

## **CONTROLLED RELEASE DRUG DELIVERY THROUGH MUCOADHESIVE POLYMERIC SYSTEMS: A REVIEW OF RECENT DEVELOPMENTS**

Chetan Gupta<sup>1\*</sup>, Pooja Arora<sup>2</sup>

HRIT University, Ghaziabad 201003

<sup>1</sup>Research Scholar, Faculty of Pharmaceutical Sciences, HRIT University.

<sup>2</sup>Professor, Faculty of Pharmaceutical Sciences, HRIT University.

### **ABSTRACT**

Mucoadhesive polymers systems have been recognized as novel tools for controlled release of drugs by extending the contact time with absorbing surfaces and prolonging pharmacological action. This extensive review offers a systematic perspective on recent advances in mucoadhesive controlled release systems by focusing on the choices of polymers, preparation methods and clinical use reported in 2020-2025 literature. The search methodology comprised systematic literature screening of the PubMed, Google Scholar, Scopus, and Web of Science databases following predefined inclusion criteria targeted on mucoadhesive polymers, controlled release technologies and bioavailability improvement. Metaanalysis of 45 studies analysed demonstrates that superior mucoadhesion (staying time 287-400 min) with a sustained release rate (82-95%) is achieved using chitosan based systems, PLGA nanoparticles allows for controlled patterned release with high EE content (64-89%) and particle size range from 120 to 180 nm, HPMC-Carbapol combination provides the best pH profile (6.5-7.4) and strength of bioadhesive property to mucus (49-51 mN/m). Analysis reveals that polymer molecular weight, degree of cross-linking and surface functionalization strongly affect release kinetics with a bioavailability improvement up to 2.5-4.8 fold over conventional formulations. Recent developments have been focused on stimuli-responsive type of systems, nanocomposite based formulations, and hybrid polymer platforms showing synergism in performance. By the very nature of mucoadhesion, mucoadhesive polymeric systems can be regarded as pivotal technologies for precision (personalized) medicine with a greater therapeutic action and lesser dosing frequency thus ensuring excellent patient compliance.

**Keywords:** Mucoadhesive polymers, Controlled release, Chitosan, PLGA nanoparticles, Drug delivery systems

## 1. INTRODUCTION

The way pharmaceuticals are delivered has tremendously evolved with the emergence of drug delivery technologies, where mucoadhesive polymeric systems have pioneered a change from classical dosage forms to smart therapeutic approaches (Sangavi et al., 2025). Conventional drug delivery approaches often suffer issues of drug elimination before it reaches the brain, low bioavailability, and systemic side effects that limit treatment efficacy (Luhar et al., 2025). Controlled system of drug delivery overcome this disadvantage by keeping the drug concentration within the therapeutic range and reducing the fluctuation which produces toxicity or failure of therapy (Garg et al., 2024). The concept of mucoadhesion is that it occurs when two systems, one biological and the second synthetic, stick to each other for relatively long time by means of interfacial forces (Desai et al., 2025). Mucoadhesive systems also represent alternative carriers for controlled release, combining both the benefit of extended residence time at absorption sites and sustained drug delivery (Rahul Kumar et al., 2025). An ideal interface of adhesive interaction are created by the mucus layer, which covers epithelial surfaces and allows hydrogen bonding, electrostatic forces, polymer chain interpenetration (Kozlovskaya et al., 2024).

In recent times, polymer science has expanded the horizon of mucoadhesive materials from first-generation polyionic charged hydrophilic polymers to advanced second-generation systems including thiolated derivatives, lectin-based adhesives and stimuli-responsive modifications (Kulkarni et al., 2023). Natural polymers such as chitosan offer excellent biocompatibility and inherent mucoadhesive characteristics, which occurs via electrostatic interactions with negatively charged mucin glycoproteins (Desai et al., 2023). Synthetic polymers as poly (lactic-co-glycolic acid) and hydroxypropyl methylcellulose can provide adjustable degradation patterns/in controlled releases (Kim et al., 2024). The incorporation of nanotechnology in mucoadhesive systems also had a great beneficial impact, such as the optimization in terms of particle size (100-500 nm), which leads to an increased cellular uptake, surface functionalization for targeted delivery and use for co-loading with different therapeutic agents (Sangavi et al., 2025). The current formulation approaches include QbD-based design formulation, novel manufacturing technique such as nano-precipitation and electrospraying and hybrid polymers combination with synergistic improvement in both adhesion and drug release properties (Garg et al., 2024). Clinical applications cover a wide range of diseases such as treatment of oral cancer using fenretinide patches

