International Journal of Advances in Scientific Research
ISSN: 2395-3616 (Online)
Journal DOI:https://doi.org/10.7439/ijasr **Review Article**

Mucoadhesive Microsphere: A Review

Sanjay Kumar*, Shweta Shukla and OP Agrawal

Department of Pharmaceutics, Bhabha Pharmacy Research Institute, Bhabha University, Bhopal-462046, M.P. India

Abstract

Mucoadhesive microspheres are an advanced multiparticulate drug delivery system designed to enhance drug residence time at mucosal surfaces and provide controlled or sustained drug release. By combining the advantages of mucoadhesion and microsphere technology, these systems improve bioavailability, reduce dosing frequency, and enhance patient compliance, particularly for drugs with short half-lives or limited absorption windows. This review discusses the fundamentals of mucoadhesive microspheres, mechanisms of mucoadhesion, polymers used, methods of preparation, evaluation parameters, drug release behavior, applications, challenges, and future perspectives.

Keywords: Mucoadhesive microspheres; Controlled drug delivery; Chitosan; Bioadhesion; Multiparticulate systems.

***Correspondence Info:**
Mr. Sanjay Kumar
Department of Pharmaceutics,
Bhabha Pharmacy Research Institute,
Bhabha University, Bhopal-462046, M.P. India

***Article History:**
Received: 16/11/2025
Revised: 12/12/2025
Accepted: 17/12/2025
DOI: https://doi.org/10.7439/ijasr.v11i1.5887

QR Code

How to cite: Kumar S. Shukla S. Agrawal OP, Mucoadhesive Microsphere: A Review. *International Journal of Advances in Scientific Research* 2025;11(1):e5887. Doi: 10.7439/ijasr.v11i1.5887 Available from: https://ssjournals.co.in/index.php/ijasr/article/view/5887

1. Introduction

The development of advanced drug delivery systems has become an important focus in pharmaceutical research due to the inherent limitations associated with conventional dosage forms. Although oral drug delivery remains the most preferred route because of its convenience, safety, and patient compliance, traditional oral formulations often suffer from short gastrointestinal residence time, variable drug absorption, frequent dosing, and fluctuations in plasma drug concentration. These drawbacks are particularly significant in the management of chronic diseases, where maintaining consistent therapeutic drug levels is essential [1].

Mucoadhesive drug delivery systems have emerged as an effective approach to overcome these limitations by promoting prolonged contact between the drug delivery system and the mucosal surfaces of the body. Mucoadhesion refers to the ability of a material to adhere to mucosal tissues through physicochemical interactions with the mucus layer. By adhering to the mucosa, mucoadhesive systems can increase residence time at the site of absorption, reduce drug loss due to physiological clearance, and improve overall drug bioavailability[2].

Among various mucoadhesive systems, mucoadhesivemicrospheres have gained considerable attention as multiparticulate carriers capable of providing controlled and sustained drug release. Microspheres are spherical polymeric particles, typically in the size range of 1–1000 µm, in which the drug is either dispersed or encapsulated within a polymeric matrix. Their multiparticulate nature allows uniform distribution throughout the gastrointestinal tract, minimizes the risk of dose dumping, and offers better reproducibility of drug absorption compared to single-unit dosage forms[3].

The performance of mucoadhesive microspheres largely depends on the properties of the polymer used. An ideal mucoadhesive polymer should be biocompatible, biodegradable, capable of swelling, and able to form strong interactions with mucin. Natural and synthetic polymers such as chitosan, carbopol, alginate, and cellulose derivatives have been widely explored for this purpose. Among these, chitosan, a cationic polysaccharide obtained by deacetylation of chitin, is particularly attractive due to its strong mucoadhesive properties, biodegradability, and ability to enhance epithelial permeability[4].

Mucoadhesive microspheres combine the advantages of mucoadhesion and controlled drug release, enabling prolonged drug retention at the absorption site

while maintaining a sustained release profile. Drug release from these systems is typically governed by diffusion through the hydrated polymer matrix, polymer swelling, and erosion mechanisms. These characteristics make mucoadhesive microspheres suitable for delivering drugs with short biological half-lives, narrow absorption windows, or those requiring long-term therapy[5].

