International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Buccal Drug Delivery Systems for Enhanced Management of Aphthous Ulcers: A Comprehensive Review of Formulation Strategies and Therapeutic Outcomes

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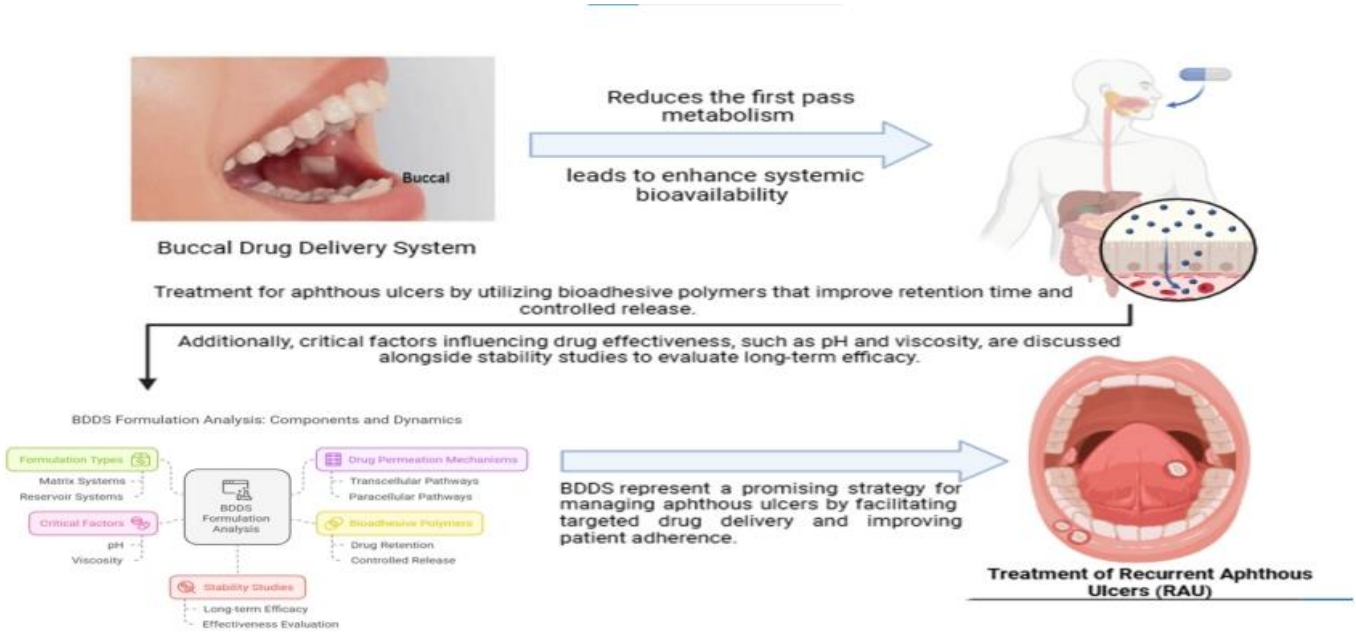
ABSTRACT



ABSTRACT

Background: Buccal drug delivery systems (BDDS) present a novel approach to enhance systemic bioavailability while circumventing first-pass metabolism. This method is especially beneficial for conditions like aphthous ulcers (canker sores), which significantly impact a patient's quality of life due to their painful nature.

Objective: To evaluate the efficacy of BDDS in managing aphthous ulcers by analyzing their formulation strategies and mechanisms of drug delivery.

Aim: The aim of this study is to highlight the advantages and methodologies of BDDS in providing localized treatment for canker sores, while ensuring improved drug absorption and patient comfort.
Materials and Methodology: The review encompasses an analysis of various BDDS formulation types, including matrix and reservoir systems. It examines the mechanisms of drug permeation, focusing on transcellular and paracellular pathways. The study also assesses the role of bioadhesive polymers in prolonging drug retention and ensuring controlled release. Additionally, critical factors influencing drug effectiveness, such as pH and viscosity, are discussed alongside stability studies to evaluate long-term efficacy.
Results: The findings demonstrate that BDDS significantly enhance localized drug treatment for aphthous ulcers by utilizing bioadhesive polymers that improve retention time and controlled release. These systems effectively address discomfort and improve therapeutic outcomes.
Conclusion: BDDS represent a promising strategy for managing aphthous ulcers by facilitating targeted drug delivery and improving patient adherence. Continued advancements in formulation techniques and a better understanding of their mechanisms can lead to tailored therapeutic solutions, effectively addressing the multifactorial triggers of canker sores.

Keywords: Buccal drug delivery, bioadhesive polymer, Buccal Dosage Form, Recurrent Aphthous Ulcers (RAU), Evaluation BDDS.

