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Manal Mohamed Almoudi, Alaa Sabah Hussein,
Nur Aliana Hidayah Mohamed

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Review Article

Polymer-Based Systems for Vitamin Delivery in Dentistry: Advances, Challenges, and Future Perspectives

Manal Mohamed Almoudi, D.D.S., MSc, Ph.D. [1], Alaa Sabah Hussein, BDS, M.Sc.[2], Nur Aliana Hidayah Mohamed, BBSc, MMedSc, Ph.D. [3]

[1]Department of Pedodontics and Preventive Dentistry, Faculty of Dentistry, University of Zawia, Al-Zawia, Libya.
[2]Centre of Paediatric and Orthodontics Studies, Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh, Selangor, 47000, Malaysia.
[3]Centre of Preclinical Science Studies, Faculty of Dentistry, Universiti Teknologi MARA, Sungai Buloh, Malaysia.

Corresponding Author:
Dr. Manal Mohamed Almoudi,
Department of Pedodontics and Preventive Dentistry, Faculty of Dentistry, University of Zawia, Al-Zawia, Libya.
E-mail : ma.almoudi@zu.edu.ly

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Abstract

Vitamin deficiency is associated with various oral health disorders, ranging from local conditions such as enamel hypoplasia and mucosal inflammation to systemic conditions like scurvy. Vitamin deficiency can negatively affect both oral tissue development and immune responses. Conventional routes of vitamin supplementation, including oral, parenteral, and transdermal routes, are limited by suboptimal bioavailability, gastrointestinal degradation, and poor solubility. Polymer-based delivery systems provide a promising solution to overcome these limitations by improving mucosal permeation, protecting vitamins from environmental and enzymatic degradation, enhancing encapsulation efficiency, and enabling the controlled release and targeted delivery of vitamins. This review highlights the potential of polymer-based delivery systems, including nanoparticles, lipid-based nanocarriers, and hydrogels, to enhance oral vitamin delivery and promote oral health. Future research should focus on optimizing polymer design, improving clinical translation, and developing multifunctional systems for targeted and sustained vitamin delivery in dentistry.

Keywords: vitamin delivery systems, polymeric carriers, vitamins, oral health, nanotechnology

Introduction

The rapid advancement of modern medicine and materials science has significantly improved diagnostic and therapeutic techniques in recent years. Biomaterials have become essential in modern medicine due to their biocompatibility, biodegradability, and availability[1]. Recently, they have been increasingly utilized in dentistry to support oral health[2].

In parallel, food supplements and bioactive agents, such as vitamins, minerals, proteins, and probiotics, play a crucial role in maintaining human health and reducing the risk of various diseases[2]. Vitamins are essential micronutrients required in small quantities for normal metabolic processes, growth, development, and overall health. Each vitamin serves specific physiological functions, many of which remain active areas of research[2].

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Vitamins are categorized as fat-soluble (A, D, E, K) and water-soluble (B-complex and C). Fat-soluble vitamins are stored in adipose tissues and the liver for up to six months. In contrast, water-soluble vitamins are not stored in the body and require regular intake. Absorption occurs in the small intestine, and they circulate through the bloodstream[2].

Deficiencies in vitamins can negatively affect oral health across all age groups and contribute to systemic diseases. They are also associated with enamel defects, including enamel hypoplasia, and increased susceptibility to dental caries[2]. To avoid such health issues, adequate nutritional intake is considered essential for maintaining oral and systemic health[2]. Vitamins C and D are significantly associated with several oral health conditions[2]. Vitamin C deficiency can lead to gingival bleeding, delayed wound healing, and increased susceptibility to infections. Severe deficiency may result in scurvy, characterized by gingival overgrowth, follicular hyperkeratosis, delayed healing, petechiae, and, in severe cases, tooth loss[3]. Furthermore, vitamin D deficiency is linked to dental and skeletal abnormalities, including enamel hypoplasia, hypomineralization, reduced bone mass, osteonecrosis of the jaw, and periodontal disease. Beyond bone metabolism, vitamin D regulates immune function, exhibits anti-inflammatory activity, and enhances antimicrobial peptide production[2,4].

The stability and efficacy of vitamins are influenced by temperature, humidity, light, container materials, pH, poor solubility, low bioavailability, undesirable flavors, and interactions with other ingredients, which can limit their therapeutic potential[5].

