A Comprehensive Review on Mucoadhesive Gel

Katkar Sujata Dayanand, Syed Abdul Azeem A., Suryawanshi Reshma B.
Shivlingeshwar college of pharmacy almala

***Abstract*—Mucoadhesive gels have emerged as one of the most promising dosage forms in Controlled and localized drug delivery, owing to their ability to adhere to mucosal Surfaces and provide prolonged therapeutic effects. The concept of mucoadhesion, First introduced in the 1980s, involves the interaction between polymeric materials And mucin present on the epithelial surface, leading to extended residence time and Enhanced bioavailability of drugs administered through mucosal routes such as Buccal, nasal, vaginal, ocular, and rectal pathways . These systems combine the Advantages of both gels and mucoadhesive polymers, offering improved patient Compliance, ease of administration, and effective site-specific delivery .Formulation of mucoadhesive gels involves selecting appropriate natural or Synthetic polymers such as carbopol, chitosan, hydroxypropyl methylcellulose (HPMC), sodium alginate, and polycarbophil, which determine rheological Behavior, swelling capacity, and mucoadhesive strength . The Physicochemical characteristics of these polymers—such as molecular weight, Degree of cross-linking, and charge—significantly influence the adhesion Mechanism and drug release profile . Several methods, including cold or hot Mechanical stirring, dispersion, and solvent evaporation, are employed to prepare These gels depending on the polymer and drug used .The mechanism of mucoadhesion primarily involves wetting, adsorption, and Interpenetration between the polymer and mucin chains, resulting in non-covalent Interactions such as hydrogen bonding, van der Waals forces, and electrostatic Attractions . Evaluation of mucoadhesive gels includes determining parameters Such as viscosity, spreadability, swelling index, pH, drug content uniformity, invitro drug release, and ex-vivo mucoadhesive strength using models like porcine or Goat mucosa**

***Keywords*— Mucoadhesive gels, bioadhesion, drug delivery, polymers, mucosal Routes, formulation, evaluation**

I. INTRODUCTION

Mucoadhesive gels have emerged as a promising class of drug-delivery systems designed to interact closely with the body's mucosal surfaces. These gels are formulated to adhere to moist tissues such as those found in the oral cavity, nasal passages, eyes, gastrointestinal tract, and vaginal region. By forming intimate contact with mucous membranes, mucoadhesive gels can prolong the residence time of therapeutic agents at the site of application, which helps improve drug absorption, enhance treatment effectiveness, and reduce dosing frequency.

The concept of mucoadhesion builds on the natural properties of mucus—a hydrated, viscoelastic secretion that protects and lubricates internal surfaces. By using polymers that can interact with mucus through physical or chemical bonding, mucoadhesive gels create a stable interface that resists quick removal by natural flushing mechanisms like saliva, tears, or mucociliary clearance. This makes them especially useful for delivering drugs that require sustained local action or that degrade quickly when exposed to digestive or systemic environments.

In recent years, advancements in polymer science, formulation methods, and characterization techniques have greatly expanded the potential of mucoadhesive gel systems. Researchers are exploring innovative materials, including natural, synthetic, and stimuli-responsive polymers, to achieve better adhesion, controlled drug release, and improved patient comfort. As a result, mucoadhesive gels are being developed for a wide range of applications, from pain management and infection control to hormone therapy and chronic disease treatment.

Mechanism of Action of Mucoadhesive Gels

The mechanism of action of mucoadhesive gels is based on their ability to interact with the mucus layer that covers mucosal tissues and to remain attached long enough to deliver therapeutic agents effectively. Although several theories have been proposed to explain mucoadhesion, the overall process can be understood in two main stages: initial contact and bond formation.

