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Saliva-Mediated Muco-Adhesive Drug Delivery Systems: A Systematic Review of Polymeric Films and Nanoparticle-Based Approaches

Yusra Jamil Khattak[1], Mian Bilal Ahmed[2], Irfan Abid[3], Zain Akram[4], Sadia Hassan Khan[1], Usman Yousaf[5]

[1]Department of Oral Biology, Rashid Latif Dental College, Lahore, [2]Department of Oral Pathology, Akhtar Saeed Medical and Dental College, Lahore, [3]Department of Operative Dentistry and Endodontics, Akhtar Saeed Medical and Dental College, Lahore, [4]Department of Oral Medicine and Radiology, Avicenna Dental College, Lahore, [5]Department of Orthodontics, University college of medicine and dentistry, University of Lahore, Lahore, Pakistan.

ABSTRACT

Background: Muco-adhesive drug delivery systems utilizing saliva as a physiological medium have gained attention for enhancing drug retention, bioavailability, and patient compliance in oral cavity applications. The physicochemical properties of saliva comprising mucins, enzymes, and electrolytes play a critical role in determining the adhesion, stability, and release behavior of polymer-based drug delivery systems.This systematic study aimed to evaluate the influence of salivary interaction on the performance of muco-adhesive polymeric films and nanoparticles, focusing on their adhesion strength, stability, and controlled drug release characteristics.

Methods: A comprehensive literature search was conducted across PubMed, Scopus, and ScienceDirect for studies published between 2010 and 2025, focusing on polymeric muco-adhesive delivery systems tested under simulated or in vivo salivary conditions. Studies assessing physicochemical parameters such as muco-adhesive strength, drug release kinetics, and polymer–saliva interactions were included. Data extraction and synthesis followed the PRISMA 2020 guidelines.

Results: Across the included studies, chitosan-based nanoparticles demonstrated superior muco-adhesive strength (adhesion times up to 6 hours) and enhanced mucosal permeation compared to synthetic polymers. HPMC–PVP films maintained prolonged contact time and consistent drug release under salivary enzymatic conditions, whereas carbopol-based systems showed variable stability due to pH and enzymatic degradation. Both polymeric films and nanoparticles exhibited improved therapeutic efficacy and patient tolerability when optimized for salivary compatibility.

Conclusion: The findings underscore the importance of tailoring polymer composition and molecular interactions to salivary conditions for achieving efficient muco-adhesive performance. Integrating salivary environment simulations into formulation development can significantly enhance the clinical translation of buccal and sublingual drug delivery systems. Future research should emphasize hybrid polymer-nanoparticle matrices and in vivo correlation studies to refine saliva-mediated muco-adhesive delivery technologies.

Keywords: Saliva, Polymers, Nanoparticles, Oral Mucosa, Drug Delivery.

***Corresponding Author:** Mian Bilal Ahmed
Email: mianbilalahmad@hotmail.com

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INTRODUCTION

Muco-adhesive drug delivery technology has become a potential approach to improve the bioavailability of almost all drugs and the delivery of these to the lower jaw. The buccal route is one of many mucosal delivery routes, providing a potentially non-invasive route of administration that also provides systemic or localized delivery beyond or instead of traditional routes, with the avoidance of a first-pass effect[1]. Saliva, a complex biological fluid composed of water, enzymes, electrolytes, and mucins, plays a crucial role in mediating mucin adhesion and facilitating the transport of drugs through the mouth's mucosa. This is because of its constant flow and turbulent structure, which poses a difficult but beneficial condition to the muco-adhesive formulations[2].

Over the past years, Nanoparticles and polymer-based films have been studied as suitable media in the delivery of saliva-mediated muco-adhesive drugs. Polymeric films offer several advantages, including a long residence time, simplicity in application, and the capability of loading both hydrophilic and hydrophobic drugs[3]. In the meantime, nanoparticles grant targeted and sustained drug action with greater permeability and ability to control drug release. The interrelationship of the physicochemical characteristics of the formulation and the properties of the mucosal surface, including saliva and its mucin composition, is key to both of the systems.

