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Review Article

Mucoadhesive buccal films: A promising approach for Controlled Drug Delivery

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Abstract

Mucoadhesive buccal films have emerged as an advanced and patient-friendly controlled drug delivery system for both local and systemic therapy. These films are designed to adhere to the buccal mucosa and release the drug in a controlled manner, thereby improving therapeutic efficacy and patient compliance. Buccal drug delivery offers several advantages including avoidance of hepatic first-pass metabolism, protection from gastrointestinal degradation, rapid onset of action, and improved bioavailability. Due to these advantages, buccal films are increasingly explored for the delivery of various drugs, particularly those with poor oral bioavailability. Mucoadhesive buccal films are commonly prepared using natural and synthetic polymers such as Hydroxypropyl Methylcellulose (HPMC), Carbopol, Polyvinyl Alcohol (PVA), and Chitosan. Among various preparation methods, solvent casting technique is the most widely employed because of its simplicity and ability to produce uniform films. Evaluation parameters including thickness, folding endurance, tensile strength, swelling index, mucoadhesive strength, drug content, and in-vitro drug release are important for optimization of film performance. Recent advances in buccal film technology include the incorporation of nanoparticles, permeation enhancers, bilayer systems, and smart polymers to improve drug permeation and controlled release behavior. Buccal films have demonstrated promising applications in the delivery of antidiabetic, antihypertensive, analgesic, antimicrobial, and peptide drugs. This review highlights the anatomy of buccal mucosa, mechanism of mucoadhesion, polymers used in buccal films, methods of preparation, evaluation parameters, advantages, limitations, recent advances, and future prospects of mucoadhesive buccal films as a promising approach for controlled drug delivery.

Keywords: Mucoadhesive Buccal Films; Buccal Drug Delivery; Controlled Drug Release; Mucoadhesion; HPMC; Carbopol; Chitosan.

1. Introduction

Controlled drug delivery systems have become an important area of pharmaceutical research due to their ability to improve therapeutic efficacy, minimize side effects, and enhance patient compliance [1-2]. Conventional dosage forms such as tablets, capsules, and syrups are widely used for drug administration; however, they are often associated with several limitations including hepatic first-pass metabolism, gastrointestinal degradation, fluctuating plasma drug concentration, and poor patient adherence [3]. These limitations have encouraged the development of novel drug delivery systems capable of improving drug bioavailability and providing controlled drug release [4-5].

Among various novel drug delivery approaches, buccal drug delivery has emerged as a promising alternative route for systemic and local drug administration [6]. The buccal mucosa, located inside the cheek cavity, offers a highly vascularized surface that allows rapid drug absorption into systemic circulation [7]. Buccal administration bypasses hepatic first-pass metabolism and protects drugs from degradation in the gastrointestinal tract, thereby improving bioavailability [8]. In addition, buccal drug delivery provides ease of administration, rapid onset of action, and easy termination of therapy if required [9].

Mucoadhesive buccal films are thin, flexible polymeric dosage forms designed to adhere to the buccal mucosa and release drugs in a controlled manner [10]. These films are generally prepared using hydrophilic polymers capable of swelling and forming intimate contact with the mucosal surface [11]. The use of mucoadhesive polymers prolongs residence time at the site of application and enhances drug absorption through the buccal membrane [12].

Buccal films offer several advantages over conventional oral dosage forms and other transmucosal systems. They are non-invasive, comfortable to use, portable, and do not require water for administration. Buccal films are especially beneficial for pediatric, geriatric, bedridden, and dysphagic patients who experience difficulty in swallowing tablets or capsules. Moreover, the films provide accurate dosing, improved stability, and better patient acceptability [13].

The success of mucoadhesive buccal films depends largely on the selection of suitable polymers and excipients. Hydroxypropyl Methylcellulose (HPMC) is widely used because of its excellent film-forming ability and controlled drug release properties [14]. Carbopol is a highly mucoadhesive polymer that enhances residence time through hydrogen bonding with mucin. Chitosan, a natural cationic polymer, improves permeation and mucoadhesion due to its bioadhesive nature and ability to transiently open tight junctions. Polyvinyl Alcohol (PVA) contributes to flexibility and mechanical strength of films [15].

Various methods have been employed for preparation of buccal films, among which solvent casting technique is the most commonly used because of its simplicity, cost-effectiveness, and ability to produce uniform films. Prepared films are evaluated for several parameters including thickness, folding endurance, surface pH, tensile strength, swelling index, mucoadhesive strength, drug content, and in-vitro drug release. Release kinetics studies are also performed to understand the mechanism of drug release from the polymeric matrix [16].

