THE ROLE OF MUCOADHESION IN MODERN DRUG DELIVERY: TECHNOLOGIES AND TRENDS

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ABSTRACT

Mucoadhesive drug delivery systems offer a novel strategy for improving both drug bioavailability and therapeutic performance by extending the duration of drug contact at mucosal surfaces. They utilize the inherent adhesive characteristics of specific polymers to bind effectively to mucosal tissues located in various regions of the body, such as GI tract, buccal cavity, nasal passages, eyes, vagina, and rectum. This review offers a thorough exploration of mucoadhesion mechanisms, detailing the physicochemical and physiological influences on adhesive behaviour, along with theoretical models that describe polymer-mucosa interactions. It also investigates the architecture and function of mucus layers, which are essential to the effectiveness of mucoadhesive systems. Moreover, it surveys a wide range of dosage forms including tablets, gels, films, patches, and ointments tailored to various routes of administration. Despite their advantages in enhancing drug retention, minimizing first-pass metabolism, and improving patient compliance, mucoadhesive systems face certain limitations including mucin turnover and challenges in formulation acceptability. The review emphasizes the ongoing innovation and potential of mucoadhesive platforms in overcoming drug delivery barriers and achieving precise, controlled therapeutic outcomes.

Keywords: bioavailability, mucoadhesion, physiological influence, drug retention, mucin turnover, therapeutic outcome.

INTRODUCTION

Oral administration remains the most widely used and favoured method for delivering therapeutic drugs. Its widespread acceptance stems from several factors includes convenient for patients, allows precise dosing, economical to produce, requires minimal sterility precautions, offers versatile formulation options, and typically ensures better product stability over time (1,2). Mucoadhesive drug delivery systems have emerged as a promising approach in pharmaceutical design, aiming to prolong the drug retention at the site of absorption or application. This strategy promotes close interaction between the formulation and the mucosal surface, thereby enhancing drug bioavailability. Additionally, these systems offer sustained drug release and allow for targeted delivery to specific areas within the body, making them highly advantageous (3).Mucoadhesive materials can serve as therapeutic agents themselves by forming a protective barrier over damaged tissues to promote healing and provide relief. lesions to promote healing and provide relief. Moreover, they can function as lubricants in sensitive areas like the mouth, eyes, or vaginal region (4). Recently, for various administration route such as oral, buccal, nasal, gastrointestinal, rectal, and vaginal it has been designed to achieve localized treatment as well as systemic therapeutic outcomes (5).

BIOADHESION AND MUCOADHESION

Bioadhesion refers to the phenomenon occurring at the interface between two materials, where at least one possesses a biological nature, and they remain connected for an extended duration due to interfacial forces. This bond can form between synthetic substances such as polymers and biological surfaces like membranes, enabling prolonged attachment (6). Adhesion refers to the attachment formed when a pressure-sensitive adhesive comes into contact with a surface, creating a bond between them. In biological systems, bio adhesion can be categorized into four distinct types:

1. Binding between two healthy cells,
2. Interaction of a cell with an external material,
3. Attachment of a healthy cell to a diseased one,
4. Adhesion involving a synthetic adhesive and a biological surface (7).

In drug delivery, bioadhesion refers to the capability of a drug carrier to stick to a targeted biological site, often involving epithelial tissues. This attachment enhances the residence time and therapeutic effectiveness of the drug at its intended location. When adhesive bonding occurs specifically with a mucus layer, the process is known as mucoadhesion. Bioadhesion is

often conceptualized by observing how bacteria bind to tissue surfaces, while mucoadhesion is illustrated through the way mucus naturally adheres to epithelial tissues (8). The mucosal lining is present across various regions including nasal cavity, GI system, respiratory passages, and sensory organs such as the ears and eyes. Mucoadhesive drug delivery systems can be designed to target these regions for more effective and localized treatment. It can be applied to various system:

- Gastrointestinal delivery system
- Sublingual delivery system
- Vaginal delivery system
- Nasal delivery system
- Ocular delivery system
- Rectal delivery system
- Buccal delivery system

MECHANISM OF MUCOADHESION

The mucoadhesion process typically involves two stages: the contact stage and the consolidation stage. The initial stage involves the interaction between the mucoadhesive substance and the mucus membrane, during which the formulation begins to spread and swell allowing it to closely engage with the mucus layer and establish a firm connection. During the consolidation phase, moisture plays a key role in activating mucoadhesive materials. It softens the system, enabling the adhesive molecules to become mobile and form weak intermolecular bonds which strengthen their attachment to the mucosal surface (9).

MUCOUS MEMBRANE

Mucosal membranes are damp, protective linings found along the inner lining of numerous body cavities like the GI tract and the respiratory system. These membranes are composed of two main layers: a connective tissue base known as the lamina propria, topped by an epithelial layer whose surface is typically kept moist by a coating of mucus. Epithelial tissues can be structured as either a single layer as seen in organs like the stomach, intestines, and bronchi or as multiple layers (stratified), which are typical in areas such as the esophagus, vagina, and cornea. In single-layered epithelia, goblet cells are present and responsible for secreting mucus directly onto the epithelial surface. In contrast, multilayered epithelia either house or lie near specialized glands that release mucus to coat the epithelial layer. It exists in two primary forms:

as a gel-like layer that clings tightly to the mucosal surface or as a soluble or suspended form within the lumen. Mucus gels are primarily made up of mucin glycoproteins, lipids, and inorganic salts, with water constituting over 95% of their total weight. This high water content makes mucus an exceptionally hydrated medium (4). The primary roles of mucus are serving as a protective coating and a natural lubricant.

Composition of mucus layer

Mucus is semi-transparent, thick fluid that spreads over mucosal epithelial surfaces that helps in maintaining hydration and protection. The thickness differs across mucosal surfaces ranging from about 50 to 450 micrometres in the gut to under 1 micrometre in the mouth.Mucin glycoproteins are large, high-molecular-weight proteins that feature linked oligosaccharide chains composed of sugar units such as L-fucose, D-galactose, N-acetyl-D-glucosamine, N-acetyl-D-galactosamine, and sialic acid.

Functions of mucous layer

- The provides protection due to its water-repelling nature (hydrophobicity).
- It affects drug bioavailability by serving as a barrier that limits the absorption of substances through tissues.
- It adheres tightly to the epithelial surface, forming a consistent gel coating.
- It plays an essential role in lubricating the mucosal membrane and preserving its moisture levels (10).

The mucoadhesive interaction: Adhesion takes place when molecular connections form across the interacting surfaces. These intermolecular bonds may develop through various ways:

a) **Ionic bond-** occurs when positively and negatively charged ions are drawn together through electrostatic attraction, creating a robust connection such as the type found in crystalline salt structures.

b) **Covalent bond**- involves the mutual sharing of electron pairs among atoms, allowing each atom to achieve a full outer orbital. This type of bond is typically strong and forms the backbone of many stable molecules.

c) **Hydrogen bond**- occurs when a hydrogen atom, already covalently linked to highly electronegative atoms like oxygen, fluorine, or nitrogen, exhibits a partial positive charge that draws it toward other nearby electronegative atoms. In this interaction, the hydrogen is effectively shared between atoms, resulting in a bond that’s generally weaker than ionic or covalent bonds.

d) **Van der Waals forces**- are the fragile type of molecular relation and stem from various temporary or induced electrical attractions. These include dipole–dipole interactions found in polar molecules, as well as dispersion forces that occur among nonpolar substances.

e) **Hydrophobic bond**- are indirect associations that occur in aqueous environments when non-polar molecular groups are present. Water molecules surrounding these non-polar areas form structured hydrogen-bond networks, which reduces the system entropy. To counteract this effect, non-polar groups tend to cluster together, effectively minimizing their exposure to water (5,11).

