MUCOADHESIVE BUCCAL DRUG DELIVERY SYSTEM - AN OVERVIEW

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Abstract

The concept of mucosal adhesive or mucoadhesive was introduced into the controlled drug delivery area, in the early 1980. Mucoadhesion can be defined as a state in which two components, of which one is of biological origin are held together for extended periods of time by the help of interfacial forces. Mucoadhesive are synthetic or natural polymer, which interact with the mucuslayer covering the mucosal epithelial surface, and mucin molecules constituting a major part of mucus. The concept of mucoadhesive as alters many investigator to the possibility that this polymer can be used over come physiological barrier in long-term drug delivery\(^1\). Buccal mucosa is the preferred site for both systemic and local drug action. The mucosa has a rich blood supply and it relatively permeable. The buccal region of the oral cavity is an attractive target for administration of the drug of choice, particularly in overcoming deficiencies associated with the latter mode of administration. Problems such as high first-pass metabolism and drug degradation in the gastrointestinal environment can be circumvented by administering the drug via the buccal route. Moreover, rapid onset of action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued. It is also possible to administer drugs to patients who unconscious and less co-operative\(^2\). In buccal drug delivery systems mucoadhesion is the key element so various mucoadhesive polymers have been utilized in different dosages form. Various bioadhesive dosages form such as Chewing gum, tablets, Patches, Hydrogel, Thiolated tablets are discussed in this review article\(^3\).
Key Words: Mucoadhesive polymers, Buccal Mucosa, permeation enhancers, Buccal formulations.

Introduction

Adhesion is a process, simply defined as the “fixing” of two surfaces to one another. There are many different terminological subsets of adhesion depending upon the environment in which the process occurs. Bioadhesion may be defined as the state in which two materials, at least one of which is of a biological nature, are held together for extend periods of time by interfacial forces[3]. Mucoadhesive polymers are synthetic or natural macromolecules which are capable of attaching to mucosal surfaces. The concept of mucoadhesive polymers has been introduced into the pharmaceutical literature more than 40 years ago and nowadays it has been accepted as a promising strategy to prolong the residence time and to improve the specific localization of drug delivery systems on various membranes.

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike[2]. The buccal mucosa lines the inner cheek and buccal formulations are placed in the mouth between the upper gingival (gums) and cheek to treat local and systemic conditions. The buccal route provides one of the potential routes for typically large, hydrophilic and unstable proteins, oligonucleotides and polysaccharides, as well as conventional small drug molecules [2]. On the other hand, the duration of buccal drug administration can be prolonged with saliva activated adhesive polymers without the problems of sublingual administration. The potential site for attachment of any bioadhesive system and hence, the mucoadhesive drug delivery system may include the following[4,5].

1. Gastrointestinal delivery system.
2. Sublingual delivery system.
3. Vaginal delivery system.
4. Nasal delivery system.
5. Ocular delivery system.
6. Rectal delivery system.
7. Buccal delivery system.
Advantages \[6,7,8\]

1. A relatively rapid onset of buccal drug delivery has a high patient acceptability compared to other non-oral routes of drug administration.

2. Action can be achieved relative to the oral route and the formulation can be removed if therapy is required to be discontinued.

3. Improved patient compliance due to the elimination of associated pain with injections.

4. It is richly vascularized and more accessible for the administration and removal of a dosage form.

5. Moreover, rapid cellular recovery and achievement of a localized site on the smooth surface of the buccal mucosa.


7. Extent of perfusion is more therefore quick and effective absorption.

8. Nausea and vomiting are greatly avoided.

9. Used in case of unconscious and less Co-operative patients.

10. Drugs, which show poor bioavailability via the oral route, can be administered conveniently.

   Ex:- Drugs, which are unstable in the acidic environment of the stomach are destroyed by the enzymatic or alkaline environment of the intestine.

Limitations \[6,7,8\]

1. Drugs which irritate oral mucosa or have bitter taste, or cause allergic reactions, discoloration of teeth cannot be formulated.