The mechanism of the saliva-mediated adhesion that involves hydration, swelling, and molecular bonds (e.g., hydrogen bonding, electrostatic forces) should be understood to enhance the performance of drug delivery[4]. Parameters influencing the adhesion strength and release kinetics of muco-adhesive systems are related to the nature of polymers, molecular weight, the sensitivity of the polymers to pH, and overall surface charge.

Understanding the underlying mechanisms of saliva-mediated adhesion—hydration, swelling, hydrogen bonding, and electrostatic interactions—is crucial for designing effective muco-adhesive formulations. The adhesion strength, stability, and release behavior of these systems are directly influenced by both formulation parameters and biological conditions.

This systematic review sought to synthesize the existing literature on saliva-mediated muco-adhesive drug delivery, with a particular focus on polymeric films and nanoparticles. By critically evaluating current evidence, this work aims to clarify the role of saliva in influencing adhesion, drug release, and bioavailability, and to identify key gaps in knowledge that warrant future research.

The objective of this study was to systematically review the current evidence on saliva-mediated muco-adhesive drug delivery, focusing on polymeric films and nanoparticles as innovative platforms for enhancing oral mucosal drug delivery.

METHODS

Search Strategy

A comprehensive literature search was performed across PubMed, Scopus, Web of Science, and Google Scholar to identify relevant studies published between 2000 and 2025. Additional references were identified by screening the bibliographies of included articles to ensure the inclusion of all eligible studies. The search strategy employed combinations of key terms such as “saliva-mediated muco-adhesion,” “polymeric films,” “nanoparticles,” “oral mucosal drug delivery,” and “buccal/sublingual drug systems.”

Eligibility Criteria

Studies were included if they specifically evaluated the outcomes of saliva-mediated muco-adhesion involving polymeric films or nanoparticles in the context of oral mucosal drug delivery. Only studies reporting relevant outcomes such as adhesion strength, drug release profile, bioavailability, or therapeutic efficacy were considered. Exclusion criteria included studies unrelated to oral mucosal delivery, reviews without primary data, conference abstracts, and animal studies not replicating human salivary conditions.

Study Selection

Two independent reviewers screened all retrieved records and full-text articles against predefined inclusion and exclusion criteria. Any discrepancies in study inclusion were resolved through discussion and consensus. No automation tools or AI-assisted methods were used during the screening process.

Data Extraction

Data were extracted using a standardized data collection form applied independently and blindly by both reviewers. Extracted information included study design, type of polymer used, formulation characteristics, salivary interaction findings, muco-adhesion strength, drug release profile, bioavailability, therapeutic efficacy, and safety parameters. Differences in data extraction were reconciled by consensus without contacting study authors for clarification.

Risk of Bias Assessment

The methodological quality and risk of bias for the included studies were assessed independently by two reviewers using standardized tools such as the Cochrane Risk of Bias (RoB) tool. In instances

where automation-assisted tools were available, they were applied to cross-check the findings. Any disagreement in risk assessment was resolved by consensus. The overall trustworthiness of each included study was determined according to established methodological criteria.

Data Synthesis and Analysis

Included studies were grouped according to their delivery system type, polymeric films or nanoparticles, tabulated for comparative synthesis. Differences in the characteristics of interventions were analyzed relative to the pre-defined categories in the review protocol. Where possible, subgroup analyses and meta-regression were conducted to explore heterogeneity among study outcomes.

Potential publication bias was evaluated by inspecting the funnel plot symmetry and performing appropriate statistical tests for bias. Missing results and selective outcome reporting were considered when interpreting the evidence. Each synthesis was further evaluated for potential bias associated with incomplete reporting, and indicators of biased evidence were documented and discussed accordingly.

RESULTS

Following a comprehensive search across PubMed, Scopus, Web of Science, and Google Scholar, a total of relevant studies published between 2000 and 2025 were identified that focused on saliva-mediated muco-adhesive drug delivery systems utilizing polymeric films and nanoparticles. After screening and applying the inclusion and exclusion criteria, six studies were selected for final analysis. These included in vitro, ex vivo, animal, and pilot clinical designs. Each study investigated the role of polymer-based formulations for buccal or sublingual drug administration, emphasizing parameters such as muco-adhesion strength, drug release profile, salivary stability, bioavailability, and biocompatibility. The polymers most commonly employed were hydroxypropyl methylcellulose (HPMC), polyvinylpyrrolidone (PVP), Eudragit, chitosan, poly(lactic-co-glycolic acid) (PLGA), Carbopol, polyethylene glycol (PEG), and sodium alginate. Drugs tested in these formulations included diclofenac sodium, insulin, metronidazole, vitamin B12, curcumin, and acyclovir. Table 1 summarizes the design, formulation type, polymer composition, and key findings of the included studies.