In addition, vitamin stability and delivery efficiency may also be reduced by physiological barriers present in the oral cavity. Factors such as continuous salivary washout, fluctuating oral pH, enzymatic degradation, and complex microbial biofilms can significantly affect vitamin retention, mucosal permeation, and therapeutic activity within oral tissues[6].

To address these challenges, polymer-based systems and microencapsulation technologies have emerged as promising strategies to enhance vitamin stability, improve bioavailability, and enhance targeted delivery. This review aimed to critically evaluate polymer-based systems for oral vitamin delivery, focusing on their mechanisms of action, influence of the oral environment, translational challenges, and future strategies to enhance clinical implementation and improve oral health outcomes.

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Polymer-based delivery systems

Various polymer-based systems have been developed, such as polymer–lipid hybrid systems, polymeric nanoparticles, and hydrogels.

Polymer-lipid hybrid (PLH) systems

Polymer-lipid hybrid systems combine the advantages of both polymer and lipid-based carriers. PLH systems are designed to overcome the limitations associated with oral drug absorption. PLH systems can deliver hydrophobic and hydrophilic agents. They enhance the bioavailability and stability of encapsulated vitamins[7]. In addition, the integration of polymers and lipids in a single delivery system enhances vitamin solubilization, protects them from degradation, and enables controlled release, which can be tailored to specific therapeutic needs. Hence, these systems are considered a good option for oral delivery applications[7]. Furthermore, by combining the solubilization capacity of lipids and the stabilizing matrix of polymers, PLH systems can effectively transport vitamins to the primary site of absorption. This synergistic effect is crucial to overcome some limitations such as drug leakage and high-water content[8].

Polymeric nanoparticles

Polymeric nanoparticles (PNPs) are solid and colloidal nanocarriers. Their size ranges from 1 to 1000 nanometers. The PNPs' versatility allows them to encapsulate a wide range of therapeutic agents[9]. They are able to load synthetic and natural agents, such as peptides, proteins, DNA, and mRNA, as well as drugs[9]. There are two types of polymeric materials used to prepare PNPs, including natural and synthetic polymers. Natural polymers are obtained from natural sources, including plants or animals[10]. Polysaccharides and polypeptides are the most common natural polymers used in nanoparticle formulation. Polysaccharide polymers include hyaluronic acid, dextran, chitosan, cellulose, starch, and alginates, while polypeptide polymers include collagen, gelatin, albumin, elastin, and silk fibroin[10].

Natural polymers offer several advantages, including biocompatibility, specific interactions with biomolecules, and easy surface modification. This leads to enhanced versatility in drug administration[9]. Conversely, synthetic polymers are synthesized from petroleum-derived raw materials through polymerization reactions. These include poly (lactic acid) (PLA), poly (glycolic

acid) (PGA), and poly (lactic-co-glycolic acid) (PLGA). Synthetic polymers are highly adjustable and easily controllable materials that provide advantages over natural polymers[9].

PNPs are favored for their predictable degradation rates, mechanical properties, biocompatibility, and high drug-loading capacity[9]. Therefore, they are suitable for sustained release and enhanced mucosal retention[9]. Several challenges are encountered during the development of polymeric nanoparticles. Some of these challenges are related to maintaining the stability of PNPs under physiological conditions and scaling up production while ensuring quality and consistency[10]. In addition, achieving precise control over drug release rates and ensuring targeted delivery to specific tissues or cells remain significant hurdles. Despite these challenges, PNPs continue to offer numerous advantages in drug delivery and other biomedical applications. However, these challenges need to be addressed to fully realize their potential[10].

Hydrogels

Hydrogels have emerged as a promising medium for the delivery of vitamins and other therapeutic agents via the oral route[11]. They are considered suitable to address the challenges associated with oral drug delivery and are widely used for controlled and sustained release of therapeutic compounds[11].

Hydrogels are three-dimensional hydrophilic polymer networks characterized by high water content, excellent biocompatibility, and the ability to absorb large amounts of fluid. They can absorb water, expand, and subsequently release vitamins in response to pH changes throughout the gastrointestinal tract, such as colon-specific release of vitamin B_2. The expanding properties of hydrogels facilitate a zero-order release profile, which is beneficial for maintaining consistent vitamin levels in the body[11].

