*https://doi.org/ 10.33472/AFJBS.6.5.2024. 522-541*

African Journal of Biological Sciences

# An Overview on Mucoadhesive Buccal Drug Delivery Systems& Approaches: A comprehensive review.

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Article History
Volume 6, Issue 5, Apr 2024
Received: 15 Apr 2024
Accepted: 22 Apr 2024
doi: *10.33472/AFJBS.6.5.2024.522-541*

Abstract:

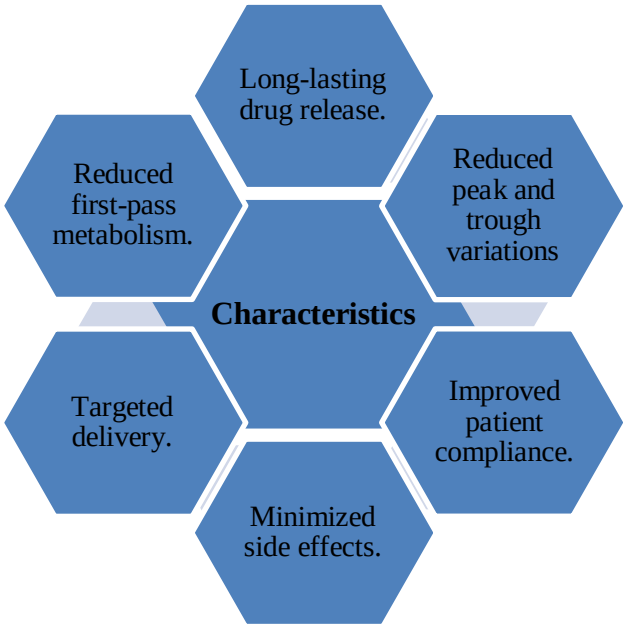
Mucoadhesive buccal drug delivery devices have attracted a lot of interest as a viable strategy for delivering medications through the mouth cavity. Due to its potential to address a number of concerns with conventional oral drug administration, including low bioavailability, first-pass metabolism, and patient compliance issues, this delivery strategy is of considerable interest. The mucosal membranes in the oral cavity are targeted by Mucoadhesive formulations, which offer an effective path for medication absorption. This abstract explores the main features, benefits, and uses of Mucoadhesive buccal drug delivery devices. The buccal mucosa, which is covered with blood vessels and provides a moderately permeable barrier to medication absorption, is utilized by these systems for its special qualities. Additionally, this method is quite practical for patients since it is simple to reach the oral cavity. In order to provide prolonged drug release and better drug bioavailability, mucoadhesive buccal drug delivery systems require the selection of appropriate polymers and excipients that can stick to the buccal mucosa. These formulations' Mucoadhesive qualities lengthen the period that the medicine is in contact with the mucosal surface, which encourages effective drug absorption. Controlled drug release, less changes in drug levels, and the possibility to prevent the hepatic first-pass impact are benefits of Mucoadhesive buccal drug delivery systems. Furthermore, they are adaptable for a range of therapeutic applications since they may be employed for both systemic and local drug administration. The expanding significance of Mucoadhesive buccal drug delivery systems as a technique of delivering medications through the mouth cavity is highlighted in this abstract. The focus of this field's study is currently on improving formulation methods and investigating cutting-edge medication delivery systems. These developments have the potential to revolutionize the pharmaceutical industry by providing patients with more practical, efficient, and patient-friendly medication delivery options.

**Keywords**: Buccal drug delivery, Oral mucosa, bioadhesion, mucoadhesion, penetration enhancer, Mucoadhesive polymer.

**Introduction:**

The aim to improve the therapeutic results of drugs while reducing side effects and enhancing patient compliance has made the development of efficient drug delivery systems a cornerstone of pharmaceutical research. Mucoadhesive buccal drug delivery systems have drawn a lot of interest among the many drug delivery methods because of its potential to completely change how drugs are transported via the mouth cavity. This cutting-edge technology offers a possible substitute for conventional oral drug delivery techniques, providing answers to various persistent problems in pharmaceutical formulation and patient care.A versatile and easy-to-access route for medication delivery is the human oral cavity. Due to its ease, oral medication delivery in the form of tablets, capsules, and liquids has historically been the main method of drug administration. It does have its drawbacks, too, including the reduced bioavailability of some medications, the potential for first-pass hepatic metabolism, and problems with swallowing in some patient populations. Mucoadhesive buccal medication delivery devices have become an innovative way to get around these challenges.Within the mouth cavity, the buccal mucosa presents a special possibility for medication delivery. It is very vascularized and possesses a barrier that is just slightly permeable, making it the perfect substrate for medication absorption. Additionally, this route of administration is quite practical for patients, particularly those who might have difficulties swallowing, pediatric and geriatric populations, or people with gastrointestinal issues, due to the simplicity of access to the buccal mucosa.The creation of formulations that can attach to the buccal mucosa is the key idea behind mucoadhesive buccal medication delivery devices. These formulations provide a prolonged residence period by retaining close contact with the mucosal surface, allowing for regulated and sustained drug release into the systemic circulation or for localized therapeutic effects. This strategy increases medication bioavailability while reducing drug level swings and perhaps avoiding the hepatic first-pass impact, making pharmacological therapy more predictable and successful.This introduction lays the groundwork for a thorough investigation of mucoadhesive buccal drug delivery systems, highlighting their features, benefits, and many drug delivery uses. This setting sets the stage for our exploration of the complex realm of mucoadhesive buccal drug delivery, an area with enormous promise to transform pharmaceutical research and enhance patient experiences with medication. (Robinson, D. H. *et al*., 1991)

