

# BUCCAL DRUG DELIVERY SYSTEMS: AN IN-DEPTH EXPLORATION OF BIOADHESION, PERMEABILITY, AND FORMULATION STRATEGIES

## Abstract

The Buccal Drug Delivery System (BDDS) has garnered much interest as a potentially effective method of administering medicinal drugs because of its distinct benefits. The complex relationships between permeability, buccal medication delivery, and bioadhesion are examined in detail in this extensive study. Enhancing medication absorption and retention in the buccal cavity is mostly dependent on bioadhesion. The intricate physiology of the mucosal membrane and the several bioadhesive mechanisms—hydration, electrostatic contacts, and covalent interactions, among others—are examined to highlight their significance for the efficacy of BDDS. Drug absorption is significantly influenced by permeability via the buccal mucosa. This article explores the physiological and anatomical properties of the buccal mucosa that affect permeability as well as methods to maximize medication absorption.

**Keywords:** Buccal Drug, bioadhesion, buccal mucosa.

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## I. INTRODUCTION

As a substitute delivery method for drugs, the buccal drug delivery system has drawn a lot of interest lately. A prolonged release profile, prevention of first-pass metabolism, and improved patient compliance are just a few benefits of this non-invasive method. The complexities of buccal drug distribution are covered in detail in this chapter, with particular attention paid to formulation techniques, permeability, and bioadhesion.

## II. AN OVERVIEW OF THE STRUCTURE OF THE ORAL MUCOSA IN THE ORAL CAVITY

Mastication, speech, and the start of the digestive process are just a few of the physiological processes carried out by the oral cavity, an intricate and dynamic anatomical area. A specialized mucous membrane that borders the mouth cavity, the oral mucosa protects underlying tissues, aids in sensation, and facilitates the absorption of certain chemicals. The buccal, sublingual, and gingival areas make up the three basic regions that make up the oral mucosa(1)

### 1. Buccal Mucosa

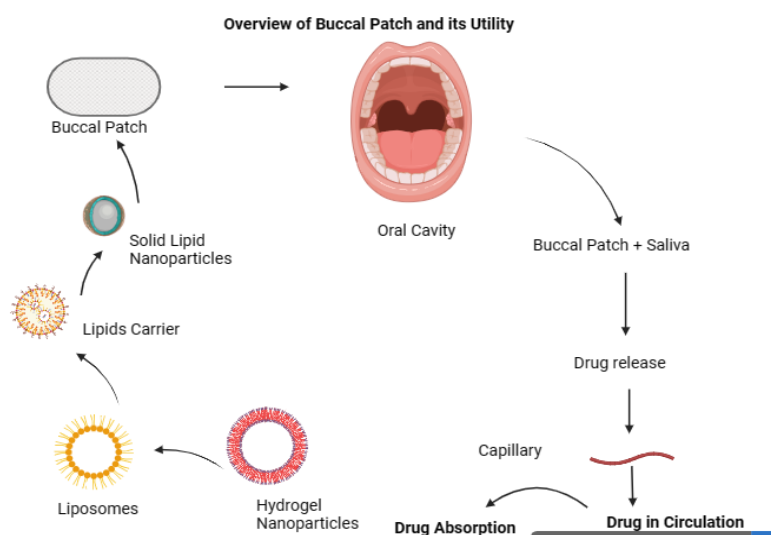
- **Location:** The lateral walls of the oral cavity are formed by the buccal mucosa, which borders the inner cheek.
- **Structural Characteristics**
  - ❖ **Squamous Epithelium Stratified:** The primary component of the buccal mucosa is a stratified squamous epithelium that protects against chemical and mechanical harm.
  - ❖ **Connective Tissue:** The connective tissue layer, which lies underneath the epithelium, is home to small salivary glands, blood vessels, and nerves.
  - ❖ **Masticatory Mucosa:** The buccal mucosa is a kind of mucosa that is used in chewing and is distinguished by its resistance to abrasion and friction (2).