Advantages

- Mucoadhesive drug delivery systems enhance the duration a drug remains at its absorption site, leading to improved bioavailability.
- They offer excellent accessibility and quick therapeutic response.
- Fast absorption is supported by rich vascularization and strong blood circulation in targeted regions.
- These systems help shield drugs from breakdown in the stomach's acidic environment.
- They also promote better patient compliance through ease of administration and effectiveness.

Limitations

- Extended contact with drugs that have ulcer-causing tendencies may lead to localized ulcerative side effects.
- A significant hurdle in advancing oral mucosal drug delivery is the absence of reliable in vitro models to effectively evaluate suitable drug candidates for this route.
- Patient approval factors such as taste, potential irritation, and the overall feel in the mouth must be carefully assessed (12).

THEORIES OF MUCOADHESION

Although the exact chemical and physical mechanisms behind mucoadhesion remain unclear, six established theories originating from research on material performance and polymer interactions offer explanations for the phenomenon. Key factors such as the

duration of contact and the contact angle significantly influence mucoadhesive behaviour (3,9,13).

Electronic Theory: It suggests that mucoadhesion takes place through electron exchange between the mucus and the mucoadhesive material, driven by differences in their electronic configurations. As electrons are transferred, a double layer of electrical charges forms at the interface between the two. This charged layer then gives rise to attractive forces that help bind the mucoadhesive system to the mucus surface (14).

Adsorption Theory: When two surfaces make initial contact, adhesion arises from surface-level forces acting between their chemical structures. This interaction leads to the development of both primary and secondary chemical bonds including covalent, electrostatic, hydrogen, hydrophobic, and Van der Waals forces between the mucus and the mucoadhesive polymer. The strength and nature of these secondary bonds are largely influenced by the characteristics of the polymer. In cases of exceptionally strong adhesion, chemisorption may occur, involving more robust chemical bonding (15).

Wetting Theory: The wetting theory, considered one of the earliest models of adhesion, is particularly applicable to liquid or low-viscosity bioadhesives. It describes adhesion as a process where the adhesive spreads into microscopic grooves and uneven areas of the surface material, eventually solidifying to form numerous bonding points. For the adhesive to move freely and establish contact, it surpasses the surface tension at the point of contact. This theory also involves calculating the contact angle and the thermodynamic energy required for adhesion to occur (4,7,16).

The amount of adhesive work is influenced by the surface tensions of both the bioadhesive and the surface it is applied to. According to the Dupre equation:

$$W_A = Y_b + - Y_{bt}$$

The specific thermodynamic work of adhesion (W_A) is determined by adding the surface tensions of the bioadhesive polymer (Y_b) and the substrate, then subtracting the interfacial tension between them (Y_{bt}). Essentially, it reflects how much energy is needed to create a bond at the interface, taking into account the balance of forces between the two contacting materials (15).

Diffusion Theory: It explains mucoadhesion as a result of polymer and mucin chains interweaving and penetrating each other. As the depth of this interpenetration increases, so

does the strength of the adhesive bond. A higher degree of structural resemblance between the mucoadhesive and the mucosal surface enhances this effect. For a strong and effective bond to form, it is generally thought that an intermingling layer of about 0.2 to 0.5 micrometers is necessary, and that greater polymer chain penetration leads to stronger adhesion forces. The extent to which mucoadhesive chains penetrate the mucus layer is influenced by several factors including the chain flexibility and composition, mobility of the molecules, and duration of contact. The penetration depth (1) can be estimated by the formula: $1 = (t\ Db)^{1/2}$

The time of contact (t) and the diffusion coefficient (Db) of the bioadhesive within the mucus play critical roles in determining how deeply the polymer penetrates. Adhesion reaches its optimal strength when this penetration depth closely matches the size of the polymer chains (15,17).