**Mucoadhesive dosage forms meet characteristics of the controlled release systems(**Ullyot, S. ***et.al*1992*)***




**Benefits of Mucoadhesive Buccal Drug Delivery Systems** ***(***Ullyot, S. C. *et al.*1992*)***

- Rapid Drug Absorption
- Avoiding First-Pass Metabolism
- Prolonged Therapeutic benefits and Less Frequent Dosing
- Improved Patient Compliance.
- Preventing Gastric Irritation.
- Lower Dose Requirement.
- Suitability for Sensitive Drugs
- Versatility.
- Enhanced Therapeutic Efficacy.
- Alternative to Injections
- Possibility of Self-Administration

**Anatomy and Structure of the Oral Cavity:**

The oral cavity, often known as the mouth, is a complex organ that is essential for a number of processes, including speaking, breathing, and, most significantly, the ingestion and early stages of food digestion. Understanding its anatomy and structure is crucial for both general knowledge and medicinal or dental applications. The major elements of the oral cavity are Lips are top and lower lips form the oral cavity's opening. They have skin, muscle, and mucous membrane they are crimson or pink along the vermilion border, Cheek are buccinators muscles form the oral cavity sides. They help keep food in the mouth during chewing. Tongue are muscular organ with

taste receptors for taste perception. Controlling food while chewing and speaking require it and Teeth break down food into tiny pieces. Different teeth include the incisor (cutting), canine (tearing), premolar, and molar (grinding) and Gingiva are pink or reddish tissue that surrounds and supports the teeth is known as the gingiva, or gums. Maintaining healthy gums is crucial for keeping teeth healthy.(Bandyopadhyay, A. K. *et al.* 2006)

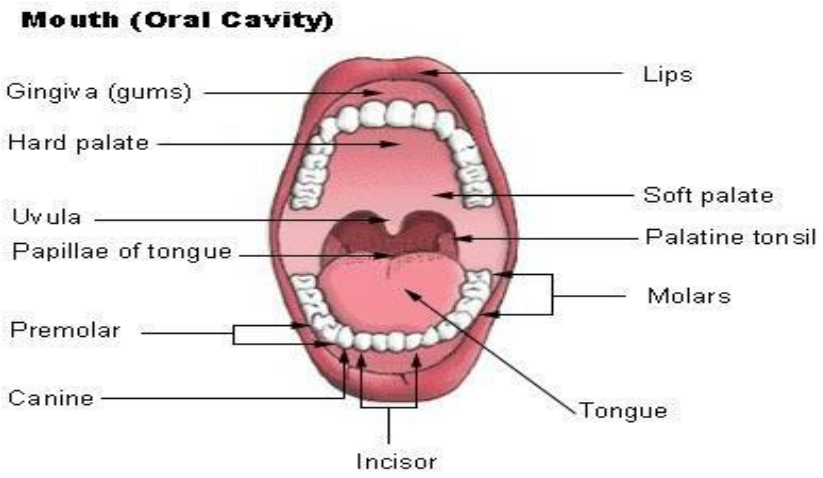



**Fig: 1Structure of the Oral Cavity**

**Composition of Buccal Mucus Layer**

Based on variables including hydration, dental health, and individual variance, the content and thickness of the buccal mucus layer might change. Buccal mucus does not have a defined or widely recognized composition with specified percentage values or thickness.

***Composition***

It contain water makes up the majority of buccal mucus, often comprising 95–99% of it, Large glycoproteins called mucins give mucus its gel-like consistency, Electrolytes and buccal mucus contains a variety of proteins, including enzymes and antimicrobial peptides, to help protect the mouth cavity.

