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Approaches of Mucoadhesive Buccal Films

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ABSTRACT: Buccal mucosa is the preferred site for both systemic and local drug action. The mucosa has a rich blood supply and it is relatively permeable. In buccal drug delivery systems mucoadhesion is the key element so various mucoadhesive polymers have been utilized in different dosage forms. Bioadhesion can be defined as a phenomenon of interfacial molecular attractive forces in the midst of the surfaces of biological substrate and the natural or synthetic polymers, which allows the polymer to biological surface for an extended period of time. These are the retentive dosage forms that release the drug directly into the biological substrate. This films are light in weight and release tropical drugs in the oral cavity at a slow and predetermined rate, provide discrate advantages over traditional dosage forms for treatment of many disease. Buccal drug delivery leads direct access to the systemic circulation through the internal jugular vien by passes drugs from the hepatic first pass metabolism leading to high bioavailability. Buccal route is an attractive route of administration for systemic drug delivery.

KEYWORDS: Buccal mucosa, buccal film, permeation, transmucosal, retentive dosage form , mucoadhesive polymer, permeation enhancers.

I. INTRODUCTION

Oral route is the most common convenient and preferred route when compared to other routes of delivery of drugs. Delivery of drug via buccal route is considered to be a foremost choice to the oral and parenteral routes of systemic drug delivery. The buccal mucosa is relatively permeable and provides affluent 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.3 The array of permeability of the oral cavity is given as Sublingual>buccal>palatal. Administration of the drug via the mucosal layer is a novel technique that delivers treatment more effective and safe, for both topical and systemic diseases.

Over the last two decades, mucoadhesion gains major interest for its potential to optimize localized drug delivery because it only retains a dosage form at the site of action (with in the gastrointestinal tract) but also keeps the formulation in intimate contact with the absorption site (in the buccal cavity). The concept of mucoadhesion has gained significant concern in pharmaceutical technology in the early 1980s.

Adhesion is a process defined as the ‘‘fixing” of two surfaces to each other.8 Bioadhesion is stated as the process in which two materials, one of which is natural in origin, are held mutually for extensive periods of time by means of interfacial forces. This phenomenon is referred to as mucoadhesion in which to a mucous membrane the adhesive is attached.

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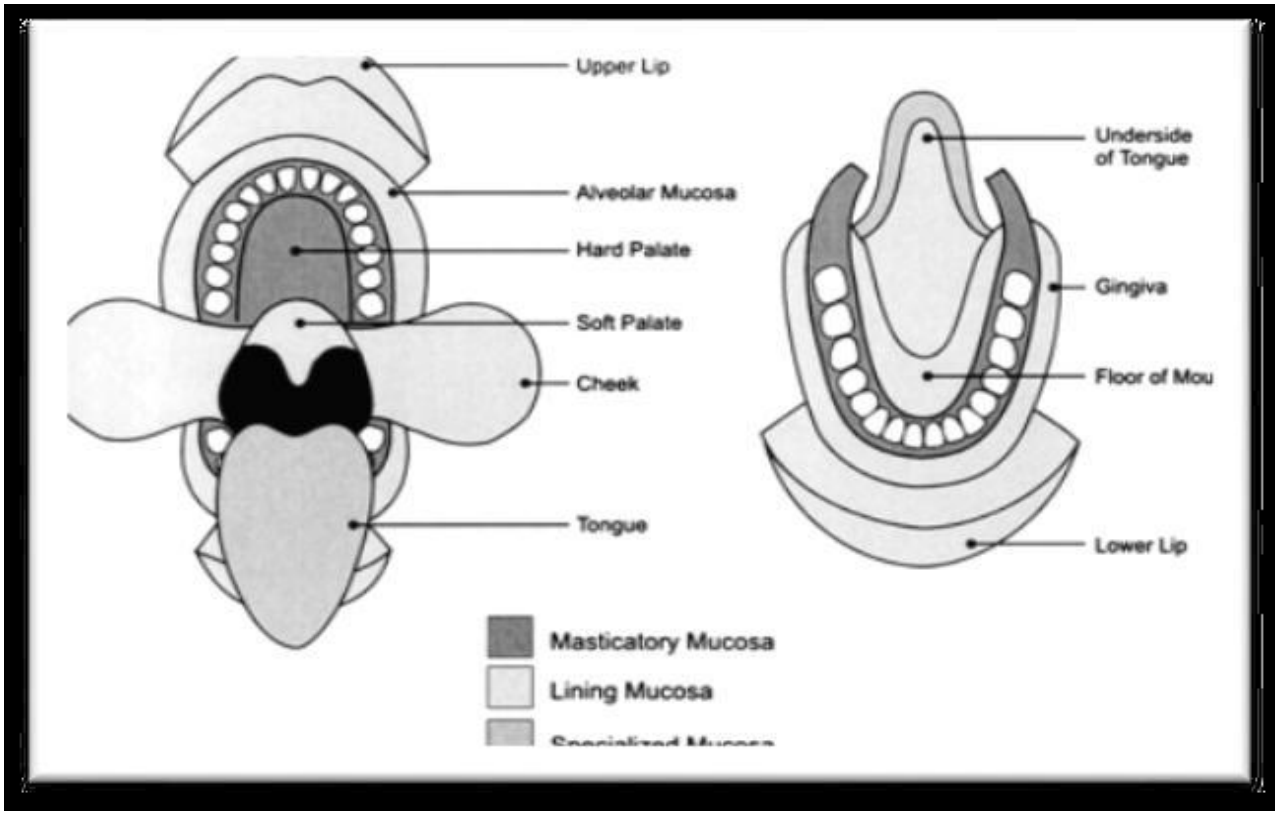