2. If formulation contains antimicrobial agents, affects the natural microbes in the buccal cavity.

3. The patient cannot eat/drink/speak.

4. Only those drugs which are absorbed by passive diffusion can be administered by this route.

5. Drugs which are unstable at buccal pH cannot be administered by this route.

6. Swallowing of saliva can also potentially lead to the loss of dissolved or suspended drug.

7. Low permeability of the buccal membrane specifically when compared to the sublingual membrane.
Mucoadhesive Polymers $^{[2,4,9,10,11]}$

Mucoadhesive polymers are water soluble and water insoluble polymers which are swellable networks jointed by cross linking agents. The polymers should possess optional polarity to make sure it is sufficiently wetted by the mucus and optimal fluidity that permits the mutual adsorption and interpenetration of polymer and mucus to take place. An ideal polymer for a mucoadhesive drug delivery system should have the following characteristics.

1. The polymer and its degradation products should be nontoxic and Non-absorbable in the gastrointestinal tract.
2. It should be nonirritant to the mucus membrane.
3. It should preferably form a strong noncovalent bond with the mucin epithelial cell surfaces.
4. It should adhere quickly to moist tissue and should possess some site specificity.
5. It should allow easy incorporation of the drug and offer nonhindrance to its release.
6. The polymer must not decompose on storage or during shelf-life of the dosage form.
7. The cost of polymer should not be high.

Some of the mucoadhesive polymers along with their mucoadhesive property are summarized below:

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Polymer</th>
<th>Mucoadhesive property</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Carbopol 934</td>
<td>+++</td>
</tr>
<tr>
<td>2</td>
<td>Carboxymethylcellulose</td>
<td>+++</td>
</tr>
<tr>
<td>3</td>
<td>Polycarbophil</td>
<td>+++</td>
</tr>
<tr>
<td>4</td>
<td>Tragacanth</td>
<td>+++</td>
</tr>
<tr>
<td>5</td>
<td>Sodium alginate</td>
<td>+++</td>
</tr>
</tbody>
</table>

Structure And Design Of Buccal Dosage Form $^{[2,8]}

Buccal Dosage form can be two types
- Matrix type
- Reservoir type
1. Matrix type: The buccal patch designed in a matrix configuration contains drug, adhesive, and additives mixed together.

2. Reservoir type: The buccal patch designed in a reservoir system contains a cavity for the drug and additives separate from the adhesive. An impermeable backing is applied to control the direction of drug delivery; to reduce patch deformation and disintegration while in the mouth; and to prevent drug loss.

Additionally, the patch can be constructed to undergo minimal degradation in the mouth, or can be designed to dissolve almost immediately. Transmucosal drug delivery systems can be bi-directional or unidirectional. Bi-directional (Figure 1) patches release drug in both the mucosa and the mouth while, Unidirectional (Figure 2) patches release the drug only into the mucosa.

**Fig. 1: Buccal Patch designed for Bidirectional drug release**

**Fig. 2: Buccal Patch designed for Unidirectional drug release**

**Buccal Permeability of Drugs through Mucosa**

There are two possible routes of drug absorption through the squamous stratified epithelium of the oral mucosa:

1. Transcellular (intracellular, passing through the cell) and
2. Paracellular (intercellular, passing around the cell).

Permeation across the buccal mucosa has been reported to be mainly by the paracellular route through the intercellular lipids produced by membrane-coating granules. Although passive diffusion is the main mechanism of drug absorption, specialised transport mechanisms have been reported to exist in other oral mucosa (that of the tongue) for a few drugs and nutrients; glucose and cefadroxil were shown to be absorbed in this way.

The buccal mucosa is a potential site for the controlled delivery of hydrophilic macromolecular therapeutic agents (biopharmaceuticals) such as peptides, oligonucleotides and polysaccharides. However, these high molecular
weight drugs usually have low permeability leading to a low bioavailability, and absorption enhancers may be required to overcome this. The buccal mucosa also contains proteases that may degrade peptide-based drugs. In addition, the salivary enzymes may also reduce stability. Disease states where the mucosa is damaged would also be expected to increase permeability. This would be particularly true in conditions that result in erosion of the mucosa such as lichen planus, pemphigus, viral infections and allergic reactions.

Overview of Buccal Mucosa

A. Structure [6,7]

![Fig. 3: Cross Section of Oral Mucosa](image)

The oral mucosa is anatomically divided into

- Epithelium
- Basement membrane and Connective tissues

1) Epithelium: [2,13] Buccal mucosa composed of several layers of different cells (fig:3).