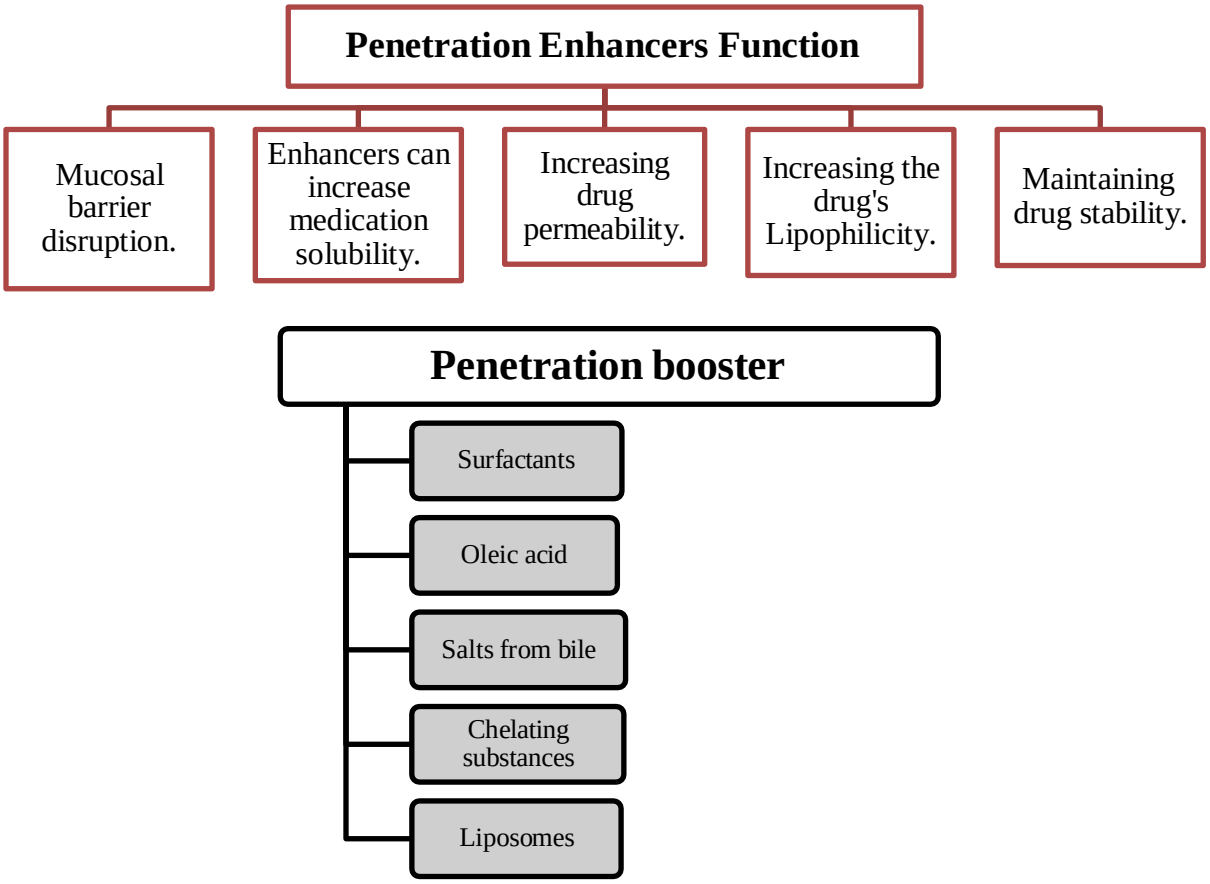
***Functions of the Mucus Layer***

- Lubrication.
- Protection.
- Pathogen defence.
- Digestion

**Buccal Penetration Enhancers**

The buccal mucosa, which borders the cheeks and the region between the mouth and the lips, helps absorb drugs and active substances. Also known as buccal absorption enhancer. This technique of medicine delivery skips the liver's first-pass processing and starts working faster than oral administration.

***BuccalPenetration Enhancers Function*** **(**Giannola, L. I. *et al.* 2008)



### *Mechanism of Permeation Enhancers*

Permeation enhancers are adjuvants or agents that increase the penetration of drugs, chemicals, or other molecules through biological barriers like skin, mucous membranes, or cell membranes. They improve penetration chemically and physically. These methods are outlined below.(Khanna, R. *et al.* 1998).

***A. Mechanisms in Chemistry***

1. Lipid Disruption
2. Solubility Enhancement.
3. Membrane fluidity alteration.
4. Competitive Binding.
5. Changes in Protein Conformation.

***B. Physical mechanisms***

1. Enhanced Diffusion.
2. Iontophoresis.
3. Microneedles.
4. Low-frequency ultrasound.
5. Thermophoresis.
6. Nanocarriers.

**Bioadhesion & Mucoadhesion**

***Bioadhesion:***

Material attachment to biological surfaces is called "bioadhesion," a wide term. This attachment can occur on mucous membranes, skin, blood components, and organs or tissues. Bioadhesive interactions usually serve medical, diagnostic, or functional purposes. The three main bioadhesion types are:

1. **Hemo-Bioadhesion:**Substances adhere to blood components including platelets and red blood cells through hemo-bioadhesion. Bioadhesion is needed for blood-contact medical devices and tailored medicine administration.
2. **Organ bioadhesion:**Organ bioadhesion attaches substances to organs or tissues. GI bioadhesion improves medicine absorption, ocular bioadhesion prolongs drug delivery to the eye, vaginal bioadhesion controls drug release, and dental bioadhesion restores teeth.

***Mucoadhesion:***

Mucoadhesion, a subtype of bioadhesion, involves material attachment to mucous membranes. Medication administration strategies that improve absorption and bioavailability use mucoadhesives. See below for mucoadhesion details: (Miller, N. S. *et al. 1998)*

1. **Interaction with mucin:**Large glycoproteins called mucins are essential to mucous membranes and secretions. Mucins interact with mucoadhesive substances via electrostatic, hydrogen bonding, van der Waals, and hydrophobic forces.
2. **Enhanced Drug Delivery:**Mucoadhesive medication delivery devices connect to buccal and gastrointestinal mucous membranes. By attaching to these surfaces, they can control and prolong drug release, increase bioavailability, and start action quickly.

