



Overview on Buccal Drug Delivery System

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Abstract

The buccal drug delivery system thus offers an exciting new route that has been found suitable to administer therapeutic agents via the buccal mucosa. Such a system, deriving advantage from the rich vascularization and permeability of the oral cavity, can promote fast absorption into systemic circulation while avoiding first-pass metabolism. Formulations in film, tablets, and gels have been developed to improve bioavailability and ease administration for patients. All these factors- drug solubility, mucosal adhesion, and release kinetics- are required to be kept in mind while designing systems for buccal delivery. Advances in materials science as well as formulation technology have further pushed the efficacy bar of these systems in applications ranging from pain control to treatment of chronic diseases. This review discusses mechanisms, advantages, challenges, and future prospects of buccal drug delivery with therapeutic perspectives in clinical practice and will highlight its utility in enhancing the outcome of treatment with improved patient compliance in clinical practices.

Research Through Innovation

Keywords

Mucoadhesion , Polymer, Penetration Enhancer.

Buccal Mucosa: An Overview

Definition

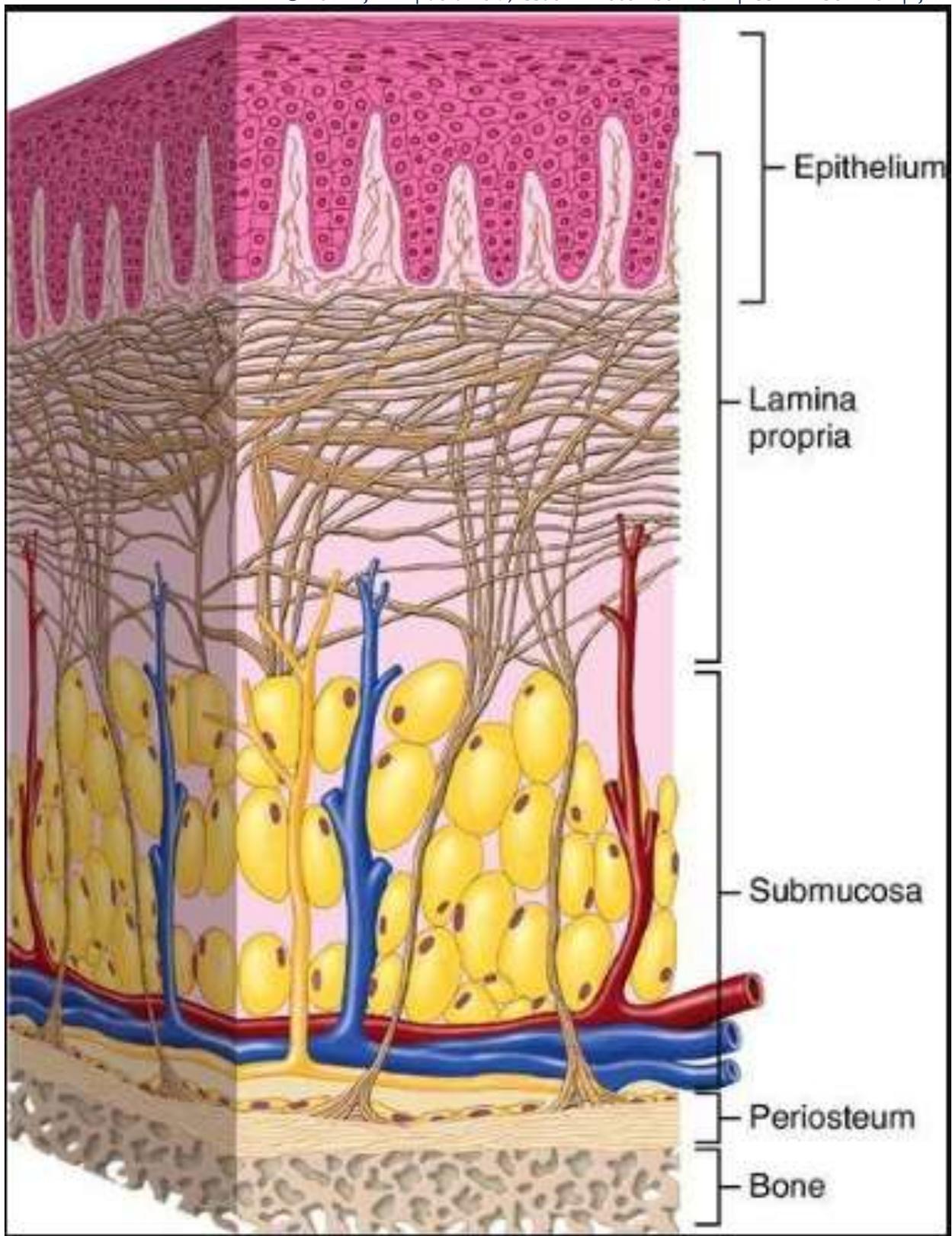
Buccal mucosa is the moist tissue lining the inner cheek and the oral vestibule. It serves some important functions in the oral cavity and, in general, forms a site for drug delivery due to its distinct physiological characteristics.

