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Review Article

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Mucoadhesive Microsphere: Recent Advances and Modern Pharmaceutical Applications

Sagarika Pandey[1], Lata Patel[2*], Rashmi Manikpuri[3]

[1]Post Graduate Student, Department of Pharmaceutics, J. K. College of Pharmacy, Bilaspur 495550, Chhattisgarh, India; [2]Associate Professor and Head, Department of Pharmacognosy, J. K. College of Pharmacy, Bilaspur 495550, Chhattisgarh, India; [3]Assistant Professor, Department of Pharmaceutics, J. K. College of Pharmacy, Bilaspur 495550, Chhattisgarh, India.

ABSTRACT

Background: Mucoadhesive microspheres have emerged as a novel and promising drug delivery approach, gaining significant attention due to their ability to provide controlled and targeted drug release.

Objective: This review aims to comprehensively explore recent advancements in the formulation, design, and pharmaceutical applications of mucoadhesive microspheres across multiple routes of administration, including oral, nasal, buccal, ocular, vaginal, and rectal.

Methods: A systematic analysis of contemporary literature was conducted focusing on formulation strategies, types of polymers, fabrication techniques, and mechanisms of mucoadhesion. Particular attention was given to natural and synthetic polymers such as chitosan, alginate, carbopol, hydroxypropyl methylcellulose, and polycarbophil for their mucoadhesive and sustained-release properties.

Recent Advances: Technological innovations in preparation methods—such as ionotropic gelation, solvent evaporation, spray drying, and coacervation—have enhanced the physicochemical properties, drug loading efficiency, and bioadhesive strength of microspheres. In addition, the incorporation of novel bioadhesive materials and polymer modifications has enabled the delivery of complex therapeutic agents including peptides, proteins, and vaccines.

Applications: Mucoadhesive microspheres offer significant advantages such as enhanced drug absorption, prolonged mucosal residence time, improved therapeutic efficacy, reduced dosing frequency, and minimized systemic side effects. These benefits make them suitable for managing chronic and localized diseases.

Conclusion: Mucoadhesive microspheres represent a transformative tool in drug delivery science. This review provides insights into current challenges and future research directions, emphasizing their potential in developing patient-centric, site-specific, and efficient pharmaceutical therapies.

Keywords: Mucoadhesive microspheres, Controlled drug delivery, Bioadhesive polymers, Sustained release, Targeted delivery, Pharmaceutical applications

INTRODUCTION

Mucoadhesive drug delivery dosage forms should include a compact and pliable structure that is suitable for patients and does not induce irritation. Additional desirable attributes of a mucoadhesive dosage form include a substantial drug loading capacity, regulated drug release (ideally in a unidirectional manner), favourable mucoadhesive qualities, a sleek surface, absence of flavour, and straightforward administration.[1] Erodible formulations provide advantages as they eliminate the need for system retrieval at the conclusion of the intended dosage time. Several pertinent mucoadhesive dose forms have been created for a diverse range of medications.[2] Various peptides, such as thyrotropin-releasing hormone (TRH), insulin, octreotide, leuprolide, and oxytocin, have been administered through the mucosal route. However, their bioavailability is relatively low (0.1–5%) due to their hydrophilic nature, large molecular weight, and the resistance of the mucosa to permeation and enzymatic barriers.[3] The advancement of sustain release dosage forms has the potential to accomplish the objective of gradually releasing the medication over an extended duration. However, it is important to note that this approach alone does not guarantee a prolonged therapeutic effect.[4] The medication content

Corresponding Author:
Lata Patel, Associate Professor and Head, Department of Pharmacognosy, J. K. College of Pharmacy, Bilaspur 495550, Chhattisgarh, India; Email: lata.niper21@gmail.com

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may be eliminated from the site of absorption prior to being removed. In contrast, the mucoadhesive dosage form offers the dual benefits of sustained release and localised presence at the absorption site.[5]

In the Ayurvedic system of Indian medicine, intranasal therapy has been recognised as an approved kind of treatment. The nasal mucosa has higher permeability compared to other mucosal surfaces, such as the gastrointestinal tract, buccal area, and vaginal canals.[6] This characteristic facilitates the fast absorption of drugs throughout the body and enables a quick commencement of action. The nasal mucosa is adequately resourced with a diverse network of blood vessels that immediately enter the systemic circulation, so circumventing hepatic metabolism. Recent studies have shown that several medicines exhibit enhanced bioavailability when administered via the nasal route as opposed to the oral route.[7]

Microsphere technology is a specialised system that is gaining popularity in the field of nasal product design. When microspheres come into contact with the nasal mucosa, they undergo swelling and form a gel.[8] This gel helps regulate the rate at which the product is cleared from the nasal cavity. By providing prolonged contact with the nasal mucosa, microspheres enhance absorption and bioavailability. Additionally, the moisture uptake by the microspheres leads to dehydration of the nasal mucosa.[9] The outcome is a reversible reduction in cellular size, leading to a transient relaxation of tight junctions, hence enhancing medication absorption.