3. **Materials:**The mucoadhesive drug delivery system can be built from proteins, liposomes, or polymers. Mucoadhesive polymers include chitosan, polyacrylic acid, and hydroxypropyl methylcellulose.

**Mechanism of bioadhesion & mucoadhesion:**

Mucoadhesion or bioadhesion allows controlled drug release and absorption from drug-containing formulations on the buccal mucosa (inside the cheek). This mechanism is needed to administer drugs continuously via the buccal route. The mechanisms affecting buccal drug administration methods are:(Vyas, S. P. *et al.*, 2002)

***A. Physcial Contacts***

1. ***Hydrogen Bonding:*** Glycoproteins containing hydroxyl and amino groups can be found in the buccal mucosa. In the drug delivery system, hydrogen bonds can develop between these functional groups and the complimentary groups on the mucoadhesive polymers, enhancing adherence.
2. ***Van der Waals forces:*** Tight contact and adhesion are facilitated by weak attractive forces between the drug delivery system and the mucosal surface.
3. ***Electrostatic forces:*** When negatively charged mucosal surfaces and cationic mucoadhesive polymers (like chitosan) interact, adhesion is facilitated.

***B. Spreading and Wetting***

- The buccal mucosa should be properly moistened by the mucoadhesive formulation, which should spread to cover its surface and adapt to its imperfections. This enhances adhesion and maximises the contact area.

***C. Gel formation and interpenetrating***

- When in contact with the buccal mucosa, some mucoadhesive polymers can expand and create a layer that resembles gel. The continuous releasing effect that results from this gel formation improves adherence.

***D. Biochemical Reactions***

- The buccal mucosa contains mucosal elements like lectins or mucins, which may interact with the mucoadhesive substance in specific ways.

***E. Considerations for Thermodynamics***

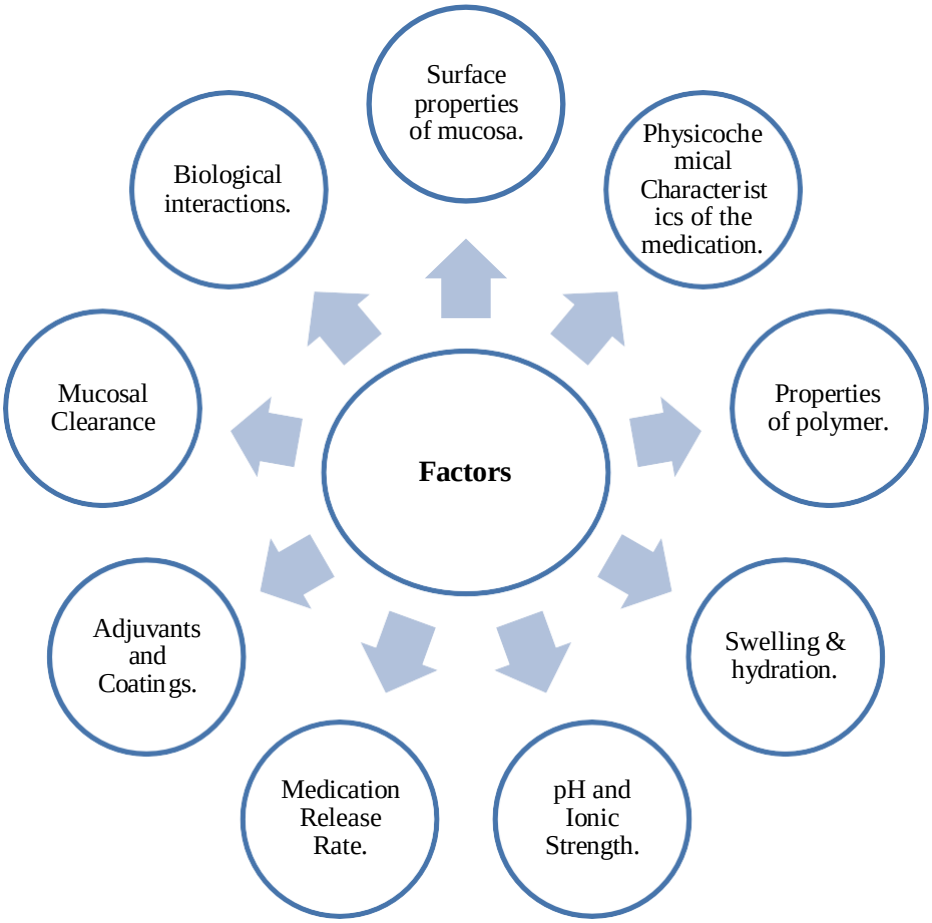
- When in contact with the buccal mucosa as opposed to when it is distributed, the mucoadhesive substance must have a lower free energy in order to produce mucoadhesion. Adhesion is fueled by this thermodynamic advantage.