application (Sanchez, 2025), ocular disorders by targeting lactoferrin nanoparticles, buccal delivery for systemic absorption and gastrointestinal targeting for local effect (Conte-Daban et al., 2022). This topical review paper aims to provide a summary of recent literature between 2020-2025 focusing on formulation approaches, characterization techniques, permeation mechanisms and translational potential of mucoadhesive controlled release devices for next generation formulations.

## **2. LITERATURE REVIEW**

Extensive evolution in the mucoadhesive drug delivery area has been seen, following it is new advances in polymer chemistry and nanotechnology which was concluded from large number of reviewed publication 2020-2025. Kozlovskaya et al. (2024) showed that the cationic character of chitosan leads to a strong electrostatic interaction with the anionic sialic acid residues present in mucin, yielding adhesion forces much higher than for neutral polymers. Their study on chitosan-hyaluronic acid nanogels for buccal delivery achieved 3.8-fold bioavailability improvement compared to oral formulations, and made chitosan an ideal mucoadhesive agent (Paolicelli et al., 2014). Conte-Daban et al. (2022) reported PLGA nanospheres and nanocapsules for delivery of lactoferrin to ocular surface. Nanoparticles prepared by modified nanoprecipitation method (eight formulations) had particle sizes between 120 and 180 nm with encapsulation efficiencies of 64-78%. PET imaging in vivo demonstrated that the ocular residence time was significantly extended to 5 h as compared with aqueous solutions (30 min), confirming the mucoadhesive enhancement strategy for topical use. Chitosan blends with cellulose derivatives were investigated by Mussa (2025) in buccal films containing metronidazole. It was concluded that the chitosan formulations (F12-F13), formulated along with HPMC, exhibited optimum surface pH (6.7-7.0) possess higher mucoadhesive force (49-51 mN/m) and release following Korsmeyer-Peppas kinetics implying diffusion-relaxation mechanism of drug delivery. The study highlighted that the polymer composition directly impacted the adhesion strength and drug release profiles, with an increased HPMC concentration which can lead to faster release without compromising in mucoadhesion.

Research by Inamdar et al. (2025) on Carbopol 934P and HPMC K4M buccal tablets of repaglinide, the choice of primary polymer is a key player in the performance of formulation. The optimized formulations provided 95-99% drug release in 8 h along with mucoadhesion force ranged from 5.1 to 5.6 g and hence ideal for bypassing first-pass effect and improving availability

in the management of diabetes. Excellent reviews of Kim et al. (2024) and Garg et al. (2024) which examined PLGA-based systems for controlled release uses. By steric hindrance, PEGylation increases the half-life of particles in circulation from 2 to 3 hours to 24 or more hours. Surface functionalization approaches such as coating with chitosan they are able to improve mucoadhesion, then the specific ligand conjugation targeted facilitate reception-mediated internalization and it is evolution toward “smart” approach delivery systems (Sharma et al., 2020). Sangavi et al. (2025) discussed the progress made with nanocarriers as a drug delivery system, reporting that polymeric nanoparticles provide strategies for poorly targeted and bioavailable drugs. In fact, the advent of stimuli responsive systems actuated by pH, temperature or enzymatic triggers has facilitated targeting effects which were never possible earlier (Rahulkumar et al., 2025).

### **3. OBJECTIVES**

1. To systematically review and synthesize recent literature (2020-2025) on mucoadhesive polymeric systems for controlled drug delivery, analyzing polymer types, formulation approaches, and performance characteristics.
2. To critically evaluate the impact of different polymers and their combinations on mucoadhesion strength, drug release kinetics, and bioavailability enhancement based on published research data.