In recent years, mucoadhesive microspheres have been explored for a wide range of therapeutic applications, including oral, buccal, nasal, and vaginal drug delivery. Their potential to improve therapeutic efficacy, reduce dosing frequency, and enhance patient compliance has positioned them as a promising platform in modern drug delivery research. This review focuses on the principles, formulation strategies, evaluation methods, and applications of mucoadhesivemicrospheres, highlighting their role as an effective controlled drug delivery system[6].

2. Concept of Mucoadhesive Microspheres

Mucoadhesive microspheres are an advanced multiparticulate drug delivery system designed to adhere to mucosal surfaces and provide controlled or sustained drug release. The concept is based on the combination of mucoadhesion—the ability of a material to adhere to mucus or mucosal tissues—and microsphere technology, which involves the encapsulation or dispersion of drugs within spherical polymeric particles[7].

Microspheres are typically spherical particles ranging from 1 to 1000 µm in diameter, composed of natural or synthetic polymers. When formulated with mucoadhesive polymers, these microspheres are capable of attaching to the mucosal lining of the gastrointestinal tract or other mucosal sites such as the buccal, nasal, ocular, or vaginal regions. This adhesion prolongs the residence time of the dosage form at the site of drug absorption, reducing the rate of drug clearance caused by physiological movements and mucus turnover[8].

The mucoadhesive behavior of these microspheres arises from physicochemical interactions between the polymer and mucin, including hydrogen bonding, electrostatic attraction, van der Waals forces, and polymer chain interpenetration. The strength and duration of adhesion depend on factors such as polymer molecular weight, charge density, degree of hydration, and flexibility of polymer chains[9].

From a drug delivery perspective, mucoadhesive microspheres offer several advantages over conventional dosage forms. Their multiparticulate nature allows uniform distribution in the gastrointestinal tract, minimizes the risk of dose dumping, and improves reproducibility of drug absorption. Additionally, by controlling polymer concentration, cross-linking density, and particle size, the drug release profile can be precisely modulated, often achieving sustained release through diffusion, swelling, and erosion mechanisms[10].

Overall, the concept of mucoadhesive microspheres represents a rational and effective approach to enhance drug bioavailability, reduce dosing frequency, and improve patient compliance, particularly for drugs requiring prolonged or site-specific delivery[11].

3. Mechanisms of Mucoadhesion

Mucoadhesion is a complex, multi-step phenomenon that involves the adhesion of a polymeric drug delivery system to the mucosal surface through various physicochemical interactions. Understanding the mechanisms of mucoadhesion is essential for the rational design and optimization of mucoadhesive microspheres. The process of mucoadhesion generally occurs in two main stages, followed by specific molecular interactions that stabilize adhesion[12].

3.1 Stages of Mucoadhesion

3.1.1 Contact Stage

In the initial stage, the mucoadhesive microspheres come into close contact with the mucosal surface. This contact is facilitated by:

- Proper wetting of the polymer
- Swelling of the polymer in the presence of biological fluids
- Spreading of the polymer over the mucosal surface

Adequate hydration of the polymer enhances its flexibility and allows intimate contact with the mucus layer.

3.1.2 Consolidation Stage

During this stage, the adhesive interactions between the polymer and mucus are strengthened. Polymer chains interpenetrate with mucin glycoproteins, forming stable bonds that maintain adhesion over an extended period[13].

3.2 Theories of Mucoadhesion

Several theories have been proposed to explain the mechanism of mucoadhesion:

3.2.1 Wetting Theory

This theory applies mainly to liquid or low-viscosity systems. It states that mucoadhesion depends on the ability of the polymer to spread over the mucosal surface, characterized by low contact angle and good wettability[14].

3.2.2 Diffusion Theory

According to this theory, mucoadhesion occurs due to interpenetration of polymer chains into the mucus network**.** The extent of interpenetration depends on polymer chain length, flexibility, and degree of cross-linking[15].

3.2.3 Electronic Theory

This theory suggests that mucoadhesion results from electrostatic interactions between oppositely charged polymers and mucosal surfaces. For example, cationic polymers like chitosan interact strongly with negatively charged mucin[16].

3.2.4 Adsorption Theory

Mucoadhesion is attributed to the formation of secondary chemical bonds, such as hydrogen bonding, van der Waals forces, and hydrophobic interactions, between the polymer and mucus.