The epithelium is similar to stratified squamous epithelia found in rest of the body and is about 50% cells layers thick. Lining epithelium of buccal mucosa is that has thickness of approximately 500-600 µ and surface area 50 cm2. The epithelium of the oral mucosa serves as a protective covering for the tissues and a barrier to the entry of foreign materials. These functions are reflected in the organization of the epithelium in which individual epithelial cells are closely opposed and stratified so there are a number of layers that show a sequence of differentiation. The uppermost layers form a surface that is resistant to physical insult and to penetration by foreign substances [6].
Membrane Coating Granules (MCG) are spherical or oval organelles (100–300 nm in diameter). MCGs discharge their contents into the intercellular space and thus form the permeability barrier. Major MCG lipid components are cholesterol esters, cholesterol, and glycosphingolipids [1]. Cells increase in size and become flattened as they progressively mature and migrate from the basal layer towards the epithelial surface, showing increasing levels of protein tonofilaments and declining levels of some cytoplasmic organelles[6].

2) Basement Membrane and Connective Tissue [2, 13]

The basement membrane (BM) is a continuous layer of extracellular materials and forms a boundary between the basal layer of epithelium and the connective tissues. This basal complex anchors the epithelium to the connective tissue and supplements the barrier function of the superficial layers of the epithelium to prevent some large molecules from passing the oral mucosa. Basement membrane, lamina propria followed by the submucosa is present below the epithelial layer5. Lamina propria is rich with blood vessels and capillaries that open to the internal jugular vein. Lipid analysis of buccal tissue shows the presence of phospholipids 76%, glucosphingolipid 23% and ceramide 0.72%. The primary function of buccal epithelium is the protection of the underlying tissues. In nonkeratinized regions. Lipid-based permeability barriers in the outer epithelial layer protect the underlying tissues against fluid loss and entry of potentially harmful environment agent such as antigens, carcinogens, microbial toxins and enzymes from food and beverages.

Methods to Increase Drug Delivery via Buccal Route

Absorption enhancers [14]

Absorption enhancers have demonstrated their effectiveness in delivering high molecular weight compounds, such as peptides, that generally exhibit low buccal absorption rates. These may act by a number of mechanisms, such as increasing the fluidity of the cell membrane, extracting inter/intracellular lipids, altering cellular proteins or altering surface mucin. The most common absorption enhancers are azone, fatty acids, bile salts and surfactants such as sodium dodecyl sulfate. Solutions/gels of chitosan were also found to promote the transport of mannitol and fluorescent-labelled dextrans across a tissue culture model of the buccal epithelium while Glyceryl monooleates were reported to enhance peptide absorption by a co-transport mechanism.
Table 2: List of Permeation Enhancers \[2\]

<table>
<thead>
<tr>
<th>Sr. no</th>
<th>Permeation Enhancers</th>
<th>Sr. no</th>
<th>Permeation Enhancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,3-Lauryl ether</td>
<td>3</td>
<td>Phosphatidylcholine</td>
</tr>
<tr>
<td>2</td>
<td>Aprotinin</td>
<td>4</td>
<td>Polyoxyethylene</td>
</tr>
<tr>
<td>5</td>
<td>Azone</td>
<td>10</td>
<td>Polysorbate 80</td>
</tr>
<tr>
<td>6</td>
<td>Benzalkonium chloride</td>
<td>11</td>
<td>Polyoxyethylene</td>
</tr>
<tr>
<td>7</td>
<td>Cetylpyridinium chloride</td>
<td>12</td>
<td>Phosphatidylcholine</td>
</tr>
<tr>
<td>8</td>
<td>Cetyltrimethyl ammonium bromide</td>
<td>13</td>
<td>Sodium EDTA</td>
</tr>
<tr>
<td>9</td>
<td>Cyclodextrin</td>
<td>14</td>
<td>Sodium glycocholate</td>
</tr>
</tbody>
</table>

**Prodrugs** \[14\]

Hussain et al delivered opioid agonists and antagonists in bitterless prodrug forms and found that the drug exhibited low bioavailability as prodrug.

Nalbuphine and naloxone bitter drugs when administered to dogs via the buccal mucosa, caused excess salivation and swallowing. As a result, the drug exhibited low bioavailability. Administration of nalbuphine and naloxone in prodrug form caused no adverse effects, with bioavailability ranging from 35 to 50% showing marked improvement over the oral bioavailability of these compounds, which is generally 5% or less.