1. Initial Contact (Wetting and Spreading)

When a mucoadhesive gel is applied to a mucosal surface, it first comes into contact with the moist

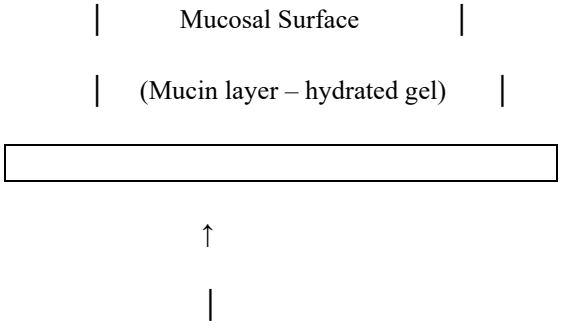
environment. The gel hydrates further, swells, and spreads across the tissue, increasing its surface area of contact. Good wetting is essential at this stage because it allows the polymer chains within the gel to come closer to the mucus layer.

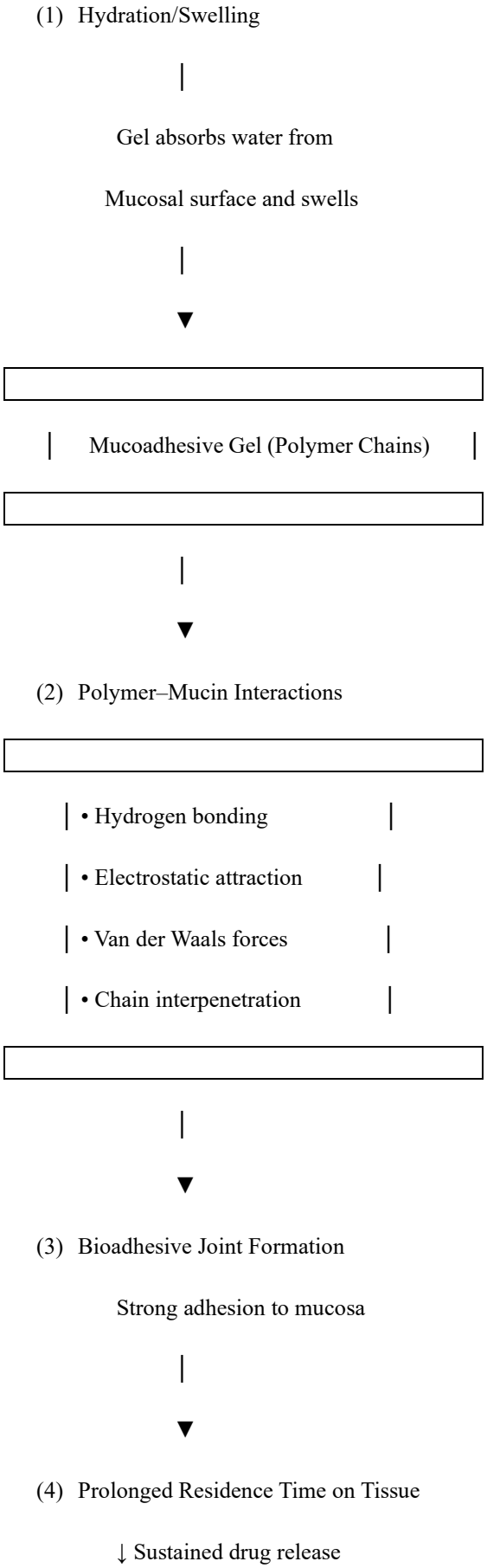
2. Interpenetration of Polymer and Mucin Chains
Once the gel is sufficiently hydrated, the polymer chains begin to interpenetrate with the mucin glycoprotein network present in the mucus. This step depends on the flexibility, length, and mobility of the polymer chains, as well as the viscosity and thickness of the mucus. The deeper and more extensive the interpenetration, the stronger the mucoadhesion.

3. Formation of Physical and Chemical Bonds
After interpenetration, various types of interactions occur between the polymer and mucin chains. These may include hydrogen bonding, ionic interactions, van der Waals forces, and hydrophobic interactions. Some polymers can even form covalent bonds with mucin components. The cumulative effect of these interactions creates a strong adhesive joint that anchors the gel to the mucosal surface.