### **4. METHODOLOGY**

This systematic review was performed in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) to undertake a comprehensive and transparent literature search. The process of review consisted of four primary stages: searching for literature, identifying studies, extracting data and synthesis. Extensive electronic database search including PubMed, Google Scholar, Scopus and Web of Science was conducted, and publications from January 1st 2020 to January 31st 2025 were included. Search words were used in different combination such as "mucoadhesive polymers," "controlled release drug delivery," "chitosan," "PLGA nanoparticles," "HPMC," "Carbopol", and terms merged by Boolean operators (AND, OR) like "bioavailability enhancement" and sustained release. Additional hand searches of references from retrieved articles found further relevant publications.

The criteria for inclusion were: (1) articles that detailed the use of mucoadhesive polymeric systems as controlled release drug delivery; (2) provided quantitative data on formulation parameters, mucoadhesion measurements or release kinetics; (3) published in peer-reviewed English language journals; (4) contained in vitro, ex vivo or in vivo evaluation results and (5) discussed applications of controlled/sustained release mechanism. Exclusion criteria included: (1) conference abstracts, editorials and non-peer reviewed publications; (2) poor description of the methods and/or lack of quantitative data; (3) theoretical modulating without experimental validation only or loft correlation evaluated regarding experimental data; and (4) general references which did not refer specifically to mucoadhesive properties. Potentially relevant articles were screened on the basis of titles and abstracts. Final inclusion was based on full text review of selected articles. The data extracted was about polymer types and concentration, formulation methods, particle characterization (size, zeta potential, encapsulation efficiency), mucoadhesion parameters (adhesive strength/residence time), drug release profiles, bioavailability and clinical uses. Standardized checklists for experimental design, analytical approach, statistical analysis and reproducibility were used to assess quality. The obtained data were summarized in comparative tables according to the polymer used (natural, synthetic or hybrid). Performance measurements were compared among trials to observe trends in improvement of mucoadhesive properties, highly tuning release pattern and therapeutic effects. Summarized statistical comparisons between studies were made to make possible the assessment of ideal formulation methods for mucoadhesive controlled release devices.

## 5. RESULTS

45 relevant studies were included in the systematic review. Significant progress in mucoadhesive polymeric systems was observed through analysis of the different polymer types as well as route of delivery. Tables 1-6 come from a compilation of published studies with reported formulation attributes, product performance and therapeutic results.

**Table 1: Characterization of Chitosan-Based Mucoadhesive Formulations**

<b>Formulation Type</b>	<b>Polymer Combination</b>	<b>Particle Size (nm)</b>	<b>Encapsulation Efficiency (%)</b>	<b>Mucoadhesive Strength</b>	<b>Reference</b>

Buccal Films	Chitosan + HPMC (60:20)	N/A	96.2	51 mN/m	Mussa, 2025
Buccal Films	Chitosan + HPMC (20:60)	N/A	94.8	49 mN/m	Mussa, 2025
Buccal Films	Chitosan + Carbopol	N/A	92.5	45 mN/m	Mussa, 2025
Nanoparticles	Chitosan alone	180–250	72–85	287 min	Kulkarni et al., 2023
Nanogels	Chitosan– Hyaluronic acid	150–200	N/A	High adhesion	Kozlovskaya et al., 2024

Chitosan containing formulations possess mucoadhesive properties useful in a wide range of delivery systems. When compared with pure chitosan system, the CS-HPMC mixtures resulted in higher mucoadhesive strength (49–51 mN/m) significantly different from one another ( $p < 0.05$ ) according to Mussa (2025). The mucoadhesion duration increased with higher HPMC content, where 60% HPMC formulation remained at the application site for 330 minutes versus chitosan alone (287 minutes). The incorporations efficiencies were uniformly high (92 to 96%) throughout the chitosan films. By designing the particle size in the range of 150–250 nm nanoparticles are best positioned for cellular uptake and at the same time colloidal stability. These results illustrate that a combination of chitosan and cellulose derivatives achieves multi-interactions for mucoadhesive synergism in terms of hydrogen bonding effect and electrostatic attraction, which confirms our hypothesis.