1. INTRODUCTION

1.1 Buccal Drug Delivery System:

The administration of medications through the buccal mucosa, the inside lining of the cheek, is known as the buccal drug delivery system. Because of its many benefits, this approach has drawn interest in pharmaceutical research as an alternative to topical, parenteral, or oral drug delivery. This system's primary characteristic is that medications enter the circulation directly through the buccal mucosa, avoiding the liver and digestive tract (first-pass metabolism). This can be particularly helpful for medications that are not well absorbed when taken orally or that are significantly broken down in the liver or gastrointestinal system [1].

1.1.1 The Buccal Drug Delivery System's salient features include:

Targeted Drug Absorption: Because of the buccal mucosa's high vascularization, medications can enter the bloodstream directly.
Avoidance of First-Pass Metabolism: Unlike oral delivery, medicines can retain better bioavailability by avoiding the liver and gastrointestinal system.
Usability: Compared to injections or intravenous administration, buccal distribution is frequently more pleasant for patients and can be non-invasive.
Fast Onset of Action: When pharmaceuticals are taken buccally, they can reach the circulation more quickly, resulting in faster therapeutic effects. This is especially true for medications that require immediate action, such as pain relievers or emergency therapies.
Localized and Systemic Delivery: The buccal system can be utilized to treat chronic disorders as well as localized conditions like oral mucosal infections [2].

1.1.2 Advantages and Disadvantages of Buccal Drug Delivery:

Advantages
Better Bioavailability: By avoiding the harsh conditions of the stomach and liver, medications are

more readily absorbed and degrade less quickly.

Convenience: By doing away with the need to swallow injections or tablets, it may increase patient compliance.

Control over Drug Release: Treatment plans may be made more flexible using buccal systems that can be made to release drugs immediately, gradually, or under control.

Decreased Side Effects: Side effects from high systemic concentrations can be reduced by offering a more direct and regulated delivery method.

Disadvantages

Drug Solubility and Size: Only specific medications that possess the right solubility and molecular size can be administered buccal.

Patient Comfort: The placement of a pill, patch, or film in the mouth may cause discomfort for certain individuals.

Local Irritation: Extended use of some formulations may cause mucosal lining irritation or injury. [3].

1.1.3 Anatomy and Physiology of Buccal route.

Both the patient and the physician believe that taking medicine orally is the most effective method. According to our current knowledge of the physiological and biochemical aspects of ingestion and metabolism, many medications cannot be efficiently delivered orally. This is because medications frequently have substantial pre-systemic clearance, preventing the formation of a relationship among membrane permeability, absorption, and bioavailability. Because of their unique benefits for systemic drug delivery compared to the traditional oral route, mucosal layers (nasal, vaginal, oral cavity, and rectal) are frequently considered as potential sites for drug administration. These advantages include the avoidance of presystemic clearance in the gastrointestinal tract and improved absorption and bioavailability as a result of a potential hepatic bypass effect [1].

Oral Mucosa: The basement membrane, connective tissue, and epithelium make up the oral mucosa. Squamous epithelium that is stratified and coated with mucus makes up the uppermost layer of the oral mucosa. The epithelium contains 40–50 cell layers at most. Cells may move more easily in relation to one another because the oral mucosa is sticky and lubricating. Drug delivery has been applied to the palate, lingual region, buccal cavity, and gingival area. As is evident, the most common method of administering medicine is the buccal route. The best site for medication administration is the buccal mucosa, which is physically located between the cheek and the gum [4]. Here in Figure No. 1 Anatomy of Buccal Mucosa Is Given Below and Also Figure No. 2 Inner Layer of Buccal Mucosa with different layers.

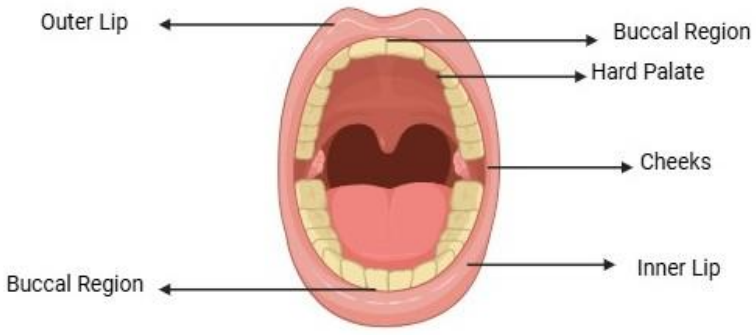


Figure 1: Anatomy of Buccal Mucosa [4]