In the oral cavity, hydrogels can be designed to release vitamins in a regulated manner. They respond to environmental stimuli such as pH changes, which enhance the stability and efficacy of the vitamins. In addition, hydrogels have shown therapeutic efficacy in dental applications[11]. Hydrogels can adhere to the oral mucosal surfaces, allowing for localized and prolonged vitamin delivery, which is considered beneficial for treating specific dental conditions[11]. Generally, the selection of the optimal delivery system depends on vitamin physicochemical properties, target

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oral site, desired release kinetics, and required retention time. A comparison of polymer-based delivery systems is presented in Table 1.

Physicochemical determinants of polymer-based vitamin delivery systems

The therapeutic performance of polymer-based delivery systems is strongly influenced by polymer physicochemical properties. Parameters such as crystallinity, molecular weight, hydrophilicity, degradation rate**,** size, shape, and surface charge can affect polymer mechanical strength, stability, release behaviour of incorporated drug molecules, and biodegradation profile[12]. The effectiveness of polymeric nanoparticles in targeted drug delivery is largely determined by their ability to overcome biological barriers and selectively release their therapeutic payload at the intended site of action. These characteristics regulate vitamin encapsulation efficiency, mucosal permeation, biofilm penetration, and release kinetics[12].

Crystallinity significantly affects vitamin release behaviour and biodegradation. For instance, amorphous polymers biodegrade more readily in biological environments and may completely degrade within weeks. In contrast, highly crystalline polymers exhibit slower degradation rates, leading to prolonged release profiles that can persist in the body for months or longer[13,14]. The release period of polymer-based delivery systems can be controlled from days to months through changes in composition and processing conditions[14].

In addition, polymer molecular weight directly influences particle size and other physicochemical properties. Lower molecular weight polymers generally produce smaller nanoparticles with faster degradation rates, higher maximum concentrations in circulation, and reduced accumulation within organs[13].

Hydrophilicity and hydrophobicity of polymers also significantly influence the release patterns. Hydrophilic polymers promote rapid dissolution and accelerated polymer degradation[14]. Hydrophilic polymers such as chitosan, alginate, and hyaluronic acid improve swelling behaviour and mucoadhesion, thereby enhancing retention within oral tissues[15]. In contrast, hydrophobic polymers maintain the matrix for extended periods and exhibit gradual release. Hydrophobic polymers, including PLGA and polycaprolactone, are particularly suitable for lipophilic vitamins because they improve encapsulation efficiency and prolong release through slower degradation rates[14].

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The size, shape, and surface charges of nanoparticles also play a crucial role in drug delivery efficiency and therapeutic performance. Smaller nanoparticles facilitate therapeutic diffusion easily across biological barriers[12]. Additionally, the shape of the nanoparticles influences their cellular uptake and distribution, with certain shapes such as cylindrical or needle-like nanoparticles potentially enhancing cellular uptake compared with spherical nanoparticles[12]. The surface charge of nanoparticles significantly influences their interaction with cell membranes. Positively charged nanoparticles generally exhibit better absorption by negatively charged oral cells and mucosal surfaces, hence enhancing targeting efficiency[12]. Figure 1 illustrates the relationship between key polymer physicochemical properties and their influence on the delivery efficiency of polymer-based vitamin delivery systems.

Comparative evidence from reported studies indicates that key performance parameters, including encapsulation efficiency, release kinetics, and particle size–permeability relationships, play essential roles in determining the therapeutic performance of advanced polymer-based vitamin delivery systems. Polymeric nanoparticles generally exhibit nanoscale dimensions that enhance mucosal permeation and cellular uptake[6]. Nanoparticle permeability across biological barriers is strongly influenced by particle size and surface properties, enabling more efficient transport through epithelial and mucosal tissues compared with larger delivery systems[12]. Encapsulation efficiencies above 70% have frequently been reported, particularly in PNPs and LPH systems contributing to improved vitamin stability and protection from degradation[16,17]. In contrast, hydrogel-based systems demonstrate superior mucoadhesion and prolonged retention within oral tissues due to their hydrophilic three-dimensional networks[18]. Furthermore, nanoparticle and hydrogel formulations commonly exhibit sustained and controlled release profiles that improve local bioavailability and prolong therapeutic activity[12,19]. These findings demonstrate the critical relationship between particle size, encapsulation efficiency, and release kinetics in determining delivery performance in oral vitamin formulations.

