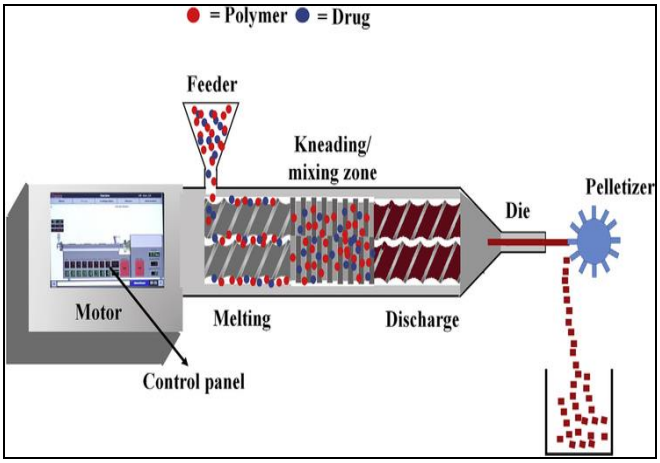


Fig 2 : Solid dispersion extrusion process

Rolling Method[11, 12] :

The solution for rolling onto the drum should have certain rheological properties, according to the layout of rolling method. Preparation of suspension of drug and polymer in water or alcohol Suspension is subjected to rollers Suspension is subjected to rollers Evaporation of solvent

EVALUATION PARAMETERS:

Thickness test:

A calibrated digital micrometre is used to measure the thickness of a film, and then a mean average is calculated. In most cases, three readings from each batch are taken and an average is produced.A film's weight variation is measured in triplicate by cutting the film and weighing each one individually. Thickness uniformity is significant since it is directly proportional to the film's dosage accuracy[13].

Tack test:

Tack refers to how firmly the film sticks to the item that has been pressed against the strip. The dehydration is also determined by this test [14].

Tensile strength:

The greatest tension at which the film breaks is described as tensile strength.

The purpose of this test is to determine the mechanical strength of films.It can be determined using the following equation: applied load at rupture divided by strip cross-sectional area.[14, 15]

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

Percentage elongation:

Deformation of the sample films happens when they are subjected to tensile stress, resulting in stretching or extension of the sample.Using a texture analyzer, it is used to estimate the ductility of polymers. It is calculated by: % Elongation = Increase in length ×100 / Original length

Folding endurance:

A piece of film is cut and continuously folded at the same location until it breaks to measure folding endurance.The folding durability value is calculated by the number of times the film could be folded at the same region without breaking. A film's typical folding endurance ranges from 100 to 150 folds[16].

Swelling property:

To verify the swelling tests of films, a simulated saliva solution is used. The initial weight of the film is established, and it is inserted in a stainless steel wire mesh that has been pre-weighed. After that, the mesh-containing film is dipped into a saliva-like solution. The mass of the film increases at fixed time intervals till there is no weight gain. These variables evaluate the extent of swelling.:

Degree of swelling = final weight (wt) – Initial weight (w0)/ Initial weight (w0)
Wt = weight of film at time interval t, w0 =weight of film at time 0.

Surface pH:

The pH value of a film is commonly measured by placing it in a Petri plate, wetting it with distilled water, and then recording the pH by contacting the film surface with a pH metre electrode.The pH of the surface must be determined since an acidic or basic pH can irritate the oral mucosa. [16,17]

Content uniformity:

The contents of a film are calculated using the standard assay method described in several pharmacopoeias for each unique drug. Analytical procedures are used to carry out the test on 20 samples. According to the Japanese pharmacopoeia, the test's acceptability value is less than 15%.The content must range from 85 % to 115 %, with a standard deviation of less than or equal to 6%, as per USP27. For calculating drug amounts in individual films, content uniformity is calculated [18, 19].

Disintegration time:

The disintegration period of a film is determined using disintegration machinery stated in official pharmacopoeias. The dissolution rate is generally a function of the film composition, as it changes with the formulation, and it typically spans from 5 to 30 seconds. This test is commonly performed using the USP disintegrating device. For estimating the disintegrating period of orally rapid disintegration films, there are no established recommendations available. There are two ways for estimating the time it takes for a film to disintegrate [20].

Slide frame method:

On the film clamped into slide frames put on the petri plate, a droplet of distilled water is poured. The length of time it takes for the film to disintegrate is recorded [21].

Petri dish method:

In a Petri plate, a film is inserted in 2 mL distilled water.The disintegration time is the amount of time it takes for the film to disintegrate entirely [22].

In-vitro dissolution test:

For conducting dissolving tests on films, standard official basket or paddle apparatus is employed. During dissolution, sink condition should be ensured. During dissolution, sink conditions should be ensured. During this process, film can float over the medium, making it difficult to perform the test effectively. Because this problem is more likely to arise with the paddle approach, the basket equipment is most commonly used.6.8 pH phosphate buffer (300 mL) and 0.1 N HCl were employed as media (900 ml).The temperature is normally kept around 37 ± 0.5 C, and the speed of rotation is set to 50 rpm.At pre-determined durations, samples of dissolved medication are collected and analysed by using a UV-spectrophotometer. Despite its widespread use, disintegration tests are still susceptible to various inaccuracies and failures [23, 24].

II. CONCLUSION

As this review demonstrates, oral fast dissolving films is a special method in pharmaceutical sciences. In comparison to traditional dose forms, they have enhanced patient acceptability and compliance, with no risk of choking and improved effectiveness and safety. The main goal of the development of ODFs was to address the difficulties in swallowing conventional oral dose forms in dysphagic juvenile, geriatric, and psychiatric patients. Presently, Because of their significance, ODFs are readily available for hypertension, acidity, allergies, pain, and other conditions. The main advantage of such dosage forms is their ability to be administered without the use of water, which meets the needs of the target demographic for convenience in drug administration while also bypassing hepatic metabolism, resulting in enhanced therapeutic response.

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