**Theories on Mucoadhesion/Bioadhesion:**

1. ***Wetting theory:*** According to the wetting theory, the intermolecular interactions between the drug delivery system and the mucosal surface cause adhesion to happen. The system wets the mucosal surface, causing adhesive forces to form that keep the device in place.
2. ***Electrostatic theory*:** Positively charged or ionizable groups on the drug delivery system and negatively charged groups on the mucosal membrane interact electrostatically, according to the electrostatic hypothesis. Adhesion is a result of these electrostatic forces.
3. ***Diffusion theory*:** In accordance with this idea, drug molecules released by the delivery system diffuse into the mucosal tissues, resulting in a gradient in concentration and the system adhering.
4. ***Interlocking*:** Bioadhesion may also be caused by a mechanical link being formed between the drug delivery system and the mucosal folds. This is known as mechanical interlocking.
5. ***Chemical bonding theory:*** According to the chemical bonding theory, certain bioadhesive systems may create covalent or ionic connections with the mucosal surface, resulting in a powerful and long-lasting adherence.
6. ***Hydration theory:*** Hydrogen bonds with the mucosal surface may occur as a result of the hydration of the polymer chains in the drug delivery system, according to the theory of hydration. The hydration of the polymer causes swelling and a larger contact surface, which might lead to adhesion.
7. ***Mucin theory:*** Mucin-Binding Theory: The mucus layer on mucosal surfaces contains glycoproteins called mucins. Certain ligands in certain bioadhesive systems bind to mucins to produce adherence.
8. ***Van der Waals Forces*:** Van der Waals forces are weak intermolecular forces that may help a medication delivery device adhere to the mucosal surface.
9. ***Polarity & surface energy:*** Systems with comparable polarity and surface energies to the mucosal tissues have a tendency to attach better due to advantageous interactions.

**Factors Influence Mucoadhesion for Buccal Drug Delivery:**

A drug delivery system's capacity to cling to mucosal surfaces for a lengthy period of time, such as the buccal (cheek) mucosa, allows for controlled drug release. For buccal medication administration, a number of variables affect mucoadhesion, including: (Veillard, M. M. *et al.*, 1987)




**Buccal Mucoadhesive Polymers:**

Buccal mucoadhesive polymers are a type of substances used in pharmaceuticals and drug delivery systems that are created to stick to the buccal (cheek) mucosa of the oral cavity. These polymers are the perfect choice for medication delivery via the oral mucosa because of their special qualities. They may come as pills, gels, patches, or other dose forms. The following are some essential qualities and uses of buccal mucoadhesive polymers: (*Alka, G.*et al, 2022).

- Adhesion to mucous membrane.
- Drug Delivery for Local and Systemic Use.
- Improved Bioavailability.
- Patient compliance.
- Drug Stability.

- Controlled Release.
- Wide Range of Polymers.

**Ideal Characteristics of Buccal Mucoadhesive Polymers (**Khanna, R. *et al*., 1998)

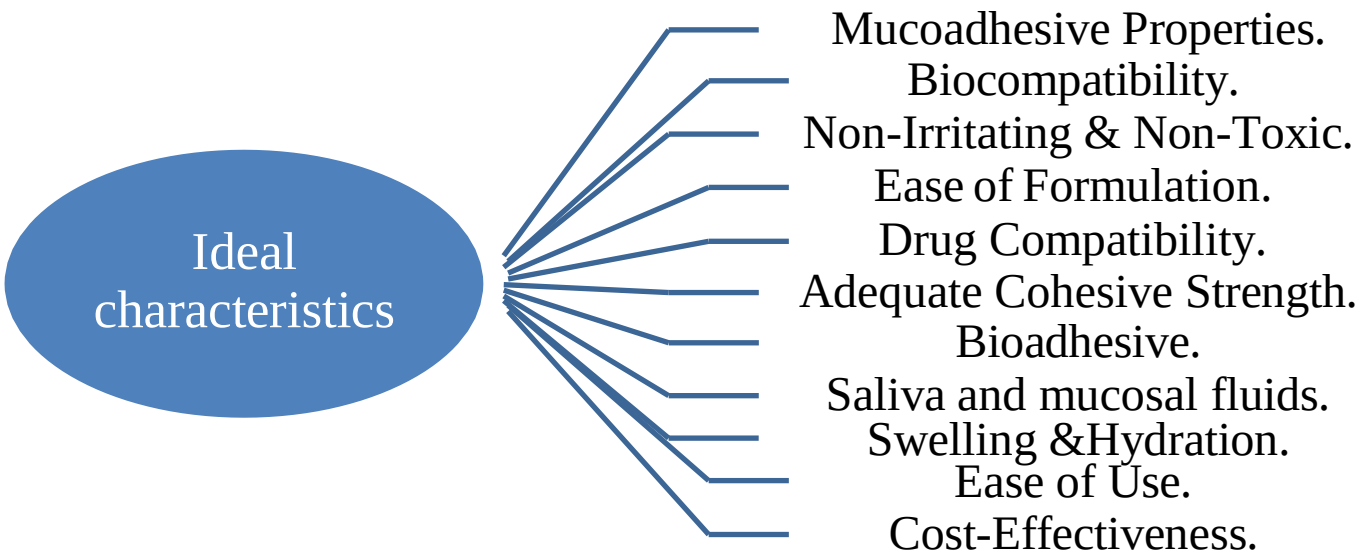



**Table: 1 Classification of Mucoadhesive Polymers in Buccal Drug Delivery:**(Khanna, R. *et al.*, 1998)

| **Main Criteria** | **Examples** | |
|---|---|---|
| | **Natural and Modified Natural Polymers** | **Synthetic** |
| Source | Hyaluronic acid, carrageenan, pectin, sodium alginate, agar, chitosan, gelatin, xanthan gum, gellan, guar gum, and agar. Derivatives of cellulose include carboxymethyl cellulose, carboxymethylthiolated cellulose, sodium carboxymethyl cellulose, | Carbopol, polycarbophil, polyacrylic acid, polyacyrlates, poly-2-hydroxyethylmethacrylate, copolymer of acrylic acid and ethylhexylacryalte, polymetahcryalate, polyalkylcynoacrylates: polyisobutylcynoacrylate, polyisohexylcyanoacrylate. Poly-N-2-hydroxypropylmethacrylamide, polyhydroxyethylene, polyvinyl alcohol, |

