ejpmr, 2020,7(3), 232-238

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

A REVIEW ON MOUTH DISSOLVING FILMS

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Article Received on 31/12/2019 **Article Revised on 21/01/2020** **Article Accepted on 11/02/2020**

ABSTRACT

Oral route is considered as one of the most convenient route for administration of various pharmaceutical dosage forms like, tablet, capsule, syrup, suspension and emulsion. Fast Dissolving Drug Delivery systems have developed various fast disintegrating preparations like mouth dissolving film, MDT. Oral thin film are new dosage form that are prepared from hydrophilic polymer which are when placed in mouth, buccal cavity disintegrate rapidly. Mouth dissolving film is superior as compare to mouth dissolving tablet as the cost of production is low. Geriatric and pediatric patients are facing difficulty in swallowing of tablet and capsule, the oral film can bypass it, along with that it has other advantages like self-administrable, fast dissolving, rapid absorption that make it versatile dosage form. The aim of present study is to enlighten specifically different polymer along with their concentrations and applications. This study also focuses on use of plasticizer, polymer, sweetener, different methods which are used for the preparation of oral films and various evaluation parameter of the film.

KEYWORDS: MDT:- Mouth Dissolving Tablet, oral films, pediatric patients, evaluation, Buccal cavity, dosage forms, Tensile strength.

INTRODUCTION

Oral film technology was first invented in the late 1970s just to overcome swallowing difficulties related to tablets and capsules faced by geriatric and pediatric patients but now is trending in pharma industry due to less fragility than other oral dosage forms, dosage accuracy, rapid release, ease of administration.[1,2]

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.[3]

The most flavoured route of drug administration is oral route due to cost efficiency and ease of administration which lead to high patient compliance for the pediatric and geriatric group, but it is still challenging route due to swallowing difficulty for pediatric and geriatric patients. The development of novel and safer drug delivery such as oral strips, buccal films are the result of patient convenience and compliance-oriented research. In recent times, an oral film drug delivery system has gained lots of popularity and acceptance. Recently, fast dissolving films are gaining interest as an alternative of fast dissolving tablets. The films are designed to dissolve upon contact with a wet surface, such as the tongue, within a few seconds, meaning the consumer can take the product without need for additional liquid. This convenience provides both a marketing advantage and increased patient compliance. As the drug is directly absorbed into systemic circulation, degradation in gastrointestinal tract and first pass effect can be avoided. These points make this formulation most popular and acceptable among pediatric and geriatric patients and patients with fear of choking.[4,5,6]

Today, Oral Thin Films are a proven and accepted technology for the systemic delivery of active pharmaceutical ingredients (APIs) for over-the-counter (OTC) medications and some prescription drugs.[7]

Fast dissolving films, a type of oral drug delivery system for the oral delivery of the drug, was developed based on the technology of the transdermal patch. This delivery system consists of a thin film, which is simply placed on the patient's tongue or mucosal tissue, instantly wet by saliva; then it rapidly disintegrates and dissolves to release the medication for oral mucosal absorption.[8,9]

Fast dissolving oral film is prepared using hydrophilic polymers that rapidly dissolve on the tongue or buccal cavity, delivering the drug to the systemic circulation via dissolution when contact with liquid is made. Fast dissolving oral film has emerged an advanced alternative to the traditional tablets, capsules and liquids often associated with prescription and OTC medications. Similar in size, shape and thickness to a postage stamp thin-film strips are typically designed for oral administration, with the user placing the strip on or under the tongue (sublingual) or along the inside of the cheek

(buccal). These drug delivery options allow the medication to bypass the first pass metabolism thereby making the medication more bioavailable. As the oral thin film dissolves, the drug can enter the blood stream through enteric, buccal or sublingually.[10,11]

The main challenges of the present study were taste masking besides improving the aqueous solubility of the drug as medications that enter the oral cavity, irrespective of mode of administration, namely, swallowing and sublingual or oral inhalation, should have an acceptable taste. One of the major barriers that prevents patient from adhering to a prescribed medication regimen has been identified as the unacceptable taste of active pharmaceutical ingredients (APIs) in these dosage forms. Taste has an important role in the development of oral pharmaceuticals, with respect to patient acceptability and compliance, and is one of the prime factors determining the market penetration and commercial success of oral formulations, especially in pediatric medicine.[12,13,14]

MECHANISM OF FILM FORMATION

Film forming system is applied directly to the skin and it forms a thin, transparent film *in situ* upon solvent evaporation as shown in fig. 1. After application of the formulation to the skin, the composition of the film forming system changes significantly due to the loss of the volatile components of the vehicle which results in formation of residual film on the skin surface. In this process the concentration of drug increases, reaching saturation level and with the possibility of reaching super saturation level on the skin surface. Supersaturation results in the enhanced drug flux through the skin by increasing the thermodynamic activity of the formulation without affecting the skin's barrier, thereby reducing the side effects or irritation.