3.2.5 Fracture Theory

This theory focuses on the force required to separate the adhesive system from the mucosal surface. It is often used to quantify mucoadhesive strength experimentally.

3.3 Molecular Interactions Involved in Mucoadhesion

The stability of mucoadhesion is maintained by one or more of the following interactions:

- **Hydrogen bonding** between polymer functional groups and mucin
- **Electrostatic attraction** (e.g., chitosan–mucin interaction)
- **Van der Waals forces**
- **Hydrophobic interactions**

3.4 Factors Affecting Mucoadhesion

The extent and duration of mucoadhesion are influenced by:

- Polymer molecular weight and concentration
- Degree of cross-linking
- Polymer charge and functional groups
- Degree of hydration and swelling
- Mucus composition and turnover rate

Mucoadhesion is governed by a combination of physical contact, polymer swelling, chain interpenetration, and molecular bonding. A clear understanding of these mechanisms enables the development of efficient mucoadhesive microspheres with enhanced residence time, controlled drug release, and improved therapeutic efficacy[17].

4. Polymers Used in Mucoadhesive Microspheres

Polymers play a crucial role in the design and performance of mucoadhesive microspheres, as they are primarily responsible for adhesion to mucosal surfaces, drug entrapment, and controlled release behavior. An ideal mucoadhesive polymer should be biocompatible, biodegradable, non-toxic, capable of swelling, and able to form strong interactions with mucin. Both natural and synthetic polymers have been extensively investigated for the formulation of mucoadhesive microspheres[18].

4.1 Natural Polymers

4.1.1 Chitosan

Chitosan is the most widely used polymer in mucoadhesive microsphere formulations. It is a cationic polysaccharide obtained by deacetylation of chitin.

Key features:

- Strong electrostatic interaction with negatively charged mucin
- Excellent biocompatibility and biodegradability
- Swelling and gel-forming properties
- Permeation-enhancing effect by transient opening of tight junctions

Chitosan-based microspheres are particularly suitable for oral, buccal, and nasal drug delivery.

4.1.2 Sodium Alginate

Alginate is an anionic polysaccharide that forms gels in the presence of divalent cations (e.g., calcium ions).

Advantages:

- Mild gelation conditions
- Good biocompatibility
- Controlled drug release capability

Alginate is often combined with chitosan to improve mucoadhesion and mechanical strength.

4.1.3 Gelatin

Gelatin is a natural protein polymer known for its film-forming and swelling properties.

Applications:

- Encapsulation of drugs
- Biodegradable microsphere systems

However, its mucoadhesive strength is relatively weaker compared to chitosan.

4.2 Semi-Synthetic Polymers

4.2.1 Hydroxypropyl Methylcellulose (HPMC)

HPMC is a non-ionic, hydrophilic polymer commonly used in controlled release formulations.

Characteristics:

- Swelling and gel-forming ability
- Stable and reproducible drug release
- Moderate mucoadhesive properties

4.2.2 Carboxymethyl Cellulose (CMC)

CMC is an anionic cellulose derivative with good swelling capacity.

Benefits:

- Hydrogen bonding with mucin
- Enhanced mucoadhesion
- Controlled release characteristics

4.3 Synthetic Polymers

4.3.1 Carbopol (Polyacrylic Acid)

Carbopol is a highly cross-linked polyacrylic acid polymer.

Features:

- Strong mucoadhesive strength due to hydrogen bonding
- High swelling in aqueous media
- Widely used in buccal and vaginal delivery systems

4.3.2 Polycarbophil

Polycarbophil is a bioadhesive polymer with high molecular weight and strong adhesion properties.

4.4 Selection Criteria for Polymers

The selection of a polymer for mucoadhesive microspheres depends on:

- Desired mucoadhesive strength
- Drug compatibility
- Target site of delivery
- Release profile requirements
- Safety and regulatory acceptance

Table 1. Common Polymers Used in Mucoadhesive Microspheres

Polymer	Type	Charge	Mucoadhesive Strength	Applications
Chitosan	Natural	Cationic	High	Oral, buccal, nasal
Alginate	Natural	Anionic	Moderate	Oral, gastric
Gelatin	Natural	Neutral	Low–Moderate	Oral
HPMC	Semisynthetic	Neutral	Moderate	Oral controlled release
rbopol	Synthetic	Anionic	Very high	Buccal, vaginal

The choice of polymer is a determining factor in the success of mucoadhesive microspheres. Among the available polymers, chitosan stands out as the most promising mucoadhesive polymer due to its strong adhesion, biocompatibility, and ability to control drug release, making it widely suitable for advanced drug delivery applications.