Fig: 1 Oral mucosa

A. ADVANTAGES:

- Rapid onset of action.
- The drug is easily administered by buccal delivery that is unstable in acidic environment of the stomach.
- Avoidance of first pass metabolism and thereby increase in bioavailability.
- Due to the intimate contact surface of the oral cavity with mucoadhesive membrane, maximized absorption rate occurs.
- The drug release is prolonged for a certain period of time.
- Flexibility in designing as multi or unidirectional release systems not only for local but also systemic actions.
- The thin film is more stable and durable than other conventional dosage forms and also improves dosage accuracy relative to liquid formulations.

B. DISADVANTAGES:

- Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property.
- One of the major limitations in the development of oral mucosal delivery is the lack of a good model for in vitro screening to identify drugs suitable for such administration.
- Drugs, which irritate the oral mucosa, have a bitter or unpleasant taste or odour; cannot be administered by this route.
- Drugs, which are unstable at buccal pH, cannot be administered by this route.
- Only drugs with small dose requirements can be administered.
- Drugs may get swallowed with saliva and loses the advantages of buccal route.
- Only those drugs, which are absorbed by passive diffusion, can be administered by this route.
- Surface area available for absorption is less.
- The buccal mucosa is relatively less permeable than the small intestine, rectum, etc.

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C. CLASSIFICATION:

1. Buccal Bioadhesive Tablets

Buccal bioadhesive tablets are dry dosage forms that are to be moistened after placing in contact with buccal mucosa. Double and multilayered tablets are already formulated using bioadhesive polymers and excipients. These tablets are solid dosage forms that ate prepared by the direct compression of powder and can be placed into contact with the oral mucosa and allowed to dissolve or adhere depending on the type of excipients incorporated into the dosage form.They can deliver drug multi- directionally into the oral cavity or to the mucosal surface.

2. Buccal Bioadhesivc Semisolid Dosage Forms:

Buccal bioadhesive semisolid dosage forms consist of finally powdered natural or synthetic polymers dispersed in a polyethylene or in aqueous solution
example: Arabase.

3. Buccal Bioadhesive Patches and Films:

Buccal bioadhesive patches consists of two ply laminates or multilayered thin film that are round or oval in shape, consisting of basically of bioadhesive polymeric layer and impermeable backing layer to provide unidirectional flow of drug across buccal mucosa. Buccal bioadhesive films are formulated by incorporating the drug in alcohol solution of bioadhesive polymer.

4. Buccal Bioadhesive Powder Dosage Forms:

Buccal bioadhesive powder dosage forms are a mixture of bioadhesive polymers and the drug and are sprayed onto the buccal mucosa the reduction in diastolic B.P after the administration of buccal tablet and buccal film of Nifedipine.

5. Buccal chewing gum:

Some commercial products of buccal chewing gum are available in the market like Caffeine chewing gum, Stay Alert, was developed recently for alleviation of sleepiness. It is absorbed at a significantly faster rate and its bioavailability was comparable to that in capsule formulation. Nicotine chewing gums (e.g., Nicorette and Nicotinell) have been marketed for smoking cessation. The permeability of nicotine across the buccal mucosa is faster than across the skin.

6. Bioadhesive spray:

Muccoadhesive sprays are gaining important over other dosage forms because of flexibility, comfort, high surface area and availability of drug in solution form. The first FDA-approved (1996) formulation was developed by fentanyl Oralet ™ to take advantage of oral transmucosal absorption for the painless administration of an opioid in a formulation acceptable to children. In 2002, the FDA approved Subutex (buprenorphine) for initiating treatment of opioid dependence (addiction to opioid drugs, including heroin and opioid analgesics) and Suboxone (buprenorphine and naloxone) for continuing treatment of addicts. In 2005, Oral-lyn buccal spray was approved for commercial marketing and sales in Ecuador..

D. MECHANISM OF ACTION:

- For bio-adhesion to occur, three steps take place:
- A close contact among a bioadhesive and a membrane either from a good wetting of the bioadhesive and a membrane or from the swelling of bioadhesive.
- Penetration of the bio-adhesive into the tissue takes place.
- Inter penetration of the chains of the bioadhesive with mucous takes place. Low chemical bonds can then settle.

The bonding between the mucus and the biological substance occurs mainly through both physical and chemical interactions results from expansion of the adhesive material and chemical bonds due to electrostatic interaction, hydrophobic interactions, hydrogen bond and dispersion forces.

