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An Overview on Buccal Drug Delivery System

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Abstract

Since the medication does not pass through the digestive system and therefore avoids the first-pass metabolism, buccal administration can provide better bioavailability and a faster onset of action for certain drugs as compared to oral administration. Buccal administration is a topical route of administration in which medications applied or retained in the buccal region (in the cheek) diffuse through the oral mucosa (tissues that line the mouth) and reach the bloodstream directly. Since the medication does not pass through the digestive system and therefore avoids the first-pass metabolism, buccal administration can provide better bioavailability and a faster onset of action for certain drugs as compared to oral administration. The present review presents various advantages, disadvantages, optimization, criteria for drug selection. The anatomy and physiology of buccal, dosage forms, factors affecting the absorption of drug from buccal cavity, absorption barriers, applications absorption enhancers and evaluation. This review also presents polymers in the buccal route of drug delivery.

Keywords: Buccal drug delivery system; BDDS, NDDS; Transmucosal drug delivery

Introduction

The buccal formulation is used to treat both local and systemic issues in the mouth, specifically between the upper gums and the cheek. Buccal mucosa lines the inner cheek and is used to treat local and systemic conditions in the mouth between the upper gums and cheek. Buccal drug delivery has higher patient acceptability than other non-oral routes of drug administration because it is more vascularized and easier to administer and remove dosage. In the harsh gastrointestinal environment, using the buccal route would result in extensive first-pass metabolism and drug degradation [1,2]. Passive diffusion into the lipoidal membrane is the primary mode of drug absorption through the buccal mucosa. After absorption, the drug is transported to the jugular vein, which then drains into the circulation, bypassing the liver and avoiding first-pass metabolism. Large, hydrophilic, and unstable proteins, oligonucleotides, and polysaccharides, as well as conventional small drug molecules, can be delivered via the buccal route. Buccal drug delivery is the administration of medication through the buccal mucosa of the oral cavity. The medication is placed between the gums and the cheek during buccal administration. Medications in the form of pills, films, or sprays are available, 1-3 cm^2 in size. It is recommended that you take 25 mg or less per day. Buccal delivery distribution takes 4-6 hours at the most [3,4] (Figure 1-3).

Advantages

- Administration is easy.
- It's simple to stop therapy.
- Allows for the long-term localization of a drug within the oral cavity.
- Can be easily administered to unconscious patients.
- Provides a good route for systemic delivery of drugs with a fast first-pass metabolism, resulting in higher bioavailability.
- It is possible to achieve a significant dose reduction, resulting in fewer dose-related side effects. This path can be used to administer drugs that are unstable in an acidic

environment and are killed by the enzymatic or alkaline environment of the intestine.

- Drugs with low oral bioavailability may be given more conveniently.
- Unlike the rectal and transdermal pathways, the presence of saliva guarantees a comparatively significant volume of water for substance dissolution.
- In this buccal drug delivery, the drug is easily absorbed by the body.
- This route can be used to administer drugs that are unstable in an acidic environment and are killed by the enzymatic or alkaline environment of the intestine.
- The buccal mucosa contains more blood vessels than the skin and has a higher permeability.

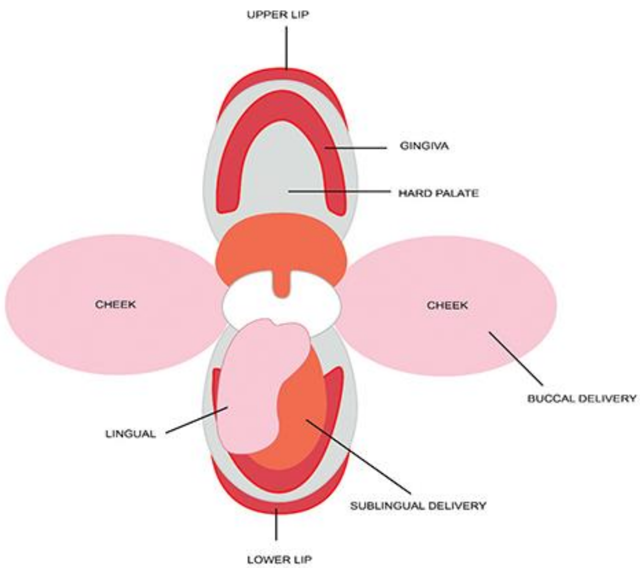

Figure 1: *The buccal area is the inner lining of the cheek and lip, representing about one third of the surface area of the oral cavity.*