The concept of supersaturation can be explained by the modified form of Fick's law of diffusion. Fick's law of diffusion given by Eq.:

$$J = \frac{DKCv}{h}$$

Where

J = rate of drug permeation per unit area of skin per unit time (flux)

D = diffusion coefficient of drug *Cv*= concentration of drug *h* = thickness of barrier to diffusion

From this equation, it is clear that the rate of drug permeation across the skin is proportional to the concentration of the drug. However this is true when the entire drug is dissolved in the vehicle. Equation describes the modified form of Fick's law of diffusion:

$J = \alpha\ D/\gamma h$

Where a=thermodynamic activity of drug within formulation γ=thermodynamic activity of drug within membrane

According to this equation, the flux of the drug is directly proportional to the thermodynamic activity of the system, which is related to saturation. However increasing the super saturation increases thermodynamic instability.

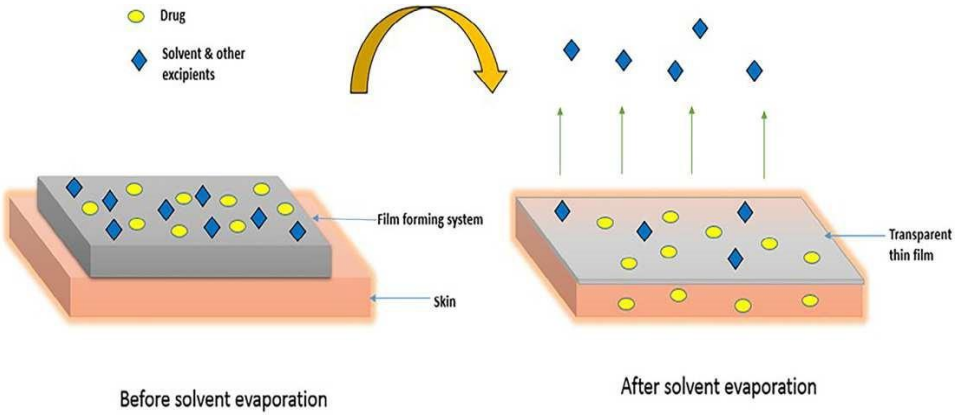

Fig. 1: Mechanism of film formation.

FFS creates supersaturated systems immediately after application to patch (EVRA®) through human epidermis *in vitro*. The film forming the skin, overcoming the problem of instability. Thus it improves the formulations showed a higher permeation than the commercial patch. drug permeation through skin compared to other transdermal dosage Without enhancer the formulation transported more than double the forms. The delivery efficiency of the film forming solutions for ethinyl ethinyl estradiol than the marketed patch. With enhancer, the estradiol was investigated. The permeation of ethinyl estradiol from formulation delivered about seven times as much ethinyl estradiol as the film forming solution prepared with enhancer or without enhancer that of the marketed patch. Thus these systems prove to be useful in was compared to the permeation from the commercially available enhancing the drug permeation.[36]

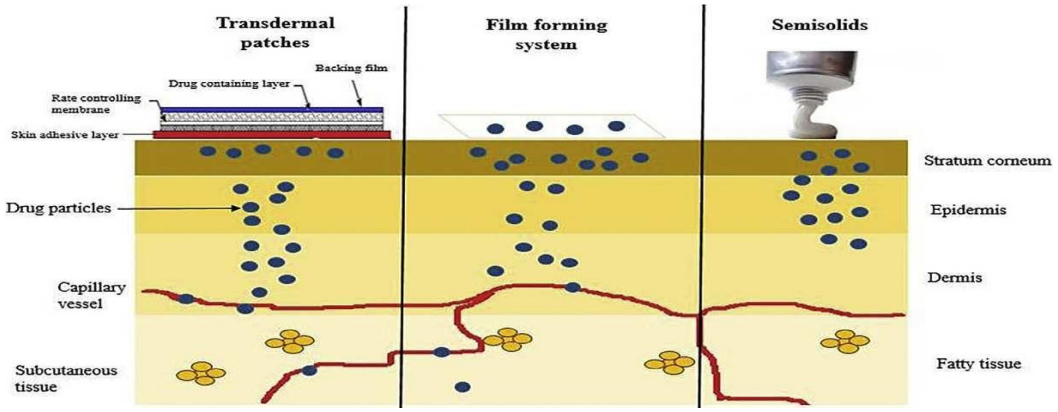

Fig. 2: Release Profile of the topical and transdermal drug delivery systems.