Composition

The anatomy of the buccal mucosa is composed of:

- Epithelium : It is the outermost layer and has been classified as being stratified squamous and nonkeratinizing, thus making it a protective layer while, simultaneously, allowing absorption.
- Lamina Propria: It is the layer of connective tissue containing blood vessels, nerves, as well as immune cells.
- Submucosa: The submucosa lies below the lamina propria with the larger blood vessels and higher support of the connective tissue.





Mucoadhesion

Definition

Mucoadhesion is said to be the adhesion of a drug delivery system to the mucosal surfaces of the body, primarily the oral cavity, gastrointestinal tract, nasal cavity, and other mucosal tissues.

This property becomes absolutely necessary to enhance the retention time of the formulation at the site of application, which in turn enhances drug absorption and efficacy.

Mechanism of Mucoadhesion

Mucoadhesion is a complex phenomenon in which adhesive material interacts with the mucosal layer through several mechanisms:

Hydrogen Bonding Hydroxyl of the mucoadhesive material and on mucin; it may interact with each other. **Van der Waals Forces** Weak attractions, which contribute to adhesion. **Ionic Interactions** Electrostatic attractions between charged groups of the mucoadhesive material and mucin. **Hydrophobic Interactions** Attractions between hydrophobic regions of the adhesive and the mucosal surface. **Factors Affecting Mucoadhesion**

Composition of Mucoadhesive Substance:

Polymers which include carbomers, hydroxypropyl methyl cellulose (HPMC) and chitosan.

pH and Ionic Strength: These may depend on ionization and solubility of mucoadhesive materials.

Surface Roughness: Topography of mucosal surface may influence attachment.

Moisture Content: There must be an adequate hydration in mucoadhesion.

Applications in Drug Delivery

Mucoadhesive systems have several applications in various drug delivery routes:

Buccal Drug Delivery : This involves the usage of buccal tablets and films, which can be retained by the buccal mucosa for the purpose of systemic absorption. **Nasal Drug Delivery:**

Nasal sprays and gels can be held within the nasal mucosa to produce prolonged drug release.

Gastrointestinal Delivery: These mucoadhesive formulations can be applied so that the intestinal mucosa remains bound in order to enhance drug absorption and deliver local treatment. **Advantage of Mucoadhesion**

Extended stay at the absorption site may enhance the bioavailability of drugs.

Local Effects Mucoadhesive systems can act specifically at the site; therefore, preparations that give site-specific action can be highly beneficial where site-specific action of the drug is required.

Greater Patient Compliance: Non-invasive and easy to use formulation shall enhance patient acceptability and compliance.

Mucoadhesion Advantages.

Increased Bioavailability of Drugs: Longer residence at the absorption site could lead to greater drug bioavailability.

Targeted Delivery: Mucoadhesive systems can effect localized action, which would be useful in clinical conditions where drugs have to act at the site of action.

Improved Compliant Profile: Non-invasive formulations that are easy to use could improve compliant profile.

Mucoadhesion Disadvantages.

Irritation and Discomfort: Mucoadhesive systems interacting with the mucosal surfaces for some period causes irritation, discomfort or inflammation, may pose a negative effect on patient compliance.

Heterogeneity of Mucosal Environment: The performance of mucoadhesive systems may depend on individual variability in mucosal characteristics like moisture content, pH, and composition of mucus leading to varied absorption of drugs.

Limited Drug Release: This may be paradoxical because high adhesion could actually inhibit drug release from mucoadhesive formulations, which can limit efficacy of therapy.

Ideal Properties of Buccal Drug Delivery Systems

An ideal buccal drug delivery system must be prepared with specific key properties to maximize its performance and compliance in the patient's side. These include:

- **Mucoadhesive Properties:** The formulation should well adhere to the buccal mucosa to provide a good retention time and allow for sustained release of the drug.
- **Biocompatibility:** Materials used for preparation should be nontoxic and nonirritating to the mucosal tissue and, thus, minimize the chance of adverse reaction.
- **Controlled Release:** The drug should be released predictably and in a controlled manner over time so that a therapeutic effect is produced without peaking and troughing.