### 2. Sublingual Mucosa

- **Location:** The sublingual mucosa covers the floor of the mouth and is located beneath the tongue.
- **Structural Characteristics**
  - ❖ **Thin Epithelium:** In comparison to other areas of the oral mucosa, the sublingual region's epithelium is comparatively thin.
  - ❖ **Vascular Network:** Due to the sublingual mucosa's high level of vascularization, some medications—particularly those taken under the tongue—can be absorbed well.

### 3. Gingival Mucosa

- **Location:** The gums are formed by the gingival mucosa, which surrounds and shields the teeth.
- **The Structural Elements Include**
  - ❖ **Gingival Epithelium:** The stratified squamous epithelium covering the gingiva is keratinized and provides resistance against the mechanical stress caused by brushing and biting.
  - ❖ **Gingival Sulcus:** The junctional epithelium fuses the gingiva to the tooth in this area, which is referred to as the gingival sulcus(3,2).



#### The oral mucosa serves several functional purposes.

- First, it provides protection against physical trauma, pathogens, and chemical irritants.
- Secondly, it contains nerves that contribute to touch, temperature, and pain perception, all of which are necessary for normal oral function.
- Lastly, saliva is secreted by small salivary glands in the connective tissue layer, which lubricates the oral cavity and aids in digestion.

For the purpose of creating efficient drug delivery systems that target the buccal, sublingual, and gingival mucosa, it is essential to comprehend their unique properties. The differences in vascularity, mechanical robustness, and epithelium thickness affect which medication formulations are best for achieving the best absorption and therapeutic results.

#### The Buccal Mucosa's Physiology

Understanding medication absorption and administration via this route requires an understanding of the physiology of the buccal mucosa. The buccal mucosa differs from other

mucosal surfaces in that it has specific characteristics that impact things like lymphatic drainage, blood flow, and medication absorption(4).

### 1. Supply of Blood to the Buccal Mucosa

- **Arterial Supply:** The buccal artery, in particular, is the major branch of the external carotid artery that supplies blood to the buccal mucosa. The vascular network makes sure that the mucosal tissues receive enough oxygen and nourishment.
- **Microcirculation:** The buccal mucosa has a highly developed microvasculature, which promotes effective medication absorption. Drugs that penetrate the buccal epithelium are rapidly delivered throughout the body thanks to capillaries in the submucosa.
- **Lymphatic Drainage:** Regional lymph nodes, especially the submandibular and deep cervical lymph nodes, receive lymphatic veins from the buccal mucosa. An important part of the clearing process for ingested compounds is lymphatic drainage, which helps with the general systemic distribution and medication removal.
- **Macromolecule Transport:** Particulate materials and large molecules may be carried by the lymphatic system, which may have an impact on the pharmacokinetics of some medications taken buccal route(5).

### 2. Particulars Affecting Drug Absorption

- **Stratified Squamous Epithelium:** Acting as a barrier of defense, a stratified squamous epithelium covers the buccal mucosa. Drug penetration is possible, nevertheless, since this epithelium is thinner than the skin.
- **Tight Junction Presence:** Paracellular transport is restricted by tight junctions between epithelial cells; nonetheless, certain medications can take advantage of these junctions by using permeation enhancers or suitable formulation techniques.
- **Rich Blood Supply:** Drugs can reach the systemic circulation without first going through the liver's first-pass metabolism because to the buccal mucosa's substantial vascularization, which facilitates quick drug absorption.
- **Moist Environment:** Saliva continuously hydrates the buccal mucosa, which promotes medication absorption and disintegration.