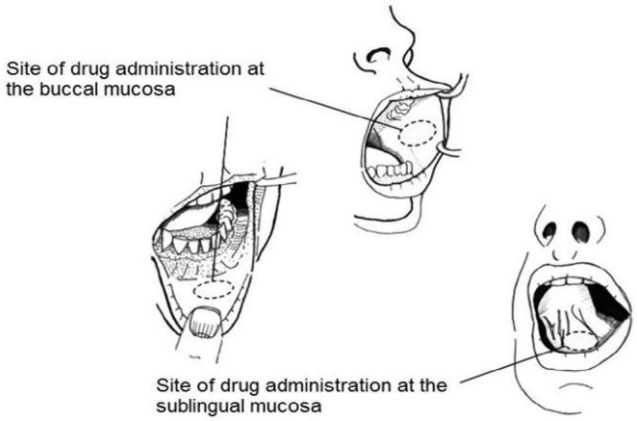

Fig. Demonstration of common site for application of film in buccal and sublingual mucosa.

METHOD OF PREPARATION

Method of preparation of fast dissolving films Fast dissolving films can be prepared by:

a. Solvent casting method
b. Semisolid casting method
c. Hot melt extrusion
d. Solid dispersion extrusion
e. Rolling method

a. Solvent casting method

In this method, water soluble polymers are dissolved in suitable solvent and the drug along with other excipients is dissolved in suitable solvent. Then both the solutions are mixed and stirred. This solution is then degassed under vacuum to settle the air bubbles. This bubble free solution is then finally casted into Petri plate and dried.[20]

b. Semisolid casting method

In this method solution of water soluble film forming polymer is prepared. And resulting solution is added to a solution of acid insoluble polymer (Examples: cellulose acetate phthalate, cellulose acetate butyrate, etc). Then the appropriate amount of plasticizer is added to obtain a gel mass. This gel mass is then casted into the films or ribbons using heat controlled drums. The thickness of the films should be about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.[21]

c. Hot melt extrusion

Hot melt extruder is used in this process. This technique involves shaping a polymer into a film via the heating process. A blend of pharmaceutical ingredients including API in dry state is filled in the hopper, conveyed, mixed and subjected to the heating process, and then extruded out in molten state melted by the extruder. The molten mass thus formed is used to cast the film. A critical step is the casting and drying process. This technique has many advantages, such as this process involves lower temperature and shorter residence times of the drug carrier mix, absences of organic solvents, continuous operation possibilities, minimum product wastage, good control of operating parameters and possibilities to scale up.[22,23]

d. Solid dispersion

The term solid dispersion refers to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers. In this method drugs are dissolved in suitable solvents and then solutions are incorporated into the melt of polyethylene glycol below 70^{o} C. Then solid dispersions are finally shaped into the films by means of dies.[24]

e. Rolling Method

In rolling method, a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on

the rollers and cut in to desired shapes and sizes. Other ingredients including active agent are dissolved in small portion of aqueous solvent using high shear processor. Water soluble hydrocolloids dissolved in water to form homogenous viscous solution.[25]

TYPES OF FILM

1] Flash release film
2] Flash dispersable film
3] Non-disintegrating mucoadhesive films
4] Medium disintegrating mucoadhesive films

APPLICATIONS

1. Film forming systems used in field of surgery.
2. It can also be used as substrate for various barrier membranes that are used in Industries.
3. Film forming polymers are used to increase the integrity of soil and elevate the soil temperature which is useful in crop production.
4. Film formners used for non-medical uses such as, the delivery of active ingredients contained in beauty products like silicone film forming technologies used to prepare cosmetic creams and ointments.
5. film forming systems were used for wound care.

Advantages[27-35]

1] Great uniformity of thickness and great clarity than extrusion.
2] Films have fine gloss and free from defect such as die lines.
3] Films have more flexibility and better physical properties.
4] As compare to tablet the on set of action is quick.
5] During administration, its doses not required water.
6] No risk of chocking.
7] Transportation is easy.
8] Rapid disintegration & dissolution in the oral cavity is provided due to large surface area.
9] For the drug delivery to the eye, opthalmic thin films can be used.

