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Newer insights in buccal drug delivery system: A comprehensive review

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Abstract
The Buccal Drug Delivery System (BDDS) has garnered significant attention in recent years as a non-invasive and effective method for systemic drug delivery. In particular, buccal patches offer numerous advantages, such as bypassing hepatic first-pass metabolism, enhancing bioavailability, ensuring ease of use, and improving patient compliance. Due to the rich vascularization of the buccal mucosa, these systems facilitate rapid drug absorption and onset of action. Advancements in BDDS are evident in the development of novel mucoadhesive polymers, nanoparticulate systems, enzyme inhibitors, and innovative drug delivery technologies, including 3D printing and thermos-sensitive patches. These advancements have markedly enhanced residence time, controlled release, and the overall effectiveness of buccal drug delivery. However, several challenges remain, such as limited permeability for larger molecules, enzymatic degradation, variability in saliva flow, and mucosal irritation. Furthermore, it underscores the existing limitations and proposes potential future directions, including personalized medicine and gene therapy through buccal administration. Overall, this review aims to provide valuable insights into the current state of buccal drug delivery, recent developments, and future opportunities within the buccal drug delivery system, thereby aiding in the design and development of more effective and patient-friendly pharmaceutical products.

Keywords: Buccal drug delivery system, buccal patch, mucoadhesive polymers, first-pass metabolism, oral mucosa

Introduction
A buccal drug delivery system refers to a technique for administering medications via the oral mucosa, particularly the inner surface of the cheeks. This method provides a practical alternative to conventional oral administration, enabling drugs to circumvent the gastrointestinal tract and evade first-pass metabolism, which may enhance bioavailability. This system is especially beneficial for medications that are unstable in the stomach's acidic environment or susceptible to degradation within the gastrointestinal tract [1-3].

The buccal route of drug delivery serves as a viable alternative among the various methods of drug administration. The oral route is arguably the most favored by patients. Within the oral mucosal cavity, the buccal region presents an appealing option for systemic drug delivery. Nevertheless, the oral administration of drugs is accompanied by certain drawbacks, such as hepatic first-pass metabolism and enzymatic degradation within the gastrointestinal (GI) tract, which hinder the oral administration of specific classes of drugs, particularly peptides and proteins. The buccal routes of drug delivery provide notable advantages over oral administration for systemic drug delivery. These benefits include the potential to bypass the first-pass effect and the avoidance of pre-systemic elimination within the GI tract, making the oral mucosal cavity a highly attractive and practical site for systemic drug delivery. Given the low patient compliance associated with rectal, vaginal, sublingual, and nasal drug delivery for controlled release, the buccal mucosa, characterized by its rich blood supply and relative permeability, stands out. The buccal mucosa lines the inner cheek, and buccal formulations are positioned in the mouth between the upper gingival (gums) and cheek to address both local and systemic conditions. The buccal route offers one of the promising pathways for typically large, hydrophilic, and unstable proteins, oligonucleotides, and polysaccharides, in addition to conventional small drug molecules [4-6].

Patents on buccal drug delivery

The true worth of any drug delivery system is determined by its innovation. The innovative characteristics of the drug delivery system or carrier are assessed based on the patents filed. These patents indicate both the progress made and the potential offered by the latest drug delivery systems. Recently, a significant number of patents have been published and approved concerning buccal drug delivery carrier systems [7-11].

Table 1: Status of the patents on buccal patches

S. No.	Patent No.	Applicant	Patent Buccal Patches	Details
	US5298256A	East Riding Laboratories	Desmopressin buccal patch composition	Desmopressin is combined with a matrix in a buccal patch designed to adhere to the oral mucosa, facilitating the release of desmopressin into the bloodstream via transmucosal absorption.
	WO1999032081A1	Orion Corporation	Transmucosal formulations of levosimendan	Levosimendan, or a suitable pharmaceutical salt of it, can be given transmucosally, particularly to the oral or nasal mucosa, for a patient. To effectively administer levosimendan to a patient using this method, it is essential to keep a source of levosimendan in contact with an intact mucous membrane for a considerable duration. Furthermore, the details of levosimendan's transmucosal formulations are provided.
	US20110160634A1	Coloplast AS	Canker sore patch	A treatment patch for canker sores consists of a mucoadhesive layer and a protective layer, with the protective layer featuring a pressure-sensitive adhesive layer.
	US20030124178A1	Halley Jaffrey.T	Soft, adherent, soluble oral patch	A hydrophilic polymer that remains liquid in the mouth at human body temperatures is integrated into a soft, adherent, and soluble oral patch designed for the delivery of topical medication. This polymer transitions into a gel at temperatures slightly lower than that of the human mouth. Oral patches feature a mesh-like structure that dissolves gradually in saliva while maintaining its solid form at human mouth temperatures. The network's pores contain both the hydrophilic polymer and a preferred medicament. The creation of the oral patch involves combining and hydrating the materials, heating them to just below boiling point, and subsequently cooling them to achieve a gel-like consistency.
	WO2015083181A3	Zim Laboratories Ltd.	water-soluble pharmaceutical film with enhanced stability	An Oral Thin Film designed to deliver an active ingredient for oral use, which remains moisture-stabilized and does not adhere or curl when subjected to 70% relative humidity at 25 °C for a duration ranging from 2 minutes to 2 hours, along with a method for its production. Additionally, a technique for creating Oral Thin Films is presented. The active component may consist of a pharmacological,nutraceutical, or cosmetic substance.