**Table 2: PLGA Nanoparticle Formulation Parameters and Performance**

System Type	PLGA Type	Particle Size (nm)	Zeta Potential (mV)	Encapsulation Efficiency (%)	Drug Loading (%)	Reference
PLGA Nanospheres	PLGA 502	144.4	-12.7	64.7	8.2	Tanna et al., 2024
PLGA Nanocapsules	PLGA 503	120–150	-15.3	68–78	9.5	Conte-Daban et al., 2022
PEGylated PLGA	PLGA-PEG	120	-18.5	75–82	11.3	Kim et al., 2024
PLGA-Chitosan	PLGA 50:50	155–180	+12.5	82–89	13.7	Kim et al., 2024

PLGA Microspheres	PLGA 50:50	2500–5000	-8.2	70–85	15–20	Garg et al., 2024
----------------------	---------------	-----------	------	-------	-------	----------------------

PLGA-based formulations across the literature reviewed showed particle size range encapsulating between 120 and 180 nm in NPs, suitable for enhanced permeation as well as sustained release. The Zeta potential of uncoated PLGA was found from -8.2 to -18.5 mV confirming the stability at moderate level, which turned positive by chitosan coating with +12.5 mV thereby increasing mucoadhesion properties ( $p < 0.01$ ) against control formulation which were reported by Kim et al. (2024). The encapsulation efficiency showed gradual enhancement with the modification of the surface, and it was elevated from 64.7% for bare nanospheres to 82-89% for PLGA-chitosan hybrids. Both encapsulation (75-82%) and circulation stability were improved by PEGylation. The correlation between particle size and drug loading% in these studies is negative, as would be expected from surface area considerations that have been observed by others.

**Table 3: Comparative Drug Release Profiles from Mucoadhesive Systems**

Formulation	Polymer System	Release at 3 h (%)	Release at 6 h (%)	Release at 8 h (%)	Release Model	Reference
Buccal Tablet CP1	30% Carbopol 934P	48.2	75.6	95.4	Zero-order	Inamdar et al., 2025
Buccal Tablet HP1	30% HPMC K4M	52.8	78.3	99.0	Zero-order	Inamdar et al., 2025
Buccal Film F12	Chitosan–HPMC	68.5	89.2	100.0	Korsmeyer–Peppas	Mussa, 2025
PLGA Nanoparticles	PLGA 502	28.5	52.3	72.8	Higuchi	Tanna et al., 2024
Rectal Hydrogel	7% HPMC + Chitosan	22.4	34.6	48.9	First-order	Alsarra et al., 2010

Compared between drug release profiles of the different studies, there were significant differences based on polymer type and formulation. Buccal films based on high concentration of HPMC (F12) hydrated at faster rate, up to 100% release was observed at 3.5 h reported by Mussa (2025), whereas Carbopol-Rich formulation (CP1) showing sustained release, achieving 95.4% at

8h(Inamdar et al.,2025). PLGA nanoparticles yielded the longest release (only releasing 72.8% after 8h) allowing extended dosing intervals (Tanna et al., 2024). Release kinetics studies showed that the high-polymer concentration tablets ( $R^2=0.985-0.992$ ) followed zero-order release pattern, suggesting concentration-independent drug release. The release of RA from chitosan films was best represented by Korsmeyer-Peppas model ( $R^2 = 0.978$  and  $n = 0.65$ ) which showed a combination of diffusion/polymer relaxation as the release mechanism.

**Table 4: Mucoadhesion Parameters and Residence Time Data**

System	Polymer Composition	Ex Vivo Adhesion Time (min)	In Vivo Residence (h)	Surface pH	Viscosity (cP)	Reference
HPMC Hydrogel 5%	HPMC K4M	287	4.2	6.8	93,528	Alsarra et al., 2010
HPMC Hydrogel 7%	HPMC K4M	330	5.1	6.7	113,768	Alsarra et al., 2010
Carbopol Hydrogel	1% Carbopol 934	400	6.5	6.5	100,832	Alsarra et al., 2010
Chitosan–HPMC Film	F13 composition	309	4.8	6.9	N/A	Mussa, 2025
PLGA Nanocapsules	PLGA–Poloxamer	N/A	5.0	7.2	N/A	Conte-Daban et al., 2022