- **High Drug Loading Capacity:** The formulation must have an adequate dose of the drug to ensure a therapeutic effect.
- **Rapid Dissolution/Disintegration:** The formulation must dissolve or disintegrate promptly in the buccal cavity to allow rapid absorption of the drug into systemic circulation.
- **Stability:** The formulation should be chemically and physically stable throughout the shelf life of the formulation, so that it does not degrade the drug as well as its activity.
- **Taste Masking:** In case the drug has a repulsive taste, then it should mask the taste so that the patient must comply.
- **Ease of Administration:** It should be easy to administer so that self-administration would not be difficult for the patient.
- **Mucosal Permeability:** The formulation should permit drug to freely penetrate the buccal mucosa thereby increasing absorption.
- **Formulation should be made in a way that saliva will not interfere with the drug's release and absorption.**

Advantages of Buccal Drug Delivery System

Buccal drug delivery systems exhibit several significant advantages over the traditional routes of administration. These include the following key advantages:

- **Rapid Absorption:** Drugs administered through the buccal route can quickly enter systemic circulation owing to the highly vascularized nature of the buccal mucosa
- **Avoids First-Pass Metabolism:** The buccal delivery avoids first-pass metabolism in the liver, which could enhance the bioavailability of many drugs that are otherwise highly metabolized upon oral administration.
- **Higher bioavailability** because it is directly absorbed into the bloodstream, compared with oral preparations.
- **Easy to administer:** the buccal system is non-invasive and not inconvenient for use; it can therefore enhance patient compliance: the patients will not accept taking pills in the mouth, for example or fear injections.
- **Controlled release systems:** drugs can be formulated to be given through controlled release: this is possible for either sustained, prolonging therapeutic effects for longer periods without dosing too often or for controlled delivery to attain a certain therapeutic effect
- **Localized Administration:** Buccal drug delivery systems can provide drugs directly to the oral cavity for localized treatment especially for oral ulcers or infections.

Disadvantages of Buccal Drug Delivery System

Despite the several advantages of buccal drug delivery systems, they do have some disadvantages:

- **Limited formulation:** No drug is appropriate for buccal delivery. Some factors that reduce the size of molecules, solubility, and stability will limit the types of drugs that can be administered effectively.
- **Irritation and discomfort:** Prolonged contact of buccal formulations with mucosal tissues may cause irritation or discomfort.
- **Variable Absorption:** Saliva secretion, pH, and mucosal individual variability can cause variable absorption and effectiveness of drugs.
- **Dosage Limitation:** Dosage volume that can comfortably be held in buccal cavity is a limitation, which sometimes may not allow high dosage of certain drugs to be administered.
- **Taste Problem:** The drug in some cases has an unpleasant taste that can't be masked, preventing the patients from using the formulation.
- **Stability Issues:** Buccal drug delivery systems can face instability if the drug degrades or loses its potency after prolonged exposure, especially humidified conditions.

Components of Buccal Drug Delivery System

The drug substance is also called the active pharmaceutical ingredient (**API**). It has a crucial role in a buccal drug delivery system and does so by having an important impact on the inherent properties of the formulation. Below is a comprehensive overview of how the drug substance influences buccal delivery:

Key Considerations for Drug Substances

Solubility : For a drug to be adequately absorbed, it has to be sufficiently soluble in saliva so it can dissolve and permeate the buccal mucosa. The drugs that are less soluble would require special formulation methods intended to increase their solubility.

Permeability : A drug needs to be permeable in order to penetrate the buccal mucosa. Molecular size and lipophilicity tend to play a critical role in the efficacy of drug absorption.

A drug must have both chemical and physical stability throughout its shelf life and in use. Formulations should be constructed to protect the drug from environmental degradation from moisture, light, and changes in temperature.

Molecular Weight : Generally, the smaller the molecule, the better it is suited for buccal absorption, since larger molecules cannot transcend the mucosal barrier easily.

Taste : Acceptability of the drug is vital to achieve patient compliance. The drugs with a bad taste may need to be masked through use of masking strategy, either flavoring agents or specialized formulation for better acceptability.

Dosage Form : The physical form that the drug takes—the solid, liquid, or semi-solid—can influence the choice of the delivery system. For example, loading and release mechanisms are different between a buccal film and tablets.