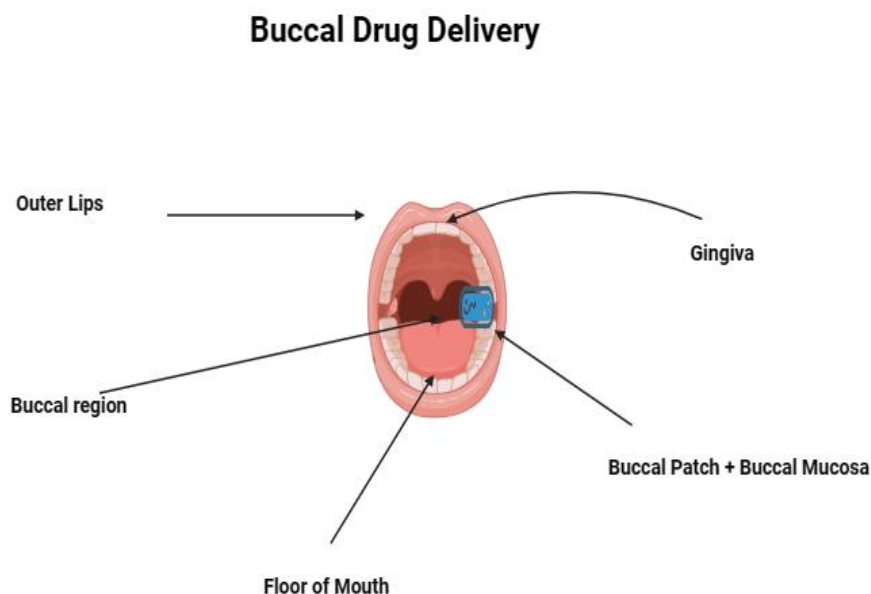
### 3. Mechanisms of Drug Absorption

Small, lipophilic compounds have the ability to passively diffuse across the buccal epithelium.

- **Facilitated Transport:** Some medications may be more easily absorbed when certain transporters on epithelial cells are present.

- **Ionization and pH:** Drug absorption can be greatly impacted by a drug's ionization state as well as the pH of the buccal environment.

It is essential to comprehend these physiological aspects while developing buccal medication delivery devices. For formulation techniques to improve medication absorption, achieve therapeutic efficacy, and guarantee patient safety, they must take into account the special qualities of the buccal mucosa(7).



### III. BIOADHESION IN BUCAL CAVITY

**1. Mechanisms of Bioadhesion:** A key component of buccal drug delivery systems, bioadhesion is the capacity of a substance to stick to biological tissues. The establishment of robust and continuous contact between the drug delivery system and the buccal mucosa is critical to the efficacy of these devices. Physical and chemical interactions can be used to classify bioadhesion processes.

#### 2. Physica Interactions

- **Van der Waals Forces:** Van der Waals forces are a type of weak attraction that exist between molecules. These pressures are involved in the first contact between the mucoadhesive substance and the mucosal surface in the context of bioadhesion. The initial contact is made possible by Van der Waals forces, which also facilitate subsequent interactions.
- **Bonding of Hydrogen:** The creation of hydrogen bridges between mucoadhesive polymer and mucosal glycoproteins is known as hydrogen bonding. By strengthening the adhesion and creating a stronger relationship between the drug delivery system and the buccal mucosa, hydrogen bonding improves adhesion.

- **Electrostatic Interactions:** refers to the attraction that exists between negatively and positively charged objects. Mucosal surfaces with opposing charges can interact with polymers with charged groups. The drug delivery system's sticky qualities can be improved by taking advantage of this interaction, which promotes mucoadhesion(7,8).

### 3. Chemicals Interactions

- **Covalent Bonds:** Covalent bonds are formed when components of the mucosal surface share electrons with the mucoadhesive polymer. Covalent bonds have the potential to promote sustained adherence, but they are less prevalent in bioadhesive systems since they need reversible interactions.
- **Ionic Interactions:** The mucoadhesive polymer and mucosal surface are subject to ionic interactions between charged groups. These exchanges could be reversible. Following drug release, the drug delivery system can separate thanks to ionic interactions, which offer a dynamic adhesion mechanism.
- **Mucoadhesive Significance in Drug Delivery:** Mucoadhesive qualities ensure longer contact for medication absorption by extending the residence duration of drug delivery systems on the buccal mucosa. Drug bioavailability is improved and sustained drug release is possible with a longer residence duration. Better medication absorption across the buccal epithelium is achieved when there is more contact between the mucosa and the drug delivery device. Lower variability in medication plasma concentrations and enhanced therapeutic effectiveness are the results of increased drug absorption(9).