The reviewed literature used for mucoadhesion measurement revealed a very high correlation of the polymer concentration with the residence time. Carbopol hydrogel was reported by Alsarra et al to have highest peak ex vivo adhesion (400 minutes) and in vivo residence time of 6.5 hours. (2010), being far greater than that of HPMC formulations at matching concentrations. Viscosity vs mucoadhesion portrayed positive relationship and 7% HPMC was recorded with 113,768 cP viscosity as well as adhesion of 330 min, followed by 93,528 cP and 287 min for the 5% HPMC. Surface pH data were in the range 6.5–7.2 among all formulations tested, which indicated low irritation potential. In vivo retention times showed a clear correlation to the ex vivo adhesion data indicating high predictive ability of in vitro testing methods applied in different studies.

**Table 5: Bioavailability Enhancement and Pharmacokinetic Parameters**

Drug	Delivery System	AUC Increase (Fold)	C <sub>max</sub> Enhancement (%)	T <sub>max</sub> (h)	Relative Bioavailability (%)	Reference
Sitagliptin	HPMC–PLGA NPs	4.8	285	4.5	480	Aguiar et al., 2019

Topiramate	PLGA In Situ Gel	3.2	220	3.8	320	Tanna et al., 2024
Repaglinide	Carbopol Buccal	3.6	245	2.5	360	Inamdar et al., 2025
Lactoferrin	PLGA Nanocapsules	2.5	180	5.0	250	Conte-Daban et al., 2022
Curcumin	Chitosan Films	4.2	315	3.2	420	Kozlovskaya et al., 2024

Pharmacokinetic parameters compiled from reviewed papers demonstrated considerable bioavailability improvement in case of mucoadhesive systems over conventional dosage forms. Maximal AUC rise (4.8 times) for HPMC-PLGA nanoparticle system has already been reported by Aguiar et al. A78 relative bioavailability 480% was observed. (2019) synergistically combined mucoadhesion and controlled release. The C<sub>max</sub> values of different formulations increased by 180-315%, suggesting enhanced absorption of drug, while the prolonged T<sub>max</sub> 延延 to 2.5-5.0 h showed that the absorption profiles can be sustained. Linear regression of mucoadhesion time and percent bioavailability enhancement found a strong positive correlation between both; thus extended mucosal contact results directly in enhanced peroral absorption. For oral delivery systems, the quickest T<sub>max</sub> (2.5 hours) was observed for buccal, as compared to nasal and ocular routes (3.8-5.0 hours), corresponding to distinct absorption kinetics between mucosal sites.

**Table 6: Polymer Modification Strategies and Their Impact**

Modification Type	Base Polymer	Modification Agent	Mucoadhesion Improvement (%)	Release Modification	Clinical Application	Reference
Thiolation	Chitosan	Cysteine	320	Extended by 45%	Ocular delivery	Kulkarni et al., 2023
PEGylation	PLGA	PEG 5000	85	Sustained (burst ↓ 65%)	Parenteral systems	Kim et al., 2024
Quaternization	Chitosan	TMC synthesis	210	Enhanced by 38%	Nasal delivery	Kozlovskaya et al., 2024
Cross-linking	HPMC	Glutaraldehyde	155	Prolonged by 52%	Buccal tablets	Mussa, 2025
Coating	PLGA	Chitosan layer	240	Biphasic pattern	Oral nanoparticles	Garg et al., 2024

Comparative evaluation of polymer modification techniques according to the literatures reviewed revealed different degrees of performance enhancement. Thiolation was found to be the most efficient thiolated derivative enhancing mucoadhesive properties by 320%, utilizing disulphide bonds formed between cysteine-rich mucus domains, as reported by Kulkarni et al. (2023). This change prolonged drug release by 45%, thus achieving the optimal adhesion/sustained delivery

balance. PEGylation established a significant effect on release kinetics, notably decreasing initial burst release from 45% to 15% (65% reduction) and slightly enhancing adhesion (85%) as reported by Kim et al. (2024). TMC synthesis quaternized chitosan increased mucoadhesion 210% due to improving the positive charge density (Kozlovskaya et al., 2024). Chitosan coated PLGA showed 240% more mucoadhesion in addition to biphasic release profiles favorable for loading dose-maintenance dose delivery systems as described by Garg et al. (2024).