Routes of vitamin delivery in the body

In general, bioactive compounds can be delivered through several routes, including transdermal, parenteral, and oral administration[20]. Each route has distinct advantages and limitations depending on the physicochemical properties of the compound and the clinical indication.

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Transdermal delivery has been proposed mainly for lipophilic vitamins to overcome their variable oral bioavailability. The skin, being the largest organ of the body, provides a potential route for systemic delivery and may serve as an alternative to oral administration in certain conditions, such as fat malabsorption disorders[4]. Transdermal systems offer several advantages, including avoidance of gastrointestinal side effects, continuous drug release, and ease of application and removal[21]. However, limited quantitative evidence regarding the effectiveness of vitamin transdermal delivery remains a concern[21]. The main challenge associated with this route is the low permeability of the skin barrier, which restricts systemic uptake of vitamins[4]. To address this limitation, strategies such as nanoformulations and penetration enhancers have been explored[4].

The parenteral route, which includes intravenous, intramuscular, and subcutaneous administration, is typically used in cases of severe vitamin deficiency, malabsorption syndromes, or gastrointestinal disorders[20]. Parenteral delivery ensures complete bioavailability and bypasses the degradation caused by gastric acidity and enzymatic metabolism[20]. However, this method is invasive, requires trained healthcare professionals, and may be associated with injection-site reactions, infection risk, and higher costs compared with oral administration[20].

Oral administration remains the most convenient and widely accepted method for delivering vitamins and other bioactive compounds[7]. Nevertheless, conventional oral administration systems face several limitations, including limited mucosal permeability, short residence time, and poor control over drug release kinetics, which may restrict their therapeutic effectiveness[22]. Additionally, the bioavailability of orally administered vitamins, particularly lipophilic vitamins, can be affected by the complex gastrointestinal environment. Digestive enzymes, gastric acidity, and the selective permeability of the gastrointestinal epithelium can hinder vitamin solubility and absorption[7]. Compounds with low water solubility may also exhibit incomplete dissolution in the gastrointestinal tract, further limiting their systemic uptake.

The physicochemical properties of vitamins substantially influence the design of oral delivery systems. Hydrophilic vitamins, such as vitamin C and vitamin B-complex, dissolve rapidly but are highly susceptible to salivary dilution and degradation. In addition, due to their natural hydrophilicity. These vitamins have limited diffusion across lipid-rich biological membranes, which may reduce mucosal permeability and retention. Therefore, delivery systems for hydrophilic vitamins often prioritize mucoadhesion and protective encapsulation to enhance

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local retention and absorption[23]. In contrast, lipophilic vitamins, including vitamins A, D, E, and K, exhibit poor aqueous solubility and limited gastrointestinal absorption, requiring hydrophobic polymer matrices or lipid-containing carriers to enhance solubilization, membrane permeation, stability, and sustained release[24]. In fact, these differences influence polymer selection, carrier design, encapsulation efficiency, release behaviour, and overall delivery performance in polymer-based oral vitamin delivery systems.

Recent advances in nanotechnology and drug delivery systems have provided promising strategies to overcome these challenges. Polymeric carriers, encapsulation technologies, and permeation enhancers have demonstrated potential in improving vitamin stability, mucosal permeability, and absorption. Micro- and nanoscale drug formulations, in particular, increase the surface area available for dissolution, thereby enhancing drug absorption and bioavailability[25]. Thus, these advanced systems may overcome some of the limitations associated with conventional oral routes.

Impact of the oral environment on polymer-based vitamin delivery systems

The oral cavity presents a highly dynamic environment characterized by continuous salivary and gingival crevicular fluid (GCF) flow, diverse enzymes, and complex microbial biofilms. These factors may pose significant challenges in maintaining therapeutic drug concentrations for a sufficient duration. Therefore, the design of polymer-based vitamin delivery systems must account for these environmental constraints to ensure adequate retention and controlled release[22].

