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Formulation and Characterization of Lanthanum Carbonate Oral Mouth Dissolving Film

Minal Ghule

Mouda College of Pharmacy
Email id: *minalghule96[at]gmail.com*

Abstract: ***The development of oral fast dissolving films, which dissolve or disintegrate instantly on the patient buccal mucosa. In response to this need, a variety of orally disintegrating tablet (ODT) formats were commercialized. Mouth dissolving films are thin solid dosage forms which when placed in the oral cavity; dissolve within few seconds without chewing and intake of water. The oral buccal mucosa being highly vascularized, drugs can absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing and enhance the efficacy and safety profile of medicament. The present study was aimed to formulate and evaluate fast dissolving oral films of lanthanum carbonate. The suitable plasticizer and its concentration were selected on the basis of flexibility, tensile strength and stickiness of the film. The films are prepared by solvent casting method and characterized by UV studies. The films were evaluated for disintegration time, Folding endurance, Tensile Strength, Mouth dissolving time, Thickness, content uniformity and In-vitro dissolution studies. In this novel drug delivery odf showed that accompanier other formulation was better therapeutic effect.***

Keywords: mouth dissolving film, lanthanum carbonate , solvent evaporation method, bioavailability enhancement

1. Introduction

Mouth dissolving films offers an elegant route for systemic drug delivery. The improved systemic bioavailability results from bypassing first pass effect and better permeability due to a well supplied vascular and lymphatic drainage. Also, large surface area of absorption, easy ingestion & swallowing, pain avoidance make the oral mucosa a very attractive and selective site for systemic drug delivery. Recent developments in the technology have presented viable dosage alternatives from oral route for wide variety of group of patients. Buccal drug delivery has lately become an important route of drug administration. Various Bioadhesive mucosal dosage forms have been developed Orally dissolving film (ODF) may be described as a small strip, composed of water soluble polymers and a bioactive ingredient that has been uniformly dispersed in the film matrix. Indeed, a number of synonym terms, such as oral film, thin-film, wafer, oral strip, oral thin film and oral soluble film, etc. viable dosage alternatives from oral route for pediatrics, geriatric, bedridden, nauseous or noncompliant patients. Buccal drug delivery has lately become an important route of drug administration. Various bioadhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving film. According to European Medicine Agency (EMA), they are designated as or dispersible film. When this film is placed on the tongue, it readily disintegrates and dissolves to release the entrapped drug that is subsequently absorbed *via* oromucosal route. It is reported that buccal mucosa has almost 4000 times greater permeability than that of skin .The delivery of drug through oral mucosa has so many advantages such as direct delivery of the drug into the blood stream, which avoids not only its exposure to the harsh conditions of gastric environment but it also eliminates its first pass metabolism in the liver.

Fast-dissolving drug-delivery systems were first developed in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experienced difficulties in swallowing traditional oral solid-dosage forms. The novel technology of oral fast-dispersing dosage forms is also known as fast dissolve, rapid dissolve, rapid melt or quick disintegration. However, the function and concept of all these dosage forms are similar. By definition, a solid dosage form that dissolves or disintegrates quickly in the oral cavity, resulting in solution or suspension without the need for the administration of water, is known as an oral fast-dispersing or fast-dissolving dosage form Fast-dissolving buccal film drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. They are usually used for pharmaceutical and nutraceutical products. It is the newest frontier in drug delivery technology that provides a very convenient means of taking medications and supplements. There are multiple fast-dissolving over the counter and prescribed products on the market worldwide, most of which have been launched recently. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology

2. Material and Method

In this mouth dissolving formulation that ingredients and methods given as below:

S. No	Ingredients	Quantity
1	Lanthanum carbonate	5-30%
2	HPMC	45
3	glycerol	0-20%
4	citric acid	2-6%
5	benzalkonium chloride,	Q.S.
6	neotame	3-6
7	orange or sweet confectionary flavor Titanium dioxide	Q.S

Manufacturing Methods

One or combination of the following process can be used to manufacture the mouth dissolving films.

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

Solvent Casting:

Fast dissolving buccal films are preferably formulated using the solvent casting method, whereby the water soluble ingredients are dissolved to form a clear viscous solution and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate and dried. Water soluble ingredients are dissolved in H2Oand API and other agents are dissolved in suitable solvent to form a clear viscous solution. Both the solutions are mixed resulting solution is cast as a film and allowed to dry film is collected Water soluble hydrocolloids used to prepare films are hydroxypropyl methylcellulose,

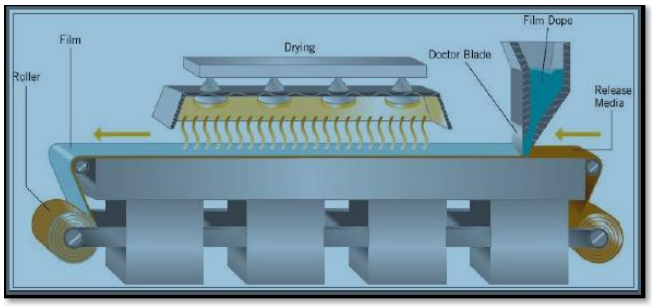

Figure 1: Solvent casting

Preparation of Artificial Saliva (AS)

The artificial saliva (AS) was prepared as described elsewhere [24]. In brief, Sodium chloride-0.844 g; Potassium chloride-1.2 g; Calcium chloride dihydrate-0.193g; magnesium chloride hexahydrate-0.111 g; potassium phosphate dibasic-0.342 g. These ingredients were added one by one to 500 mL of distilled water and then the volume was made up to 1000 mL using the same. The pH was adjusted with 0.1N hydrochloric acid to 5.7.