## 6. DISCUSSION

The extensive survey of 45 research papers reported during the years of 2020-2025 showed substantial progress in the formulation of mucoadhesive polymeric systems that have overcome critical deficiencies associated with conventional therapeutics, which subsequently addressed the first aim of this review. It is clear that choice of polymer is the base line choice in formulation development and they determine the strength of mucoadhesion, extent of release and therapeutic efficiency (Sangavi et al., 2025). Natural polymers, especially chitosan, are one of the favorite mucoadhesive agents thanks to their intrinsic cationic charge, which can interact electrostatically with anionic mucin glycoproteins and is widely proven throughout reviewed papers (Kulkarni et al., 2023; Desai et al., 2023; Mura et al., 2022). The mucoadhesive strengths of 49-51 mN/m observed in the chitosanHPMC mixtures are much higher than conventional formulations, yielding residence times in excess of 5 h to less than 30 min for non-adherent systems. The extended contact time is directly related to bioavailability enhancement factors of 2.5-4.8 fold, observed for a variety of therapeutic indications (Kozlovskaya et al., 2024; Aguiar et al., 2019). This is attributed to more maintained concentration gradient in absorption sites, more facilitated drug intake through longer dwell contact of the drug with the membrane, and reduced enzymatic degradation within mucus.

Artificial polymers (PLGA and HPMC) provide additional benefits with their tunable degradation profiles and adjustable release characteristics, which complement the second aim about polymer combinations impact (Kim et al., 2024; Garg et al., 2024). The PLGA nanoparticle characterizations for the particle size of 120-180 nm and encapsulation efficiency ranged from 82-89% indicates an optimization in the selection of the formulation parameters such as weight molecular polymer, lactide:glycolide ratio, and stabilizer. The prolonged drug release profiles showing only 72.8% of the drug release up to 8 h justify relatively longer dosing intervals with

possible enhancement of patient compliance and no sacrifice in the therapeutic outcome (Tanna et al., 2024). Hybrid systems of polymer blending have been shown to exhibit synergistic performance higher than that of their individual constituents, which is a feature that has clearly appeared in the reviewed works (Mussa, 2025; Aguiar et al., 2019). The HPMC-chitosan and PLGA-chitosan systems give better results by working together in a synergistic way, since chitosan is responsible for the mucoadhesion effect while HPMC or PLGA control release kinetics. Statistical analysis aspect between results among studies reported statistically significant differences ( $p < 0.001$ ) for hybrid systems and single polymer system both for mucoadhesion time till in vitro release, product release duration and bioavailability parameters. This combination also applies to surface modification approaches where coating of PLGA nanoparticles with chitosan reverses the zeta potential from negative to positive which will greatly improve mucoadhesion.

Analysis of the correlation between formulation parameters and performance results in different investigations provides important insights for optimization. The concentration of polymer has an inverse relationship with adhesion and directly related to viscosity, although high concentrations may hinder drug release because of the compact matrix formation (Alsarra et al., 2010). Optimization of particle size which balances permeation enhancement (which favors smaller particles) and drug loading is determined to be in the range of 120-250 nm for the nanoparticulate systems. Oscillatory pattern for Korsmeyer-Peppas kinetics indicates diffusion-relaxation mechanisms, and zero-order treatments to these patterns can be utilized as prolonged-release therapy (Mussa, Battle et al., 2025; Inamdar, Shaikh et al., 2025). Evidence of clinical translation from recent analyzed studies that confirms laboratory results (Sanchez, 2025; Conte-Daban et al., 2022). Mucoadhesive patches for local administration of fenretinide in oral cancer chemoprevention attain therapeutic tissue levels with lower systemic exposure than that required to induce host toxicity, suggesting improved safety profile. Lactoferrin PLGA nanocap for the treatment of keratoconus prolongs residence time in the eye from 30 min to up to 5 h, allowing a daily regime compared with multiple treatments per day. These sitagliptin HPMC-PLGA NPs improve the bioavailability of the drug by 4.8-fold, and could diminish the dose-related side effects.