Fracture Theory: Fracture theory focuses on measuring the force needed to pull apart two surfaces that have adhered. It's especially useful for assessing the bond strength of rigid mucoadhesive materials. This approach is commonly used to evaluate tensile strength, particularly in systems like microspheres and powdered formulations. The peak tensile strength observed during the separation process is calculated by dividing the highest detachment force (F) by the area (A) over which the adhesive interaction occurred. This ratio provides a measure of how strongly the mucoadhesive material is bonded to the surface (9,18). The equation can be written as: $S_m = F_m / A_m$

Although it might unable to provide a detailed mechanistic framework for bioadhesive behavior, they are valuable for pinpointing the key variables that influence the bioadhesion process (19).

ELEMENTS INFLUENCING MUCOADHESION

Molecular weight: The ideal molecular weight for achieving strong mucoadhesion varies depending on both the specific polymer used and the type of tissue involved. Generally, as the molecular weight of the polymer chain increases, its ability to adhere improves. Polymers with molecular weights of 100,000 or higher are typically considered suitable for biomedical use. For instance, polyethylene glycol (PEG) with a molecular weight of 20,000 exhibits weak adhesion, while PEG at 200,000 shows better adhesive properties, and PEG at 400,000 demonstrates significantly stronger mucoadhesion (20,21). For polymers with lower molecular weights, their effectiveness as bioadhesives relies more heavily on how

well they interact and interpret the surrounding environment. In contrast, polymers with higher molecular weights achieve strong adhesion primarily through the physical entanglement of their long chains with the mucosal surface (22).

Flexibility: Mucoadhesion initiates as polymer chains begin to diffuse into the interface where they interact with mucus. To ensure effective entanglement, these chains must exhibit considerable flexibility, allowing them to intertwine with the mucosal surface (23). Enhanced interpenetration of polymer chains is largely due to the increased structural flexibility achieved by adding polyethylene glycol (PEG). Typically, a polymer has ability to move and flexibility is linked to its viscosity and diffusion coefficient, greater flexibility allows the polymer to diffuse more effectively throughout the mucus layer (24).

Charge: Previous studies have suggested that the adhesive performance of polymers is influenced by their charge. Nonionic polymers typically exhibit weaker adhesion, while polymers with a strong anionic charge tend to demonstrate more pronounced mucoadhesive properties. A strong negative charge is considered an essential feature for effective mucoadhesion (25). Certain positively charged (cationic) polymers tend to exhibit stronger mucoadhesive behavior, particularly when placed in environments that are neutral or mildly alkaline in pH. Moreover, certain cationic polymers with high molecular weights like chitosan have demonstrated strong mucoadhesive capabilities (26). Although there is limited research on how membrane charge directly impacts mucoadhesion, the membrane pH plays a more influential role. It affects the ionization state of the polymers altering whether they exist in ionized or unionized forms which in turn influences their adhesive behavior (4).

Hydration: Swelling behavior is influenced by both the nature of the mucoadhesive material and the surrounding environment. Factors such as polymer concentration, ionic strength, and water availability play key roles in this process. In laboratory conditions, optimal bioadhesion is achieved when the water content is balanced. However, excessive hydration can lead to the formation of a slippery, gel-like layer that diminishes adhesive effectiveness (27).

Environmental Related Factors:

Applied Strength: Establishing a stable bioadhesive system requires the application of a specific amount of force. The adhesive strength tends to rise with increased application pressure or density up to an optimal level. The initial pressure at the tissue–mucoadhesive

contact site significantly influences how deeply the polymer penetrates. When high pressure is sustained over a sufficient duration, even polymers lacking direct affinity for mucin can develop mucoadhesive properties through physical interpenetration (28).