| | | |
|---|---|---|
| | hydroxypropyl methyl cellulose, hydroxypropyl methyl cellulose, methyl cellulose, and methylhydroxypropyl methyl cellulose. | polyvinyl pyrrolidone, and thiolated polymers are among others. |
| | **Water-Soluble** | **Water-Insoluble** |
| **Solubility in water** | **Cellulose derivatives:** Hydrophilic Polyethylene Carbonate (HPC), Hydroxypropyl Methylcellulose (HPC), Hydroxypropyl Methylcellulose (HPC), Hydroxypropyl Methylcellulose (HPC), Hydroxypropyl Methylcellulose (HPC) (water-soluble), CarboxyHPMC (at 38 degrees Celsius), PAA, sodium CMC, sodium alginate Poly(N-2-hydroxypropylmethacryl amide), poly(hydroxyethylene), poly(vinyl alcohol), poly(vinylpyrrolidone), and thiolated polymers are among more. | **Polymers based on poly (meth) acrylic acid:** The following are examples of polymers: carbopol, polycarbophil, polyacrylic acid, polyacyrlates, poly-2-hydroxyethylmethacrylate, copolymer of acrylic acid and ethylhexylacryalte, polymetahcryalate, polyalkylcynoacrylates: polyisobutylcynoacrylate, polyisohexylcyanoacrylate. Cellulose ethylenate.<br><br>Chitosan, which dissolves in weak aqueous acid solutions. |

| | **Cationic and Anionic** | **Non-Ionic** |
|---|---|---|
| **Charge** | Aminodextran, chitosan, dimethylaminoethyldextran, and trimethylated chitosan are all **cations.**<br>Chitosan EDTA, CMC, CP, pectin, PAA, PC, sodium alginate, sodium CMC, and xanthan gum are other examples of **anionic** substances. | Hydroxyethyl starch, HPC, poly(ethylene oxide), PVA, PVP, scleroglucan. |
| Potential bioadhesive forces | **Covalent**<br>**Hydrogen bond**<br>**Electrostatic interaction** | Cyanoacrylate<br>Acrylates [hydroxylated methacrylate, poly(methacrylic acid)], CP, PC, PVA<br>Chitosan |

**New-Generation Mucoadhesive Polymers:**

You've named three different kinds of new-generation mucoadhesive polymers: "Lactin," "Thiolated," and "Polyox." These represent certain groups or classes of mucoadhesive polymers, each with particular uses and characteristics.(Lehr, C. M. 2000)

***1. Lactin***

Type: In the context of mucoadhesive polymers, the name lactin is not frequently used. You might be referring to a particular polymer, a lactose or lactulose derivative, or both. To describe the characteristics and uses of a certain polymer or chemical in relation to mucoadhesion, it would be required to provide more detailed information.

***2. Thioloated Polymers***

Type: Mucoadhesive polymers that include thiol (sulfhydryl) groups are known as thiolated polymers. They are frequently synthetic polymers that have had thiol groups added to them.Thiol groups in thiolated polymers are capable of forming covalent connections with mucosal surfaces. Drug delivery is improved by the covalent connection, which increases adhesion and prolongs contact with the mucosa, Applications: Nasal, ocular, and buccal formulations all employ thiolated polymers in their drug delivery systems. They are made to enhance the polymer's mucoadhesive characteristics, enhancing the efficiency of medication administration.

### *3. Polyethylene Oxide, or Polyox*

Type: Polyox is a synthetic water-soluble polymer commonly referred to as polyethylene oxide (PEO) or polyethylene glycol (PEG)., Characteristics: Although Polyox is employed in many drug delivery and medicinal applications, it is not often thought of as a mucoadhesive polymer. It has regulated drug release capabilities and is hydrophilic and water-soluble. Because of how well it dissolves and gels, it is frequently utilised., Applications: Although polyox is not naturally mucoadhesive, it may be added to formulations to alter the kinetics of drug release and improve the stability of drug delivery systems.(Chen, Y. S. *et al.* 1984)

### **Mucoadhesive Buccal Dosage Forms:**

Buccal Mucoadhesive dosage forms cling to the oral cavity's inner cheek lining. Some drugs benefit from avoiding the gastrointestinal tract and liver with these dose formulations. They cross the mucosal membrane to deliver drugs or active ingredients.(Weinberg, D. S. *et al.*, 1988) Here some essentials about buccal Mucoadhesive dose forms Medications with limited oral bioavailability, rapid liver metabolism, or stomach acid sensitivity taken in this way. They deliver drugs directly to the bloodstream and the term "Mucoadhesive" refers to a dose form's ability to adhere to the buccal mucous membranes, and their dosage forms are buccal tablets, buccal films, buccal gels, buccal patches, and buccal microspheres. For the administration Put the buccal Mucoadhesive dosage form in the patient's mouth, usually on the inner cheek, and let it stick & release.(Harris, D. *et al.*, 1992)