4. Sustained Retention and Drug Release
Once adhesion is established, the gel remains attached to the mucosa for an extended period, resisting natural clearance mechanisms such as saliva flow, blinking, or mucociliary movement. During this retention period, the drug embedded within the gel gradually diffuses out and is absorbed either locally or systemically, depending on the formulation design. The prolonged contact time enhances drug availability and can improve therapeutic outcomes.

5. Detachment and Clearance
Over time, the adhesive bonds weaken due to dilution, enzymatic degradation, or natural turnover of the mucus layer. The gel eventually detaches and is cleared from the site without causing damage to the tissue.





↓ Improved local absorption

↓ Reduced dosing frequency

Hydration – Gel absorbs moisture from mucosa and swells.

Polymer–mucin interactions – Swollen polymer chains interact with mucin via hydrogen bonds, electrostatic forces, and chain entanglement.

Adhesion – A stable adhesive bond forms between gel and mucosa.

Drug release – The gel remains in place longer, allowing sustained drug delivery.

Natural Mucoadhesive Polymers

- Chitosan
- Sodium alginate
- Pectin
- Gelatin
- Guar gum
- Xanthan gum
- Carrageenan
- Tragacanth
- Locust bean gum
- Hyaluronic acid

Semi-Synthetic Polymers

- Hydroxypropyl methylcellulose (HPMC)
- Hydroxypropyl cellulose (HPC)
- Carboxymethyl cellulose (CMC)
- Methylcellulose (MC)

Synthetic Mucoadhesive Polymers

- Poly(acrylic acid) (Carbopol / Carbomer)
- Polycarbophil
- Polyvinyl alcohol (PVA)
- Polyvinylpyrrolidone (PVP)
- Polyethylene glycol (PEG)
- Eudragit (e.g., Eudragit RL, RS, NE grades)

Specialized / Modified Polymers

- Thiolated polymers (thiomers)
- Cyclodextrin-based mucoadhesives
- Grafted chitosan derivatives (e.g., trimethyl chitosan)
- Lectin-modified polymers

Method of Preparation of Mucoadhesive Gel

Ingredients Commonly Needed

- Mucoadhesive polymer (e.g., Carbopol, HPMC, Chitosan, Sodium alginate)
- Active drug (optional)
- Solvent (usually distilled water)
- Neutralizing/adjusting agents (e.g., Triethanolamine for Carbopol)
- Preservatives (optional)
- Humectants (e.g., glycerin) if required

Procedure

1. Polymer Dispersion

- Measure the required amount of polymer.
- Sprinkle it slowly into distilled water with continuous stirring.

- Allow it to hydrate and swell completely (may require 1–2 hours depending on polymer).

2. Drug Solution/Dispersion Preparation

- Dissolve or disperse the active drug in a suitable amount of water.
- Add humectants or preservatives if needed.

3. Mixing

- Add the drug solution/dispersion slowly into the hydrated polymer base.
- Stir gently to avoid air bubble formation.

4. pH Adjustment / Neutralization (If Required)

- For Carbopol and some acidic polymers: add neutralizing agent (e.g., TEA).
- Gel forms as the pH increases and viscosity rises.

5. Homogenization

- Mix using a homogenizer or gentle mechanical stirrer until a smooth, uniform gel forms.

6. Deaeration

- Allow the gel to stand or use vacuum to remove entrapped air bubbles.

7. Packaging

- Transfer into suitable containers (laminated tubes, jars, or syringes).