### Factor Influencing Bioadhesion

#### 1. Material Properties

- **Polymer Kind:** Bioadhesion is greatly influenced by the kind of polymer utilized in the formulation. Since they interact with mucosal surfaces, mucoadhesive polymers such as chitosan, cellulose derivatives, and carbomers are often used.
- **Molecular Weight of the Polymer:** Polymers with a higher molecular weight often have superior bioadhesive qualities. Prolonged contact with the mucosa is encouraged by longer polymer chains, which also increase mucoadhesive strength.
- **Polymer Concentration:** Adhesive strength is influenced by the amount of mucoadhesive polymer in the formulation. More concentrations usually lead to more bioadhesion.
- **Chemical Structure:** The kind and intensity of contacts with mucosal surfaces are dictated by the mucoadhesive polymer's chemical structure. Functional groups that form hydrogen bonds, such hydroxyl or amino groups, can improve adhesion.

- **Establishing Cross-Links:** The stability of the mucoadhesive system can be improved by crosslinking within the polymer matrix, which affects the strength and persistence of adhesion(10).

## 2. Physiological Factors

- **Mucosal Surface Characteristics:** Individual differences exist in the composition and topography of the buccal mucosa. The degree of hydration, surface charge, and roughness can all affect how well mucoadhesive systems interact.
- **Saliva Composition:** The adhesive qualities of saliva are influenced by its composition, which includes its mucin concentration and viscosity. Saliva has properties that can either help or inhibit bioadhesion.

## 3. Formulation Factors

- **Drug Properties:** The drug's size, charge, and lipophilicity are among its physicochemical characteristics that affect how it interacts with mucoadhesive polymers and the mucosal surface.
- **Drug Loading:** Bioadhesion may be impacted by the quantity of medicine included in the mucoadhesive formulation. Adhesion strength and rheological characteristics may change with high drug loading (10,11).

## 4. Patient-Related Factors

- **Individual Variability:** Due to variations in salivary content, mucosal features, and oral physiology, bioadhesive systems may behave differently in different people.
- **Patient Compliance:** The efficacy of the mucoadhesive system may be impacted by patient acceptability and convenience of administration. Convenience and comfort have a role in patient compliance.

## Buccal Drug Delivery Using Bioadhesive Polymers

- **Natural Polymer**
- **Synthetic Polymer**

### 1. Natural Polymers

- **Chitosan:** Made from the polysaccharide chitin, which is present in the exoskeleton of crustaceans. Electrostatic and hydrogen bonding interactions between positively charged amino groups and negatively charged mucosal surfaces are made possible. It is used for prolonged medication release, used in gels, pills, and buccal films.
- **Sodium Alginate:** It is used for films and mucoadhesive patches for controlled medication release.

- **Hyaluronic Acid:** It Promotes mucoadhesion by forming hydrogels with a high water content. Because of its biocompatibility and capacity to hold moisture, buccal medication administration uses it.

## 2. Synthetic Polymers

- **Poly (Acrylic Acid) (PAA):** Include the formation of hydrogen bonds with mucosal surfaces. Because of its bioadhesive and prolonged release qualities, it is included into buccal films and patches.
- **Polyvinylpyrrolidone (PVP):** Create a cohesive and flexible coating on the mucosal surface. Because of its mucoadhesive and film-forming properties, it is used in buccal patches and tablets.
- **Polyethylene Glycol (PEG):** Bioadhesive Properties: Promotes mucoadhesion by increasing formulation viscosity. To increase adhesive strength, combine this polymer with others in buccal formulations(12, 13, 14).

