IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
June 2017 Vol.:9, Issue:3

Buccal Film: An Emerging Technology for Oral Drug Delivery

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Ashinaa Benedict*, Dr. Manju Maria Mathew, Jishnu Sathyan, Jaise Thomas

Dep. of pharmaceutical science, Nirmala college of pharmacy, Muvattupuzha, Ernakulam, Kerala.

Submission: 5 June 2017
Accepted: 10 June 2017
Published: 25 June 2017

Keywords: Buccal film, Mucosal membrane, Mucoadhesion

ABSTRACT

Among the various routes of administration, the oral route is the most convenient, easy and preferred one. However, orally administered drugs are either prone to hepatic first-pass metabolism or metabolism in the gastrointestinal tract or both. The mucoadhesive drug delivery systems improve the bioavailability of the drugs by bypassing the first-pass effects and avoiding the presystemic elimination of the drug within the GI tract. Out of the various sites available for mucoadhesive drug delivery, the buccal mucosa is the most suited one for local as well as systemic delivery of drugs. Buccal film drug delivery uses a dissolving film or oral drug strip to administer drugs via absorption in the mouth. A film is prepared using hydrophilic polymers that rapidly dissolves in the mouth, delivering the drug to systemic circulation when contact with the liquid is made. Buccal drug delivery options allow the medication to bypass the first pass metabolism thereby making medication more bioavailable.

INTRODUCTION

We know that different types of routes of administration for medicaments are available, like injectables, inhalable, transdermal, oral and nasal routes of administration. Among this oral route is the most convenient and preferred route when compared to other routes of delivery of drugs. Mucoadhesion gains major interest over the last two decades for its potential to optimize localized drug delivery because it only retains a dosage form at the site of action but also keeps the formulation in intimate contact with the absorption site. Mucoadhesion concept has gained significant concern in pharmaceutical technology in the early 1980s.[2] Adhesion is a process of fixing of two surfaces to each other. Bio-adhesion (and mucoadhesion) is the process in which synthetic and natural macromolecules adhere to mucosal surfaces in the body by means of interfacial forces

Buccal drug delivery is an important route of drug administration. Buccal administration refers to a topical route of administration in which drugs held or applied in the buccal area, diffuse through the oral mucosa and enter directly into the bloodstream. In biological term, the product is placed between upper gums and cheeks to treat local and systemic conditions. The buccal mucosa is relatively permeable and provides rich blood supply and permits a prolonged retention of a dosage form, especially with the use of mucoadhesive polymers without much interference in processes such as mastication, unlike the sublingual route. The order of permeability of the oral cavity is given as Sublingual>buccal>palatal.[8] Buccal administration shows better bioavailability and rapid onset of action compared to oral administration because the medication does not pass through the digestive system and thereby avoids first pass metabolism.

The buccal film can be defined as the dosage form that employs a water dissolving polymer which allows the dosage form to dissolve into the buccal mucosa or mouth and releases the medicament to provide local or systemic drug delivery.

The ideal buccal film drug delivery system must have the following characteristics:

- After administration, there should be no residue present in the buccal cavity.
- Should adhere for a few hours to the site of attachment.
- The polymer used should be non-toxic as well as non-irritant.

- Drug release should be in a unidirectional way toward the mucosa.
- Should have sufficient hardness.
- Having a taste masking property.
- Facilitate the rate and extent of drug absorption.
- Should not cause any inconvenience to the patient and
- Should not interfere with the normal functions like talking, drinking etc.

Advantages of the buccal film:

Buccal films have the following advantages.

- Fast dissolution rate when compared to other conventional dosage forms.
- Avoid acid/enzyme metabolism.
- Ease of administration and termination.
- High patient compliance.
- Stable.
- Cost effective.
- Avoids hepatic first pass metabolism and thereby increasing the bioavailability.
- The high rate of absorption due to the intimate contact surface of the oral cavity with the mucoadhesive membrane.
- Suitable for geriatric, pediatric, unconscious or comatose patients where complete dosing is difficult.
- Low intersubject variability when compared to transdermal patches.
- Preferred over adhesive tablets in terms of flexibility and comfort.
- Effective in oral disease.