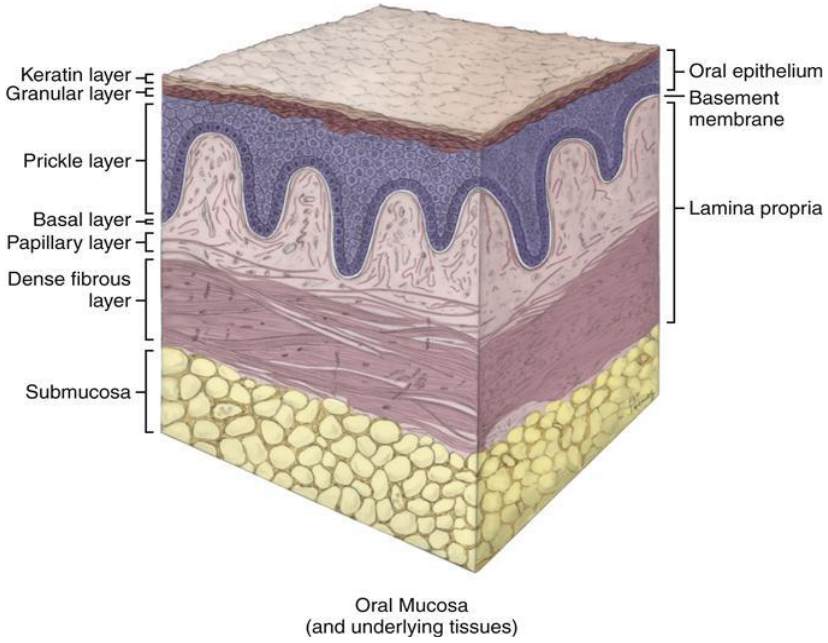


Figure 2: Inner Layer of Buccal Mucosa [4]

Table 1: Oral Cavity Composition for Permeability Enhancer Mechanism [1]

S. No.	Oral Physiology and Functions	Thickness	Enhancing Drug Permeability Mechanism
1.	Epithelium layer-The layer of the epithelium.	500 to 800µm	As an anionic surfactant, sodium lauryl sulphate may be used to expand the protective layer's pores. It is a cation, cetyl pyridinium chloride. Non-ionic compounds like Poloxamer, Brij, Span, and Myrj.
2.	Basement membrane-The basement membrane forms a distinct layer between the connective layer and the epithelium. provides the epithelial layer with mechanical support by making it easier for the epithelium to adhere to connective tissue.	1 to 2µm	Anionic polymers, chelators, cyclodextrins, and surfactants can all be used to increase drug permeability. Or cationic polymers to resist Ca^{+} ions and provide a negative charge on the mucosal surface.
3.	**Mucus:** A gel-like secretion that was clear and persistent; composition **Water:** 95–99% Mucin, a water-insoluble glycoprotein, makes up 1-5% of	500–600 µm of buccal (nonkeratinized) with 2.40 - 0.97 milliliters per minute per	Bile salts like sodium glycocholate, sodium tauro cholate, and sodium tauro deoxycholate, fatty acids like oleic acid, caprylic acid, and lauric acid, cyclodextrin,

	proteins, enzymes, electrolytes, and nucleic acids. **Role**: The viscoelastic hydrogel's function is to act as a barrier between the environment and the cell.	centimeter for sublingual (nonkeratinized) - 100 to 200 µm 200 µm gingival (keratinized) with 1.47 ml/min/cm^2 and 250 µm palatinal (keratinized) with 0.89 ml/min/cm^2 Viscosity ranges from 1.05 to 1.29 cP.	chelator (ethylenediaminetetraacetic acid), sodium salicylate, and methyl ethyl ketone, as well as anionic and cationic surfactants, will either make the phospholipid domain more fluid. Drug Permeation enhancement mechanism: by augmenting the BDDS with bile salt and fatty acids, will either improve the fluidity of phospholipid domains.
4.	**Saliva:** Saliva helps in swallowing by moistening food, which starts the digestive process. Salivary amylase, an enzyme found in it, starts the process of breaking down carbs into simpler sugars. The first stage of starch digestion in the mouth depends on this enzymatic activity.	Saliva thickness differs depending on the area of the mouth, from the back of the tongue to the hard palate, which is 0.01 mm thick.	Surfactants: These can facilitate medication penetration by lowering the mucosal barrier's surface tension. Fatty acids, like lauric acid, have the capacity to damage cell membranes and make drugs more permeable. One biopolymer that might improve mucosal membrane permeability is chitosan. Cyclodextrins can improve a drug's solubility.

1.2 Mucoadhesive & Bioadhesive:

In the pharmaceutical and biomedical sciences, mucoadhesive and bioadhesive materials are essential ideas, especially for tissue engineering, wound healing, and drug delivery systems. Despite their frequent interchange ability, these names have varied meanings and uses depending on how well they adhere to various biological surfaces. Materials that particularly stick to mucosal surfaces-like the lining of the mouth, gastrointestinal system, nasal cavity, eyes, or other mucosal membranes-are known as mucoadhesive materials. Glycoproteins, water, and other secretions make up the mucus layer that coats the mucosal surfaces.

Bioadhesive materials refer to those that adhere to any biological tissue or surface, not limited to mucosal layers. These materials can form bonds with a wide variety of biological tissues such as skin, bone, and other soft tissues [5].