Initial Contact Time: The duration of contact between the mucoadhesive material and the mucus layer plays a vital role in how much the polymer swells and penetrates. Longer initial contact times allow greater intermingling of the polymer chains with the mucus, resulting in stronger mucoadhesive bonding (29).

pH at polymer substrate interface: The pH level can affect the electric charge present on the mucus surface and alter the ionization state of certain mucoadhesive polymers, both of which play a role in adhesion strength (20). The charge density of mucus varies with pH because the dissociation behavior of functional groups—present in both the carbohydrate segments and the amino acid residues of the polypeptide chain—changes with the acidity or alkalinity of the environment (27).

Physiological Variables:

Disease state: Medical disorders like the common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, and infections or inflammatory responses in the eyes and reproductive tract can alter the physicochemical nature of mucus (30). Although the precise structural modifications under these circumstances are still not fully understood, it is crucial to assess the performance of mucoadhesives within these altered environments to ensure their effectiveness (31).

Mucin Turnover: The regular renewal of mucin molecules in the mucus layer plays a key role in limiting how long mucoadhesives can remain attached. Regardless of how strong their adhesive properties are, mucoadhesives eventually detach as mucin is naturally replaced. Interestingly, the rate at which mucin turns over may vary depending on whether a mucoadhesive is present. Secondly, the continuous renewal of mucin produces a significant amount of soluble mucin molecules. These soluble components may bind to mucoadhesive agents prematurely, preventing them from effectively adhering to the actual mucus layer (26,32,33).

Potential sites for Mucosal Drug Delivery The main goals is to ensure close interaction between the formulation and the site of absorption, and to extend its retention at that location—ultimately enhancing and prolonging the therapeutic effect of the drug (34).

Mucoadhesive formulations have been extensively utilized for precise and regulated drug delivery to various mucosal membrane-associated tissues. These systems can administer active pharmaceutical ingredients (APIs) either locally or systemically, while also reducing or bypassing bioavailability challenges like enzymatic breakdown or hepatic metabolism (35).

Buccal Drug Delivery: The buccal cavity provides several benefits for drug administration, with key advantages including easy access and minimal enzymatic degradation. Moreover, if adverse effects arise, treatment can be quickly discontinued by removing the drug form, making this approach both safe and convenient (29). While gels and ointments are generally the most convenient for patients, other forms like tablets, patches, and films have also been explored. Delivering drugs to easily reachable areas like the mouth typically ensures high patient compliance, minimal irritation, and simplified administration. Additionally, though less frequently highlighted, benefits include a fast therapeutic effect thanks to the richly vascularized buccal mucosa (36). A range of mucoadhesive polymers have been utilized in designing buccal drug delivery systems. These include cyanoacrylates, polyacrylic acid, sodium carboxymethylcellulose, hyaluronic acid, hydroxypropylcellulose, polycarbophil, chitosan, and gellan (35,37).

Nasal Drug Delivery: The nasal cavity presents a promising site for developing drug formulations that incorporate mucoadhesive polymers. Its mucosal lining offers a substantial surface area of approximately 150–200 cm^2, making it an effective platform for drug delivery. An important benefit of intranasal drug delivery is the presence of a broad, highly vascularized surface in the nasal cavity, which enables direct absorption into the systemic circulation and effectively bypasses hepatic first-pass metabolism (38). The retention time of particles within the nasal mucosa typically ranges from 15 to 30 minutes, largely due to icreased mucociliary activity triggered by the presence of foreign materials. To enhance nasal drug delivery, several polymers are employed in formulation development, including methyl vinyl ether copolymer, hydroxy propyl methylcellulose (HPMC), sodium carboxymethylcellulose, Carbopol 934P, and Eudragit RL 100 (39,40).