This explains why the pharmacologic properties of the drug itself are of paramount importance to successful buccal drug delivery systems. It determines everything, from formulation to patient compliance. To develop truly efficacious and patient-friendly pharmaceuticals, it is crucial that such factors be understood.

Bioadhesive Polymers in Buccal drug delivery system

Bioadhesive polymers play a crucial role in buccal drug delivery systems. These innovative materials significantly improve the adhesion of formulations to the buccal mucosa, which in turn enhances drug retention and absorption. This means that medications can be more effectively delivered directly through the mouth, leading to better therapeutic outcomes for patients. With their ability to prolong the presence of drugs in the oral cavity, bioadhesive polymers are redefining how we approach medication delivery, making it more efficient and user-friendly for everyone.

Characteristics of Polymer for buccal drug delivery system

In the selection of polymers for buccal drug delivery systems, some of the primary properties are taken care of so that it will function properly. Here is an overview of the critical properties that these polymers must provide:

Mucoadhesive Properties : The selected polymer should have good adhesive interactions with the buccal mucosa for the retention time at the application site and sustaining the release of drugs.

Biocompatibility : The selected polymers should not be toxic and do not irritate the oral mucosa, thus ensuring the assurance and comfort of the patient.

Hydrophilicity : Polymers should have good water-absorbing characteristics, which promote gel formation after hydration and further improve drug dissolution and delivery.

Mechanical Strength : Their mechanical properties should be suitable in that they should be able to resist the mechanical stress of oral movements such as chewing and swallowing without being removed from the buccal cavity.

Flexibility and Elasticity : Polymers should be flexible enough to enable them to track the contour of the buccal mucosa and hence enhance comfort and adhesion.

Controlled Release Profile : It must assure sustained and controlled drug release for a long duration. Polymers should allow sustained and controlled drug release for a long time and therefore sustain therapeutic levels.

pH Sensitivity : Controlled release is beneficial in the fluctuating oral environment of saliva composition, which varies in pH.

Examples of Polymers

1. Natural Polymers:

- Chitosan
- Gelatin
- Alginates
- Pectin

2. Synthetic Polymers:

- Carbomers (e.g., Carbopol)
- Polyvinyl Alcohol (PVA)
- Hydroxypropyl Methylcellulose (HPMC)
- Polyethylene Glycol (PEG)

3. Semi-Synthetic Polymers:

- Sodium Carboxymethylcellulose (CMC).

4. Thermosensitive Polymers:

- Ploxamers

5. Mucoadhesive Copolymers:

- Eudragit

Penetration Enhancers in Buccal Drug Delivery System

Penetration enhancers are drugs that have been added to buccal drug delivery systems to increase the penetration of the buccal mucosa. The therapeutic agents, through this increased permeability, get absorbed. Here is an account of the roles, types, and mechanisms of penetration enhancers in buccal drug delivery:

Role of Penetration Enhancers :

Increase Permeability: They overcome the barrier properties of the buccal mucosa, thus making it easier to drug molecules whose size is larger or less permeable.

Improving Bioavailability: Penetration enhancers may improve the bioavailability of certain drugs by improving absorption.

Modulate release rates: Some of them can be used to control the release of the drug from the formulation to ensure the maintenance of a therapeutic effect.

Examples of Penetration Enhancers

Surfactants:

1. Sodium Lauryl Sulfate (SLS)
2. Polysorbates (for example, Tween 80)

Fatty Acids:

1. Oleic Acid
2. Capric Acid

Alcohols:

1. Ethanol
2. Isopropanol

Amino Acids : L-Arginine

Chitosan

Glycols : Propylene Glycol

Biological Enhancers : Enzymes

Physical Enhancers:

1. Iontophoresis
2. Ultrasound

Backing Membrane

The backing membrane is a critical component of buccal drug delivery systems, especially in formulations like buccal patches and films. It serves multiple functions that contribute to the overall efficacy and usability of the delivery system.

Examples Backing Membrane

- Polyethylene
- Polyvinyl Chloride (PVC)
- Ethylene Vinyl Acetate (EVA)
- Polyurethane

- Aluminium Foil
- Polypropylene

Plasticizers

Plasticizers are substances added to polymers in drug delivery systems to enhance their flexibility, workability, and mechanical properties. In buccal drug delivery systems, plasticizers play a vital role in improving the performance and comfort of formulations like films, patches, and tablets. Here's an overview of their importance, common types, and mechanisms of action.