Table 2: Types of Bioadhesive & Mucoadhesive Polymers

Types	Examples	Reference
Natural and Modified natural Polymers	Agarose,Chitosan,Gelatin,Pectin,Sodium aliginate,CMc,NaCMCHPc,HPMC,Methyl Cellulose	6
Synthetic	Carbopol,Polycarbpphil,Polyacrilic acid,Polyacrylates	7
Cationic & Anionic	Aminodextrain,Chitosan,Chitosan EDTA,Dimethylaminoethyldextran	8
Thiolated Polymers	Thiolated CTS Thiolated PAA	9

1.2.1 Bio-adhesion Theories:

It is simple to understand the theoretical polymer-polymer adhesion. Expanded to explain that how polymeric materials with biological surfaces adhere to one another. The electronic, adsorption, wetting, diffusion, and fracture theories are among the pertinent theories.

Electronics Theory -The electrical theory, electron transfer is probably going to occur on A double layer of electrical charge will form at the bioadhesive interface as a result of contact between the bioadhesive polymer and the glycoproteinic network, which have distinct electronicst.

Adsorption Theory- bioadhesive systems adhere to tissue because of Vander walls, hydrogen bonding, and related forces.

Wetting Theory- Intimate molecular contact is a pre - requisite for development of strong adhesive bond, requiring examination of the wetting equilibrium and dynamic behavior of the bioadhesive candidate material with the mucus. Some important characteristic for liquid bioadhessive materials include I. A zero or near zero contact angle. II. A relatively low viscosity and III. An intimate contact that exclude air entrapment. The specific work of adhesion between bioadhesive controlled release system and the tissue is equal to the sum of the two surface tensions and less than the interfacial tension.

Diffusion Theory-A sufficiently deep layer of chains may form as a result of the interpenetration of polymer and mucus chains. The diffusion mechanism is the intimate contact of two polymers or two pieces of the same polymer. During chain interpenetration, the molecules of the polymer and the dangling chains of the glycoproteinic network make intimate contact [71].

Dehydration Theory-Water removal's function in the adhesion process between bioadhesive materials and biological tissues is the main focus of the dehydration bioadhesive hypothesis. Understanding how some bioadhesive systems work well in wet environments—like the human body—is made easier with the help of this hypothesis.

Mechanical Theory:- The physical interlocking of sticky materials with biological tissue surfaces is how the mechanical bioadhesion hypothesis explains the adhesion process. The significance of surface roughness and texture in improving adhesion is emphasized by this hypothesis [10]. In Figure No. 3 Different Bioadhesion theories are explained with Diagram.

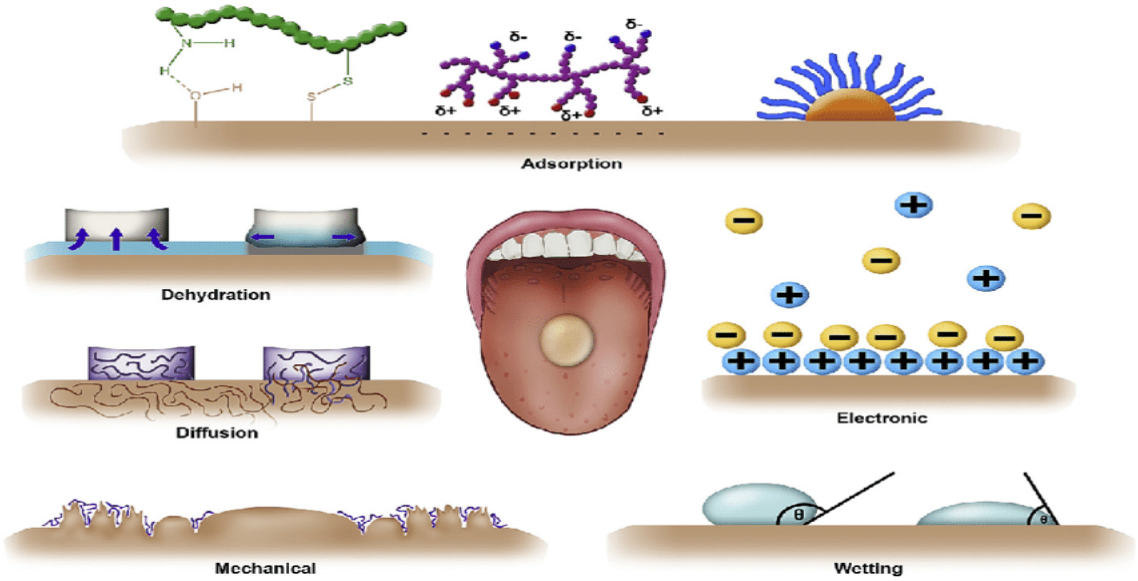


Figure 3: Diagram of Bioadhesive Theories [10]

1.3 Mechanism and formulation of Buccal drug delivery system.

Drugs are administered via the buccal mucosa, the cheek lining, in a process known as buccal drug delivery. Avoiding first-pass metabolism, increasing systemic bioavailability, and offering a practical way to self-medicate are just a few benefits of this strategy. There are two main methods that drugs are transported through the buccal mucosa:

Transcellular Pathway: In this method, the medication travels through the buccal mucosa's cells. It is frequently applied to lipophilic medications that readily permeate the lipid bilayer of cell membranes. **The paracellular route**: which is better suited for hydrophilic medicines, permits medications to move across cells. The degree of medication penetration may vary depending on how well the cells' tight connections hold together.