In recent years, significant advancements have been made in buccal film technology. The incorporation of nanocarriers, permeation enhancers, bilayer systems, and smart polymers has improved the performance of buccal films. Buccal films are now being investigated for the delivery of a wide range of therapeutic agents including antidiabetic drugs, antihypertensive agents, analgesics, antifungal drugs, peptides, proteins, and vaccines [17].

Despite several advantages, buccal drug delivery also has certain limitations such as limited surface area for absorption, continuous saliva secretion, and possible accidental swallowing of the dosage form. Nevertheless, ongoing research and technological advancements continue to overcome these challenges and expand the scope of buccal drug delivery systems [18].

Overall, mucoadhesive buccal films represent a promising and innovative approach for controlled drug delivery. Their ability to bypass first-pass metabolism, improve bioavailability, provide sustained drug release, and enhance patient compliance makes them an attractive alternative to conventional dosage forms. Consequently, buccal film technology has gained considerable attention in modern pharmaceutical research and development [19].

2. Anatomy and Physiology of Buccal Mucosa

The buccal mucosa is an important site for transmucosal drug delivery due to its rich vascularization, relatively high permeability, and ease of accessibility. Buccal drug delivery systems are designed to deliver drugs through the lining of the cheek directly into systemic circulation, thereby bypassing hepatic first-pass metabolism and gastrointestinal degradation.

The oral mucosa covers the inner lining of the oral cavity and is divided into three major regions:

- Buccal mucosa
- Sublingual mucosa
- Gingival mucosa

Among these, the buccal mucosa is widely used for controlled drug delivery because of its adequate surface area, smooth texture, and relatively low enzymatic activity.

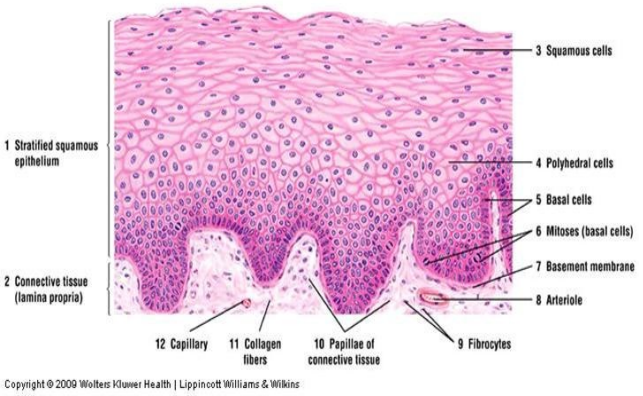

Figure 1: Anatomy and Physiology of Buccal Mucosa

3. Mucoadhesion and Mechanism

Mucoadhesion is defined as the adhesion between a polymeric material and the mucosal surface for an extended period of time. In buccal drug delivery systems, mucoadhesion plays a significant role in improving residence time, drug absorption, and therapeutic efficacy. Mucoadhesive buccal films adhere to the buccal mucosa and release the drug in a controlled manner, thereby enhancing bioavailability and patient compliance [20].

The mechanism of mucoadhesion generally occurs in two stages: the contact stage and the consolidation stage. During the contact stage, the polymer comes into close contact with the mucosal membrane and undergoes hydration and swelling. In the consolidation stage, interpenetration of polymer chains with mucin occurs, resulting in the formation of secondary chemical bonds such as hydrogen bonding, van der Waals forces, and electrostatic interactions [21].

Several theories including wetting theory, diffusion theory, adsorption theory, and electronic theory

have been proposed to explain the mucoadhesion phenomenon. The strength of mucoadhesion depends on factors such as polymer molecular weight, flexibility, swelling behavior, pH, and mucosal environment [22].

Polymers such as HPMC, Carbopol, Chitosan, and PVA are commonly used in mucoadhesive buccal films due to their excellent film-forming and adhesive properties. These polymers improve drug retention at the site of absorption and provide controlled drug release.

Mucoadhesive buccal systems offer several advantages including avoidance of first-pass metabolism, enhanced bioavailability, reduced dosing frequency, and improved patient compliance, making them a promising approach for controlled drug delivery [23].

4. Polymers Used in Buccal Films

Various natural and synthetic polymers such as HPMC, Carbopol, Chitosan, and PVA are widely used in the preparation of buccal films.

Table 1: Polymers Used in Buccal Films

Polymer	Type	Major Properties	Role in Buccal Films
HPMC (Hydroxypropyl Methylcellulose)	Semi-synthetic hydrophilic polymer	Excellent film-forming ability, swelling property, biocompatibility	Controls drug release and forms smooth flexible films
Carbopol 934P	Synthetic polyacrylic acid polymer	Strong mucoadhesion, high swelling capacity	Enhances mucoadhesion and prolongs residence time
Chitosan	Natural cationic polymer	Biodegradable, permeation enhancer, mucoadhesive	Improves drug permeation and sustained release
Polyvinyl Alcohol (PVA)	Synthetic water-soluble polymer	High mechanical strength, flexibility, transparency	Improves elasticity and mechanical stability of films

5. Recent Advances in Buccal Film Technology

Recent advances in buccal film technology have focused on improving drug loading, mucoadhesion, permeation, mechanical strength, patient acceptability, and controlled drug release. Conventional solvent-cast buccal films are now being modified using advanced polymers, nanocarriers, multilayer systems, and modern manufacturing technologies to enhance therapeutic performance [24].