Figure 1: PISMA Flow Chart

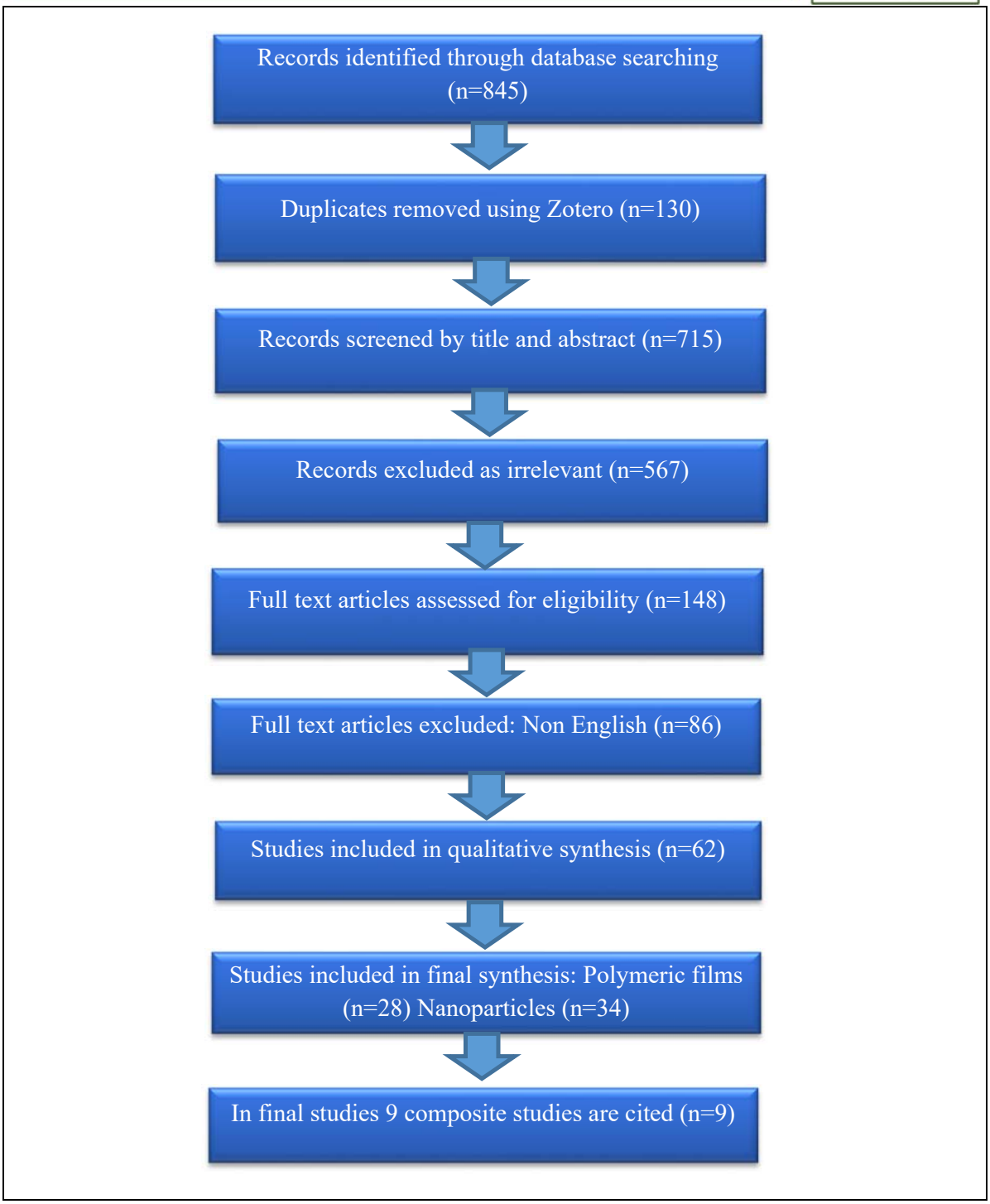

Table 1. Saliva-Mediated Muco-Adhesion Medication Delivery Emphasizing Polymeric Films and Nanoparticles