Examples of Plasticizers

- Glycerin
- Propylene Glycol
- Polyethylene Glycol (PEG)
- Triethyl Citrate (TEC)
- Acetyl Tributyl Citrate (ATBC)

Stabilizers and Preservatives

To ensure safety, efficacy, and longer drug stability in the buccal drug delivery formulation, stabilizers and preservatives play very important roles. Here, I will take some space to present an overview of their functions, types, and importance in the buccal system.

Examples

- Citric Acid
- Paraben
- Tocopherol
- Ascorbic Acid
- EDTA

Flavouring and Sweetening Agents

These flavoring and sweetening agents are integral in a buccal drug delivery system, especially in making formulations palatable. It is important because it improves compliance with treatment, especially in patients who have a sensitive response to bad tastes and as is common with geriatrics and pediatrics.

Examples

- Saccharin
- Aspartame
- Monosodium Glutamate (MSG)
- Steviol Glycosides (Stevia)
- Sorbitol
- Honey

Release Control Modifiers

Release control modifiers are crucial components in buccal drug delivery systems that influence the rate and duration of drug release from the formulation. By modifying the release profile, these agents help achieve the desired therapeutic effect while improving patient compliance.

Examples

- Hydroxypropyl Methylcellulose (HPMC)
- Ethyl Cellulose
- Xanthan Gum
- Guar Gum

Saliva Stimulating Agents

Saliva inducing agents can be of great importance when developed buccal drug delivery systems focusing on increasing patients drug absorption and enhancing their comfort.

Examples

Pilocarpine and Cevimeline: These agents may be formulated as buccal agents that cause direct stimulation of salivary secretion.

Natural Extracts: Citrus extracts or even mint can be added to the formulations to induce the stimulation of saliva flow.

Approaches in Buccal drug delivery System

Buccal drug delivery systems prove to be a unique route for the administration of drugs through the oral cavity, with direct absorption into systemic circulation. Some of the most relevant approaches used in buccal drug delivery are depicted below:

1. Formulation Types

Tablets: Buccal tablets are slow-dissolving tablets that release drugs slowly in the buccal cavity.

Films: In this system, thin films can be associated with buccal mucosa to provide a sustained release of drugs.

Gels and Pastes: They can be applied directly in the buccal area, where localized or systemic drug delivery can be achieved.

Lozenges: These are solid forms that slowly dissolve in the mouth and provide a slow release of the drug.

2. Mucoadhesive Systems

Mucoadhesive Polymers: These polymers that make them stick to the mucosal surface add adhesion properties to these, which in turn prolong drug retention and absorption.

Bioadhesive Hydrogels: These hydrogels can help maintain moisture and enhance the contact of the drug with the mucosa.

3. Permeation Enhancers

Chemical Enhancers: Chemical enhancers in the form of surfactants or fatty acids can be used to swell the mucosa. This is followed by an increase in the permeability of the drug.

Physical Enhancers: In this category, techniques like iontophoresis and sonophoresis enhance the delivery of drug by the application of electrical or ultrasound energy to the mucosa.

4. Controlled Release Systems

Matrix Systems: The technique brings about a controlled release rate of the drug by a matrix of polymers.

Reservoir Systems: In this system, there is a drug reservoir which is covered by rate controlling membrane, and always there is a consistent release profile.

5. pH-Sensitive System

Formulations which are pH dependent respond to the oral environment and can release the drug in a controlled manner based on the saliva pH.

6. Nanoparticle Systems

Nano-carriers: The entrapment of a drug using nanoparticles increases solubility as well as provides targeted delivery to the buccal mucosa.

Liposomal Systems: Liposomes enhance the stability of drugs and help in absorption by the mucosal membrane.

7. Taste Masking Technique

Employment of taste-masking agents or technique and formulation palatability helps the patients to comply

Conclusion

In conclusion, buccal drug delivery systems constitute promising alternatives to traditional oral and injectable routes with a host of advantages such as improved bioavailability, rapid onset of action, and an increased possibility of patient compliance. They have the ability to bypass first-pass metabolism and gain direct access into systemic circulation, which lends importance to its use in drugs having low oral bioavailability or that require quicker therapeutic effects.

All these systems depend on several factors, including formulating designing, choice of excipients, and mucoadhesive and permeation-enhancing agents. Advances in nanotechnology with the use of particle carriers as well as controlled release add more to their potential.

Overall, with advancing knowledge in this delivery route, buccal systems can be a significant player in modern pharmacotherapy.

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