## IV. PERMEABILITY ACROSS BUCCAL MUCOSA

One essential component of buccal medication delivery systems is permeability across the buccal mucosa. Drugs' bioavailability, effectiveness, and therapeutic results are influenced by their capacity to cross the mucosal barrier. The permeability across the buccal mucosa is influenced by many factors(15):

- **Epithelial Structure:** Stratified squamous epithelium, which is less keratinized than skin epithelium, makes up the buccal mucosa. This increases the permeability of the buccal mucosa to several medications.
- **Junctions between Cells:** Transport between cells within an epithelium is controlled by tight junctions. The tightness of these junctions can affect the permeability of the buccal mucosa, facilitating or obstructing the transfer of medications between cells.
- **Mucus Layer:** The buccal mucosa's mucus layer serves two purposes. It functions as a reservoir for prolonged drug release as well as a barrier that prevents drug penetration, particularly in the case of mucoadhesive formulations.
- **Blood Supply:** Drugs are rapidly absorbed into the circulation thanks to the buccal mucosa's extensive vascular network. Small, lipophilic substances can enter the bloodstream through the submucosal blood arteries.
- **Lipophilicity:** Because the cell membranes of lipophilic medicines are lipid-rich, these medications often exhibit increased permeability across the buccal mucosa.
- **Molecular Size:** Because they can fit through the narrow gaps between cells, small molecules are more permeable than bigger ones.



- **pH and Ionization:** Drug ionization can be impacted by the pH of the buccal environment. Electrostatic interactions may cause altered permeability in ionized medicines. For the best possible medication absorption, buccal administration systems might need to take the mouth cavity's physiological pH into account.
- **Drug Concentration:** Through concentration-driven mechanisms such as passive diffusion, higher drug concentrations can improve drug permeability.
- **Enhancers of Permeation:** To increase medication permeability across the buccal mucosa, permeation enhancers are frequently used. These enhancers have the ability to change the mucosal membrane's structure, allowing more medications to flow through.
- **Vehicle Formulation:** Permeability may be impacted by how the drug delivery system is formulated. Gel formulations, for example, may improve medication absorption and contact time.
- **Drug Metabolism in Buccal Tissues:** Drugs can be metabolized by the enzymes found in buccal tissues. The bioavailability of several medications taken via buccal administration may be impacted by this metabolic activity.
- **Disease States:** The buccal mucosa's permeability may change as a result of specific illnesses or diseases. Drug absorption may be impacted by oral cavity diseases or inflammation.
- **Temperature:** Drug permeability can be impacted by temperature because it can change the fluidity of cell membranes. Increased warmth may improve medication dispersion across the buccal mucosa(16,17).

## V. FORMULATION STRATEGIES FOR DRUG DELIVERY SYSTEM

- **Dosage Form:** Films, Gels, Tablets, and Patches: Provide regulated medication release, extended residence duration, and convenience of administration.
- **Selecting Polymers:** Chitosan and poly(acrylic acid) are examples of natural and synthetic polymers that improve adherence for prolonged medication release.
- **Techniques for Enhancement:** Enhancers of Permeation: Increase a drug's capacity to pass through the mucosal barrier.
- **Cutting-Edge Technologies:** Improve medication solubility, stability, and targeted delivery with nanoparticles and liposomes.
- **Formulations Suitable for Patients:** Oral disintegrating tablets and fast-dissolving films: Boost adherence with quick and easy administration.

- **Systems of Adaptive Release:** Optimizing treatment results through controlled medication release is made possible by responsive hydrogels.
- **Combination Products:** Create medications with complimentary effects to increase their effectiveness.
- **Stabilizers and Antioxidants:** guarantee medication stability by halting deterioration.
- **Tasting-Making Methods:** Masking technologies and flavoring agents can help patients accept medications that are delivered buccally.
- **Technologies for Microfabrication:** Microneedles and microdevices: Provide exact control over the kinetics of medication release.
- **Regulatory Aspects to Take into Account:** Adherence to Regulations: Guarantee effectiveness and safety, hasten approval.
- **Customized Formulations:** Take into account aspects unique to each patient to improve treatment results.
- **Adherence to Regulatory Bodies:** For buccal medication delivery systems to be approved, compliance with regulations established by regulatory organizations like the FDA and EMA is essential (18).