1.3.1 Matrix type: The purpose of matrix systems in buccal drug administration is to regulate the release and absorption of medications via the buccal mucosa. Bioadhesive polymers are frequently used in these systems to prolong the drug's retention at the absorption site. Because it influences the drug's release profile, bioavailability, and patient compliance, matrix type selection is essential.

1.3.2 Reservoir type: In buccal drug delivery, reservoir-type devices are specialized mechanisms intended to distribute medicine via the buccal mucosa, the inside lining of the cheeks, in a regulated manner. These systems are distinguished by having a separate reservoir or cavity that houses the medication and additives, apart from the layer of adhesive that binds the device to the buccal mucosa[11].

1.4 New Buccal Dosage Form

Based on their shape, buccal mucoadhesive dosage forms may be divided into three categories:

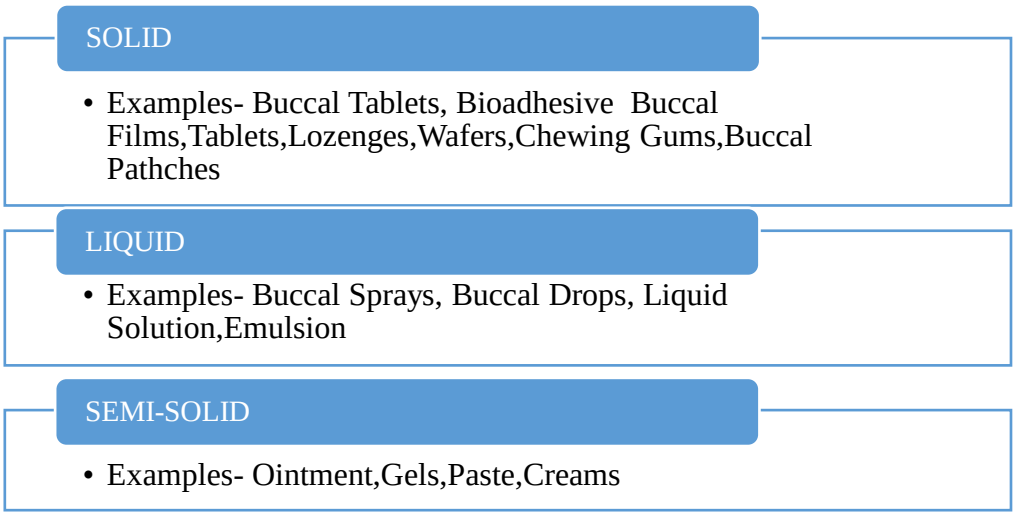
Types 1- interface just need one layer and have several directions. Drugs being released Issues with this dosage kind includes significant medication loss as a result of swallowing.

Type 2- devices; in order to construct a gadget with two layers, the drug-loaded bioadhesive layer is covered with an impermeable backing layer. This prevents drug leaking through the top of the dosage form. By solely delivering medication from the side nearest to the buccal mucosa, **Type 3-** reduces drug loss. Except for the area that comes into touch with the buccal mucosa, cover every surface of the dosage

form. The device should be made to maximize the swelling rate of the bioadhesive polymer for extended bioadhesion and controlled drug released.

Four groupings can be used to classify buccal adhesive dosage types in their most basic forms: Numerous buccal medication delivery systems have been created by scientists for both local and systemic effects. The articles' BDDS were split into their individual preparation forms, which were divided into liquid, solids, semisolids, and other materials [12].

1.4.1 Different types of Buccal Drug Formulations [13]



1.4.1.1 Types of Solid Buccal Drug Formulation: -

Solid buccal medication formulations come in a variety of forms, each with special qualities and uses.

Buccal Tablet- Small, flat, and frequently disc-shaped, buccal tablets are made to stick to the buccal mucosa. They release the medication gradually as they disintegrated buccal tablets offer regulated drug release, which can increase patient compliance and therapeutic efficacy [14].

Buccal Films- The buccal mucosa is adhered to via buccal films, which are thin, flexible strips. They are made to gradually disintegrate or erode, releasing the medication as they go. Buccal films can be more pleasant and less noticeable than tablets, and they have a greater surface area for medication absorption. They are especially appropriate for pediatric and elderly populations, as well as those who have trouble swallowing pills [15].

Buccal patches-Adhesive patches that adhere to the buccal mucosa are known as buccal patches. They may be made to release medications gradually. Buccal patches give a degree of control over drug delivery since they release medication continuously and may be taken off T if needed. When long-term medication administration is advantageous for chronic illnesses, they are frequently utilized [16].