Ocular Drug Delivery: Frequent tear production and blinking lead to swift elimination of active drugs from the ocular cavity, resulting in reduced bioavailability. This challenge can be addressed by administering medication through ocular inserts or patches (35). Mucoadhesive polymers are typically designed to adhere specifically to the conjunctival

mucus in vivo. However, their migration can lead to the unintended accumulation of semisolid material on the corneal surface, potentially impairing visual clarity (41). Mucoadhesive polymers commonly utilized in ocular drug delivery systems include thiolated poly(acrylic acid), poloxamers, cellulose acetate phthalate, methyl cellulose, hydroxyethyl cellulose, poly(amidoamine) dendrimers, poly(dimethyl siloxane), and poly(vinyl pyrrolidone) (42).

Rectal and Vaginal Drug Delivery: Both the vaginal and rectal lumens have been investigated as routes for delivering active agents, targeting either systemic or localized effects. This method of administration allows drugs intended for systemic delivery to avoid hepatic first-pass metabolism. However, a common challenge is the migration of the delivery system within these lumens, which may interfere with precise drug targeting. Incorporating mucoadhesive polymers into drug delivery systems helps limit their migration, thereby enhancing therapeutic effectiveness. Commonly used polymers include mucin, gelatin, polycarbophil, and poloxamer (43,44).

Gastrointestinal Drug Delivery: Mucoadhesive polymers can enhance contact with the gastrointestinal (GI) tract lining, thereby improving drug bioavailability. Additionally, specific 'absorption windows' within the GI tract such as regions associated with gut associated lymphoid tissue can be targeted to facilitate the uptake of larger and poorly soluble therapeutic compounds (45). A key goal of oral mucoadhesive drug delivery systems is to significantly extend the drug residence time in the gastrointestinal tract, enhancing its local therapeutic effect and enabling once-daily dosing. Various dosage forms such as sustained-release tablets, semisolids, powders, and micro- or nanoparticles have been extensively researched for this purpose (33). Matharu and Sanghavi formulated mucoadhesive tablets for captopril using Carbopol 934P and poly(acrylic acid) cross-linked with 0.001% ethylene glycol (46). There is growing interest in second-generation delivery systems, including the use of thiolated chitosan tablets for oral insulin administration. Additional progress in this area includes the incorporation of second-generation mucoadhesives onto microsphere surfaces (47).

Mucoadhesive Dosage Forms

Tablets: Mucoadhesive tablets are typically compact, flat, and oval-shaped, measuring around 5–8 mm in diameter (48). Unlike traditional tablets, they permit activities like drinking and speaking with minimal discomfort. Upon administration, they gradually soften,

adhere to the mucosal surface, and remain in place until they fully dissolve or release their active ingredients. It perhaps engineered to attach to various mucosal surfaces, like those in the gut, enabling both localized and systemic controlled drug release. Targeting the gastric epithelium allows for site-specific delivery of medications. These tablets are widely favored due to their ability to provide sustained drug release, reduce dosing frequency, and enhance patient adherence to treatment (27,49).

Gels and ointments: Semisolid formulations easily disperse across the surface of mucous membrane. To tackle their short retention time at the application site has been addressed through the use of mucoadhesive formulations. Specific polymers, such as sodium carboxymethylcellulose, carbopol, hyaluronic acid, and xanthan gum, exhibit a phase transition from liquid to semisolid, enhancing their adherence and effectiveness (50–52). This viscosity enhancement facilitates prolonged and regulated drug release. Hydrogels, in particular, represent an effective dosage form. They are created from polymers that swell in hydrated conditions and encapsulate drug compounds, enabling gradual release through either diffusion or erosion (53). Mucoadhesive gels are beneficial in oral drug delivery due to their prolonged retention time, effective tissue penetration, and high therapeutic efficiency, all while maintaining patient comfort. One of their key uses is in treating periodontitis which is an inflammatory infection that leads to gum-pocket formation and may result in tooth loss. Research suggests that when antimicrobial agents are formulated with mucoadhesive polymers, they can be conveniently administered into periodontal pockets via a syringe, enhancing the treatment effectiveness (54–56). HPMC has been incorporated as a mucoadhesive component in ointment formulations. Moreover, a dense gel composed of Carbopol and hydroxypropylcellulose has been formulated for topical applications, capable of adhering to tissue surfaces for durations of up to eight hours (57).