## VI. REGULATORY CONSIDERATION AND FUTURE PERSPECTIVE IN BUCCAL DRUG DELIVERY SYSTEM

Getting regulatory clearance requires meeting strict requirements for quality, safety, and efficacy. Clinical and preclinical data must be meticulously documented. Regulatory submissions need thorough testing for safety, bioavailability, and stability. Maintaining quality control procedures and ensuring uniformity in manufacturing operations are crucial. For regulatory compliance, adherence to Good Manufacturing Practices (GMP) is essential(19).

## VII. FUTURE DEVELOPMENTS AND TRENDS: NANOTECHNOLOGY PROGRESS

### 1. Nanotechnology Advancement

- Nanocarrier research and development should continue to improve medication transport, targeting, and therapeutic results.
- Combining materials at the nanoscale to solve issues with medication stability and absorption.

## **2. Advanced Drug Delivery System**

- Study of cutting-edge drug delivery technologies, including as hydrogels, implanted controlled-release devices, and smart polymers.
- Using 3D printing technology to create customized, demand-driven medication distribution systems.

## **3. Innovation Dosage Forms**

- Improvements in dose forms, such as smart buccal films, mucoadhesive nanoparticles, and microneedle patches.
- Investigating novel materials and configurations to achieve better medication release profiles.

## **4. Digital Health and Data Integration**

- Integration of digital health technologies to track treatment compliance, general health, and patient adherence.
- Using big data analytics to get understanding of the results of buccal drug delivery.

## **5. Patient focus Approaches**

- Concentrate on creating formulations that are more palatable to patients and have better taste masking and acceptance.
- When creating buccal drug delivery systems, patient preferences and lifestyles are taken into account.

## **6. Environment Technology**

- Emphasis on sustainable production methods and eco-friendly materials.
- Investigating environmentally friendly and biodegradable polymers for oral medication administration(19, 20).

## **VIII. CONCLUSION**

The buccal drug delivery system has emerged as a promising alternative for drug administration, offering advantages such as prolonged release, avoidance of first-pass metabolism, and enhanced patient compliance. This chapter provides a comprehensive overview of the structure of the oral mucosa in the oral cavity, focusing on the buccal, sublingual, and gingival mucosa. Understanding the unique properties of these mucosal regions is crucial for developing efficient drug delivery systems. The physiology of the buccal mucosa, including blood supply, permeability, and drug absorption mechanisms, is discussed in detail. The role of bioadhesion in buccal drug delivery is emphasized, with physical and chemical interactions playing a key role in ensuring continuous contact between the drug delivery system and the buccal mucosa. Factors influencing bioadhesion, such as material properties, physiological factors, formulation factors, and patient-related factors, are highlighted. The use of both natural and synthetic polymers in buccal drug delivery, along

with permeability across the buccal mucosa, is explored. Various formulation strategies, including dosage forms, polymer selection, enhancement techniques, and cutting-edge technologies, are presented to optimize drug delivery efficiency. Regulatory considerations for buccal drug delivery systems are discussed, emphasizing the importance of meeting quality, safety, and efficacy requirements. Future developments and trends in buccal drug delivery, including nanotechnology advancements, innovative dosage forms, digital health integration, patient-focused approaches, and environmentally friendly technologies, are explored. In the evolving landscape of pharmaceuticals, buccal drug delivery systems hold great potential for addressing challenges associated with traditional drug administration routes. Continued research, technological advancements, and adherence to regulatory standards will contribute to the further development and implementation of effective buccal drug delivery systems, ultimately enhancing patient outcomes and treatment options.

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