One important advancement is the development of nanocarrier-loaded buccal films, where nanoparticles, liposomes, nanoemulsions, solid lipid nanoparticles, and nanostructured lipid carriers are incorporated into polymeric films. These systems improve the solubility, stability, and mucosal permeation of poorly water-soluble drugs [25].

Another recent approach is the use of bilayer and multilayer buccal films. These films contain a drug-loaded mucoadhesive layer and a backing layer. The backing layer prevents drug loss into saliva and promotes unidirectional drug release toward the buccal mucosa, thereby improving bioavailability [26].

The use of smart and stimuli-responsive polymers has also gained attention. These polymers respond to changes in pH, temperature, or moisture and provide controlled or site-specific drug release. Such systems are useful for achieving prolonged therapeutic action and reducing dosing frequency [27].

Advanced manufacturing techniques such as hot-melt extrusion, electrospinning, and 3D printing are increasingly being explored for buccal film development. These methods improve dose accuracy, scalability, and customization of films. 3D printing also allows personalized drug dosing, which may be useful for pediatric and geriatric patients [28].

Permeation enhancers are another important area of advancement. Agents such as chitosan, bile salts, surfactants, and fatty acids are incorporated to improve drug transport across buccal mucosa. These enhancers help overcome the permeability barrier and increase systemic absorption [29].

Table 2: Recent Advances in Buccal Film Technology

Recent Advance	Description	Major Benefit
Nanocarrier-loaded films	Incorporation of nanoparticles, liposomes, nanoemulsions, or lipid carriers into films	Improved solubility and permeation
Bilayer/multilayer films	Films with drug layer and backing layer	Unidirectional drug release
Smart polymers	pH-, temperature-, or moisture-responsive polymers	Controlled and site-specific release
Electrospun films	Nanofiber-based films with high surface area	Rapid hydration and improved release
3D printed films	Computer-aided personalized film manufacturing	Dose customization
Permeation enhancer-based films	Use of chitosan, surfactants, bile salts, or fatty acids	Enhanced mucosal absorption
Taste-masked films	Use of sweeteners, flavors, and masking agents	Improved patient acceptability

Overall, recent advances in buccal film technology have expanded their application from conventional small-molecule drugs to peptides, proteins, vaccines, and poorly soluble drugs. These innovations make buccal films a promising platform for controlled, targeted, and patient-friendly drug delivery [30].

6. Applications of Buccal Films

Mucoadhesive buccal films have gained significant importance in pharmaceutical drug delivery due to their ability to provide controlled and systemic drug release through the buccal mucosa. These films are widely used for drugs that undergo extensive first-pass metabolism, exhibit poor gastrointestinal stability, or require rapid onset of action. Buccal films also improve patient compliance because of their ease of administration and non-invasive nature.

Buccal films are used for both local and systemic delivery of drugs. They are especially suitable for pediatric, geriatric, and dysphagic patients who have difficulty swallowing conventional oral dosage forms.

Major Applications of Buccal Films

- Controlled and sustained drug delivery
- Delivery of drugs with poor oral bioavailability
- Rapid systemic absorption
- Local treatment of oral diseases
- Delivery of peptides and proteins
- Improved patient compliance in chronic therapy

Table 3: Applications of Buccal Films

Therapeutic Category	Example of Drug	Purpose/Application
Antidiabetic drugs	Glimepiride, Metformin	Improved bioavailability and controlled release
Antihypertensive drugs	Propranolol, Atenolol	Avoidance of first-pass metabolism
Analgesics	Fentanyl, Diclofenac	Rapid pain relief
Antiemetic drugs	Ondansetron	Rapid onset of action
Antifungal drugs	Clotrimazole, Miconazole	Local treatment of oral infections
Antimicrobial agents	Chlorhexidine	Oral cavity disinfection
Hormones and peptides	Insulin, Testosterone	Improved systemic absorption
Smoking cessation therapy	Nicotine	Sustained nicotine delivery
Vaccines	Buccal vaccine formulations	Non-invasive immunization approach

Applications in Controlled Drug Delivery

Buccal films provide prolonged residence time on the buccal mucosa, enabling sustained and controlled release of drugs. This helps maintain therapeutic drug concentration for an extended period and reduces dosing frequency.