Films: Compared to adhesive tablets, mucoadhesive films offer greater patient compliance. They overcome the limited retention time typical of oral gels, which tend to washed away by saliva. In treating oral conditions, these films not only aid in localized drug delivery but also shield the affected area, thereby alleviating pain and enhancing therapeutic effectiveness. An optimal mucoadhesive film should combine softness, elasticity, and flexibility with sufficient mechanical strength to resist tearing caused by oral movements. It should also exhibit robust mucoadhesive properties to remain securely in place within the oral cavity throughout the intended period of drug release (5,58).

Patches: Patches are multilayered systems composed of protective backing that prevents permeability, a reservoir layer that holds and gradually releases the drug, and a mucoadhesive surface designed for attachment to mucosal tissues. Their design closely resembles that of transdermal drug delivery systems. Adhesive patches are commonly fabricated using either solvent casting or direct milling techniques. In the former approach, the drug-polymer mixture is poured onto a backing layer to form an intermediate sheet, which is then shaped into patches following the evaporation of the solvent (59). In the latter technique, the formulation ingredients are thoroughly blended and compressed to achieve a uniform thickness, after which patches of specific dimensions and shapes are punched out. To enhance performance, an impermeable backing layer can be added to regulate drug release direction, reduce drug loss, and protect the patch from deformation or breakdown during use (60).

Table 1.: Different types of mucoadhesive dosage forms

Delivery routes	**Dosage form**				
	Tablet	**Ointment**	**Gel**	**Patch**	**Film**
Buccal	Theophylline, multiple polymers (61)	Benzyl nicotinate, multiple polymers(62)	Benzydamine, chitosan derivatives (63)	Miconazole, PVA/PVP (64)	Fentanyl, PVP (65)
Nasal	N/A	Mupirocin, glycerin ester	Insulin, starch (66)	Insulin, chitosan/PEG (67)	Chlorpromazine, chitosan/ pectin (68)
Ocular	Diclofenac, poly(acrylic) acid (40)	Sulphadicramide multiple polymers(69)	Puerarin, poloxamer/Carbopol (70)	Ciprofloxacin, PVA/CMC (71)	Fluorescein, HPMC (72).
Vaginal	Metronidazole, chitosan (73)	Terameprocol, white petroleum (74)	Amphotericin, pluronic (75)	ALA, PMVE/MA (76)	SDS, multiple polymers (77)
Rectal	Ramosetron, Carbopol (78)	Zinc oxide, petroleum	Quinine, HPMC (79)	N/A	Theophylline, pHEMA (80)

CONCLUSION

Mucoadhesive drug delivery systems have emerged as a promising approach for achieving targeted and sustained release of therapeutic agents across mucosal surfaces. By maintaining extended contact with the mucosa, these systems improve drug absorption, reduce dosing frequency, avoid first-pass hepatic metabolism, and enhance patient compliance. The effectiveness of these formulations relies on a delicate interplay between polymer properties—such as molecular weight, flexibility, surface charge, and hydration capacity—and physiological factors like pH levels, mucin turnover, and the presence of disease. A wide variety of dosage forms tailored to different mucosal routes have been developed, offering distinct benefits for localized or systemic drug administration.

Despite the clear advantages of mucoadhesive systems, several hurdles persist—such as the need for robust in vitro models, ensuring patient comfort, and adapting to the constantly changing mucosal environment. Future advancements should focus on the development of second-generation mucoadhesive with enhanced specificity, biocompatibility, and responsiveness to environmental cues. The convergence of nanotechnology and intelligent drug delivery platforms offers promising avenues for overcoming existing limitations and enhancing therapeutic performance Overall, mucoadhesive drug delivery continues to be a dynamic and impactful area in pharmaceutical science with significant clinical and commercial relevance.

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