**pH** \[14\]

Shojaei et al evaluated permeability of acyclovir at pH ranges of 3.3 to 8.8, and in the presence of the absorption enhancer, sodium glycocholate. The in vitro permeability of acyclovir was found to be pH dependent with an increase in flux and permeability coefficient at both pH extremes (pH 3.3 and 8.8), as compared to the mid-range values (pH 4.1, 5.8, and 7.0).
Patch design\cite{14}

Several in vitro studies have been conducted regarding on the type and amount of backing materials and the drug release profile and it showed that both are interrelated. Also, the drug release pattern was different between single-layered and multi-layered patches.

Toxicity and Irritancy Associated With Buccal Drug Delivery: \cite{11}

Formulations that produce local damage at the site of application, such as ulceration of the mucosa, would preclude their widespread usage as a result of the associated pain and discomfort. This is particularly important in buccal drug delivery where the formulation is in contact with the mucosa for extended periods. Toxic effects can arise from the drug itself, the bioadhesive or from other components of the formulation. For example, carbomers have been reported to produce mucosal irritation believed to result from a localised low pH, whereas lectins have been shown to be cytotoxic. Excipients such as absorption enhancers (e.g., sodium dodecyl sulfate) have also been reported to be irritant.

List of Drugs Delivered Via Buccal Route\cite{15}

In an effort to determine the feasibility of buccal route as a novel route of drug delivery, several drugs (Table 2) have been studied. The variation in class of compounds illustrates that the pharmaceutical industries have an alternative and novel routes of administration for existing drugs.

Table-3: List of Active Ingredients delivered via a buccal route\cite{15}

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Active Ingredients</th>
<th>Sr. No.</th>
<th>Active Ingredients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acitretin</td>
<td>11</td>
<td>Metronidazole</td>
</tr>
<tr>
<td>2</td>
<td>Acyclovir</td>
<td>12</td>
<td>Melatonin</td>
</tr>
<tr>
<td>3</td>
<td>Arecoline</td>
<td>13</td>
<td>Metoprolol tartrate</td>
</tr>
<tr>
<td>4</td>
<td>Buprenorpine</td>
<td>14</td>
<td>Morphine sulphate</td>
</tr>
<tr>
<td>5</td>
<td>Carbamazepine</td>
<td>15</td>
<td>Nalbuphine</td>
</tr>
</tbody>
</table>
Mechanism Of Buccal Absorption $^{[16,17]}$

**Fig.4: Comparative Drug Absorption between Oral & Buccal Route**

Buccal route provides the potential pathway to bypass first-pass effect following oral administration. The mechanisms by which drugs cross biologic lipid membranes are passive diffusion, facilitated diffusion, active transport and pinocytosis. Among these, majority of drugs move across oral mucosa by passive mechanism which is governed by the laws of diffusion. In case of simple diffusion, two potential routes of drug transport are the paracellular or aqueous pore pathway and transcellular or lipoidal pathway.
Theories of Mucoadhesion [18]

The electronic theory: Transfer of electrons amongst the surfaces resulting in the formation of an electrical double layer thereby giving rise to attractive forces.

The wetting theory: The contact angle of liquids on the substrate surface is lower, then there is a greater affinity for the liquid to the substrate surface.

The adsorption theory: The presence of intermolecular forces, viz. hydrogen bonding and VanderWaal’s forces, for the adhesive interaction amongst the substrate surfaces.

The diffusion theory: The diffusion of the polymer chains, present on the substrate surfaces, across the adhesive interface thereby forming a networked structure.

The mechanical theory: The diffusion of the liquid adhesives into the micro-cracks and irregularities present on the substrate surface thereby forming an interlocked structure which gives rise to adhesion.

The cohesive theory: The phenomena of bioadhesion are mainly due to the intermolecular interactions.

Factors Affecting Mucoadhesion

Mucoadhesion may be affected by a number of factors, including hydrophilicity, molecular weight, cross-linking, swelling, pH, and the concentration of the active polymer. [18,19,20]

Hydrophilicity: Bioadhesive polymers possess numerous hydrophilic functional groups, such as hydroxyl and carboxyl. These groups allow hydrogen bonding with the substrate, swelling in aqueous media, thereby allowing maximal exposure of potential anchor sites. In addition, swollen polymers have the maximum distance between their chains leading to increased chain flexibility and efficient penetration of the substrate.

