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Formulation and Evaluation of Fast Dissolving Oral Films

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ABSTRACT:

Oral fast dissolving is one of such approach to increase consumer accepted by virtue of rapid dissolving, self-administration without water and chewing. The film is an ideal intraoral fast dissolution drug delivery system. The films are designed to dissolve upon contact with wet surface such as tongue. There are many techniques were available to prepare the oral fast dissolving films at the mouth or buccal cavity. Buccal cavity is one of part of mouth and it's having a mucosal layer and having the saliva glands for the rapid absorption of films. Orally fast dissolving drug is the type of drug delivery system which in the oral cavity, dissolve within few min or seconds without intake of water. Oral films are very similar to postage stamp in their shape, size, and thickness. This review describes about types and preparation of method of oral films, selection of polymer for the formulation of oral films, evaluation parameter and its application.

KEYWORDS:

Rapid dissolving films, permeability, solvent casting and disintegration, oral strips, polymer.

INTRODUCTION:

The oral route is one of the most preferred routes of drug administration as it is more convenient, cost effective, and ease of administration lead to high level of patient compliance. The oral route is problematic because of the swallowing difficulty for pediatric and geriatric patients who are afraid of choking. Patient convenience and compliance-oriented research has resulted in bringing out safer and newer drug delivery systems. Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing. Fast dissolving drug delivery systems were first invented and in the late 1970s as to overcome swallowing difficulties associated with tablets and capsules for pediatric and geriatric patients.(1)

These dosage forms have a shelf life of 2-3 years, depending on the active pharmaceutical ingredient but are extremely sensitive to environmental moisture.

An ideal fast dissolving delivery system should have the following properties: High stability, transportability, ease of handling and administration, no special packaging material or processing requirements, no water necessary for application, and a pleasant taste.

The first of the kind of oral strips (OS) were developed by the major pharmaceutical company Pfizer who named it as Listerine pocket packs and were used for mouth freshening. Chloraseptic relief strips were the first therapeutic oral thin films (OTF) which contained 7 benzocaine and were used for the treatment of sore throat. Formulation of fast dissolving buccal film involves material such as strip-forming polymers, plasticizers, active pharmaceutical ingredient, sweetening agents, saliva stimulating agent, flavoring agents, coloring's agents, stabilizing and thickening agents, permeation enhancers, and super disintegrant.

The concept of oral dissolving film:

This delivery system consists of a thin film after placing it on the top of the tongue, the film dissolves within seconds, avoiding first pass metabolism and may increase the bioavailability of drug. (3) Accessibility of larger surface area leads to quick disintegration and dissolution in the oral cavity within seconds due to rapid wetting by saliva.

Oral dissolving film is flexible, so they are not as fragile and need not any kind of special package for protection during transportation and storage as compared to fast dissolving tablets.

No need of water has led to better satisfactoriness amongst the dysphasic patients and to better acceptance during travelling without carrying water. No fear of chocking as compared to fast dissolving tablets.

The large surface area available in the film dosage form allows rapid wetting by saliva then quickly disintegrates and dissolve and absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism and on increase the bioavailability. (5)

Fast dissolving oral films have advantages like, more stable, durable, and quicker than other conventional dosage forms; avoid first pass metabolism, pleasant mouth feel, accurate dosing, and rapid onset of action and no need of water with patient compliance. Moreover, ease of handling and transportability (1)

Special features of mouth dissolving films

• Thin elegant film

• Available in various size and shapes

• Unobstructive

• Excellentmucoadhesion

• Fast disintegration

• Rapid release

(8) Advantages :

• Convenient dosing.

• No water needed.

• No risk of chocking.

• Taste masking.

• Enhanced stability.

• Improved patient compliance.

• The drug enters the systemic circulation with reduced hepatic first pass effect.

• Site specific and local action.

• Availability of large surface area that leads to rapid disintegration and dissolution within oral cavity.

• Dose accuracy in comparison to syrup.

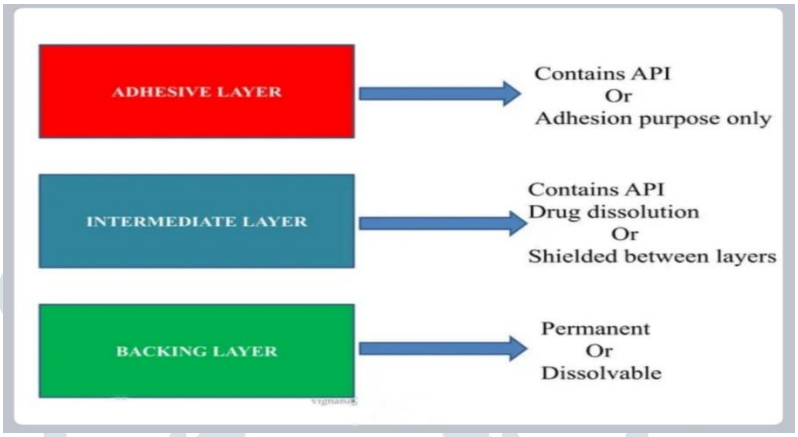
• Disadvantages:

• Drugs which are unstable at buccal pH cannot be administered.