Applications of Mucoadhesive Gels

1. Oral and Buccal Applications

- Treatment of mouth ulcers
- Delivery of analgesics and antimicrobials
- Periodontal therapy
- Systemic drug delivery through buccal mucosa

2. Vaginal Applications

- Antifungal therapy
- Contraceptive delivery
- Hormone delivery
- Treatment of bacterial vaginosis

3. Nasal Applications

- Prolonged retention of nasal decongestants
- Delivery of peptides, proteins, and vaccines

4. Ocular Applications

- Increased contact time for eye medications
- Treatment of conjunctivitis, dry eye, or postoperative inflammation

5. Rectal Applications

- Anti-inflammatory and anesthetic applications
- Treatment of hemorrhoids

6. Dermatological and Wound Applications

- Healing of burns, cuts, and chronic wounds
- Delivery of antimicrobial or healing agents
- Long-lasting hydration of skin

7. Gastrointestinal Applications

- Targeted delivery to gastric or intestinal mucosa
- Treatment of ulcers and inflammatory bowel disease

8. Cosmetic and Personal Care

- Long-adhesive cosmetic formulations

- Skin hydration gels

Recent Advancements in Mucoadhesive Gel

1. Living, Self-Regenerating Mucoadhesive Hydrogels

    - Scientists have engineered living hydrogels by using genetically modified bacteria that produce mucoadhesive fibers (e.g., curli fibers) that stick to mucosal surfaces. These bacteria remain viable inside the gel and can regenerate the hydrogel over time, improving longevity and adaptability of the mucoadhesive system.
    - This means the gel is not just passive: it can self-repair and potentially respond dynamically to the mucosal environment.

2. Functionally Modified Polymers for Stronger Adhesion & Controlled Release

    - New polymers are being designed with functional groups (e.g., thiol, lectin, or other bioactive moieties) to improve adhesion to mucus, increase retention, and enable more precise control of drug release.
    - Stimuli-responsive polymers (responding to pH, redox conditions, or enzymes) are being integrated into mucoadhesive gels so that drug release can be triggered by local conditions in the body.

- Mucoadhesive Nanocarriers in Gels

    - Nanoparticles that have both mucoadhesive and mucus-penetrating properties are being embedded within hydrogels. These hybrid systems help deliver drugs more deeply into the mucosal layer while still maintaining prolonged residence time on the surface.

    - This is particularly useful for oral or gastrointestinal delivery: the gel holds the nanocarriers in place, and the carriers themselves can navigate the mucus barrier more effectively.

- Clinical Antiseptic Gels with Mucoadhesion

    - There are new gel formulations intended for clinical antiseptic use that are mucoadhesive. These gels can adhere to mucosal surfaces (e.g., in the oral cavity) and maintain antiseptic action over a longer period, reducing the frequency of re-application.

    - This makes them more effective and user-friendly for patient care.

- Improved Gastrointestinal Retention Systems

    - For gastric (stomach) delivery, researchers are using mucoadhesive gels to prolong the residence time of drugs in the stomach. For example, nanoparticle-based gels adhere to gastric mucosa, allowing for more sustained local treatment of gastric diseases.

    - These systems could significantly improve treatment of diseases like ulcers or infections by ensuring the drug stays where it is needed.

New Mucoadhesive Gel Formulations for Vaginal Delivery

- Novel mucoadhesive gel formulations (e.g., using combinations of different mucoadhesive polymers) are being developed to deliver drugs like adapalene more effectively to vaginal tissue. These gels are optimized for adhesion, spreadability, and drug absorption.

- Such gels aim to improve therapeutic outcomes and patient compliance by providing sustained drug release and good tissue contact

Limitations of Mucoadhesive Gels

1. Limited Residence Time

    - Despite mucoadhesion, gels may be removed quickly by saliva, mucus turnover, or bodily fluids, reducing effectiveness.

2. Irritation or Discomfort

- Some polymers or formulations can cause local irritation, burning, or discomfort, especially in sensitive mucosal areas.

3. Variability in Mucoadhesion

- Adhesive strength can vary with pH, mucosal hydration, and individual physiology, leading to inconsistent drug delivery.

4. Limited Drug Loading

- Highly viscous gels can have low drug solubility or loading capacity, restricting the amount of drug delivered.

5. Stability Issues

- Gels can undergo phase separation, microbial growth, or polymer degradation, reducing shelf life.

6. Poor Penetration

- Some mucoadhesive gels stick well to mucus but fail to penetrate deeply into tissue, limiting drug absorption.

7. Taste and Palatability

- For oral gels, unpleasant taste or texture may reduce patient compliance.

