



Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Buccal adhesive tablet

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ABSTRACT

In pharmaceutical science various transmucosal routes are here but buccal route is suitable for local and systemic drug delivery. Buccal route is approachable route for therapeutic agent and avoid the enzymatic degradation and first pass metabolism that will lead the higher bioavailability. Current review include the advantages, disadvantages, buccal mucosa: overview, mechanism action of drug, ideal properties for permeation of drug, factors affecting bioavailability, mucoadhesive polymers, classification of various mucoadhesive polymers, theory of bioadhesion, evaluation of buccoadhesive dosage form and conclusion.

Keywords: Transmucosal routes, buccal route, first pass metabolism, bioavailability.

INTRODUCTION

Oral route have some disadvantages like enzymatic degradation and first pass metabolism. Proteins and peptides mostly shows above disadvantages, so these drugs are mostly administered by parenteral routes.[1]

Some drugs given through oral route shows 'low-bioavailability' and 'first pass metabolism'. Alternate routes are required in above case, parenteral route fixed some limitations like pain. Other alternative routes (i.e. ocular, vaginal, rectal, sublingual, buccal, pulmonary, transdermal) are available for drugs delivery. Among these routes transmucosal route may be advantageous route, oral cavity is highly vascularized and more suitable for dose termination and administration. High bio-availability can be achieved through direct administration into systemic circulation by the internal veins (jugular) of oral cavity. Buccal route is highly compliance to the patients comparison to other alternative routes. It has some limitations like low permeability in comparison of sublingual route.

The drug delivery is classified into following categories:

- 1)Sublingual delivery: Drug delivered through the mucosal membranes situated in the floor of mouth.
- 2)Buccal delivery: Drug delivered through the mucosal membrane of cheeks.
- 3)Local delivery: Drug delivered into oral cavity.[2][3]

ADVANTAGES

- Drug goes directly into the blood.
- Drug can terminate any time.
- Local stress or damage may be recovered rapidly.
- Large surface area for drug delivery.
- Rich blood supply.
- Sustained/control drug delivery.
- The potential for delivery of peptide molecules unsuitable for the oral route.[3-10][21]

DISADVANTAGES

- Formulation should not be disturbed.

- Eating and drinking are restricted.
- There is ever present possibility that the patient may swallow the formulation.
- Drug swallowed with saliva is lost.
- Drug with bad taste can't be administered by this route.
- Over hydration may lead to formation of slippery surface and structural integrity of formulation may get disrupted. [4][11-12]

BUCCAL MUCOSA: OVERVIEW

1)Structure: on the behalf of anatomy, oral mucosa is divided into following parts:

A. Epithelium: Epithelium is made up of about 40-50 stratified squamous layer of epithelial cells (thickness: 500-800µm). Epithelium layer's main function is protection to the tissues and act as a barrier for the foreign materials.

B. Basement membrane and connective tissue: Basement membrane is consist of continuous layers of extracellular materials (tissues) which are present between epithelium layer and connective tissues.

2)Environment of buccal mucosa: In the buccal mucosa saliva is secreted by salivary glands.

A. Role of saliva:

- Work as protection for buccal tissue.
- Mineralization or demineralization of tooth enamel.
- Hydrate the oral dosage form.

B. Role of mucus:

- Act as lubrication.
- Major role is bio-adhesion.
- Mucus is composed of mucin (proteins) and carbo-hydrate. [13-15]

MECHANISM ACTION OF DRUG

1)Simple diffusion: Absorption depends on random motion of molecules from a zone of higher concentration to one of low concentration to substance placed on mucosa.

2)Facilitated diffusion: Absorption involves a carrier system which leads to more rapid absorption such a carrier system exhibit stereo specificity in D- glucose and L-arabinose. Absorption of nicotinic acid and nicotinamide across the buccal mucosa has been shown to depend upon the presence of sodium ions.