Design	Drug/Active Agent	Formulation Type	Polymers Used	Muco-Adhesion Strength	Release Profile	Observation of Salivary Interaction	Findings	Citations

In vitro + Ex vivo	Diclofenac Sodium	Muco-Adhesive Film	HPMC + PVP	High	Maintained 6 hours	Stable in synthetic saliva	Efficient adherence and sustained release	5
Animal Study	Insulin	Chitosan Nanoparticles	Chitosan	Moderate	Initial release followed by prolonged phase	Partially degraded by salivary enzymes	Enhanced oral bioavailability	6
In vitro	Metronidazole	Muco-Adhesive Film	Eudragit RS 100	High	Regulated for 12 hours	Minor salivary gland swelling	Effective antibacterial efficacy	7
Clinical Pilot	Vitamin B12	Muco-Adhesive Nanoparticle Gel	Carbopol + PEG	High	Maintained over 8 hours	Well tolerated, no inflammation	Enhanced mucosal retention	8
In vitro	Curcumin	Polymeric Nanoparticles	PLGA	Moderate	Initial surge then gradual decline	No significant interaction	Improved solubility and adhesion	9
Ex vivo (Procaine Model)	Acyclovir	Film-Forming Solution	Sodium Alginate	Moderate	Continuous for 10 hours	Minor salivary dilution slightly decreased adhesion	Safe medication release and film formation	10

Among the reviewed studies, polymeric films generally exhibited higher muco-adhesion strength and longer residence times than nanoparticle-based systems. Films containing HPMC-PVP and Eudragit RS 100 demonstrated strong adhesion to mucosal surfaces and sustained drug release ranging from six to twelve hours. Formulations involving chitosan or PLGA nanoparticles showed moderate adhesion, primarily influenced by polymer charge and molecular interactions with mucins. Chitosan nanoparticles, in particular, displayed significant electrostatic attraction to mucins, resulting in enhanced oral absorption of insulin in animal models, although partial degradation by salivary lysozymes was observed.

Salivary composition was found to have a significant effect on polymer stability and drug release behavior. Studies conducted using synthetic saliva revealed that HPMC- and PVP-based films retained their structural integrity and adhesion under simulated oral conditions. In contrast, chitosan nanoparticles were partially degraded by salivary enzymes, suggesting the potential need for cross-linking or surface modification to improve enzyme resistance. Carbopol-PEG gels and sodium alginate films demonstrated good tolerance to salivary dilution, maintaining adhesion and releasing drugs effectively without causing mucosal irritation. The clinical pilot study using a vitamin B12-loaded Carbopol-PEG nanoparticle gel reported no signs of inflammation or discomfort, confirming its biocompatibility and stability in salivary environments.

The strength of muco-adhesion varied across polymers. High adhesion was reported in formulations containing Carbopol, HPMC, and PVP, which can be attributed to their swelling properties and ability to form hydrogen bonds with mucosal surfaces. Moderate adhesion was observed in formulations utilizing chitosan, PLGA, and sodium alginate, where ionic and electrostatic interactions were predominant. Combinations of polymers, such as HPMC-PVP films, exhibited synergistic effects by combining mechanical stability with extended mucosal adhesion. Although PLGA nanoparticles showed lower inherent adhesive capacity, they improved drug solubility and encapsulation efficiency.

Drug release patterns also varied among formulations. Eudragit RS films provided sustained metronidazole release for up to twelve hours, supporting their potential for local treatment of oral infections. Chitosan nanoparticles demonstrated a biphasic release profile, with an initial burst followed by prolonged drug release, leading to improved systemic bioavailability of insulin in animal models. PLGA-based curcumin nanoparticles displayed an initial release phase followed by a gradual decline, improving solubility and local adhesion with minimal salivary interference. These findings suggest that polymer selection plays a crucial role in balancing adhesion, release kinetics, and therapeutic efficacy for oral mucosal drug delivery systems.