8. Sensitivity to Environmental Conditions

- Temperature, humidity, and pH changes can alter viscosity and adhesion, affecting performance.

9. Manufacturing Challenges

- Producing uniform gels with consistent viscosity, spreadability, and mucoadhesion can be technically challenging.

10. Limited to Local or Mucosal Delivery

- Mainly useful for mucosal surfaces; systemic delivery is sometimes inefficient unless specially designed.

Marketed preparation

Gelclair®

- An oral gel used to protect mucosal surfaces and relieve pain from oral mucositis, ulcers, or other lesions. Wikipedia+2Gelclair Patient Website+2

- Key components: Polyvinylpyrrolidone (PVP) and sodium hyaluronate (hyaluronic acid). Gelclair+1

- Form is concentrated gel (sachets) that you dilute with water before rinsing in the mouth.

Gengigel®

- Oral gel formulated with high molecular weight hyaluronic acid. Truemeds+1

- Used for soothing gums, helping heal ulcers, and promoting mucosal recovery after dental procedures.

Aloclair Plus® Bioadhesive Gel

- Mucoadhesive gel for minor oral ulcers and mucositis symptoms. MDPI

- Contains high-molecular-weight hyaluronic acid

II. CONCLUSION

Mucoadhesive gels are a versatile drug delivery system designed to adhere to mucosal surfaces, prolonging residence time and enhancing local or systemic drug absorption. Their ability to control drug release, reduce dosing frequency, and improve patient compliance makes them valuable in oral, nasal, vaginal, ocular, and rectal applications.

Despite their advantages, they face limitations such as variable adhesion, limited drug loading, potential irritation, and stability challenges. Recent advancements, including stimuli-responsive polymers, nanocarriers, and self-regenerating hydrogels, are addressing these challenges and expanding their therapeutic potential.
Overall, mucoadhesive gels represent a promising platform for targeted, sustained, and patient-friendly

drug delivery, with ongoing innovations likely to broaden their clinical applications and effectiveness in the future.

REFERENCES

[1] Yeruva, T., Morris III, R. J., Kumar, S., Zhao, L., Kofinas, P., & Duncan, G. A. (2025). Rapid in situ forming PEG hydrogels for mucosal drug delivery. Biomaterials Science, 13, 4390–4399. RSC Publishing

[2] Baus Domínguez, M., Aguilera, F.-R., Vivancos Cuadras, F., et al. (2024). Mucoadhesive Pharmacology: Latest Clinical Technology in Antiseptic Gels. Gels, 10(1), 23.

[3] Boddupalli, B. M., Zulkar, N. K., Nath, R., & Banji, D. (2010). Mucoadhesive drug delivery system: An overview. Journal of Advanced Pharmaceutical Technology & Research, 1(4), 381–387. PMC

[4] Sahin, A. B., Karakurt, S., & Bilecen, D. S. (2025). Development of a mucoadhesive drug delivery system and its interaction with gastric cells. Beilstein Journal of Nanotechnology, 16, 371–384. Beilstein Journals

[5] Kulkarni, R., et al. (2025). Mucoadhesive in situ forming gels: Bridging formulation. International Journal of Pharmaceutics. ScienceDirect

[6] Halder, J., Mishra, S., Saha, I., et al. (2025). Optimization and preparation of in situ mucoadhesive gel of azithromycin hydroxypropyl-β-cyclodextrin inclusion complex. BMC Pharmacology and Toxicology, 26, 93. BioMed Central

[7] Patil, K. H., & Mobin, S. A. (2024). Advances in Mucoadhesive Drug Delivery System: Enhancing Efficacy and Patient Compliance. Journal of Drug Delivery & Therapeutics, 14(10), 166–174. Drug Delivery Journal

[8] John, C. V., Vavre, N. A., Sawant, S. S., Sharma, A. L., & Patil, S. D. (2024). Oral mucoadhesive drug delivery system: Formulation strategies and evaluation techniques. World Journal of Advanced Research and Reviews, 24(01), 1706–1719. WJARR