- Directly and easily modifies microenvironment.
- Avoid dose-dependent side effects by decreasing the dose.
- An alternative route for proteins and peptides.
- Follows passive diffusion and does not require any activation.
- The presence of saliva ensures a large amount of water for dissolution of drug unlike in the case of the rectal and transdermal route.

Disadvantages of the buccal film:

Disadvantages of the buccal film are as follows:

- Only small dose drugs are suitable for the buccal film.
- Buccal films are moisture sensitive.
- The buccal mucosa has low permeability when compared to sublingual mucosa.
- Eating and drinking are restricted.
- Drugs which are unstable at buccal pH and those which irritate the mucosa or have a bitter or unpleasant taste and odor cannot be administered by this route.
- Drugs causing allergic reactions as well as discoloration of teeth cannot be formulated as the buccal film.
- The requirement of frequent dosing due to the flushing action of saliva.
- The buccal mucosa has low permeability when compared to sublingual mucosa.
- Chance for over-hydration which in turn leads to the formation of slippery surface and structural integrity of formulation may get disrupted.

Overview of Oral Mucosa

The oral cavity is that part of the mouth bounded anteriorly and laterally by the lips and the cheeks, posteriorly and medially by the teeth and/or gums, and above and below by the

reflections of the mucosa from the lips and cheeks to the gums. The lining of the oral cavity is referred to as the oral mucosa and it consists of stratified squamous epithelium termed oral epithelium and an underlying connective tissue termed lamina propria (Fig-1).

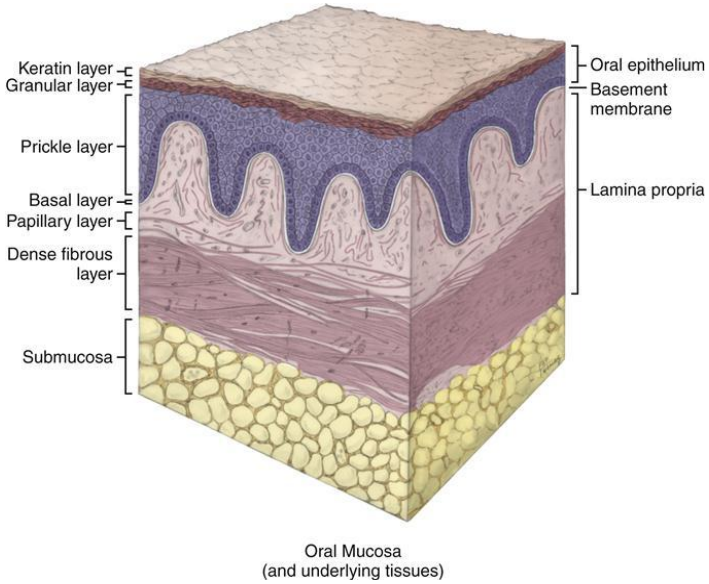

Fig-1

Oral mucosa in the oral cavity can be divided into three main categories based on function and histology:

- **Masticatory mucosa** keratinized stratified squamous epithelium, present in the hard palate (the upper surface of the mucosa) and the gingiva (gums).

- **Lining mucosa**, non-keratinized stratified squamous epithelium, present in the lips, cheeks, soft palate and a lower surface of the tongue.

- **Specialized mucosa**, both keratinized and non-keratinized epithelium, present in the regions of the taste buds on lingual papillae on the dorsal surface of the tongue that contains nerve endings for general sensory reception and taste perception.

Mechanism of Mucoadhesion

The mechanism of mucoadhesion is generally divided into two steps (Fig-2):

- The contact stage involves intimate contact between the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with mucus layer.

- The consolidation stage involves penetration of the mucoadhesive into the surface of the mucous membrane (interpenetration).

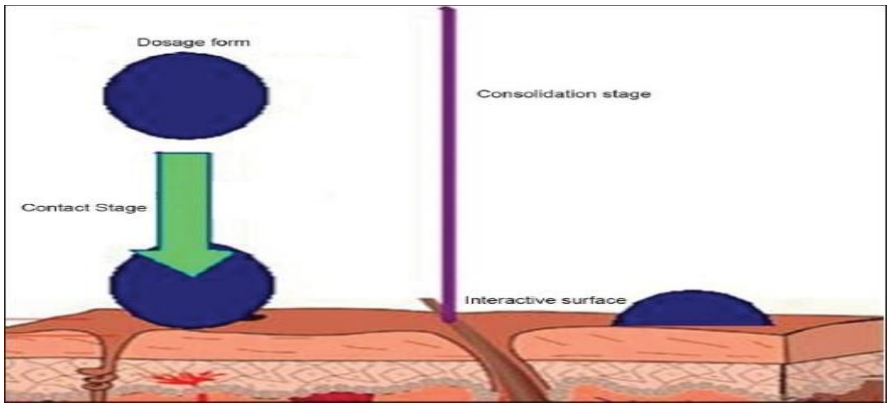

Fig-2

Manufacturing methods of buccal films

Following methods may be used to manufacture the buccal film:

- Solvent casting method
- Hot-melt extrusion method
- Solid dispersion extrusion method
- Rolling method

Solvent Casting Method

Solvent casting method is the most widely used method for the manufacturing of buccal film due to its excellent uniformity in thickness, easy and low-cost processing. In this method, the drug and other excipients are dissolved in the appropriate solvent to form a clear viscous solution and the formed solutions are mixed well. Then, the solution is cast as a film and allowed to dry. Film is collected.[2]

Hot Melt Extrusion Method

Hot melt extrusion is widely used to prepare granules, sustained release tablets, and transmucosal drug delivery systems. It is an anhydrous method and exhibits better content uniformity than extrusion method. In this method, the drug is mixed with the carriers in the dry state. The mixture is then melted by using an extruder having heaters. It is then shaped into films with the help of dies. The film is collected.

Solid dispersion extrusion method

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, the drug is dissolved in a suitable liquid solvent. The solution is then incorporated into the melt of polymer below 70^0C. Finally, solid dispersion is shaped into films with the help of dies. The film is collected.

Rolling method

In this method, the film is prepared by making a pre-mix by using the film forming the polymer, polar solvent and other additives.[1] The solvent used is mainly water and mixture of water and alcohol. The pre-mix is then added to feed tank. Then the required amount of drug is added to the desired mixer. Blend the drug with pre-mix to give a uniform matrix. Then by using metering pumps a specific amount of uniform matrix is fed to the pan. The film is finally formed on the substrate and carried away by the roller. The wet film is dried and collected.

Evaluation of the buccal film

Drug Content Uniformity:

Three films of each formulation were taken in the separate 100ml volumetric flask; 100ml of pH 6.8 phosphate buffer was added and stirred continuously for 24 h. The solutions were filtered, suitably diluted and analyzed on a UV spectrophotometer. The average of drug contents of three films was taken as final reading.[7]

Folding Endurance:

Folding endurance is measured by manual repeated folding of the film at some place till it broke. The number of time the film is folded without breaking is the folding endurance value.

Film weight and thickness:

The weight of each film was measured with the help of a digital balance from different positions of the film and the average weight was calculated. Similarly, the thickness of each film was measured with the help of screw gauge and the average was calculated.

Surface pH of the film:

Surface pH of the film can be determined by allowing three films of each formulation to swell for two hours on an agar plate surface. The surface pH was measured with the help of pH paper which is placed on the surface of the swollen film and a mean was calculated.

Swelling index:

Three films of each formulation were weighed individually. Then the sample is placed on the surface of an agar plate which is kept in an incubator (hot air incubator) maintained at 37^0c. An increase in the weight of the film was noted at 1 h intervals up to 5 h. The percent swelling, % S was calculated using the following equation (1)

$$\text{Percent swelling (\%S)} = [(X_t - X_o) / X_0] \times 100 \ldots\ldots\ldots\ldots (1)$$

Where, X_t = the weight of the swollen film after time t,

X_o = the initial film weight at zero time.

Moisture content:

The prepared films are weighed individually and then placed in a desiccator which contains calcium chloride at room temperature for 24 h. After a specific time interval, the films are to be weighed again until they show an unvarying weight. The % moisture content was calculated by using the following formula.

$$\% \text{ moisture content} = \frac{\text{initial weight} - \text{final weight}}{\text{Final weight}} \times 100$$

In-vitro release study

Dissolution studies are carried out in a USP dissolution apparatus using 900ml of dissolution medium at 37± 0.5^0C, and a rotation speed of 50 rpm was used. An aliquot of sample is periodically withdrawn and replaced with fresh medium. The samples were filtered through Whatman filter paper and analyzed spectrophotometrically.