• Drugs which irritate the mucosa cannot be administered by this route.

• Drug with small dose requirement can only be administered.

• Taste masking- Most drugs have bitter taste and need taste masking.



• Applications of Orally Dissolving Film:

1) Topical Application: The use of dissolved film may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other topical condition.

2) Gastro Retentive Dosage System: dissolved films are being considered in dosage forms for which water soluble and poorly soluble molecules of various molecular weight are contained in the film formats. Manufacturing Methods: Following are the process that can be used to manufacture the mouth dissolving films.

I) Solvent casting method

II) Semisolid casting method

III) Hot melt extrusion

IV) Solid dispersion extrusion

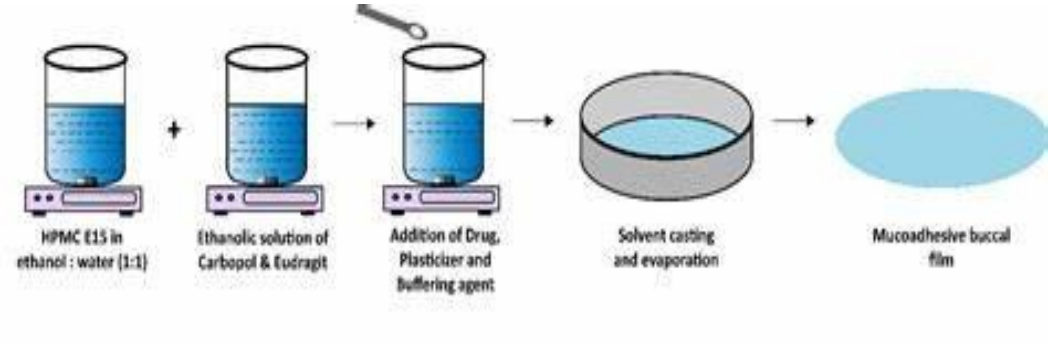
V) Rolling method

I) Solvent Casting Method:

It is very old film making method. In this method, firstly the water-soluble polymers are dissolved in water at 1,000 rpm and can be heated up to 60°C.

All the other excipients like colors, flavoring agent, sweetening agent, etc. are dissolved separately. Then both the solutions obtained are mixed thoroughly stirring at 1,000 rpm. The obtained solution is incorporated with the API dissolved in suitable solvent. The entrapped air is removed by vacuum.

The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the de sired size.



II) Semisolid Casting Method:

Semisolid casting method is generally used when acid insoluble polymers are used .in this method a solution of water-soluble film forming polymer is made then this solution is poured in the solution of acid insoluble polymer, which is prepared in sodium or ammonium hydroxide. After this plasticizer is added to form the gel mass. Amount of plasticizer added affect the property of gel mass formed. The gel mass formed is then casted into film of ribbons using heatcontrolled roller/drum. The ratio of acid insoluble polymer and film forming polymer. The film thickness formed by this method is a about 0.015- 0.05 inches.

Advantages and disadvantages of the solvent casting method

- Films are of uniform thicknesses

- Films are clear and bright

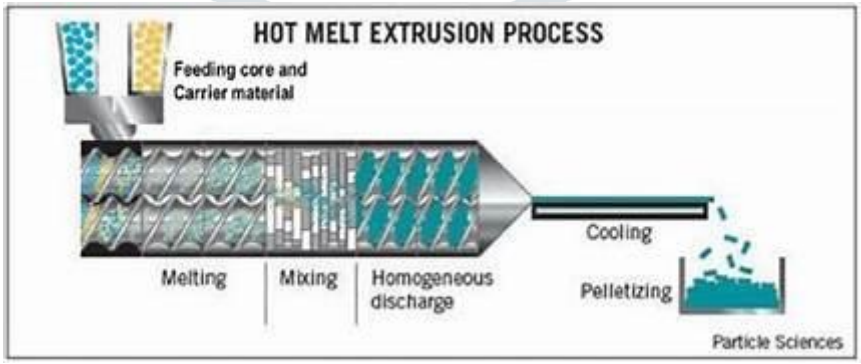
- Films are quite flexible - Prepared films are quite thin (12-100 µm)

- Offers better physical properties

- The method cost is suitable

III) Hot Melt Extrusion:

In hot melt extrusion method firstly, the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally, the melt is shaped into films by the dies. There are certain benefits of hot melt extrusion. Less operation units-better content uniformity an anhydrous process. The API's and others ingredients leading to improved dissolution rate and bioavailability. Subjected to the heating process where the mixing gets molten and then extruded out producing thin films. The solvent is completely removed by suitable technique.



IV) Rolling method:

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and alcohol. The film is dried on the rollers and cutter into desired shapes and sizes other ingredients including active agents dissolved in small portion of aqueous solvent using high shear processor Water soluble hydrochloride dissolved in water to form homogenous viscous solution.