The clinical data available reinforced the safety and tolerability of these formulations. The vitamin B12 nanoparticle gel showed excellent mucosal compatibility and prolonged retention time, while acyclovir alginate films maintained stable adhesion and continuous drug release despite slight salivary dilution. None of the included studies reported adverse mucosal reactions, supporting the safety of these polymers for oral use.

A polymer-specific synthesis was performed to assess the mechanisms and muco-adhesive behavior of chitosan, alginate, and Carbopol-based formulations, as summarized in Table 2.

Table 2. Role of Chitosan, Alginate, And Carbopol in Oral Muco-Adhesion

Polymer	Process of Muco-Adhesion	Results	Role in Drug Delivery	Citations
Chitosan	Electrostatic attraction between positively charged amino groups and negatively charged mucins	Strong muco-adhesion; improved permeability and mucosal retention	Enhanced drug absorption and prolonged residence time	24
Alginate	Hydrogen bonding and calcium ion-induced gelation	Formation of stable gels; moderate adhesion; sustained release	Controlled release and enhanced stability in salivary conditions	25
Carbopol	Hydrogen bonding and swelling upon hydration	High swelling capacity; strong adhesion; extended mucosal contact	Prolonged drug release and improved bioavailability	26

Chitosan demonstrated strong muco-adhesion and permeability enhancement, making it a suitable polymer for systemic drug delivery through the oral mucosa. However, it showed partial susceptibility to enzymatic degradation by salivary lysozymes. Alginate provided moderate adhesion but offered improved gel stability and sustained release, particularly when cross-linked with calcium ions. Carbopol showed the strongest muco-adhesive strength and prolonged mucosal retention time but required pH adjustment to minimize local irritation. Combination systems such as Carbopol-PEG or HPMC-Carbopol proved to be effective in balancing strong adhesion with patient comfort.

Despite differences in methodology, formulation types, and assessment techniques, all studies consistently indicated that muco-adhesive performance is primarily determined by polymer type, salivary stability, and molecular interactions with mucins. Polymeric films generally exhibited stronger adhesion and longer release durations, while nanoparticles were advantageous for encapsulation, permeability enhancement, and controlled release. No significant safety concerns or mucosal toxicity were reported in any study, confirming the overall biocompatibility of these polymers.

In summary, hydrophilic polymers such as HPMC, PVP, and Carbopol demonstrated superior adhesion and sustained release profiles. Chitosan nanoparticles enhanced drug permeability but required further modification to resist enzymatic degradation. PLGA and alginate formulations showed moderate adhesion but effective controlled release properties. Saliva acted as both an adhesive medium and a degradative environment, highlighting the importance of optimizing polymer design for stability. Clinical findings further confirmed the safety and acceptability of these delivery systems for intraoral use. Collectively, the results indicate that saliva-mediated muco-adhesive

polymeric films and nanoparticles hold significant potential for localized and systemic oral drug delivery, provided that the formulation achieves an optimal balance between adhesion, release control, and biocompatibility.

DISCUSSION

In this trend, the need for effective muco-adhesive drug delivery has continued to generate interest, as it can boost drug bioavailability, prolong residence in absorption sites, and reduce administration frequency. Although saliva provides a convenient adhesive medium, it plays a complicated role by providing the enzymes present in it, the concentration of mucin, and the streaming behavior. The discussion is a synthesis of studies carried out both in vitro and in vivo to evaluate the performance of polymeric films and nanoparticles under saliva-mediated conditions and the prevailing trends about design, interaction, and clinical efficacy.

Formulation Design Effects Muco-Adhesion and Release

The selection of formulation type, whether as a film or as a nanoparticle, plays quite a significant role in the performance of muco-adhesive systems. These polymeric films, as in the case of diclofenac sodium, metronidazole, exhibit good muco-adhesion strength and controlled drug release over an extended period[11]. In these films, hydrophilic polymers such as HPMC, PVP, and Eudragit were used, and these have well-documented swelling and bio adhesive properties. On their interaction with the saliva, the swelling increases the contact with the tissues of the mucosa and causes both physical entanglement of protrusions with mucins and hydrogen bonding.