[9] Cevher, E., et al. (2008). Effect of thiolated polymers on the textural and mucoadhesive properties of vaginal gels. International Journal of Pharmaceutics. PMC

[10] Feder Erg, C., Wagner, B., Beyerle, A., & Bernkop Schnürch, A. (2020). Thiolated chitosans: A multi talented class of polymers for mucoadhesive drug delivery. Journal of Pharmaceutical Sciences. PMC

[11] Kulkarni, R. (2023). Mucoadhesive drug delivery systems: A review of recent advances. Journal of Pharmacy & Bioallied Sciences. Taylor & Francis Online

[12] Vigani, B., Rossi, S., Bonferoni, M. C., & Caramella, C. (2023). Mucoadhesive polymers in substance based medical devices: Functional ingredients or what else? Frontiers in Drug Safety and Regulation, 3, 1227763. Frontiers

[13] Sharma, R., Kumar, S., Malviya, R., Prajapati, B. G., & Puri, D. (2024). Recent advances in biopolymer-based mucoadhesive drug delivery systems for oral application. Journal of Drug Delivery Science and Technology. ScienceDirect

[14] Jawadi, Z., et al. (2022). Bio Inspired Muco Adhesive Polymers for Drug Delivery. Pharmaceutics. PMC

[15] Naveen, N. R., & Bernkop Schnürch, A. (2018). A spotlight on thiolated natural polymers and their applications in mucoadhesive drug delivery. European Journal of Pharmaceutical Sciences. ScienceDirect

[16] Ghodrati, A. D., & Comoglu, T. (2024). Mucoadhesive Polymers in Colon Targeted Drug Delivery Systems: A Comprehensive Review. Journal of the Faculty of Pharmacy, Ankara University. DergiPark

[17] Kavitha, M. G., Rupesh Kumar, M., & Singh, S. J. (2011). Novel Mucoadhesive Polymers – A Review. Journal of Applied Pharmaceutical Science. J Appl Pharm Sci

[18] Anitha, A., et al. (2011). Development of mucoadhesive thiolated chitosan nanoparticles for biomedical applications. International Journal of Pharmaceutics. ScienceDirect

[19] Cho, I. S., et al. (2018). Synthesis and characterization of thiolated hexanoyl glycol chitosan for mucoadhesive thermosensitive hydrogel systems. Biomaterials Research, 22, 33. BioMed Central

[20] Pardo Rendón, A. G., et al. (2024). Development and evaluation of the biological activities of mucoadhesive hydrogels with enhanced retention. Gels, 10(9), 574. MDPI

[21] Peppas, N. A. (1996). Hydrogels as mucoadhesive and bioadhesive materials. Journal of Controlled Release. ScienceDirect

[22] Shahid, F., et al. (2025). Synthesis and characterization of a highly stable mucoadhesive

hydrogel for oral drug delivery. Frontiers in Dental Medicine. Frontiers

[23] Hanafy, N., & Wahab, M. (2019). Mucoadhesive Hydrogel Nanoparticles as Smart Carriers for Drug Delivery. Applied Sciences, 9(5), 825. MDPI

[24] Demina, N. B., Larionova, N. I., & Kharenko, E. (2009). Mucoadhesive drug delivery systems: Review. Pharmaceutical Chemistry Journal, 43(4), 200–208. ResearchGate

[25] Alawdi, S., & Solanki, A. B. (2021). Mucoadhesive Drug Delivery Systems: A Review of Recent Developments. Journal of Scientific Research in Medical and Biological Sciences, 2(1), 50–64. Baynoon Centre

[26] Dhutwalia, P., et al. (2014). A review on mucoadhesive drug delivery systems: A novel approach. International Journal of Pharma and Bio Sciences. IJPCBS

[27] Cevher, E., & Şahin, M. (2008). Effect of thiolated polymers to textural and mucoadhesive properties of vaginal gels. European Journal of Pharmaceutics and Biopharmace