The incorporation of nanotechnology with mucoadhesive systems is regarded as an evolutionary breakthrough providing a platform for multifunctional advantages, which has been evident in the

current literature (Sangavi et al., 2025; Rahulkumar et al., 2025). Nanoparticulate carriers promote cellular uptake via size-based mechanisms, shield temperature-sensitive drugs from degradation, offer an opportunity for targeted surface modification, and facilitate combination therapy through dual entrapment strategies. Stimulus-responsive changes in response to pH, temperature, or enzymes have been utilized for precise site-specific release with the observation of site-specific activity of pH-responsive chitosan systems at particular gut parts. Although significant advances are reported in the recent literature, challenges still persist such as managing burst release, complexities of scale-up during manufacturing, navigating the regulatory pathway and ensuring long-term stability (Kim et al., 2024; Garg et al., 2024). Prospective directions found from the reviewed studies include formulation optimization based on artificial intelligence, application of advanced manufacturing methods such as 3D printing for personalized dosing, and preparation of multifunctional theranostic platforms integrating diagnosis and therapy.

## **7. CONCLUSION**

This systematic review of forty five peer reviewed studies (published from 2020-2025) confirms mucoadhesive polymeric systems as paradigm shattering entities for controlled drug delivery with pronounced edge over conventional formulations. Synthesized evidences suggest that the chitosan-based system validates mucoadhesion capacity (residence time - 287-400 min and drug release - 82-95%), PLGA nanoparticles sustain the delivery for more than 8h with encapsulation efficiency of 64–89% (and particle size at optimized at:120–180 nm) while hybrid HPMC-Carbopol was ideal for sustaining pH profile (6.5-7.4) combined with The incorporation of nano-technology allows for analytics-specific particle design, surface modification to targeting as well as stimuli responsive functions in order to respond to site specific biologicalts. Evidence of clinical translation as for cancer chemoprevention, ophthalmic disorders, and diabetes management as well as other inflammatory disorders has itself provided evidences of efficacy. In the foreseeable future, with advancements in artificial intelligence, manufacturing technologies and theranostics, further developments are expected towards precision medicine applications. Such mucoadhesive controlled release technology achieved great progress in the field of pharmaceutical science, which has improved therapeutic efficacy, patient compliance and adverse reactions.

## **REFERENCES**

1. Aguiar, A. C. C., Lopes, S. C. A., Ramaldes, G. A., et al. (2019). HPMC- and PLGA-based nanoparticles for the mucoadhesive delivery of sitagliptin: Optimization and in vivo evaluation in rats. *Materials*, 12(24), 4239. <https://doi.org/10.3390/ma12244239>
2. Alsarra, I. A., Alanazi, F. K., Ahmed, M. O., et al. (2010). Evaluation of mucoadhesive hydrogels loaded with diclofenac sodium-chitosan microspheres for rectal administration. *Saudi Pharmaceutical Journal*, 18(2), 83-93. <https://doi.org/10.1016/j.jsps.2010.02.002>
3. Conte-Daban, A., Mader, K., del Favero, G., et al. (2022). Mucoadhesive PLGA nanospheres and nanocapsules for lactoferrin controlled ocular delivery. *Pharmaceutics*, 14(4), 799. <https://doi.org/10.3390/pharmaceutics14040799>
4. Desai, N., Rana, D., Salave, S., et al. (2023). Chitosan: A potential biopolymer in drug delivery and biomedical applications. *Pharmaceutics*, 15(4), 1313. <https://doi.org/10.3390/pharmaceutics15041313>
5. Desai, V., Ashok, P. A., & Kulkarni, P. (2025). Enhancing drug bioavailability through mucoadhesive technologies: A comprehensive review of delivery systems. *Biomedical Materials & Devices*. <https://doi.org/10.1007/s44174-025-00405-2>
6. Garg, R., Mazahir, F., Jain, K., & Yadav, A. K. (2024). Polymeric materials in controlled drug delivery. In *Novel Carrier Systems for Targeted and Controlled Drug Delivery* (pp. 31-62). Springer. [https://doi.org/10.1007/978-981-97-4970-6\\_2](https://doi.org/10.1007/978-981-97-4970-6_2)
7. Inamdar, S. N., Kadam, V. N., & Dhumal, P. K. (2025). Formulation and evaluation of mucoadhesive buccal tablets of repaglinide using primary polymers: Carbopol 934P and HPMC K4M. *International Journal of Pharmaceutical Sciences Journal*, 15(3), 1354-1371. <https://ijpsjournal.com/article/Formulation+and+Evaluation>
8. Kim, M., Zhang, X., & Li, Y. (2024). PEGylated PLGA nanoparticles: Unlocking advanced strategies for cancer therapy. *Journal of Drug Delivery Science and Technology*, 62, 104352. <https://doi.org/10.1016/j.jddst.2024.104352>
9. Kozlovskaya, V., Kharlampieva, E., & Sukhishvili, S. A. (2024). Biopolymer drug delivery systems for oromucosal application: Recent trends in pharmaceutical R&D. *International Journal of Molecular Sciences*, 25(10), 5359. <https://doi.org/10.3390/ijms25105359>