### ***Advantages***

1. Rapid commencement.
2. Avoids First-Pass Metabolism
3. Avoids Gastric Degradation

**General Considerations in Designing Dosage Forms**

When designing dose forms, such as physiological, pathological, pharmacological, and pharmaceutical issues. The following important factors:(Hillery, A. M., *et al.*, 2001)

***A. Biological Considerations***

1. ***Route of Administration*:**Consider physiological effects of the selected administration route. Oral medications must withstand the stomach's acidity, whereas intravenous pharmaceuticals reach the blood instantaneously.
2. ***GI Transit:***Understanding gastrointestinal transit physiology affects oral drug absorption. Create time-resistant dose forms that provide the correct amount of medicine.
3. ***Drug Absorption:***Consider efflux transporters and stomach pH variations throughout the tract when assessing medication absorption.
4. ***First-Pass Metabolism:***Consider the first-pass effect, where medicines are metabolized in the liver before being disseminated. This may impact medication bioavailability.
5. ***Metabolism & elimination:***Understanding the drug's metabolism and excretion can help you create dosage forms. Certain drugs must be released continuously to maintain therapeutic levels.

***B. Pathological features***

1. ***Disease State:***Consider the treated sickness. Some illnesses need immediate treatment, while others need continual medicine supply.
2. ***Tissue Targeting*:**To optimize drug distribution to disease-damaged organs and tissues, the dosage form should be designed
3. ***Pathological Changes*:**Some diseases alter physiological factors like pH or blood flow, which might affect medication absorption and distribution. Change the dosage form to reflect these changes.

***C. Pharmaceutical Considerations***

1. ***Properties of drug:*** Understanding the drug's pharmacokinetic profile, which includes elements like half-life, peak concentration, and therapeutic range, is important. The dose form's release profile is influenced by this information.

2. ***Pharmacodynamics:*** Take into account the drug's therapeutic impact and mode of action. The medicine should be administered in a way by the dosage form that maximises its pharmacological action.
3. ***Dosage form:*** Design the dosage form to obtain the intended dose-response relationship in order to ensure that the therapeutic effect is attained within a range that is both safe and effective.
4. ***Unwanted Effects:*** By enhancing medication release and pharmacokinetics, minimise unwanted effects. For instance, sustained-release formulations can lessen negative effects and peak concentrations. (de Boer, A. G. *et al.,* 1990)

***D. Aspects of pharmaceuticals***

1. ***Drug property:***Drug characteristics should be taken into account while formulating and manufacturing decisions since they affect the drug's solubility, stability, and particle size.
2. ***Excipient Selection:*** Pick excipients that work well with the medicine and the dosage form you have in mind. Binders, fillers, disintegrants, and lubricants are a few examples of these.
3. ***Dosage form*:**Depending on the characteristics of the medicine and the patient, choose the best dose form (such as a tablet, pill, suspension, or transdermal patch).(Singh, J. *et al.,* 1989)
4. 
5. ***Stability*:**Make that the dosage form is stable for the course of its shelf life. It is necessary to handle issues like chemical deterioration and moisture sensitivity.
6. ***Regulatory Compliance*:** Verify that the dosage form conforms with all applicable laws, regulations, and good manufacturing practises (GMP).
7. ***Packaging and labeling*:**Develop suitable packaging and labelling to safeguard the dose form, offer crystal-clear patient instructions, and ensure product integrity.(Singh, J. *et al.,* 1989)

**Approaches to the Use of Mucoadhesive Formulations:**

1. ***Adhesion to mucosal surfaces:*** The oral cavity's mucosal surfaces are capable of being adhered to by mucoadhesive polymers. Maintaining drug contact with the mucosa and avoiding drug washout, or removal from the medication due to saliva and swallowing, depend on this adhesion. (Motwani, J. G, *et al.,* 1991)

2. ***Extended medication release***: The use of Mucoadhesive polymers aids in regulating and prolonging the release of pharmaceuticals. Over time, the medicine may be delivered more consistently and sustainably because to this regulated release.
3. ***Enhanced drug bioavailability:*** By preventing first-pass hepatic metabolism, buccal drug administration can increase the bioavailability of certain medications. This is especially crucial for medications with low oral bioavailability.(vanHoogdalem, E, *et al*., 1991)
4. ***Minimized systemic adverse effects:*** By delivering the medication locally through the buccal mucosa, it is possible to lessen the possibility of systemic side effects from other administration routes, such oral or intravenous delivery.
5. ***Enhanced patient compliance:*** By providing patients with a comfortable and non-invasive method of taking their prescriptions, buccal drug delivery systems may enhance patient compliance and adherence to treatment plans.