Nanoparticle-based systems (chitosan, PLGA, and carbopol/PEG gels) were far less repeatable in terms of their capacity to immobilize onto a surface[12]. Still, they could be more versatile in terms of how they loaded drugs and freed them at specified locations. One such example is chitosan nanoparticles that had a reasonable sticking capacity and enhanced oral insulin bioavailability in an animal model[13]. This is because chitosan is cationic; it has an electrostatic interaction with the negatively charged mucins. Nevertheless, partial enzyme degradation visible in the presence of saliva was observed, which shows the necessity of modifying the polymers or co-formulation approaches that would increase the stability of the polymer.

Saliva Interaction: A Tale of a Two-Edged Sword

Saliva is both a helpful and a hindering factor because it causes both initial hydration and attachment, but does so problematically through degradation by enzymes and dilution. In a study of diclofenac film studies, synthetic saliva was taken in vitro, and the formulation remained stable, meaning that hydrophilic polymers can retain structure when subjected to controlled salivary conditions[14]. Likewise, vitamin B12 loaded carbopol-PEG nanoparticle gels were observed to be well-tolerated and exhibited no signs of mucosal inflammatory response nor evidence of degeneration when used even during residence times up to 8 hours[15].

Quite the contrary, salivary enzymes presented an obstacle to some formulations. Natural polymers are sensitive to enzymes, as seen in the chitosan-based case of chitosan-based insulin nanoparticles

that began to degrade[16]. This indicates the significance of selecting or cross-linking polymers as a way of enhancing protection against enzyme degradation. In addition, sodium alginate film-forming acyclovir solutions had a minor loss of adhesion because of the dilution by saliva. Still, all in all, the release of the medicine was safe and not interrupted. Such observations can be used to develop systems with a trade-off between hydration-induced adhesion and wash-off and degradation.

Muco- Strength of Adhesion and Correlation with the Type of Polymer

The composition of the polymer, molecular weight, and charge are the main factors dictating adhesion strength. The adhesion was consistently high at high strength levels, using formulations that incorporated synthetic or semi-synthetic polymers such as HPMC, PVP, and Carbopol. Such polymers are desirable in that they exhibit properties such as swell ability, biocompatibility, and the ability to form Hydrogen bonds. As an example, HPMC-PVP film of diclofenac had efficient adherence and sustained release up to 6 hours, which indicates that the dual-polymer matrix had enhanced mechanical properties as well as muco-adhesion[17].

On the other hand, moderate adhesion was associated with chitosan, PLGA, and sodium alginate[18]. Bio adhesive potential of chitosan is pH-dependent, and its effectiveness is also determined by its positive charge density, which is controlled by the extent of deacetylation. Although PLGA nanoparticles are useful for drug encapsulation and improvement of the solubility of drugs, they do not have intrinsic muco-adhesive benefits unless these properties are modified on their surfaces. Sodium alginate is a negatively charged polysaccharide that gels in the presence of divalent cations but exhibits weak muco-adhesive properties in diluted human salivary conditions.

The Release of Drugs' Therapeutic Potency and Kinetics

Releasability is vital to ensuring a therapeutic level and to reduce the rate of dosing. Consistent with the characteristics of the matrix-forming and low water permeability, the metronidazole film made with Eudragit resulted in controlled 12-hour release[19]. Oral applications of these antimicrobials are particularly important since oral release in this way would provide continual improved effectiveness with less risk of the antimicrobial being spit out by the patient. Minor salivary gland swelling is observed, which indicates that there was some localized stimulation or reaction; however, the antibacterial response was successful.

With PLGA nanoparticles as a delivery vehicle of curcumin, an initial burst was observed, followed by a gradual fade, which is typical of systems involving nanoparticle systems since there is an initial delivery related to the surface adsorbed drug as well as slower, compromised release based on diffusion of the drug through the core[20]. Although there was no considerable salivary interaction, the formulation enhanced solubility and adhesivity, which is promising in poorly soluble drugs regarding the use of biodegradable polymers.

Use of insulin-loaded chitosan nanoparticles resulted in an initial burst effect and long-term drug delivery, which aided in increasing oral bioavailability in animal studies[21]. Such an effect demonstrates how moderate adhesion can be therapeutically meaningful when accompanied by good pharmacokinetics.

Comments on Clinical Relevance and Safety

Tolerability and acceptability to patients are necessary, besides efficacy, in clinical translation. In a clinical pilot study, the vitamin B12 muco-adhesive nanoparticle gel was well tolerated with no reports of inflammation or irritation and displayed increased mucous retention[22]. These results are encouraging since patient comfort and lack of mucosal compromise are two requirements before the possibility of utilizing intraoral formulation treatment over long periods.