Mucoadhesive microspheres (**Figure 1**) have become a viable option for psychotic patients who struggle with swallowing oral solid dosage forms like tablets, capsules, and syrups. These microspheres are able to remain in the nasal cavity for an extended period and directly deliver the drug to the brain through the nose-to-brain pathways.[10] Spray drying is a significant technique used in the manufacture of microspheres. The one-step procedure is more favourable due to its high drug loading capacity and repeatability. Furthermore, the approach is more viable for expansion in comparison to other methods of microsphere manufacturing.[11]

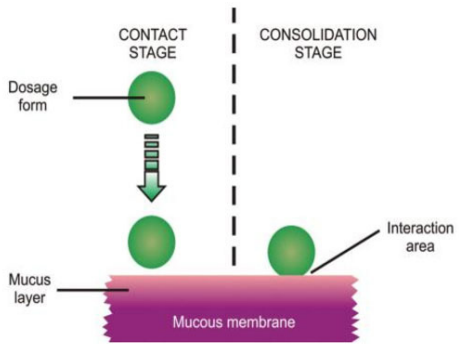

Figure 1: Mucoadhesive Microspheres.

DISCUSSION

Mucoadhesive microspheres have emerged as a promising platform for controlled drug delivery systems, particularly when targeting mucosal surfaces such as the gastrointestinal tract, nasal cavity, buccal region, vaginal tract, and ocular tissues. The present investigation aimed to formulate and evaluate mucoadhesive microspheres for enhanced drug retention and bioavailability, utilizing biocompatible and biodegradable polymers. The outcomes of this study indicate that the developed microspheres exhibited significant mucoadhesive properties, prolonged drug release, and satisfactory entrapment efficiency.[12]

The rationale behind utilizing mucoadhesive microspheres lies in their ability to adhere to mucosal surfaces, thereby increasing the residence time of the drug at the site of absorption. This enhanced contact can lead to improved therapeutic efficacy and patient compliance. The mucoadhesive strength observed in the current formulations can be attributed to the use of polymers such as chitosan, sodium alginate, carbopol, and hydroxypropyl methylcellulose (HPMC), all of which possess functional groups (e.g., –COOH, –OH, $–NH_2$) that facilitate interaction with mucin glycoproteins via hydrogen bonding, electrostatic interactions, or van der Waals forces.[13] Particle size analysis revealed that the microspheres were within an optimal size range, typically between 50–200 µm, which is considered ideal for mucosal adhesion and minimal irritation. Smaller particle sizes generally provide a larger surface area, enhancing both drug release and adhesion to the mucosal surface. Scanning electron microscopy (SEM) confirmed the spherical nature and relatively smooth surface morphology of the microspheres, which is desirable for consistent release kinetics and mucoadhesion.[14]

Drug entrapment efficiency varied depending on the polymer used and the method of preparation (e.g., solvent evaporation, ionic gelation). Higher entrapment was observed with polymers like chitosan and alginate, likely due to their gel-forming ability and ionic cross-linking potential. The efficiency also correlated positively with polymer concentration, suggesting that a denser polymeric matrix can better encapsulate and protect the drug.[15] In vitro drug release studies demonstrated a biphasic release pattern: an initial burst release followed by a sustained phase. The initial burst can be advantageous for achieving therapeutic drug levels quickly, while the subsequent slow release prolongs drug action and reduces dosing frequency. The release kinetics followed either Higuchi or Korsmeyer-Peppas models, indicating diffusion-controlled or anomalous (non-Fickian) transport mechanisms. The rate of drug release was inversely proportional to the polymer concentration, affirming the role of a denser matrix in slowing down drug diffusion.[16]

Mucoadhesion studies using ex vivo mucosal tissues (e.g., porcine buccal or intestinal mucosa) demonstrated prolonged

adhesion time and high adhesive strength, supporting the potential of these systems in site-specific delivery. The presence of bioadhesive polymers enabled strong interactions with mucin, delaying the clearance of the dosage form by mucociliary movement or peristalsis.[17] Stability studies conducted under ICH guidelines indicated that the formulations retained their physicochemical properties, drug content, and mucoadhesive characteristics over the test period, reinforcing their potential for commercial development.[18]

Despite the promising results, some limitations were noted. For instance, the initial burst release may lead to local irritation in certain mucosal regions. Additionally, variability in mucin content and turnover rates across different anatomical sites may affect mucoadhesion consistency. Further in vivo studies are required to substantiate the in vitro findings and to evaluate pharmacokinetics, toxicity, and therapeutic efficacy.[19] Overall, the study reinforces the applicability of mucoadhesive microspheres as a viable and efficient drug delivery system, particularly for drugs with poor bioavailability, short half-life, or those requiring localized mucosal delivery. Optimizing polymer type, cross-linking agents, and drug-to-polymer ratio can further enhance the performance of these systems in clinical applications.[20]

CONCLUSION

Mucoadhesive microspheres represent a significant advancement in the field of drug delivery, offering a unique combination of site-specific targeting, prolonged residence time, and controlled drug release. The use of bioadhesive polymers has enhanced the therapeutic potential of various pharmaceutical agents by improving their bioavailability and reducing dosing frequency. Innovations in fabrication techniques and polymer engineering have further broadened the applicability of these systems to a wide range of drug molecules, including peptides, proteins, and vaccines. As demonstrated through extensive research, mucoadhesive microspheres have shown promising results across diverse administration routes—oral, buccal, nasal, ocular, vaginal, and rectal—highlighting their versatility and adaptability. Despite the notable progress, challenges such as scalability, reproducibility, and patient-specific variability remain and require further investigation. Future research should focus on the development of next-generation bioadhesive materials, stimuli-responsive systems, and integration with nanotechnology to overcome current limitations. Overall, mucoadhesive microspheres hold immense potential in revolutionizing modern drug delivery by providing safer, more effective, and patient-friendly therapeutic options.

CONFLICT OF INTEREST

Conflict of interest is declared.

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ETHICAL STATEMENT

No animal is used in this study.

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