Recent advancements in buccal drug delivery

Recently, numerous researchers have been engaged in traditional drug design technology. However, the present situation is markedly different, as research is actively being conducted on innovative and improved drug delivery systems to mitigate adverse drug reactions and enhance patient compliance. Advanced drug delivery technologies have made it feasible to enhance both the bioavailability and safety of medications. Notably, advancements have been observed in the buccal drug delivery system in recent times [12-17].

Table 2: Recent progress in buccal drug administration

S. No.	Researchers (Year)	Advancement details
	Parmar and Solanki (2025) [12]	Buccal drug delivery presents a promising alternative to traditional oral administration, circumventing hepatic first-pass metabolism and gastric degradation that frequently restrict drug bioavailability. This review investigates the anatomical and physiological features of the buccal mucosa that facilitate drug absorption, analyzing essential formulation strategies such as Quality by Design (QbD) principles, the incorporation of mucoadhesive polymers, and the application of permeation enhancers. Additionally, the review emphasizes recent progress in buccal drug delivery systems, particularly focusing on nanotechnology-based methods for improving the delivery of small and macromolecules, as well as biologics. A thorough literature review illustrates the potential of buccal delivery to enhance therapeutic outcomes by utilizing the distinctive properties of the buccal mucosa and optimizing drug absorption through advanced formulation design and innovative technologies.
	Cheng *et al.*, 2025 [13]	With the swift advancement of buccal films (BFs), there has been a notable increase in the demand for materials that form films and the techniques used for their preparation. Cellulose ethers (CEs) possess advantageous characteristics, including efficient film formation, mucosal adhesion, and biocompatibility; consequently, they are predominantly utilized as film-forming materials, which are crucial for the fabrication of BFs. CE-based BFs, which are categorized as orodispersible and buccal mucoadhesive films, can be produced using methods such as solvent casting, inkjet printing, three-dimensional printing, electrospinning, and hot melt extrusion. Hydrophilic CE-based orodispersible films can quickly dissolve or disintegrate upon interaction with saliva, facilitating drug release. High-viscosity or hydrophobic CEs can act as protective layers for BFs, regulating the unidirectional release of drugs and reducing the impact of saliva and buccal movements. These mucoadhesive films can securely adhere to the buccal mucosa for an extended duration, thereby extending the drug release time and improving bioavailability. CEs are available in various types and grades, each exhibiting distinct rheological and physicomechanical properties, which also allow for tailored designs to meet the needs of specific patients. This review offers a comprehensive overview of CE-based BF technology, examines the challenges and future directions of this film, and highlights critical areas for scientific inquiry, such as the interactions of bioadhesive materials in buccal mucosal drug delivery. The aims of this review are to underscore the significance of their application in oral drug delivery and encourage the wider implementation of BF-based patient-centric dosing.
	Ahmad *et al.*, 2025 [14]	Both local and systemic medication delivery significantly benefit from the sublingual and buccal methods of administration. They have proven to be an effective alternative to the traditional oral route, especially in circumstances that necessitate a rapid onset of action. Through venous drainage to the superior vena cava, medications can swiftly and directly enter the systemic circulation. Consequently, they are advantageous for patients who experience difficulties in swallowing, as well as for drugs that are extensively metabolized by the liver or degraded within the gastrointestinal tract. Historically, medications administered via buccal and sublingual routes are available in three primary dosage forms: liquid (such as sprays and drops), semi-solid (such as gels), and solid (such as tablets, wafers, films, and patches). Physiological factors often affect traditional dosage forms, which can diminish the formulation's interaction with the mucosa and lead to unpredictable drug absorption. Numerous advancements in formulation development have been made to improve drug absorption and retention in the buccal and sublingual regions. This review will primarily focus on the