Molecular weight: The interpenetration of polymer molecules is favored by low-molecular-weight polymers, whereas entanglements are favored at higher molecular weights. The optimum molecular weight for the maximum mucoadhesion depends on the type of polymer, with bioadhesive forces increasing with the molecular weight of the polymer up to 100,000. Beyond this level, there is no further gain. [21]
Cross-linking and swelling:

Cross-link density is inversely proportional to the degree of swelling \(^{[22]}\). The lower the cross-link density, the higher the flexibility and hydration rate; the larger the surface area of the polymer, the better the mucoadhesion. To achieve a high degree of swelling, a lightly cross-linked polymer is favored. However, if too much moisture is present and the degree of swelling is too great, a slippy mucilage results and this can be easily removed from the substrate \(^{[23]}\). The mucoadhesion of cross-linked polymers can be enhanced by the inclusion in the formulation of adhesion promoters, such as free polymer chains and polymers grafted onto the preformed network \(^{[20]}\).

Spatial conformation: Besides molecular weight or chain length, spatial conformation of a polymer is also important. Despite a high molecular weight of 19,500,000 for dextrans, they have adhesive strength similar to that of polyethylene glycol (PEG), with a molecular weight of 200,000. The helical conformation of dextran may shield many adhesively active groups, primarily responsible for adhesion, unlike PEG polymers, which have a linear conformation \(^{[18]}\).

Ph:

The pH at the bioadhesive to substrate interface can influence the adhesion of bioadhesives possessing ionizable groups. Many bioadhesives used in drug delivery are polyanions possessing carboxylic acid functionalities. If the local pH is above the pK of the polymer, it will be largely ionized; if the pH is below the pK of the polymer, it will be largely unionized. The approximate pK\(^a\) for the poly(acrylic acid) family of polymers is between 4 and 5. The maximum adhesive strength of these polymers is observed around pH 4–5 and decreases gradually above a pH of 6. A systematic investigation of the mechanisms of mucoadhesion clearly showed that the protonated carboxyl groups, rather than the ionized carboxyl groups, react with mucin molecules, presumably by the simultaneous formation of numerous hydrogen bonds \(^{[24]}\).

Concentration of active polymer:

Optimum concentration of polymer corresponding to the best mucoadhesion. In highly concentrated systems, beyond the optimum concentration the adhesive strength drops significantly. In concentrated solutions, the coiled molecules become solvent-poor and the chains available for interpenetration are not numerous. This result seems to
be of interest only for more or less liquid mucoadhesive formulations [19]. Solid dosage forms such as tablets, the higher the polymer concentration, the stronger the mucoadhesion [25].

**Drug/excipient concentration:**

Drug/excipient concentration may influence the mucoadhesion. [26] The effect of propranolol hydrochloride to Carbopol® (a lightly cross-linked poly(acrylic acid) polymer) hydrogels adhesion. Author demonstrated increased adhesion when water was limited in the system due to an increase in the elasticity, caused by the complex formation between drug and the polymer. While in the presence of large quantities of water, the complex precipitated out, leading to a slight decrease in the adhesive character. Increasing toluidine blue O (TBO) concentration in mucoadhesive patches based on Gantrez® (poly(methylvinylether/maleic acid) significantly increased mucoadhesion to porcine cheek tissue [27] This was attributed to increased internal cohesion within the patches due to electrostatic interactions between the cationic drug and anionic copolymer.

**Other Factors Affecting Mucoadhesion**

Mucoadhesion may be affected by the initial force of application. [28] Higher forces lead to enhanced interpenetration and high bioadhesive strength. [29] In addition, the greater the initial contact time between bioadhesive and substrate, the greater the swelling and interpenetration of polymer chains. [30] Physiological variables can also affect mucoadhesion. The rate of mucus turnover can be affected by disease states and also by the presence of a bioadhesive device.

**Buccal Formulations**

1. The size of the delivery system varies with the type of formulation, i.e., a buccal tablet may be approximately 5–8mm in diameter, whereas a flexible buccal patch may be as large as 10–15cm² in area.
2. Mucoadhesive buccal patches with a surface area of 1–3 cm² are most acceptable.
3. It has been estimated that the total amount of drug that can be delivered across the buccal mucosa from a 2-cm² system in 1 day is approximately 10–20 mg.
4. The shape of the delivery system may also vary, although for buccal drug
5. Administration, an ellipsoid shape appears to be most acceptable.
6. The thickness of the delivery device is usually restricted to only a few millimeters. The location of the delivery device also needs to be considered.