Lozenges- Lozenges: These are solid dosage forms that dissolve slowly in the mouth, releasing the drug gradually. They are commonly used for delivering drugs for throat infections and for nicotine replacement therapy [17].

1.4.1.2 Types of Liquid Buccal Drug Formulation.

Solution: - Solutions: These are uniform concoctions in which the medication has been fully dissolved in a solvent. Because solutions are liquid and make it easier to reach the mucosal surface, they are simple to give and can offer quick medication absorption [18].

Suspension: - .Suspensions: The medication is dissolved in a liquid media in these formulations. For medications that are insoluble in water, suspensions are helpful because they enable the administration of insoluble medications in a liquid state [19].

Emulsion: - .A combination of two immiscible liquids, usually water and oil, in which one is dissolved in the other, is called an emulsion. Certain medications can be made more stable and soluble by emulsions, which make them appropriate for buccal administration [20].

Micro-Emulsion: - .Clear, thermodynamically stable mixes of water, oil, and surfactant often with a co-surfactant—are known as micro emulsions. They provide better medication absorption and solubilization properties than traditional emulsions [21].

Sprays: - The buccal mucosa is intended to receive a thin mist of medication solution or suspension from these formulations. Because sprays cover a big surface area, they are handy and can enable quick medication absorption [22].

1.4.1.3 Types of Semisolid Buccal Drug Formulation:

Gels- Gels are semi-solid structures made up of a liquid phase scattered across a network of three-dimensional polymers. Depending on the type of gel-forming agent being employed, they might be either hydrophilic or hydrophobic [23].

Ointment:- Ointments, which can be either water-soluble or water-insoluble, are viscous treatments with a significant oil content. They offer a barrier of protection to the mucosal surface and are usually oily [24].

Creams:- Creams are emulsions with a semi-solid consistency that combine phases of water and oil. They can be water-in-oil (W/O) or oil-in-water (O/W) emulsions [25].

Paste:- Pastes have a larger percentage of solid particles and are thicker than creams and ointments. Because of their adhesive qualities, they are often utilized [26].

1.5 Apthous ulcers (Canker Sores)

The contemporary word "aphtha," which denotes an uncomfortable or inflammatory state, comes from the ancient Greek word "aphthi," which means "burning." The establishment of this name honors Hippocrates, who first used these terms to describe these disorders. Recurrent aphthous ulceration (RAU), a painful inflammatory condition with an unknown origin, presents as one or more oral mucosal ulcerations. . Severe and frequently recurrent intraoral cavity inflammation affects between 5–25% of the population. Systemic medication is required for recurrent instances of aphthous ulcers once topical therapies such as corticosteroids have failed. Recurrent episodes of aphathous stomatitis sometimes referred to as canker sores, all medical professionals who come into touch with RAS benefit from reading this review as it integrates essential elements of the condition at the clinical, histological, and molecular levels. RAS manifests clinically as recurrent episodes of one or more painful ulcerations that are unrelated to systemic diseases. AS should be used to describe ulceration when there is no systemic disease present.

5.1 Reasons and Initiators

Immune System Malfunction: White blood cells attacking the oral mucosal cells are considered to be the cause of canker sores during an immune system malfunction [28].

Nutritional Deficiencies: Canker sores have been associated with deficiencies in specific vitamins and minerals, including iron, vitamin B12, and folate.

Hormonal Changes: Canker sores can be brought on by changes in hormones, especially during menstruation [29].

Stress: It is commonly known that emotional stress can cause canker sores. Research has indicated that people may encounter breakouts more frequently when they are under stress.

Food Sensitivities: Some people may get canker sores as a result of eating certain foods, particularly those that are hot or acidic [30].

Oral Injuries: Minor mouth injuries, including those brought on by dental procedures, excessive brushing, or unintentional bites, can result in the formation of canker sores.

Underlying Medical Conditions: Recurrent canker sores may be linked to long-term illnesses including HIV infection, inflammatory bowel disease, or celiac disease.

Hereditary Predisposition: Given that canker sores can run in families, there might be a hereditary component [31].

Immune System Weakness: People who have a compromised immune system are more susceptible to canker sores.

Lifestyle Factors: It has been proposed that smoking and inadequate dental hygiene may be risk factors [32].

1.5.2 Classification of Canker Sores

Minor Canker Sores:

Dimensions: Usually little than 1 centimeter across.

Features: These are the most prevalent kind and frequently manifest as tiny, round or oval ulcers with a red halo surrounding a white or yellow core. Usually, they go away without leaving any scars in one to two weeks. Minor canker sores can repeat many times a year, especially in younger people [33]. In Figure No. 4 Minor Canker sores are shown.

Figure 4: Minor Canker Sores [34]

Major Canker Sores:

Size: Usually more than 1 centimeter, larger than little canker sores.