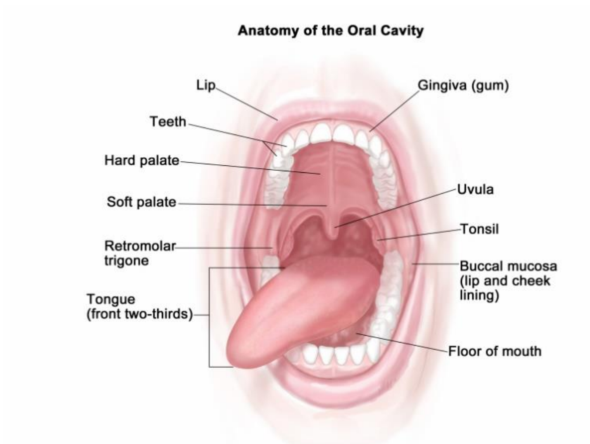

Figure 2: *Anatomy of oral cavity.*

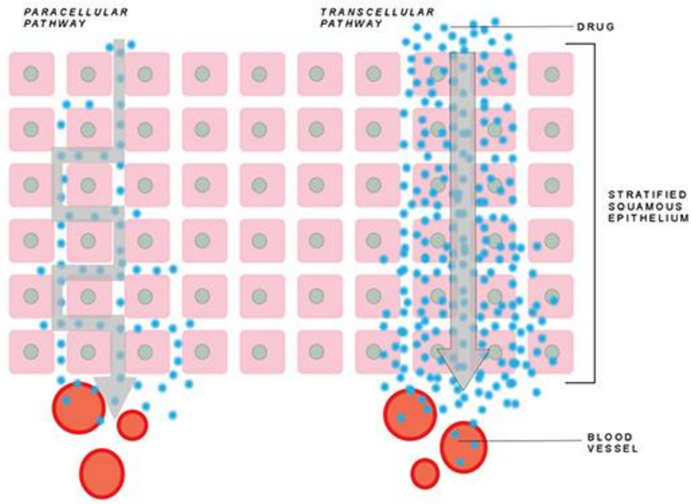

Figure 3*: Drug transport across the mucosa can be transcellular or paracellular.*

Disadvantages

- Drugs with a bitter or unpleasant taste or odor that irritate the oral mucosa are not permitted to be administered via this path.
- This path cannot be used to administer drugs that are unsafe at buccal pH.
- Only medications with low dosing criteria can be given out.
- Drugs may be swallowed with saliva, which negates the benefits of the buccal route.
- This path can only be used to administer medications that are absorbed by passive diffusion.
- The ability to eat and drink may be limited.

Limitations

- Mucus is continually being wiped away from the surfaces. It will ultimately wash the dosage type away from the application site.
- Since the mucous turnover rate varies from person to person, creating a dosage type is difficult.
- Due to disease, physiological factors, and other factors, the dosage form's adhesion rate in the body can vary from the proposed specification.
- Due to disease, physiological factors, and other factors, the dosage form's adhesion rate in the body can vary from the proposed specification.
- There are fewer strong mucoadhesive polymers that will meet all the requirements.
- Polyelectrolytes are mucoadhesive polymers. Slight variations in pH and mucus charge have a direct impact on the polymer's mucoadhesion properties.

- Drugs that cause tissue inflammation are not appropriate from this route of the drug delivery system.

Ideal Characteristics of Buccal Adhesive Drug Delivery System

- It should adhere to the attachment site for several hours.
- The drug should be distributed in a controlled manner.
- It can deliver medication to the mucosa in a unidirectional manner.
- It can make it easier for drugs to be absorbed in a faster rate and to a greater degree.
- It should not irritate or inconvenience the patient, and it should not prevent the patient from performing usual functions such as talking or drinking.

Uses of Buccal Delivery

- Local and systemic therapy may also be delivered through the mouth.
- Local treatment can be used to treat oral infections, dental caries, mouth ulcers, stomatitis, gingivitis, and other disorders.
- The buccal route is of particular interest when it comes to the systemic transmission of small molecules that are subjected to the first-pass metabolism.