3)Intercellular movements: Oral epithelium has loose junctions and is leaky therefore is likely to allow passage of substance through intercellular space. Molecules with a molecular weight more than 70,000 passage the basal lamina.

4)Endocytosis: Oral mucosal cells are able to absorb substances by endocytosis it is likely that this mechanism has only a minor role in drug transport from buccal i.e. oral cavity. [16]

IDEAL PROPERTIES FOR PERMEATION OF DRUG

Drug should be follow the under mention properties for the easy permeation of drug through the buccal mucosa:

1)Molecular size: The absorption rate of hydrophilic substances is a function of molecular size. Small molecules (<75-100Da) appear to cross the mucosa rapidly, thus permeability decreased with increasing molecular size.

2)Lipid solubility: For un-ionizable compounds, their relative permeabilities are function of their oil water partition coefficient, with the more lipid compounds having higher permeabilities.

3)Ionization: The degree of ionization of permeants is a function of both its pKa and pH at mucosal surface. For many weak acids and bases, only the unionized form possesses appreciable lipid solubility. The absorption of many compounds showed maximal at which they are mostly unionized tailing off as the degree of ionization, increase.[5,21]

FACTORS AFFECTING BIOAVAILABILITY

1)Inherent permeability of the epithelium: The permeability of the oral mucosal epithelium is intermediate between that of the skin epithelium, that for barrier function and the gut. Thus, in the oral cavity, the buccal mucosa is less permeable comparison to sublingual mucosa.

2)Thickness of epithelium: The thickness of the oral epithelium varies considerably between sites in the oral cavity. The thickness of buccal mucosa is approx. to 500-800µm.

3)Blood supply: High blood supply or lymphatic network in the lamina propria serve the oral cavity, thus drug moieties which traverse the oral epithelium are readily absorbed into the systemic circulation.

4)Metabolic activity: Drug moieties adsorbed via the oral epithelium are delivered directly into the systemic circulation and avoid the hepatic first pass metabolism effect. Mucosal drug delivery particularly attractive for the delivery of enzymatically labile drugs such as therapeutic peptides and proteins.

5)Saliva and mucous: The activity of the salivary gland means that the oral mucosal surfaces are constantly washed by saliva, i.e. approx. to 0.5-2.0 liter/day. Particular sublingual area comes to a lot of saliva which can enhance drug dissolution and therefore increase bioavailability.

6) Transport routes and mechanism: Drug permeation across the epithelium barrier is via two main routes:

- The para-cellular route: Drug across between adjacent epithelial cells,
- The transcellular route: Across the epithelial cells by among the following mechanism: passive diffusion, carrier mediated transport and endocytic processes.[17,21]

MUCOADHESIVE POLYMERS

As the contact between formulation and buccal mucosa is one of the key factors in successful buccal delivery, use of mucoadhesive polymers in the formulation of buccal drug delivery systems may increased the contact time. Mucoadhesive polymers are used to improve drug delivery by enhancing the dosage form's contact time and residence time with mucous membranes.

Mucoadhesion may be defined as, the process where polymers attach to biological substrate or a synthetic or natural macromolecule, to mucosal or an epithelial layer.[13,15]

An ideal polymer for buccal adhesive drug delivery systems should have following characteristics:

- Mucoadhesive polymer should be compatible with buccal environment.
- It should be non-toxic, non-irritant, free from leachable impurities and absorbable from mucous layer.
- Polymer should adhere quickly to surface of moist tissue and possess some site specificity.
- It should not decompose during the shelf life of dosage form.
- Should be low cost.
- Easy incorporate to the drug into formulation.
- Should have good spread-ability, swelling, wet ability, solubility and biodegradability properties.
- Should adhere quickly to buccal mucosa and possess sufficient mechanical strength.
- Polymer should posses tensile strength and shear strengths at the bioadhesive range.
- Polymer should show bioadhesive properties in any physical state.
- Should have optimum molecular weight.
- Mucoadhesive polymer should sufficiently cross-linked but not to the degree of suppression of bond forming groups.
- It should not develop the secondary infections such as dental caries [13,15,18].