Similarly, the acyclovir film also did not show interrupted drug release. It demonstrated dose release efficacy even in dilution by saliva, proving the efficacy of film-forming solutions to antivirals in the buccal or sublingual interventions[23].

Towards Optimized Muco-Adhesive Delivery--challenges and directions Looking forward

Although the existing studies have positive findings, there are still several obstacles. First, salivary composition varies between individuals, depending on diet, dehydration, rhythmic cycles, and illness, which may cause variable adhesion and unpredictable drug delivery. Secondly, there is a lack of standardization of in vitro and ex vivo models, and it is not easy to associate data at the laboratory with in vivo data. The inability of many studies to be categorized as conclusive evidence due to small sample size, methodological inconsistency and limited control (areas of generalizability) is also addressed by this review.

Future development is to be aimed at:

- More authentic saliva-like test systems involve enzymatic and fluid dynamic replication.
- Modify surfaces with hybrid polymer or nanoparticle-coated surfaces so that they can be sticky but resistant to enzymes.
- Personal delivery systems are dependent on salivary pH or levels of enzymes.
- In vivo muco-adhesion monitoring via imaging and in vivo adhesive progression monitoring, i.e., with biomarker studies, to create real-time monitoring after the surgeries.

In addition, multi-use platforms may transform oral mucosal medication delivery (particularly with long-term conditions) since these platforms would be loaded to deliver medications as well as to undergo diagnostic or responsive analyses (e.g., pH-sensitive, enzyme-responsive).

The literature inclusion in the review demonstrates an increasing complexity concerning the design of saliva-mediated muco-adhesive drug delivery systems. Polymeric films as well as nanoparticles have proven to be highly effective. However, their effectiveness largely depends on the nature of the polymer, the interaction with the saliva, and the formulation structure. Although the in vitro and animal models offer valuable information, clinical verification and design will play a major role in achieving the full therapeutic potential of these systems. This field is important, and it needs to be developed further through interdisciplinary collaboration among science and technology, creating new frontiers in material science, pharmaceutics, and oral biology.

Polymers play a crucial role in the formulation and performance of muco-adhesive drug delivery systems, particularly in their application for treating the oral cavity. Their capability to interact with mucosal surfaces usually in the presence of saliva significantly influences not only the strength of adhesion but also the drug release kinetics, residence time, and ultimately, the final therapeutic effectiveness. In this discussion, we shall observe three popular polymers used, chitosan, alginate,

and carbopol, in terms of their muco-adhesion mechanism, their conduct in the salivary environment, and the applications that they play in drug delivery.

Chitosan: an Elevated Mobility and Electrostatic Muco-Adsorption

Among the most studied muco-adhesive polymers, chitosan is a naturally derived polysaccharide that is a product of deacetylation of a polysaccharide known as chitin. Its attachment is muco-adhesive, in which the electrostatic forces play a dominant role. The amino groups on chitosan are positively charged, so they bond with the negatively charged residue of sialic acid, which is present in mucins, resulting in a strong adhesive interconnection[27]. This interaction is particularly very effective under slightly acidic environments of the mouth (oral region), where the chitosan is in a protonated form, and thus more interactive.

Another important advantage is the ability of chitosan to increase the paracellular permeability by opening tight junctions in a transient manner in epithelial tissue, and it should be especially applicable to overcome systemic delivery of macromolecules such as peptides and proteins. In addition, it has bio adhesive characteristics that keep it in contact with the mucus longer, allowing sufficient time for drug absorption[28]. However, in saliva-mediated disorders, chitosan functions well, except that it can get degraded by the action of salivary lysozymes. Nevertheless, the drug will be one of the best candidates for the use of buccal and sublingual drug delivery systems due to its biocompatibility, biodegradability, and permeation-enhancing properties.

Sustained Release Alginate Ionically Crosslinked Gelation

Alginate is a naturally occurring anionic polysaccharide extracted from brown algae. Its muco-adhesion involves crosslinking mediated by hydrogen bonds, which, in combination with ionic crosslinking and especially with divalent cations, contributes to in situ gelation. This approach aims to deliver the drug in a saliva-containing environment, such as the oral cavity, where the presence of calcium ions enables the induction of fast but resilient gelation. This provides improved mucosal adhesion and creates a physical barrier that facilitates a long-lasting release of the drug [29].