Anatomy of Oral Mucosa

A layered squamous epithelium and a thicker lamina propria make up the oral mucosa. The stratum basale (base layer), stratum spinosum (prickle layer), stratum granulosum (granular layer), and stratum corneum (corneum layer) are the four layers that make up the epithelium of keratinized oral mucosa (keratinized layer). The two deep layers (basale and spinosum) remain the same in the nonkeratinized epithelium, but the outer layers are referred to as the intermediate and superficial layers. Depending on the area, the mouth epithelium may be nonkeratinized or keratinized. Nonkeratinized squamous epithelium covers the soft palate, inner lips, inner cheeks, the floor of the mouth, and the ventral surface of the tongue (Figure 2). Keratinized squamous epithelium can be found on the gingiva and hard palate, as well as parts of the tongue's dorsal surface [4,5]. Keratinocytes in the stratum granulosum divide into nonvital surface cells or squamous cells, resulting in the stratum corneum. As they move from the stratum basale, where progenitor cells are found, to the superficial surface, the cells terminally differentiate. Nonkeratinized epithelium, unlike keratinized epithelium, does not have keratinized superficial layers. In response to frictional or chemical trauma, the nonkeratinized epithelium can easily transform into keratinizing epithelium, resulting in hyperkeratinization. When the linea Alba appears, a white ridge of calloused tissue that extends horizontally at the stage where the maxillary and mandibular teeth come together and occlude, the buccal becomes hyperkeratinized. The tissue has all of the layers of orthokeratinized tissue, including the granular and keratin layers, and there is an abundance of keratin on the tissue's surface. Patients who clench or grit their teeth (bruxism) have a wider region of the buccal mucosa that becomes hyper keratinized than just the linea alba. This larger white, rough, raised lesion should be documented to account for the patient's parafunctional behavior in the dental care plan [6,7] (Figure 4).

Functions of Oral Mucosa

Actions like eating, drinking, and talking constantly put mechanical stress on the oral environment. Since the mouth is subjected to rapid changes in temperature and pH, it must be able to adapt rapidly. The only part of the body where taste can be detected in the mouth. The oral mucosa must perform a variety of functions as a result of its particular physiological characteristics. Protecting the underlying tissues from mechanical pressures, bacteria, and toxins in the mouth is one of the most essential functions of the oral mucosa. The hard palate and gingivae are closely bound by keratinized masticatory mucosa. It makes up one-quarter of all oral mucosa. It protects the underlying tissues by withstanding the loading forces of mastication. When chewing and talking, the mucosa covering the cheeks, lips, and mouth floor shifts to make room. It allows food to quickly move through the mouth during mastication while shielding the underlying tissues from trauma. It accounts for 60% of the oral mucosa [8,9]. Saliva is the most important secretion of the oral mucosa. Lubrication, pH buffering, and immunity are only a few of their functions. Saliva's lubricating and antimicrobial functions are primarily preserved by resting; saliva produces a flushing effect and aids in the removal of oral debris and noxious Saliva contains a variety of antimicrobial proteins that aid in the protection of the oral ecosystem against infectious agents. Salivary lysozyme, lactoferrin, salivary peroxidase, myeloperoxidase, and thiocyanate concentrations function as a defense mechanism. Three pairs of major salivary glands (parotid, submandibular, and sublingual) and several minor salivary glands produce saliva. It also helps in chemical digestion because it includes the enzyme amylase, which breaks down carbohydrates into sugars [9,10]. Sensation - The oral mucosa is highly sensitive to pain, touch, temperature, and taste because it is densely innervated. The trigeminal (V), facial (VII), glossopharyngeal (IX), and Vagus nerves are among the cranial nerves involved in mouth sensations (X). Specialized mucosa surrounds the dorsum of the tongue. It makes up about 15% of your oral mucosa and is made up of taste buds that allow you to taste stuff [9]. Swallowing, gagging, and hunger are all mouth-related reflexes. While not as important in humans, some animals, such as dogs, rely on panting to control their temperature because sweat glands are only found in their paws [9,11].

Environment of Buccal Mucosa

The oral cavity is distinguished by the presence of saliva, which is an intercellular ground fluid that covers the cells of the oral epithelia and is supplied by the salivary glands. The primary and minor salivary glands secrete mucus, which is contained in saliva [12].