In-vitro residence time

The *in-vitro* residence time was determined with the help of an IP disintegration apparatus which is maintained at a temperature of 37±2^0C using 900ml of the disintegration medium. A piece of porcine buccal tissue was used for this study, which is attached to a rectangular glass piece using cyanoacrylate adhesive from the non-mucosal surface. The glass piece containing tissue and film placed into the basket of disintegration apparatus and set in motion. The time required for complete detachment of the film from the mucosal surface was observed and recorded.

Ex vivo mucoadhesive strength

The force which is required for the detachment of film from the mucosal surface is taken as a measure of the mucoadhesive strength. The *ex-vivo* mucoadhesive strength was determined by using a modified balance method. The porcine buccal mucosa was taken by removing the underlying fat tissues the mucosal membrane was separated. The mucosa was attached to a dry petri dish which was moistened with a few drops of simulated saliva. The balance was adjusted by keeping sufficient weight on the left pan for equal oscillation. From the left pan, a weight of 5g (w_1) was removed and the film was brought in contact with pre-moistened mucosa for 5 min. Then weights were increased until the attachment breaks (w_2) on the left pan. The difference in the weight ($w_2 - w_1$) gives the mucoadhesive strength. The mucoadhesive force was calculated by using the following equation:

$$\text{Mucoadhesive force} = \frac{\text{mucoadhesive strength (g)} \times \text{acceleration due to gravity } (9.8\text{m/s}^{-1})}{(\text{kg/m/s}) \qquad 1000}$$

In-vitro buccal permeation study

The *in-vitro* buccal permeation study using goat mucosa was performed using a Keshary-Chien type glass diffusion cell at 37º±0.2°C. Goat buccal mucosa obtained from a local slaughterhouse should be used within 2hrs of slaughter. Freshly obtained goat buccal mucosa is mounted between the donor and receptor compartments. The film is attached with the mucosa and the compartments were clamped together. The donor compartment is filled with 1 ml of phosphate buffer (pH 6.8) and the receptor compartment of 20 ml capacity is filled with phosphate buffer (pH 7.4). By stirring with a magnetic bead at 50 rpm the hydrodynamics in the receptor compartment were maintained. Required quantity of the sample is withdrawn at predetermined time intervals and analyzed. The experiments were performed in triplicate, and mean values were calculated.

CONCLUSION

It can be concluded that buccal film drug delivery is an emerging technology in the mucoadhesive system. The buccal mucosa is a promising delivery route especially for drugs that need to avoid the gastrointestinal tract due to degradation by the gastric pH, intestinal enzymes, or due to substantial hepatic first pass effect.

REFERENCES

1. Shubham Verma, Nitin Kumar, Pramod Kumar Sharma. Buccal Film: An Advance Technology for Oral Drug Delivery. Advances in Biological Research 2014; 8 (6):260-267.
2. Sravanthi R.R, Rajalakshmi R, Krishna Moorthy S.B, Rupangada V, Ramya Sudha E. Mucoadhesive Buccal Films: An Innovative Drug Delivery System. International Journal of PharmTech Research 2014; 6(5):1665-1678.
3. N. G. Raghavendra Rao, B Shravani, Mettu Srikanth Reddy. Overview on Buccal Drug Delivery Systems 2013; 5(4):80-88.
4. Parth S. Patel, Ashish M. Parmar, Nilang S. Doshi, Hardik V. Patel, Raxit R. Patel, Chetan Nayee. Buccal Drug Delivery System: A Review 2013; 5(3):35-48.
5. Izhar Ahmed Syed, S.Krishna. Buccal Films Drug Delivery Device: A Review. Asian Journal of Pharmaceutical Education and Research 2013; 2(3):1-30.
6. Mishra A, Ramteke S. Formulation, and Evaluation of Mucoadhesive Buccal Film of Flurbiprofen. International Journal of PharmTech Research 2011; 3(3):1825-1830.
7. Umesh D Shivhare, Parag D Bodkhe, Kishor P Bhusari, Vijay B Mathur. Formulation and Evaluation of Mucoadhesive Films of Losartan Potassium. Scholars Research Library 2010; 2(5):251-260.
8. Amir H Shojaei. Buccal Mucosa As A Route For Systemic Drug Delivery: A Review. J Pharm Pharmaceut Sci 1998; 1(1):15-30.