CLASSIFICATION OF VARIOUS MUCOADHESIVE POLYMERS [15,19]:

A. Natural polymers:

- Tragacanth
- Sodium alginate
- Guar gum
- Xanthan gum
- Soluble starch
- Gelatin
- Chitosan

B. Synthetic polymers:

- Cellulose derivatives (Methylcellulose, Ethyl cellulose, Hydroxy ethyl cellulose, Hydroxyl propyl cellulose, Hydroxy propyl methylcellulose, Sodium carboxy methylcellulose).
- Poly acrylic acid, Polymers (Carbomers, Polycarbophil).
- Poly hydroxyl ethyl methylacrylate.
- Poly ethylene oxide.
- Poly vinyl pyrrolidone.
- Poly vinyl alcohol.

THEORY OF BIOADHESION ^(22,23)

The theoretical framework for polymer-polymer adhesion can be easily extended to describe the bioadhesion of polymeric materials with biological surface. Theories of bioadhesion are shortly described below:

A. Electronic Theory

Under this theory, electron transfer on contact of the bioadhesive polymer and the glycoprotein net work which have different electronic structures, which will in turn lead to the formation of a double layer of electrical charge at the bioadhesive interface.

B. Absorption Theory

Absorption theory includes bioadhesive systems adhere to tissue because of Vander walls, hydrogen bonding, and related forces.

C. Wetting Theory ⁽²⁴⁾

For the development of strong adhesive bond intimate molecular contact is a pre-requisite, adhesive bond requires the examination of the wetting equilibrium and dynamic behavior of the bioadhesive candidate material with the mucus membrane.

Following are the qualities for liquid bioadhesive materials:

1. A zero or near zero contact angle.
2. A relatively low viscosity and
3. An intimate contact that exclude air entrapment.

The specific adhesion work should be equal to the sum of the two surface tensions and less than the interfacial tension.

D. Diffusion Theory ⁽²⁵⁾

Under the diffusion theory, the associate contact of two pieces of the same polymer or two different polymers. During chain interpenetration, the molecules of the polymer and the hanging chains of the glycoprotein are associated. Due to the concⁿ gradient, the bioadhesive polymer chains enter at the rates which are depend on the diffusion coefficient of a macromolecule through a cross-linked network and the chemical potential gradient.

In addition, good solubility of the bioadhesive medium in the mucus is required for bioadhesion. So the difference of the solubility parameters of the bioadhesive medium and the glycoprotein should be as close to zero as possible. Thus the bioadhesive medium must be of similar chemical structure to the glycoprotein.

E. Fracture Theory

Fracture theory includes hardly separation of two surfaces after adhesion to the adhesive bond strength.

EVALUATION OF BUCCOADHESIVE DOSAGE FORM [17,20,21]**A. In vitro/ Ex vivo methods**

- Tensile strength
- Shear strength
- Other method
- ✓ Adhesion weight method
- ✓ Fluorescent probe method
- ✓ Flow channel method
- ✓ Mechanical spectroscopic method
- ✓ Falling liquid film method
- ✓ Colloidal gold staining method
- ✓ Isometric method
- ✓ Thumb method
- ✓ Adhesion number
- ✓ Electrical conductance

B. In vivo method

- Radioisotopes
- Gamma scintigraphy
- Pharmaco scintigraphy
- Electron paramagnetic resonance
- Isolated loop technique
- X-ray

CONCLUSION

Buccal mucosa offers many advantages over the oral route, which are avoid first pass metabolism, high bioavailability, reduced dose frequency, increase patient compliance. Drug is directly goes into systemic circulation without any pain, it's an advantage over the parenteral route. Buccal route may an alternate route for systemic delivery. Buccal delivery is achieved by buccal tablet, patch, gel and powders.

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