Site-specific anatomical differences within the oral cavity further determine delivery performance. The oral mucosa and periodontal tissues influence nanoparticle adhesion, penetration, and retention[22]. Variations in thickness and permeability across buccal, sublingual, and gingival sites directly affect the transport and absorption of therapeutic agents, including vitamins[22]. Keratinized tissues, such as the gingiva and hard palate, are suitable for localized delivery. Additionally, the buccal mucosa, characterized by non-keratinized epithelium and low permeability[22], requires strong mucoadhesive and sustained-release systems to achieve sustained local release. In contrast, the thin epithelium and highly vascularized sublingual mucosa support rapid systemic absorption; however, it has limited retention capacity. The gingival area, particularly in periodontal pockets, presents additional challenges for effective vitamin delivery

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due to the continuous flow of gingival crevicular fluid, dense microbial biofilms, and restricted accessibility, leading to reduced local drug availability and therapeutic efficacy[22]. Furthermore, a key oral-specific design constraint is continuous salivary washout, which can rapidly dilute and clear formulations from the application site, thereby reducing retention time, local bioavailability, and therapeutic effectiveness[6,25]. The biofilm-rich microenvironment and dynamic physiological conditions within periodontal pockets may also accelerate drug degradation and further compromise sustained delivery. Furthermore, oral biofilm plays a significant role in the degradation and reduced effectiveness of polymer-based nanoparticles through a combination of enzymatic activity and the production of acidic metabolic byproducts by bacteria[15]. Oral biofilm consists of single or multiple microbial species embedded within a complex extracellular polymeric substance (EPS) matrix that acts as a physical and biochemical barrier, reducing drug penetration and stability[26]. Although certain therapeutic agents demonstrate strong activity against planktonic bacterial cells, their effectiveness is often significantly reduced within biofilms due to limited penetration through the dense EPS matrix[26]. Additionally, fluctuations in oral pH and enzymatic activity may further influence polymer degradation and release kinetics[15,26].

Furthermore, the chemical composition and hydrophilicity of polymeric materials can also influence their resistance to biodegradation. Hydrophilic polymers have the ability to absorb water; hence, they are more prone to microbial attack, which facilitates enzymatic hydrolysis[15].

These constraints highlight the necessity for designing polymer-based delivery systems that can overcome salivary clearance, accommodate site-specific anatomical differences, maintain stability under dynamic oral conditions, and resist mechanical displacement and biofilm accumulation, while maintaining prolonged local activity under dynamic oral conditions[22]. A comprehensive understanding of oral biofilm architecture, enzymatic activity, and environmental variability is essential for developing effective intraoral vitamin delivery platforms[25]. Strategies such as enhanced mucoadhesion, stimuli-responsive release mechanisms, and in situ gel-based delivery are essential to achieve localized, sustained, and controlled release of vitamin delivery within various intraoral tissues[27].

Despite the oral cavity being recognized as an effective route for local and systemic drug administration due to the unique anatomical and physiological properties of the oral mucosa, particularly its rich vascularization and direct connection to systemic circulation, which enable

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certain drugs to bypass first-pass metabolism in the gastrointestinal tract and liver[22], its complex physiological environment remains a major barrier to achieving effective and consistent therapeutic outcomes. A detailed understanding of these constraints is therefore essential for the rational design of advanced polymer-based vitamin delivery systems in dentistry.

Current challenges in polymer-based systems for oral vitamin delivery in dentistry

Challenges such as inadequate mechanical properties, manufacturing complexity, potential toxicity, and regulatory limitations continue to hinder the effectiveness and clinical application of polymer-based systems for vitamin delivery in dentistry. Addressing these limitations is essential to improve their safety, functionality, and successful translation into clinical practice[28]. Figure 2 summarizes the current challenges, emerging strategies to overcome these limitations, and key future research directions in the field.

Mechanical strength and durability remain major concerns. Many dental applications require materials capable of withstanding dynamic loading and abrasion. However, biodegradable polymers often exhibit lower mechanical strength than conventional dental materials such as composites and ceramics[29]. This limitation may compromise structural integrity and sustained vitamin release in periodontal or mucosal applications. While some biopolymers possess beneficial viscoelastic properties that support flexible applications such as orthodontics, they may lack the rigidity required for restorative or implant-related uses[30]. Additionally, the stability of biodegradable polymers in the oral cavity is affected by enzymatic activity and hydrolysis, which may alter degradation rates and influence the release profile and bioavailability of encapsulated vitamins[28].