Disadvantages[27-35]

1] The polymer must be soluble in a volatile solvent or water.
2] The stable solution with reasonable minimum solid content and viscosity should be formed.
3] Special packaging for product stability and safety is required.
4] It absorb moisture from the external atmosphere.

FORMULATION[18,19]

SR. NO.	NAME OF INGRIDIENT	USES	AMOUNT	EXAMPLE
1	Drug	Therapeutic activity	5-30%w/w	All drugs are suitable
2	Polymers	Ability to forming film	45%w/w	HPMC
3	Plastisizers	Increase flexibility reduce bitterness of film	0-20%w/w	Glycerol, Polytheleneglycol
4	Surfactant	Solubilizing agent &wetting agent	9.5%w/w	Tween 80, SLS
5	Sweetning agent	Enhance the palatability	3-6%w/w	Saccharine, Aspartaine
6	Saliva stimulating agent	Increase saliva stimulation	2-6%w/w	Citric acid
7	Flavours	To mask the odour of drug	Should not exceed 1% w/w	Menthol
8	Colors	To give elegancy to film	Should not exceed 1%w/w	Titanium dionide

EVALUTION PARAMETER

1. Thickness: The thickness of the all different films was measured using a baker precision measuring instrument, china. It was measured by placing each film between the anvil and the presser foot of the dial guage is 5 different location and the average thickness was calculated.[37]

2. Tensile strength: Tensile strength is maximum stress applied to at which film specimen breakes. It is calculated by the load at rupture divided by the cross section area of the film.[38]

Tensile strength = F max/A film

3. Youngs modulus: - It is use to estimate stiffness. It is found as balance applied stress to the strain in the region. it is determind by,

Youngs modulus = force of corresponding strain/cross sectional area.[39]

4. Tail flick test: The ventral surface of the tail of the animal was placed on the heating coil of digital analgesiometer and the basal reaction times were noted. About 3-5 basal coxib was fixed of 10 mg/kg body weight.[40]

5. Thermodynamic stability test: Optimize formulations then subjected to different thermodynamic stability study test namely centrifugation and freeze thaw cycles by thermodynamic stability test.

6. Viscosity: Evaluate the viscosity of the optimized formulation by Brookfield viscometer.[41]

7. Drug content: Determine the percentage of drug content of formulation from the calibration curve by using uv spectrometer.

8. Weight of films: Oral fast dissolving films can be weighed on analytical balance and average weight can be

determined for each film. It is desirable that films should have nearly constant weight. It is useful to ensure that a film contains the proper amount of excipients and APIs.[42]

9. pH value: P^H is measured by the dissolving one oral film in 10ml distilled water and measuring the pH of the obtained solution should have nearly uniform pH value.[43]

10. Elongation: When stress is applied, a film sample stretches and this is referred to as strain. Strain is basically the deformation of film divided by original dimension of the sample. Generally elongation of film increases as the plasticizer content increases.[44]
Percent elongation= $L*100/L^o$
L = Increase in length of film L^o = Initial length of film

11. Swelling property: Each film sample is weighed and placed in a pre-weighed stainless steel wire mesh. Then the mesh containing film sample is submerged into 15ml medium (simulated saliva solution) in a plastic container. Increase in the weight of the film was determined at preset time interval until constant weight was observed.[45]
Degree of swelling = Wt – Wo/ Wo
Where, Wt is weight of film at time t, and Wois weight of film at time zero.

12. Stability Studies: Stability studies on the optimized oral fast dissolving film is carried out for determination of effect of temperatures and humidity on the stability of the drug. The film are stored in an aluminum foil and subjected to stability at room temperature. The sample can withdraw at 3 months and 6 months and subjected for cumulative % drug release and in vitro dissolution studies to determine disintegration time and disintegration test.[46]

Table: Comparison between oral films and oral tablets.[17]

Oral films	Oral tablets
1. Oral films have greater dissolution due to large surface area	1. Oral tablets have lesser dissolution area as compared to oral films
2. They have better longevity than oral tablets	2. They have less longevity than oral films
3. They have more patient compliance than oral tablets	3. They have less patient compliance as compared to oral film
4. There is no risk of choking	4. There is a risk of choking

CONCLUSIONS

Recently pharmaceutical companies embraced fast dissolving films as a practical and accepted alternative to traditional medicines. This technology is good for increasing patent life of existing product in pharmaceutical company.

Fast dissolving oral films have better patient compliance and improve efficiency and better safety, compared with conventional oral dosage forms. Industrially feasible approach to overcome the problems of low oral bioavailability associated with the lipophilic drugs.

This study explores the possibilities of loading a wide variety of plant actives as their scale up is convenient and economical.

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