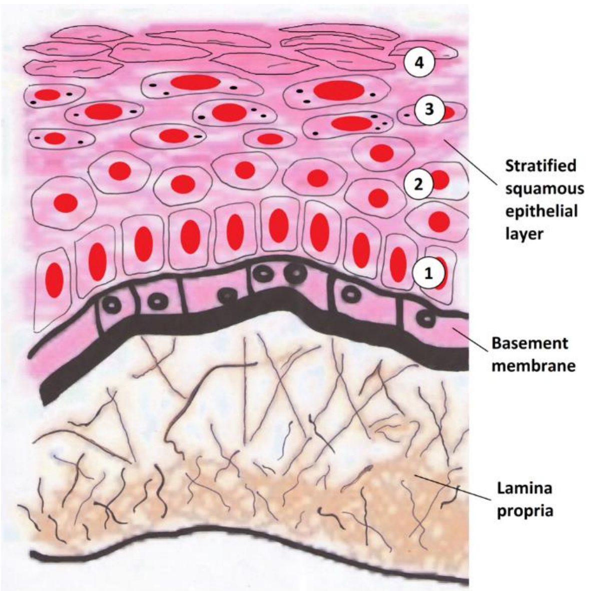

Figure 4*: Schematic illustration of the layers found in keratinized oral mucosa that include a deeper lamina propria and basement membrane in-between and superficial layers of strafied squamous epithelium that include from deepest to most superficial: 1: Stratum basale, 2: Stratum spinosum, 3: Stratum granulosum, 4: Stratum corneum*

Role of Saliva

- The mineralization and demineralization of tooth enamel is a continuous process [13].
- Both oral cavity tissues are protected by this fluid.
- Hydration takes the form of an oral mucosal dose.

Role of Mucus

- Bioadhesion
- Consists of proteins and carbohydrates
- Consists of proteins and carbohydrates
- Promotes cell-to-cell adhesion
- Provides lubrication

Design of Buccal Dosage Form [14] (Figure 5)

Matrix type: A Buccal patch with a matrix structure contains a combination of drug, adhesive, and additives. Bidirectional patches deliver the medication to the mucosa and the mouth [14] (Figure 5). Drug + Mucoadhesive Matrix

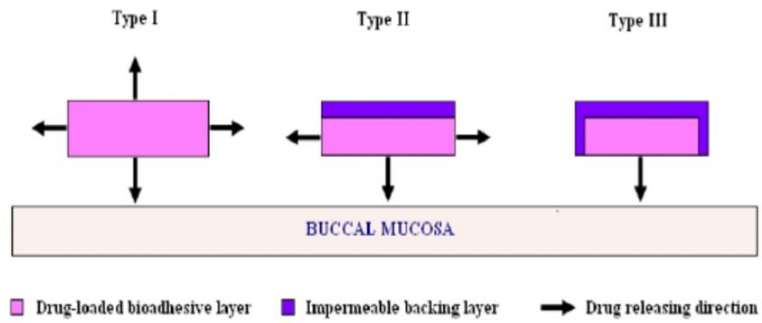

Figure 5*: Design of buccal mucoadhesive dosage forms.*

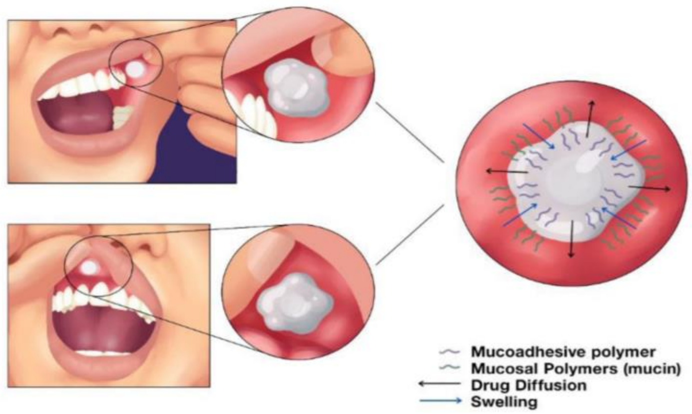

Figure 6: *Mucoadhesive Buccal Tablets.*

Reservoir type: A reservoir device buccal patch has a cavity for the medication and additives that is separate from the adhesive. Impermeable backing is used to guide the course of drug delivery, avoid drug loss, and minimize patch deformation and disintegration when in the mouth.

Buccal Drug Delivery and Mucoadhesivity

The device's mucoadhesion is important. Mucoadhesive materials bind to the mucin layer of a biological membrane to achieve systemic drug delivery and include tablets, patches, tapes, films, semi-solids, and powders [15].

Types of Buccal Mucoadhesive Dosage Forms [16]

Based on their geometry, there are three distinct groups.