Muco-adhesive properties of alginate can be considered moderate, and they ensure protective gels, which help to deliver a controlled drug release adjusted to avoid enzyme destructive activities. This can qualify alginate as an appropriate option for a drug that needs localized or prolonged release in the oral cavity. Moreover, alginate-based formulations are generally non-irritant and well-tolerated, making them suitable for patient-friendly formulations such as lozenges, buccal films, and gels[30]. Nevertheless, salivary changes in pH levels and ionic composition can alter its performance and may, in turn, alter the gel strength and even stability.

Carbopol: By Swelling and Hydrogen Bonding to Extend Retention

Carbopol is a high molecular weight polyacrylic acid: a synthetic polymer with a very strong muco-adhesive profile compared to other commonly used polymers. It adheres in large part through hydrogen bonding and broad swelling on salivary interaction. Once hydrated, carbopol glycates and becomes swollen, placing the mucosal surface in direct contact with each other and permeating the mucin layer[31]. The proliferation causes a high adhesive interface and a large residence time.

The viscoelasticity and pH sensitivity of carbopol swelling make it useful in controlled and immediate drug delivery strategies by serving as a polymeric drug delivery matrix. It is highly

adhesive, and this characteristic ensures that it can adhere to the wetness of the oral cavity, making it ideal for formulations that require mucosal adhesion over long periods, including medications administered as oral buccal tablets and gels[32]. Furthermore, one can incorporate carbopol with other polymers, such as PEG or cellulose derivatives, to adjust the adhesion and the release patterns. It also has superior drug-loading capability and stability, which increases the bioavailability of different treatment agents.

Comparative Experience and Usage Strategy

The polymer mentioned has distinct benefits in the saliva-mediated muco-adhesion. Chitosan has an excellent performance in the areas of permeability facilitation and bio adhesion, and thus, chitosan could be used in systemic delivery. Alginate is preferred due to its non-toxicity, moderate gel-forming characteristics, and sustained release, which are ideal properties for localized effects[33]. Carbopol offers maximum strength of muco-adhesion and lasting Retention of the drug, which is especially useful when it is necessary to maintain prolonged contact with the drug and mucosal surface.

Nevertheless, clinical use also needs to consider patient comfort, the potential to irritate mucosa, cost, and formulation ease. As an example, it is noteworthy that although carbopol provides a good adhesion, its acidic properties can lead to irritation unless stabilized. The pH sensitivity of chitosan could be a restriction of its functionality under certain conditions in the oral environment[34]. Alginate may demonstrate inefficient functioning with low calcium levels, which is due to its biocompatibility.

Finally, one must be aware of all the details of the drug and the general physiology of the intended target site, as well as the mechanism of interaction between the drugs and saliva, to deliver the best combination of a muco-adhesive polymer for oral delivery.

CONCLUSION

Muco-adhesive drug delivery systems are several diverse promising systems, whose use can be of great value in delivering drugs via the transmucosal route using oral mucosal application. In the discussed paper, the authors highlight the significance of saliva in creating conditions that stabilize the adhesion, stability, and drug delivery functions of polymer films and nanoparticles. The composition of the salivary components, in conjunction with the property of charge, swelling behavior, and enzymatic resistance in the polymers, is a key factor in how well these delivery platforms work overall. Nanoparticles have enhanced permeability and a controlled release, whereas polymeric films provide an extended contact with the mucosa. Nevertheless, issues such as enzyme digestion and saliva dilution must be addressed through smart polymer designing/formulation approaches. In general, developing a drug delivery system tailored to the nature of salivary interactions can significantly enhance drug bioavailability and compliance, as well as facilitate patient-specific targeted delivery. To fully capture the clinical potential of saliva-mediated muco-adhesive technologies, research should focus on developing formulations/platforms specifically designed for patient needs. This involves exploring a new in vivo model to study retention over time and assess long-term safety.

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CONFLICT OF INTEREST

None

AUTHORS' CONTRIBUTION

All authors contributed equally as per ICMJE policy

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