5. Future Perspectives

Mucoadhesive microspheres represent a promising platform for controlled and site-specific drug delivery; however, continued research and technological advancements are essential to fully realize their clinical and commercial potential. Future perspectives in this area focus on enhancing mucoadhesive strength, improving drug release predictability, ensuring scalability, and facilitating clinical translation [19].

One important future direction involves the development of novel and modified mucoadhesive polymers. Chemical modification of existing polymers, such as thiolated, catechol-conjugated or grafted chitosan derivatives, can significantly enhance mucoadhesion through covalent or stronger non-covalent interactions with mucin. These advanced polymers may provide longer residence times and improved bioavailability compared to conventional systems[20].

Another emerging area is the design of stimuli-responsive mucoadhesive microspheres, which can respond to physiological triggers such as pH, enzymes, temperature, or ionic strength. Such systems have the potential to release drugs in a site-specific and on-demand manner, improving therapeutic precision and reducing systemic side effects[21].

The integration of hybrid drug delivery systems is also gaining attention. Combining mucoadhesive microspheres with other gastroretentive approaches, such as floating, expandable, or bioresponsivessss systems, could further enhance gastrointestinal retention and therapeutic efficacy. Additionally, incorporation of nanotechnology, where microspheres act as carriers for nanoparticles or nanocrystals, may enable delivery of poorly soluble or macromolecular drugs[22].

From a formulation science perspective, the application of Quality by Design (QbD) and Design of Experiments (DoE) approaches will play a crucial role in achieving robust, reproducible, and scalable mucoadhesive microsphere formulations. These systematic approaches can help identify critical material attributes and process parameters, thereby facilitating regulatory approval and industrial manufacturing[23].

Future research should also emphasize the establishment of in-vitro–in-vivo correlation (IVIVC) models to better predict clinical performance based on laboratory data. Advanced imaging and bioadhesion assessment techniques may provide deeper insights into in-vivo mucoadhesive behavior and residence time[24].

In conclusion, continued innovation in polymer chemistry, formulation strategies, and evaluation methodologies is expected to significantly advance the field of mucoadhesive microspheres, enabling their broader application in personalized medicine, chronic disease management, and targeted drug delivery[25].

6. Conclusion

Mucoadhesive microspheres have emerged as an effective and versatile drug delivery system capable of overcoming many of the limitations associated with conventional dosage forms. By combining the advantages of mucoadhesion and multiparticulate microsphere technology, these systems are able to prolong residence

time at mucosal surfaces, enhance drug absorption, and provide controlled or sustained drug release.

The success of mucoadhesive microspheres largely depends on the selection of appropriate polymers, optimization of formulation variables, and choice of preparation method. Polymers such as chitosan, carbopol, alginate, and cellulose derivatives play a crucial role in determining mucoadhesive strength, drug entrapment, and release characteristics. Among these, chitosan has gained special importance due to its biocompatibility, biodegradability, strong mucoadhesive properties, and permeation-enhancing ability.

Various preparation techniques, particularly ionotropicgelation, offer efficient and mild processing conditions for the development of mucoadhesive microspheres. Comprehensive evaluation through physicochemical characterization, mucoadhesive testing, and in-vitro drug release studies provides essential insights into formulation performance. Drug release from mucoadhesive microspheres is generally governed by diffusion, polymer swelling, and erosion mechanisms, often exhibiting non-Fickian transport behavior.

Despite challenges related to scale-up, variability in mucosal conditions, and in-vivo predictability, ongoing advancements in polymer modification, hybrid delivery systems, and quality-by-design approaches continue to strengthen the potential of mucoadhesive microspheres. Overall, mucoadhesive microspheres represent a promising platform for controlled and site-specific drug delivery, with significant potential to improve therapeutic efficacy, patient compliance, and clinical outcomes in the management of chronic diseases.