**Evaluation of Mucoadhesive Buccal Drug Delivery Systems:**

**1)** ***Experimental Methodologies for Buccal Absorption/Permeability Study:***

***A. In Vitro Methodologies:***

1. ***Ex Vivo Buccal Tissue Models*:** To assess drug penetration, remove buccal tissue, often from an animal or human source. These investigations are helpful in determining a compound's permeability and absorption. Because it is relevant, human tissue is chosen if it is accessible. Franz diffusion cells and Ussing chambers are common methods.
2. ***Cell Culture Models:*** Permeability can be evaluated using cultured buccal epithelial cell lines, such as TR146 and H413. These cell models are useful for predicting buccal absorption and assessing transport pathways.

***B. In Vivo Methods:***

1. ***Animal Studies:*** Testing the buccal absorption of substances by using animal models, such as rats or rabbits. These researches contribute to our understanding of pharmacokinetics and systemic exposure.
2. ***Human Clinical Trials:***The most pertinent information on buccal absorption may be obtained from clinical trials involving human participants. However, because of safety and ethical concerns, these studies are usually carried out later in the drug development process.

***C. Physical-chemical Examination:***

1. ***Solubility Studies*:** Knowing a drug's solubility in buccal fluids might help determine how well it may be absorbed.

2. ***Permeability Assays:*** To determine the permeability of medications and substances, methods such as the Caco-2 cell test or the PAMPA (Parallel Artificial Membrane Permeability test) are used.

***D. Research on Pharmacokinetics:***

1. ***Saliva sampling:*** Tracking medication concentrations in saliva over time to evaluate the kinetics and absorption of the agent.
2. ***Blood Sampling:*** After a drug is administered buccaly, blood samples are taken to assess pharmacokinetic parameters and drug concentrations.(vanHoogdalem, E, *et al*., 1991)

**E.** ***Techniques to Study Mucoadhesive Strength***

1. ***Tensile testing:*** In this technique, a mucoadhesive formulation is attached to a probe, and the force needed to separate it from the mucosal tissue is measured. It offers numerical information about the degree of adherence. (Singh, J. *et al.*, 1989)
2. ***Texture Analyzer:*** A mucoadhesive formulation in the oral cavity can be subjected to mechanical stresses that can be replicated using a texture analyzer. It gauges characteristics like the maximum separation force and the work of adhesion.

3. ***In Vitro Mucoadhesion Testing:*** In vitro techniques use mucin-coated surfaces or excised buccal tissue from humans or animals. After applying the formulation to the surface, the force needed to separate it is calculated. Compared to in vivo research, these experiments are more regulated.
4. ***Rheological Methods:*** Rheological analyses can evaluate the mucoadhesive compositions' viscoelastic characteristics. The formulation's rheological behaviour can shed light on its sticky qualities.
5. ***Measurements of the Contact Angle:*** The wetting qualities of a mucoadhesive formulation droplet on a mucosal surface may be evaluated by measuring the contact angle of the droplet. Good wetting and adhesion potential are indicated by a low contact angle.
6. ***Biological Models:*** In vivo investigations in animal models or human clinical trials might yield important insights into a formulation's mucoadhesive characteristics in a physiological context. However, the utilisation of human trials may be restricted due to ethical and legal issues.
7. ***Peel Test:*** This test involves applying a formulation to a mucosal surface, followed by the attachment of a strip of material (such as a piece of adhesive tape) to the formulation. It is assessed how much force is needed to remove the strip from the mucosa.
8. ***Studies on Swelling:*** Measuring how much a mucoadhesive formulation swells when it comes into touch with mucosal surfaces might reveal information about its adhesion characteristics.

**Conclusion:**

Drug delivery technologies that promote patient compliance and convenience are essential in today's healthcare setting. Thus, efforts are underway to create innovative dosage forms to meet patients' growing need for more accessible remedies. Oral mucosal delivery helps the public beyond those with swallowing difficulties. Mucoadhesive dose forms reduce enzymatic activity, are cost-effective, improve patient adherence, and are easy to administer and remove. Mucoadhesive polymers prolong medication activity at the delivery site and prevent early drug metabolism in the gastrointestinal system and liver, improving treatment effectiveness. Several in vitro and in vivo methods can evaluate mucoadhesive drug delivery systems. Buccal drug administration can systemically distribute ineffective oral drugs, making it a non-invasive way to provide strong peptide and protein therapy. This makes its exploration intriguing. Researchers worldwide are improving buccal adhesive systems by adding pH modifiers, enzyme inhibitors, and permeation enhancers to increase oral medicine bioavailability. Despite advances in mucoadhesives, more has to be done. A multidisciplinary strategy is needed to overcome the challenges of using mucoadhesive buccal dosage forms to administer innovative and pre-existing medicines with local or systemic effects. More research is needed to validate these novel mucoadhesive formulations for treating localised and systemic diseases.

## Acknowledgements:

The writers appreciate Dr. Anand chaurasia, Dr. Dharmendra Rajput (MPU, Bhopal) encouragement of their creative endeavours. Dr. Naveen gupta Dean of Patel college of pharmacy, Madhyanchal Professional University (MPU), Bhopal, MP. India, has been very helpful to the authors, and they are very grateful to him.

## Conflict of interest:

There are no conflicting interests, as the authors have stated.

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