Applications in Chronic Diseases

Buccal films are highly useful in chronic diseases such as diabetes mellitus, hypertension, and pain management, where prolonged therapy and improved patient adherence are essential.

Applications for Poorly Soluble Drugs

Drugs with poor aqueous solubility and extensive hepatic metabolism can achieve improved therapeutic efficacy through buccal delivery due to direct systemic absorption.

Applications in Pediatric and Geriatric Patients

Buccal films are thin, flexible, and easy to administer, making them suitable for patients who have difficulty swallowing tablets or capsules.

Mucoadhesive buccal films have broad pharmaceutical applications for both local and systemic drug delivery. Their ability to improve bioavailability, provide controlled drug release, and enhance patient compliance makes them a promising alternative to conventional dosage forms.

7. Future Perspectives

Mucoadhesive buccal films have shown significant potential as an advanced drug delivery system due to their ability to improve bioavailability, provide controlled drug release, and enhance patient compliance. Continuous advancements in polymer science, nanotechnology, and pharmaceutical manufacturing are expected to further expand the applications of buccal films in the future.

One important future direction is the development of nanotechnology-based buccal films, where nanoparticles, nanoemulsions, liposomes, and solid lipid carriers are incorporated into films to improve solubility, permeability, and targeted drug delivery. These systems may enhance therapeutic efficacy of poorly water-soluble drugs.

The use of smart and stimuli-responsive polymers is another promising area. Such polymers can respond to changes in pH, temperature, or moisture and release drugs in a controlled and site-specific manner. This approach may help achieve prolonged therapeutic action with reduced dosing frequency.

Advancements in 3D printing technology are expected to revolutionize buccal film manufacturing by enabling personalized dosage forms with precise drug loading and customized shapes. Personalized buccal films may be particularly useful in pediatric and geriatric therapy. Future research is also focused on the buccal delivery of proteins, peptides, vaccines, and biologics, which are usually degraded in the gastrointestinal tract. Buccal films may provide a non-invasive alternative to injectable formulations.

Further improvements in permeation enhancers and mucoadhesive polymers are likely to increase drug permeation across buccal mucosa and improve residence time. Combination of buccal films with controlled-release and targeted-delivery technologies may provide superior therapeutic outcomes.

Table 4: Future Perspectives of Buccal Film Technology

Future Area	Expected Advancement	Potential Benefit
Nanotechnology-based films	Incorporation of nanoparticles and lipid carriers	Improved solubility and bioavailability
Smart polymers	Stimuli-responsive drug release systems	Controlled and site-specific delivery
3D printed buccal films	Personalized drug delivery systems	Customized dosing and better compliance
Peptide and protein delivery	Buccal delivery of biologics	Non-invasive alternative to injections
Advanced permeation enhancers	Improved transmucosal absorption	Enhanced systemic delivery
Combination drug therapy	Multi-drug loaded buccal films	Improved therapeutic effectiveness
Commercial scale-up	Automated manufacturing systems	Large-scale production feasibility

Despite the promising advancements, further studies including long-term stability, large-scale manufacturing, regulatory approval, and clinical trials are necessary before widespread commercialization of buccal film products can be achieved.

Overall, mucoadhesive buccal films are expected to play a major role in the future of controlled and patient-friendly drug delivery systems due to their versatility, convenience, and therapeutic advantages.

8. Conclusion

Mucoadhesive buccal films have emerged as a promising and effective approach for controlled drug delivery due to their ability to provide prolonged residence time, improved bioavailability, and enhanced patient compliance. Buccal drug delivery offers several advantages over conventional oral dosage forms, including avoidance of hepatic first-pass metabolism, protection from gastrointestinal degradation, rapid onset of action, and ease of administration.

The successful performance of buccal films largely depends on the selection of suitable polymers such as HPMC, Carbopol, Chitosan, and PVA, which contribute to film formation, mucoadhesion, flexibility, swelling behavior, and controlled drug release. Various preparation methods, particularly solvent casting technique, enable the development of uniform and stable films with desirable physicochemical and mechanical properties.

Recent advancements including nanocarrier-loaded films, multilayer systems, smart polymers, electrospinning, and 3D printing technologies have significantly improved the therapeutic potential of buccal films. These developments have expanded their applications for systemic delivery of antidiabetic, antihypertensive, analgesic, antimicrobial, peptide, and protein drugs.

Despite certain limitations such as limited drug loading capacity and influence of saliva on adhesion, buccal films continue to attract considerable research interest because of their versatility and patient-friendly nature. Future innovations in polymer science, permeation enhancement, and personalized drug delivery are expected to further enhance the clinical and commercial applicability of buccal film technology.

Overall, mucoadhesive buccal films represent a valuable platform for controlled and targeted drug delivery and hold strong potential as an alternative to conventional dosage forms in modern pharmaceutical therapy.

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