7. The maximal duration of buccal drug retention and absorption is approximately 4–6 h because food and/or liquid intake may require removal of the delivery device.

Physiology of mucus membrane under disease condition need to be accounted for (e.g.: Cancer patients suffer from oral candidosis)

   a. Buccal Tablets
   b. Buccal Patches and Films
   c. Buccal Semisolids (ointments and gels)
   d. Buccal Powders

A. Buccal tablets:-

   a) Adhesive tablets are held between the gum and cheek.
   b) Generally flat, elliptical or capsule-shaped.
   c) Troches & lozenges are two other types of tablets used in oral cavity where they are intended to exert a local effect in the mouth or throat.
   d) Muccoadhesive tablet may be monolithic or bilaminated system.
   e) Monolithic is multidirectional release
   f) Bilayered containing core layer & backing layer.
   g) Backing layer may be of water insoluble material like Ethyl cellulose or hydrogenated caster oil or may be polymeric coating layer
   h) Backing layer avoids sticking of the tablet to the finger during application.

Limitations of buccal tablets

1. The small surface of contact with mucosa.

2. Their lack of physical flexibility.

Evaluation of buccal tablets [31]

· In vitro swelling rate and bioadhesion studies
· In vitro surface pH studies
· In vitro drug release studies
· In vitro permeation studies
· In vitro mucoadhesion strength
· In vitro residence time
· In vivo release studies
· Stability studies in human saliva
· Ex vivo mucoadhesion time
· Ex vivo mucoadhesion force
· Ex vivo transmucosal permeation studies

**B. Buccal patches and films:**

1. Buccal patches consists of two ply laminates or multilayered thin film round or oval as 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.

2. Isosorbid dinitrate in the form of unidirectional erodible buccal film are developed and characterised for improving bioavailability.

3. Buccal film of salbutamol sulphate and terbutalin sulphate for the treatment of asthma.

**C. Buccal semisolid dosage forms:**

1. A buccal semisolid dosage form consists of finally powdered natural or synthetic polymer dispersed in a polyethylene or in aqueous solution.

   E.g:- Gels, Ointments, oral base.

2. Gels are usually clear, transparent, semisolids containing solubilized active substances.

3. Forming hydrophilic polymers is typically used to prepare lipid-free semisolid dosage forms.

   E.g:- Methylcellulose, carbopols, hydroxyl ethylcellulose etc.

4. Vehicles containing therapeutic agents are especially useful for application to mucus membranes and ulcerated or burned tissues, because their high water content reduces irritancy.
5. Due to plastic rheological behaviour they can remain to the surface of application for a reasonable duration before they are washed off.

6. In comparison to solutions, gels can significantly prolong residence time and hence improve bioavailability. Eg. Glibenclamide.

7. One of the original oral mucosal-adhesive delivery systems- “orabase” consists of finely ground pectin, gelatin and sodium carboxy methyl cellulose dispersed in a poly (ethylene) and a mineral oil gel base, which can be maintained at its site of application for 15-150 minutes\textsuperscript{[31]}. 

D. Buccal powder dosage forms:

Buccal bioadhesive powder dosage forms are a mixture of bioadhesive polymers and the drug and are sprayed onto the buccal mucosa. Yamamoto et al., have described a hydroxypropyl cellulose and beclomethasone dipropionate containing powder that was sprayed onto the oral mucosa of rats. A significant increase in the residence time relative to an oral solution was seen, and 2.5% of beclomethasone was retained on buccal mucosa for over 4 hours\textsuperscript{[32,33]}. 

Conclusion:

The buccal mucosa offers several advantages for controlled drug delivery for extended periods of time. The mucosa is well supplied with both vascular and lymphatic drainage and first-pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract are avoided. The area is well suited for a retentive device and appears to be acceptable to the patient. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled and manipulated in order to accommodate drug permeation. Buccal drug delivery is a promising area for continued research with the aim of systemic delivery of orally inefficient drugs as well as a feasible and attractive alternative for non-invasive delivery of potent peptide and protein drug molecules. However, the need for safe and effective buccal permeation/absorption enhancers is a crucial component for a prospective future in the area of buccal drug delivery.
References:


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