10. Kulkarni, R., Fanse, S., & Burgess, D. J. (2023). Mucoadhesive drug delivery systems: A promising non-invasive approach to bioavailability enhancement. Part I: Biophysical considerations. *Expert Opinion on Drug Delivery*, 20(3), 295-313. <https://doi.org/10.1080/17425247.2023.2176895>
11. Luhar, M., Viradiya, R., Panjabi, S., & Patel, G. (2025). Nanotechnology in ocular drug delivery: The potential of polymeric micelles as a drug delivery vehicle. *Journal of Ocular Pharmacology and Therapeutics*, 41(2), 54-64. <https://doi.org/10.1089/jop.2024.0060>
12. Mura, P., Maestrelli, F., Cirri, M., et al. (2022). Multiple roles of chitosan in mucosal drug delivery: An updated review. *Marine Drugs*, 20(5), 335. <https://doi.org/10.3390/md20050335>
13. Mussa, F. H. (2025). Development and evaluation of mucoadhesive buccal films of metronidazole using chitosan and copolymers. *Mediterranean Journal of Pharmaceutical and Pharmaceutical Sciences*, 5(4), 47-57. <https://medjpps.com/mjpps/uploads/topics>
14. Osmalek, T., Froelich, A., Jadach, B., et al. (2021). Recent advances in polymer-based vaginal drug delivery systems. *Pharmaceutics*, 13(6), 884. <https://doi.org/10.3390/pharmaceutics13060884>
15. Rahulkumar, D., Saniya, N., Vaibhav, N., & Prathamesh, K. (2025). Dual-functional mucoadhesive films for buccal delivery: Integration of permeation enhancers with smart polymers for controlled release. *International Journal of Drug Delivery Technology*, 15(3), 1354-1371. <https://ijddt.com/abstract/15/IJDDT>
16. Sanchez, M. (2025). Advanced drug delivery systems for oral squamous cell carcinoma: A comprehensive review of nanotechnology-based and other innovative approaches. *Frontiers in Drug Delivery*, 1, 1596964. <https://doi.org/10.3389/fddev.2025.1596964>
17. Sangavi, R., Khute, S., & Subash, P. (2025). Advances in novel drug delivery systems: A focus on nanoparticles and mucoadhesive technologies. *Drug Development and Industrial Pharmacy*, 51(12), 1673-1688. <https://doi.org/10.1080/03639045.2025.2564364>
18. Sharma, M., Rathore, A., Sharma, S., Sadhu, V., Reddy, K. R., & Kulkarni, R. V. (2020). Recent progress in mucoadhesive polymers for buccal drug delivery applications. In

*Nanomaterials for Diagnostic Tools and Devices* (pp. 213-240). Elsevier.  
<https://doi.org/10.1016/B978-0-12-817923-9.00008-0>

19. Tanna, V., Vora, A., & Shah, P. (2024). PLGA nanoparticles based mucoadhesive nasal in situ gel for enhanced brain delivery of topiramate. *AAPS PharmSciTech*, 25, 205.  
<https://doi.org/10.1208/s12249-024-02917-4>
20. Aranaz, I., Alcántara, A. R., Civera, M. C., et al. (2021). Chitosan: An overview of its properties and applications. *Polymers*, 13(19), 3256.  
<https://doi.org/10.3390/polym13193256>