		physiological factors that influence buccal and sublingual drug delivery, as well as innovations in nanoparticulate drug delivery methods for sublingual and buccal administration. Additionally, it will address the clinical development pipeline, which encompasses formulations that have received approval and those currently undergoing clinical trials.
	Mauceri *et al*., 2025 [15]	Oral lichen planus (OLP) and recurrent aphthous stomatitis (RAS) are regarded as the most painful oral inflammatory conditions, exhibiting a high prevalence worldwide and significantly affecting patients' quality of life. In recent decades, researchers have been investigating mucoadhesive drug delivery systems (MDDS) to enhance the safety and efficacy of medications through optimized formulations that improve patient compliance while overcoming the drawbacks of semisolid products. Thirteen observational studies involving individuals suffering from OLP or RAS were analyzed. The lack of standardized therapies concerning MDDS, medication, and dosing regimens was emphasized. All MDDS provided various advantages, such as extended drug release, protection against mechanical irritation, and alleviation of pain and inflammation. MDDS enhanced patient adherence by reducing the frequency of daily applications and minimizing systemic side effects. Therefore, MDDS may offer a promising alternative for the treatment of both OLP and RAS, addressing significant limitations associated with conventional formulations.
	Lou *et al*., 2023 [16]	The oral route is the most favored method for both systemic and local drug administration. Nevertheless, the oral drug delivery system encounters the challenging physiological and physicochemical conditions of the gastrointestinal tract, which restricts the bioavailability and targeted design of the oral drug delivery system. Innovative pharmaceutical strategies, such as nanoparticulate formulations, biomimetic drug formulations, and microfabricated devices, have been investigated to enhance drug targeting and bioavailability. This review discusses the anatomical, biochemical, and physiological factors that affect drug delivery via the oral route, and it highlights recent advancements in both conventional and novel oral drug delivery methods aimed at improving drug bioavailability and targeting capabilities.
	Liu *et al*., 2025 [17]	Pharmacological treatment represents a vital domain in contemporary medicine, and enhancing its delivery mechanisms is of paramount importance. Conventional approaches are fundamentally constrained by first-pass metabolism, the potential for severe adverse effects, and issues related to patient adherence, which considerably limits the efficacy and applicability of pharmaceuticals. The delivery of drugs via the oral mucosa has emerged as a minimally invasive and effective strategy. The distinctive anatomical characteristics of the oral mucosa enable the swift absorption of medications into the systemic circulation, thereby yielding rapid therapeutic responses. Nevertheless, a complex oral microenvironment and the mucosal barrier hinder drug absorption. Biomaterials have emerged as a significant catalyst for the innovative advancement of oral therapeutics, due to their unique and superior properties. They are extensively utilized in the prevention, diagnosis, treatment, and rehabilitation of oral health conditions. This review examines the latest developments in biomaterial-assisted oral mucosal drug delivery systems, scrutinizing essential physiological factors and absorption obstacles that influence therapeutic efficacy. By concentrating on innovative material engineering techniques, it underscores notable advancements in prolonging drug retention time and enhancing delivery accuracy within the oral cavity. Additionally, the research highlights critical obstacles in translating these innovations from laboratory settings to clinical applications, stressing the necessity for solutions to close this gap.

Buccal drug delivery commercial aspect

The medication can be commercially administered via the buccal drug delivery system. This method offers numerous benefits, such as bypassing the gastrointestinal tract and hepatic portal system, facilitating easier drug administration, significantly reducing the likelihood of nausea and vomiting, and enhancing patient compliance by eliminating the pain associated with injections. It is particularly advantageous for unconscious or less cooperative patients, making this delivery system a preferred choice. Additionally, multiple drugs can be administered to patients using this approach [18-32].

Table 3: Drugs administered through buccal drug delivery system

S. No.	Drug	Polymer Used	Category
1.	Atenelol	Sodium alginate, carbapol 33	Anti-hypertensive
2.	Baclofen	NaMC, Na alginate and Methocel K15M	Anti-Inflammatory
3.	Carvedilol	HPMC K4M and CP 934P	Congestive Heart Failure
4.	Chlorhexidine diacetate	Chitosan and Na alginate	Antiseptic
5.	Diltiazem	NaCMC, HPMC, Na alginate and guar gum	Antihypertensive, Anti-Arrhythmic, Anti-Anginal
6.	Ergotamine tartarate	Carboxyvinyl and HPC	Migraine Or Cluster Headache
7.	Flurbiprofen	HPMC K15M, HEC, CP971 and Carbomer	Osteoarthritis And Rheumatoid Arthritis
8.	Isosorbide dinitrate	Carbopol 934P, PVP, Eudragit 100M	Anti-Anginal
9.	Metronidazole	CP 934P, HEC	Antibiotics
10.	Nicotine	CP 934 and HPC	stimulant in the brain
11.	Omeprazole	Na alginate, HPMC	Indigestion, heartburn, acid reflux
12.	Prednisolone	HPMC, CP 934 and NaCMC	Steroids
13.	Propranolol HCl	HPMC K4M, Xanthan gum, EC	Anti-hypertensive
14.	Salbutamol sulphate	HPMC K4M and EC	Anti-Asthamatic
15.	Tizanidine	CP 934, HPMC K4M, HPMC K15M	Muscle Relaxant

Conclusion

Buccal drug delivery offers numerous advantages, including ease of administration, accessibility and withdrawal, retention, high patient compliance, cost-effectiveness, and low enzymatic activity. This approach can be employed to circumvent first-pass metabolism in the liver, as well as pre-systemic clearance occurring in the gastrointestinal tract. This site is also considered suitable for a retentive device and is acceptable to any patient. Buccal drug administration holds the potential to serve as a practical and intriguing method for non-invasive delivery of potent peptides and protein therapeutic agents, as well as a means for systemic distribution of orally ineffective drugs. Mucoadhesive systems may become increasingly important in the development of new pharmaceuticals due to the significant influx of novel substances emerging from pharmacological research. Consequently, the buccal mucosa offers numerous benefits for long-term regulated drug administration, as well as a suitable environment for systemic distribution.

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