Features: Severe canker sores can cause more agony and take weeks to cure, and they may leave scars behind. They might manifest as a single ulcer or, in certain situations, as many sores that arise at the same time. Because of their size and degree of pain, these sores can have a major effect on speaking and eating [34]. In figure No. 5 Major canker Sores are shown.

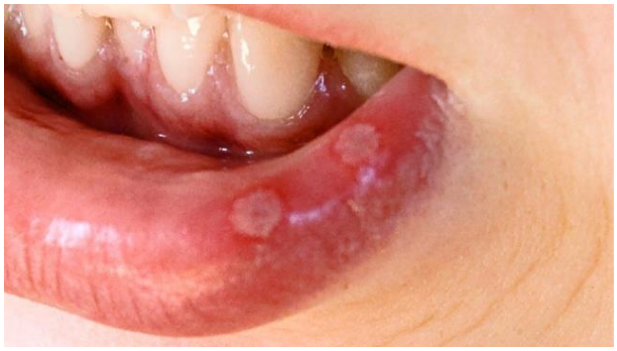


Figure 5: Major Canker Sores [34]

Herpetiform Canker sores:

Size: Extremely tiny, about 1-2 millimetres across

Features: The herpes virus is not the cause of herpetiform canker sores, despite their name. They can combine to produce bigger ulcers and can occasionally be found in clusters of 10 to 100. These sores are quite painful and often go away in a week or two [35]. In figure No.6 Canker sore that is Herpetiform are shown.

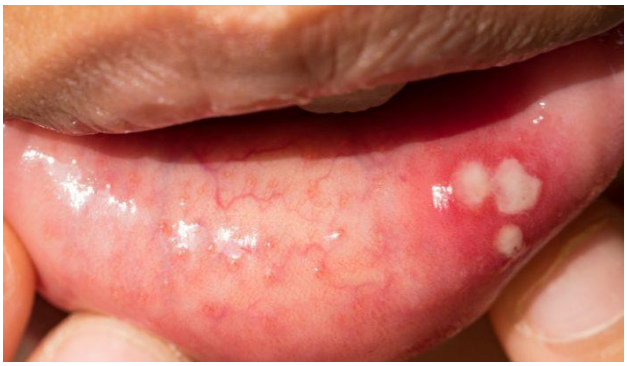


Figure 6: Canker Sores that are herpetiform [35]

1.5.3 The Biological Mechanism of Canker Sore Development

Environmental triggers, genetic variables, and immune system reactions interact intricately in the pathophysiology of canker sores. Among the principal biological mechanisms are:

1.5.3.1 Immune System Involvement.

Cell-Mediated Immune Response-Canker sores are primarily driven by a T cell-mediated immune response. The process begins when the immune system detects an antigen, which can be a foreign substance such as a protein, polysaccharide, lipid, or nucleic acid. This detection triggers an immune response involving various white blood cells, including neutrophils, lymphocytes, macrophages, and mast cells, which are recruited to the site of the antigen[36].

Cytokine Involvement- In people with RAS, pro-inflammatory cytokines such as TNF-α, IL-6, and IL-17 are increased. These cytokines aid in the recruitment and activation of immune cells at the ulcer site and contribute to the inflammatory process. Interleukin-17 (IL-17), a component of the Th17-type adaptive immune response, is essential for limiting tissue invasion and microbial proliferation. But in canker sores, this reaction may become dysregulated, resulting in tissue damage and excessive inflammation [37].

Toll-Like Receptors (TLRs) - A class of receptors known as TLRs is able to identify chemicals that come from infections. The TLR2 pathway exhibits aberrant activation in RAS, which might impact the induction of an aberrant Th1 immune response and hence contribute to the disease process [38].

Table 3: Different Routes of Administration of API & Polymer in which Dosage Form Used:

S.No	BDDS Formulation	Routes of administration	API & polymer	Ref.
1.	Buccal Film	Oral	Triamcinolone Acetonide, Pectin & Gellan Gum	41
2.	Buccal Tablet	Oral	Hydrocortisone Carbopol & HPMC	42
3.	Buccal Patches	Oral	Triamcinolone Acetonide Carbopol & HPMC	43
4.	Lozenges	Oral	Benzocaine Polyethylene Glycol	44
5.	Wafers	Oral	Lidocaine HPMC	45
6.	Chewing Gums	Oral	Benzocaine Gum Acacia,Carragenan	46
7.	Buccal Sprays	Oral	Fentanyl Carbopol,HPMC	47
8.	Buccal Drops	Oral	Midazolam Chitosan, Sodium Carboxy Methyl Cellulose	48
9.	Ointment	Oral	Chlorhexidine Carbopol,PEG,Gum Arabic,Aliginate	49
10.	Buccal Gel	Oral	Hyaluronic Acid Carbopol, PEG,Aliginate,HPMC	50
11	Adhesive Alginate	Oral	Sodium alginate adhesive	72
12	Oradisc	Oral	Collagen	**73**
13	Pellicle	Oral	Amlexanox 2mg	**74**

14	Solid (lozenges)	Oral	Nicotine Lozenges	**75**
15	solid (paste)	Oral	Licorice Paste	**76**
16	Liquid (mouthwash)	Oral	Alcohol-aqueous mouthwash with chlorhexidine gluconate	**77**

Table: Evaluation Parameters of Buccal Drug Delivery system [1].