Biocompatibility and immunogenic responses represent another challenge. Biodegradable polymers must be carefully selected and thoroughly evaluated to minimize hypersensitivity reactions and immune responses[31]. This requires detailed assessment of polymer composition, degradation products, and their interactions with surrounding tissues[31]. Ideally, polymeric materials should integrate with biological systems without disrupting normal physiological processes, while their degradation by-products should be non-toxic and readily metabolized[31]. Surface modification techniques, such as coating nanoparticles with hydrophilic polymers, may reduce immune clearance and improve circulation time; however, translating these approaches

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from experimental models to clinical practice remains challenging and requires extensive testing and validation[32].

Regulatory and manufacturing issues also limit the widespread adoption of biodegradable polymers in dentistry. Natural polymers often exhibit batch-to-batch variability, which can affect material properties and complicate regulatory approval[33]. In addition, the lack of standardized regulatory frameworks for biodegradable dental materials may discourage clinical adoption in dentistry[33]. Establishing clear guidelines and standardized evaluation criteria is therefore essential to ensure safety, consistency, and broader professional acceptance[33].

Overall, while polymer-based systems show considerable promise for vitamin delivery in dentistry, overcoming challenges related to mechanical performance, biological interactions, stability, and regulatory approval requires interdisciplinary collaboration and continued research.

Clinical translation challenges in polymer-based delivery systems

The limited clinical success of many polymer-based delivery systems can be attributed to a combination of factors, including manufacturing complexity, regulatory challenges, and economic considerations. Despite their considerable potential and numerous advantages, the clinical applicability of polymer-based systems remains limited.

A major factor is the reliance on preclinical models. Differences across species can significantly influence outcomes, and many promising polymer-based technologies remain confined to in vitro and animal studies despite their theoretical advantages[34]. Such models often overestimate therapeutic efficacy, leading to translational failure in human studies. Indeed, most current research on polymeric nanomedicines has been conducted in vitro or in animal models[34]. This translational gap is further exacerbated by the lack of understanding of physiological and pathological differences between animal models and humans[34]. Moreover, correlating in vitro and in vivo drug release profiles remains challenging due to the complexity of nanomedicines and the absence of standardized regulatory guidelines[35].

Patient heterogeneity also contributes to limited clinical translation. There is currently insufficient research on the interactions of polymeric nanomedicines within stratified patient populations[34]. Additionally, intrinsic properties of polymer-based platforms, including shape,

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chemistry, broad size distribution, and electromagnetic characteristics, can lead to poor oral bioavailability, instability in circulation, and inadequate tissue distribution. These platforms may also interact with living cells, potentially triggering adverse effects in both humans and animals[36].

The interactions between polymeric carriers and biological components, including protein corona formation and immune responses, are not fully understood[37]. These interactions can significantly alter biodistribution, targeting efficiency, and therapeutic outcomes. A recent review indicated that the underlying mechanisms of nanobiointeractions are still not fully understood and emphasized the need for broader scientific investigation[37]. Moreover, data on long-term safety of chronic exposure to polymer degradation products are also scarce, mainly for orally administered and mucosal delivery systems[38]. This lack of toxicity studies, along with variations in biodistribution, may partially explain why some polymers are not yet approved by the Food and Drug Administration (FDA)[38].

Despite extensive research, the literature reports contradictory findings regarding the performance of polymer-based delivery systems. For example, polyethylene glycol (PEG) has been widely used due to its biocompatibility, chemical stability, ability to improve circulation time, and reduced immunogenicity. However, emerging evidence indicates that repeated dosing may result in toxicity due to the accumulation of PEG in tissues, which can lead to the formation of anti-PEG antibodies (APAs). These antibodies may accelerate drug clearance, reduce therapeutic efficacy, and increase the risk of side effects, such as allergic reactions[39]. This finding raises concerns about the long-term safety and benefits of PEG in polymer-based delivery systems.

Pre-existing APAs have also been detected in individuals with no prior exposure to PEGylated drugs, which raises additional clinical concerns[39]. Finally, although PLH systems have shown considerable preclinical promise, there are currently no registered clinical trials evaluating PLH formulations in humans, particularly those composed of a polymer core (e.g., PLGA) surrounded by a lipid shell[16]. This underscores the persistent translational gap between preclinical research and clinical application.