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II. EVALUATION TESTS

A.WEIGHT VARIATION:

For evaluation of film weight, three films of every formulation are selected randomly and individual weight of each 1x1cm patch was taken on digital balance. The average weight was calculated.

a. Film thickness:

Thickness of the film is measured by using screw gauge with a least count of 0.01 mm at different places on the film. The thickness of the film was measured at three different places and the average of thickness is measured.

b. Surface PH:

For determination of surface pH three films of each formulation is allowed in contact with 1ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of films and allowing equilibrate for 1 min. A mean of three reading is recorded.

c. Folding endurance:

Folding endurance of the film is determined by repeatedly folding one film at the same place till it broke, which was considered satisfactory to reveal good films properties. The number of times of films could be folded at the same place without breaking gave the value of the folding endurance. This test was done on randomly selected three films from each formulation.

d. Drug content uniformity:

This parameter was determined by dissolving film of 1 × 1cm diameter containing drug in 50 ml simulated salivary fluid with occasional shaking. Filtration was carried out to remove insoluble residue, 1 ml of the filtrate was diluted to 10 ml with simulated salivary fluid (pH 6.8). The absorbance was measured at spacified nm using an UV spectrophotometer. The experiments were carried out in triplicate for the films of all formulations.

e. *In-vitro* dissolution studies:

Dissolution study was carried out in USP basket type apparatus using the stimulated salivary fluid (pH 6.8) as a dissolution medium at 50 rotations per minute. 10 ml aliquots were withdrawn at one minute time intervals and same amount of fresh dissolution medium was added. The aliquots were assayed for drug content at spacified wavelength using UV-spectrophotometer. The cumulative percentage drug release was calculated.

f. Moisture absorption:

The moisture absorption study of films was done at a relative humidity of 75% for a period of three days. The low moisture uptake by all the formulations was observed at 75% relative humidity. The low moisture uptake by all the buccal films can help to retard any hydrolytic degradation, and films will remain stable.

g. Swelling studies:

The degree of swelling is determined in phosphate buffer pH 6.8. All batches have good swelling properties which remain hydrated for longer time. All formulations were swelled within 10 min and which

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delayed the swelling after 2 h i.e. constant weight of the buccal patch is seen. It is highlighted that swelling properties are important when film integrity is evaluated.

h. Percent elongation at break:

For the determination of percentage elongation of the film formulations, the distance between the tensile grips of the tensile strength testing machine was measured before and after the fracture of the film and calculated the % elongation of patch by using the following formula Then the percentage elongation of the films was computed with the help of the formula given below.

% Elongation at break =Increase in length Initial weight×100 .

i. Dispersion test:

A strip equivalent to 5 mg of drug placed in 200 ml of 6.8pH phosphate buffer and was stirred for 3 minutes. The resulting solution was passed through sieve number 22. The film is said tosed the dispersion test only when no residue is left on the sieve.45.

j. *In vitro* residence/mucoadhesion time :

The in vitro adhesion time of films was evaluated by assessing the time for the patch to detach from goat buccal mucosa in a well stirred beaker filled with 500 ml phosphate buffer pH 6.8 at 37 °C. The mucosal membrane was fixed on the side of the beaker with cyanoacrylate glue. The patch was attached to the membrane by applying light force with finger tip for 60 sec. The beaker was then magnetically stirred at an approximate rate of 150 rpm to simulate buccal and saliva movement. The time necessary for complete erosion or detachment of the films from the mucosal membrane was taken as an indication of the in vitro adhesion time.

k. Tensile strength:

Tensile strength of the buccal films was determined by using universal strength testing machine. The sensitivity of the machine is one gram. It consists of 2 load cell grips. The lower one is fixed and upper one is movable as shown in the figure. The test patch of specific size is fixed between these cell grips and force was gradually applied, till the patch breaks. The tensile strength of the patch was taken directly from the dial reading.

l. Percentage Moisture content :

The buccal patches is weighed accurately and kept in desiccators containing anhydrous calcium chloride. After three days, the patches were taken out and weighed. The moisture content (%) was determined by the formula47.

% Moisture content =Initial weight – Final weight Initial weight×100

m. Effect of temperature and humidity:

Effect of temperature and humidity of optimization formulation was carried out for one month at 40 °C ± 2 °C,75 % ± 5% RH maintained in environmental stability chamber. The patches were wrapped in aluminium foil and exposed to the said conditions. Samples were evaluated at 0, 7, 14, 21 and 28 days for the parameters as

i. Appearance
ii. Surface pH
iii. Folding endurance
iv. Drug release

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III.CONCLUSION

Due to success, advantages and ease of access of drug delivery through oral mucosal tissue the buccal and sublingual routes have favourable opportunities and many formulation approaches; although the current commercially available formulation are mostly limited to tablets and films. The buccal mucosa offers several advantages for controlled drug delivery for long period of time and also favourable area for systemic delivery of orally unsatisfactory drugs and attractive alternative for non-offensive delivery of potent peptide and protein drug molecule. There is renewed interest and active product development activity for following generation of oral mucosal delivery system. Oral mucoadhesive dosage forms will continue be an exciting research focus for improving drug absorption especially for the new generation

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