V) Solid Dispersion Extrusion:

Term solid dispersion refers to dispersion of active ingredients in an inert carrier in solid state in the presence of amorphous hydrophilic polymers. In starting, the drug is dissolved in suitable liquid solvent and later this solution is added in the melt of polyethylene glycol at below 70 ° C without removing the liquid solvent and at last the solid dispersions are passed through dies to shape them in form of strips.

Now a day, both natural and synthetic polymers are utilized for the preparation of fast mouth dissolving film.

Characterization of oral fast dissolving films:

Film forming capacity It is ability of polymer about formulation of desired strip. It is categorized according to strip forming capacity such as very poor, poor, average, good, better, best. (Dixit RP et. al., 2009, Patel R. et. al., 2009) Appearance of films Appearance of strip was evaluated by visual observation such as transparent and semitransparent nature of strip. (Mashru RC et. al., 2005, Patel R. et. al., 2009) Disintegration time The Disintegrating test was carried out in 900 ml phosphate buffer (pH 6.8) at 37±0.5 0C. All studies were performed in triplicate for each batch.

Evaluation of the films:

Pre formulation is required to reach the set objective(9).

1)Thickness: It is important to ensure that the thickness of films is directly affected on the uniformity of drug content.

The film should be thick between 5 and 200 mm.

2)Dryness test: It should be dry to touch, dry hard, dry to handle, and dry print free.

Formulation table :

Components	Concentrations
1.API's	1-2%
2.Film forming agent	45-48%
3.surfactant	q.s
4.sweeting agent	3-6%
5.faloving agent	q.s
6.plasticizers	0-20%
7. vehicles	q.s

Active ingredients used in OTFs

The API must be dissolved for absorption to occur. If the active substance is very lipophilic, it is insoluble in the aqueous medium, and absorption may not be at the desired level. Therefore, there is a delicate balance between the lipophilicity and solubility of the drug. The primary mechanism of drug absorption is passive diffusion. As a result, the partition coefficient, degree of ionization, and molecular weight have a major influence on the transport of drugs across the oral mucosal membranes. The API's pKa and the degree of ionization at ambient pH must be considered when considering bioavailability. The degree of absorption is generally proportional to the lipophilicity or partition coefficient of the API. However, the solubility of the drug also plays a significant role. The nonionized form of the drug shows more lipid-soluble properties and therefore penetrates by diffusion through biological membranes.

Film-forming polymers used in OTFs

The selection of polymers is one of the most critical and important parameters in the successful preparation of oral films due to their tensile strength, which depends on the type and number of films used. According to the total weight of the dry film, at least 45% polymer by weight must be present, but 60%-65% by weight of the polymer is chosen to achieve the desired properties. Polymers can be utilized alone or in combination to achieve the desired film properties. Because OTFs are rapidly dispersed and dissolved in the oral cavity, the film_forming polymers utilized must be water-soluble. At the same time, the films obtained must be durable, which will not cause any damage during transport and storage.

Properties of an ideal polymer for OTFs are the following.

- The polymer used must be nontoxic and non-irritating

- There should not be impurities

- It must have enough wetting and spreading properties

- It must have sufficient stress and tensile strength

- It should be accessible and not too expensive

- The shelf life should be reasonable

- It should not cause secondary infections in the dental areas or oral mucosa

- It should have a good feeling in the oral cavity

- It must not be an impediment to the disintegration time

Film forming polymers :

- Hrydroxy Propyl M ethyl cellulose (HPMC) E15 ,K15 and E5
- Methyl cellulose A3,A6,and A15
- Pullulan, carboxy methyl cellulose (CMC)
- Poly vinyl pyrroliodone (PVP)
- Pectin
- Gelatine
- Sodium alginate

Plasticizers used in OTF's :

Plasticizers helps to increase the flexibility and lower the tg of polymer by reducing the friability of the film. Plasticizers also increase tensile strength. Plasticizers must be compatible with drug, solvent, and polymer used. It reduce the brittleness, impart flexibility, and enhance toughness for films.

- Glycerol
- Di-butyl phthalate
- Polyethylene glycol
- Dimethyl phthalate
- Diethyl phthalate

Saliva stimulating agent:

This agent is using for the purpose of increase the rate of production of saliva that would aid in the faster disintegration of rapid dissolving films formulations more saliva production help in the faster disintegration of fast dissolving films formulation. some of those agents are

- Citric acid
- Tartaric acid
- Malic acid
- Ascorbic acid

Citric acid being used more preferred amongst them.

Flavouring agent :

Flavours are used in the formulations must be non toxic, soluble, stable and compatible with the excipients. The quantity of flavouring agents required to mask the taste depend on the flavor type and its strength. commonly used are

- Vanilla
- Cocoa
- Peppermint oil
- Cinnamon oil
- Orange

Sweeting agents:

sucrose is the best commonly used sweeting agent. sucrose is very soluble in water and being colourless dose not impact any undesirable color to the final formulations.

- Dextrose
- Sucrose
- Fructose
- Glucose
- Sorbitol
- Mannitol

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