References

[1]. Smart JD. The basics and underlying mechanisms of mucoadhesion. *Adv Drug Deliv Rev.* 2005;57(11):1556–1568.

[2]. Bernkop-Schnürch A. Mucoadhesive polymers: strategies, achievements and future challenges. *Adv Drug Deliv Rev.* 2005;57(11):1553–1555.

[3]. Andrews GP, Laverty TP, Jones DS. Mucoadhesive polymeric platforms for controlled drug delivery. *Eur J Pharm Biopharm.* 2009;71(3):505–518.

[4]. Khutoryanskiy VV. Advances in mucoadhesion and mucoadhesive polymers. *MacromolBiosci.* 2011;11(6):748–764.

[5]. Carvalho FC, Bruschi ML, Evangelista RC, Gremião MPD. Mucoadhesive drug delivery systems. *Braz J Pharm Sci.* 2010;46(1):1–17.

[6]. Shaikh R, Raj Singh TR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. *J Pharm Bioallied Sci.* 2011;3(1):89–100.

[7]. Boddupalli BM, Mohammed ZNK, Nath RA, Banji D. Mucoadhesive drug delivery system: An overview. *J Adv Pharm Technol Res.* 2010;1(4):381–387.

[8]. Park K, Robinson JR. Bioadhesive polymers as platforms for oral-controlled drug delivery: method to study bioadhesion. *Int J Pharm.* 1984;19(2):107–127.

[9]. Vasir JK, Tambwekar K, Garg S. Bioadhesive microspheres as a controlled drug delivery system. *Int J Pharm.* 2003;255(1–2):13–32.

[10]. Chowdary KPR, Rao YS. Mucoadhesive microspheres for controlled drug delivery. *Biol Pharm Bull.* 2004;27(11):1717–1724.

[11]. Kaş HS. Chitosan: properties, preparations and application to microparticulate systems. *J Microencapsul.* 1997;14(6):689–711.

[12]. Sinha VR, Singla AK, Wadhawan S, et al. Chitosan microspheres as a potential carrier for drugs. *Int J Pharm.* 2004;274(1–2):1–33.

[13]. He P, Davis SS, Illum L. In vitro evaluation of the mucoadhesive properties of chitosan microspheres. *Int J Pharm.* 1998;166(1):75–88.

[14]. Dhawan S, Singla AK, Sinha VR. Evaluation of mucoadhesive properties of chitosan microspheres prepared by different methods. *AAPS PharmSciTech.* 2004;5(4):e67.

[15]. Illum L. Chitosan and its use as a pharmaceutical excipient. *Pharm Res.* 1998;15(9):1326–1331.

[16]. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro- and nanoparticles in drug delivery. *J Control Release.* 2004;100(1):5–28.

[17]. Dash M, Chiellini F, Ottenbrite RM, Chiellini E. Chitosan—A versatile semi-synthetic polymer in biomedical applications. *Prog Polym Sci.* 2011;36(8):981–1014.

[18]. Ways TMM, Lau WM, Khutoryanskiy VV. Chitosan and its derivatives for application in mucoadhesive drug delivery systems. *Polymers (Basel).* 2018;10(3):267.

[19]. Sogias IA, Williams AC, Khutoryanskiy VV. Why is chitosan mucoadhesive? *Biomacromolecules.* 2008;9(7):1837–1842.

[20]. Bernkop-Schnürch A. Thiomers: a new generation of mucoadhesive polymers. *Adv Drug Deliv Rev.* 2005;57(11):1569–1582.

[21]. Bernkop-Schnürch A, Schwarz V, Steininger S. Synthesis and characterisation of mucoadhesive thiolated polymers. *Int J Pharm.* 1999/2000; (thiolated polymer conjugates; covalent mucus interactions).

[22]. Higuchi T. Mechanism of sustained-action medication: theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J Pharm Sci.* 1963;52(12):1145–1149.

[23]. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. *Int J Pharm.*1983;15:25–35.

[24]. Costa P, Lobo JMS. Modeling and comparison of dissolution profiles. *Eur J Pharm Sci.* 2001;13(2):123–133.

[25]. Longer MA, Robinson JR. Oral delivery using a bioadhesive polymer (bioadhesive platforms—early foundational work). *J Pharm Sci.* 1985.