Type - l (Multidirectional)

- Multidirectional release from a single-layer interface.
- A significant amount of medication is lost due to swallowing.

Type - 2 (Bi-layered)

- An impermeable backing layer is layered over the top.
- Preventing drugs from being swallowed.

Type - 3 (Unidirectional)

- Drug loss is minimal with this unidirectional release system.
- Achieved by applying a coating to all surfaces except the contact face.

Buccal Formulation

Buccal mucoadhesive tablets allow for drinking and speaking without causing severe pain, unlike conventional tablets. They soften, bind to the mucosa, and remain in place until full dissolution and/or release. These tablets may be used to treat the palate, the mucosa lining the jaw, and the region between the lip and the gum [17,18] (Figure 6).

Buccal Tablets

- Direct compression is the most common method for making these tablets, but wet granulation techniques may also be used [17,18].
- A multilayered tablet can be made by layering and compressing the ingredients in a specific order. Several newer approaches use tablets that melt at body temperature.
- The two bioadhesive buccal tablets "Bucastem" (Nitroglycerine) and "Suscard bucca" are two commercially available mucoadhesives.
- For example, nitroglycerin bioadhesive tablets are used to treat angina pectoris, while sumatriptan succinate buccal adhesive tablets are used to treat migraine and cluster headaches.

Buccal Patch/Film

- Buccal Patch/Film has three layers: an impermeable backing layer, a drug-containing reservoir layer, and a bioadhesive surface for mucosal attachment [17,18].
- There are two methods for producing adhesive patches: solvent casting and direct milling.
- The intermediate sheet on which patches are punched is prepared using the solvent casting process, which involves casting a drug and polymer solution onto a backing layer sheet and then allowing the solvents to evaporate.
- An impermeable backing layer can be added to prevent drug leakage and minimize deformation and disintegration of the device during the application phase in the direct milling method, where formulation constituents are homogeneously blended and compressed to the desired thickness, and patches of predetermined size and shape are then cut or punched out to monitor the direction of drug release and avoid drug leakage.
- For example, isosorbide dinitrate is produced and characterized as a unidirectional erodible buccal film to improve bioavailability. b) Salbutamol sulfate and terbutaline sulfate buccal film for asthma care. c) Clindamycin mucoadhesive film for pyorrhea therapy.

Buccal Gel/Ointment

- These semisolid dosage types such as buccal gel/ointment have the benefit of quick dispersion in the oral mucosa.
- To solve the issue, bioadhesive formulations were used.
- Some bioadhesive polymers undergo a phase shift from liquid to semisolid, increasing viscosity and allowing for sustained and regulated drug release.

Evaluation of Buccal Tablets [19-21]

- One of the measurement criteria in determining the residence time.
- Research on permeation.
- Swelling study
- Research the release rate.
- Toxicity and irritability study.
- Quantification of Bioadhesion
- Endurance Material Uniformity in Folding
- Surface pH: 1 percent agar solution for 2 hours and 1 minute of equilibrium

List of Drugs Delivered *via* Buccal Route

Acyclovir, Carbamazepine, Cetyl Pyridinium Chloride, Chitosan, Chlorpheniramine maleate, Chlorhexidine diacetate, Diclofenac sodium, Diltiazem Hydrochloride, Glucagon-like peptide (GLP)-1, Ergotamine tartrate, Flurbiprofen, Fluoride, Melatonin, Metronidazole, Morphine sulphate Nalbuphine, Nicotine, Nifedipine, Omeprazole, Piroxicam, Pindolol, Propranolol, Propolis, Rh EFG (Recombinant human epidermal growth factor), Sodium fluoride, Salmon calcitonin [22].

Product

- Oral bioadhesive formulation: Corlan – hydrocortisone succinate, Bonjela – Hypromellose, Daktarin – miconazole, Corsodyl – chlorohexidine [23]
- Buccal mucosa formulation: Buccastem –nausea, vomiting, vertigo, Suscard- angina

Conclusion

Buccal drug delivery is a non-invasive option for potent peptides and potential protein drug molecules, as well as systemic delivery of drugs that are ineffective when taken orally. We conclude that it is critical to not only create new drugs but also to refine the various routes of administration to maximize efficiency while minimizing side effects. The buccal mucosa has several benefits when it comes to managed drug delivery over long periods of time. The first-pass metabolism in the liver and pre-systemic clearance in the gastrointestinal tract are avoided since the mucosa is well supplied with both vascular and lymphatic drainage.

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