S. no.	Characterization Parameter	Method Used	Instrument	Used For Dosage Form
1	Surface ph	Visual colour change	pH meter	Mucoadhesive tablet, Patch, tablet Films
2	Swelling index	Swelling of Tablet and patch in pH 6.4 phosphate buffer	Agar gel plates	Tablet films, wafers, Patches, films
3	Drug compatibility	Spectral analysis, Thermal analysis	DSC, XRD, FTIR	Films Tablets, Wafers, patches
4	Folding endurance	constant folding at the same point	Manually folded	Patches, Films
5	Thickness	Standard deviation	Electronic digital micrometer, vernier calipers, screw gauze	Films tablets, wafers, patches
6	Water absorption capacity test	Agar plate technique	desiccator	Patches or film
7	Mucoadhesive strength	Tensile strength	Texture analyzer	Films tablet, patches
8	In-vitro drug release	Beaker method; Rotating peddle method; Dissolution method	Kesary chein cell; Franz diffusion cell	Tablets, Microspheres, patches or films
9	Hardness	Crushing force	Monsanto hardness tester	Tablets, wafers

10	Friability	weighing	Roche friabilator	tablets
11	Drug content	Titration	UV spectrophotometer, RPHPLC	Tablets, patches or films
12	Flatness	Constriction	Vernier Calipers	Patches, films
13	Contact angle	Optical tensiometer	Optical tensiometer	Films
14	Bio-adhesion	Colloidal gold staining method, Florescence probe method	Dissolution cells	Patches, Films
15	Water vapour transmission rate	Dressing method	Ovens	Patches, Films
16	Drug entrapment	Assay	UV spectrophotometer	Films, Patches, Microspheres
17	Transparency	Transmittance	UV spectrophotometer	Films
18	Ex- vivo residence time (rt)	Disintegration test	Modified disintegration test apparatus	Patches, Films Tables
19	Percentage moisture loss	Gravimetry method	Desiccator	Patches, Films
20	Morphology	Microscopy	Scanning Electron Microscopy (SEM)	Tablets, Patches, film

Table 4: Patent List BDDS for RAU

Sr. No.	Formulation Details	Patent Number	Reference
1	Mucoadhesive Buccal Film (Trilaminate Film)	US4900552A	59
2	Solid nano particles (either alcohol-in-fluorocarbon microemulsions, liquid hydrocarbon-in-fluorocarbon microemulsions)	US7153525	60

3	Personalized 3D-Printed Buccal Tablets (3D-printing preparation method for tablet medicines through spraying medicaments on a matrix material)	CN105687153A	61
4	Mucoadhesive Buccal Film Having Dual Permeation Enhancer (statin-hydroxypropyl-beta-cyclodextrin inclusion complex and a statin-loaded mixed micelle composition)	US10709662B1	62
5	Sublingual and Buccal Film (Morphinan derivatives, e.g. morphine, codeine)	US9687454B2	63
6	Sublingual and Buccal Film (Buprenorphine/Naloxone Films)	US-10034833-B2	64
7	Transmucosal drug Delivery Devices(buprenorphine Drug)	US-9901539-B2	65
8	Orodispersible Film (Buprenorphine and Naloxone Drug)	US20150283067A1	66
9	Orodispersible Film (Araliaceae (Ginseng family), e.g. ivy, aralia, schefflera or tetrapanax)	US20170182105A1	67
10	Buccal Tablet (Dyclonine hydrochloride Drug)	US20110160634A1	68
11	Buccal Lozenges(lidocaine)	US4191750A	69
12	Buccal Lozenges Devices (Lactic Acid Solution)	US5389679A	70

CONCLUSION:

In conclusion, buccal drug delivery systems (BDDS) utilizing bioadhesive polymers have emerged as a promising approach for managing aphthous ulcers, also known as canker sores. BDDS offer targeted drug absorption and localized treatment, addressing the discomfort and improving therapeutic outcomes for patients. The use of bioadhesive polymers in buccal dosage forms ensures prolonged drug retention and controlled release, enhancing patient adherence and comfort. Continued advancements in formulation techniques and a deeper understanding of the mechanisms of buccal drug delivery hold the potential to provide tailored therapeutic solutions for addressing the multifactorial triggers of canker sores. For college students studying pharmaceutical sciences, exploring the developments in buccal drug delivery systems and bioadhesive polymer formulations can offer valuable insights into the innovative strategies for localized drug treatment.

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