Evaluation: Characterization of fast dissolving films:

Weight variation of the film:

2.25 cm2 films were cut at five different places in the caste film. The weight of each filmstrip was taken and the weight variation was calculated

Thickness

Thickness test can be carried out using an electronic micrometer. The thickness of the film sample should be measured at five locations (center and four corners), and the mean thickness is calculated. Samples with air bubbles, nicks or tears and having mean thickness variation

Folding endurance

To determine folding endurance, a strip of film is cut and repeatedly folded at the same place tillit broke. The number of times the film could be folded at the same place without breaking gives the value of folding endurance.

Swelling index

The studies for swelling index of the film are conducted in stimulated salivary fluid. The film sample is weighed and placed in a preweighed stainless steel wire sieve. The mesh containing the film is submerged into 50 ml of stimulated salivary medium contained in a mortar. Increase in weight of the film is determined at each interval until a constant weight is observed. The degree of swelling is calculated using the formula:

$$SI = wt - wo / wo$$

Where SI is the swelling index,
wt is the weight of the film at time "t", and
wo is the weight of film at t = 0

Uniformity of drug content:

This parameter can be determined by dissolving known weight of film by homogenization in 100ml of stimulated saliva of pH 6.8 for 30 min with continuous shaking.

Palatability test

Palatability study is conducted on the basis of taste, after bitterness and physical appearance. All the batches are rated A, B and C grades as per the criteria. When the formulation scores at least one A grade, formulation is considered as average. When the formulation scores two A grade then it would be considered as good and the one with all three A grade it would be the very good formulation.
Grades: A= very good, B= good, C=poor

Tensile strength

The tensile strength (psi) is the property of the film that requires a load to cause load deformation failure of film. Nafee *et al.*, 2003 evaluated this mechanical property by using Instron Universal Testing Instrument (model F. 4026),with a 5-kg load cell .Film strips in special dimension and free from air bubbles or physical imperfections were held between two clamps positioned at a distance of 3 cm. During measurement, the strips were pulled by the top clamp at a rate of 100 mm/min; the force and elongation were measured when the film broke. Results from film samples, which broke at and not between the clamps, were not included in the calculations. Measurements were run in triplicate for each film. Tensile strength is also defined as the maximum stress applied to a point at which the film specimen breaks and can be computed from the applied load at rupture as a mean of three measurements and cross sectional area of fractured film from the following equation .

Tensile strength (N/mm2) = breaking force (N) / cross sectional area of sample (mm2)

Disintegration test:

Disintegrating time is defined as the time (second) at which a film breaks when brought into the contact with water or saliva. The disintegration time is the time when a film starts to break or disintegrate. Thickness and mass play a role in determining the dissolvable films physical properties. Disintegration test is done by Disintegration apparatus.

Dissolution test:

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature and solvent concentration. Invitro release studies are carried out in modified USP XXIII apparatus (paddle over disk).

Stability study

Stability study of fast dissolving films is carried out for all the batches according to ICH guidelines. After predetermined time intervals, the films are evaluated for the drug content, disintegration time and physical appearance

3. Result and Discussion

Physical characterization of fast dissolving oral films

The physical characterization of the formulated oral films were done by various techniques various parameters like weight variation of the films, thickness of the films, Tensile strength of the films, Folding endurance of the films, Disintegration time, Mouth dissolving time, Drug content uniformity of films, *In-vitro* dissolution. Weight variation varies as the polymer concentration increases the thickness, folding endurance and disintegration time of the film also increases. The formulation F5 shows56 sec (disintegration time). The formulation shows the maximum value of tensile strength 1.80 mpa in that formulation increase concentration of polymer that also increase of tensile strength and folding endurance was 170 this might be due to the formation of strong hydrogen bonds between polymer and plasticizer there by imparting flexibility to with stand rupture. In this percentage of elongation was found to be if increase of increase polymer concentration of filim. The *In-vitro* drug release from the formulation f5 was 98.5% within 7mins of time.

4. Conclusion

From the present investigation it can be concluded that oral thin film formulation can be a potential novel drug dosage form for geriatric and also for general population. Hence fast dissolving films were found to be suitable for eliciting better therapeutic effect. The films take 5 to 8 min for complete dissolution in artificial saliva medium. Addition of sweetener, saliva stimulator and surfactant delay the dissolution process.

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