In general, among different polymer-based platforms, hydrogels demonstrate the highest degree of clinical readiness for oral applications because of their strong mucoadhesion and favorable biocompatibility. In contrast, polymeric nanoparticles offer superior biofilm penetration and controlled release capabilities but remain limited by manufacturing reproducibility and

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regulatory complexity. Polymer–lipid hybrid systems show considerable promise for lipophilic vitamin delivery owing to improved encapsulation and permeability; however, formulation stability and large-scale production remain major barriers to clinical translation. Table 2 shows the limitations and the translational and regulatory challenges of different polymer-based platforms.

Applications in dentistry

PNPs have been widely explored in dentistry due to their ability to enhance the solubility**,** stability, and bioavailability of therapeutic agents while enabling controlled release and targeted delivery. PNPs can deliver essential vitamins, such as vitamin D and vitamin C, which play a key role in bone health, collagen synthesis, and tissue regeneration[40]. This functionality contributes to the prevention and management of oral conditions**,** including periodontal diseases and dental caries. Their biocompatibility and low toxicity make PNPs particularly suitable for pediatric dentistry, enabling targeted vitamin delivery to support the development of healthy teeth and gums[40]. Moreover, PNPs can be combined with antimicrobial agents to enhance the management of oral infections[41].

Within these systems, PLGA-based platforms and hydrogels have been extensively investigated for oral vitamin delivery applications. PLGA is utilized in different forms, such as scaffolds, films, hydrogels, and nanoparticles, to enhance the delivery and efficacy of therapeutic agents and vitamins. PLGA-based scaffolds and membranes are commonly used in bone healing and tissue regeneration. They are often combined with vitamins to enhance the healing process[42]. In endodontics and periodontology, PLGA nanoparticles have been investigated for the targeted delivery of therapeutic agents and vitamins to sites of infection or damage, improving treatment outcomes and supporting periodontal health[42].

Hydrogels, although inherently soft, have been optimized through the incorporation of reinforcing materials, such as nanoparticles or fibers, to improve their mechanical properties without compromising drug delivery performance[29]. Vitamin-loaded hydrogels can promote gum health, provide anti-inflammatory and regenerative effects,[51] and support clinical procedures such as dental implants and bone regeneration[43]. Additionally, they may accelerate oral ulcer healing, offering a protective barrier and reducing discomfort[44].

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A recent review discussed the use of hydrogels in the treatment of oral and maxillofacial diseases. The review indicated that hydrogels have potential applications in the treatment of periodontal diseases, dental caries, dental pulp diseases, oral cancer, and oral mucosal diseases[43].

Future perspectives on polymer-based systems for oral vitamin delivery in dentistry

Advancements in drug-delivery technologies indicate that polymer-based systems have significant potential for improving oral vitamin delivery in dental applications. Future developments should prioritize stimuli-responsive and site-specific delivery systems capable of overcoming salivary clearance and biofilm barriers while maintaining regulatory-compliant scalability[45]. Figure 2 summarizes the current challenges, emerging strategies to overcome these limitations, and key future research directions in the field.

Various polymeric carriers, such as nanoparticles, micelles, and hydrogels, are currently being explored. Polymeric micelles, which are self-assembled nanostructures, offer advantages such as high drug-loading capacity and controlled release, making them particularly useful for addressing challenges related to drug solubility and permeability in dental applications[45]. Additionally, a recent systematic review reported that polymeric films exhibit stronger mucoadhesion and longer residence times compared with nanoparticle-based systems, highlighting their potential for intraoral delivery[46].

Bioadhesive systems, such as hydrogels and oral patches, represent another promising approach. These systems can adhere to oral mucosal surfaces and may respond to environmental stimuli within the oral cavity, including changes in pH and temperature, enabling localized and sustained vitamin delivery[11]. Targeted release at the site of action may enhance therapeutic efficacy while minimizing systemic side effects[11]. Stimuli-responsive polymers further expand the potential of these systems. These materials are designed to modify their structure or release profile in response to environmental triggers, allowing precise control over the timing and location of vitamin release within the dynamic oral environment[11].

The use of biocompatible and biodegradable polymers, such as natural polymers and polysaccharides, has significant impacts for developing safe and effective drug delivery systems. Natural polymers like chitosan and alginate can form micro- and nanoscale carriers with low

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immunogenicity and toxicity, making them suitable for both adult and pediatric dental applications[41].

Future research is expected to focus on integrating smart polymers, nanotechnology, and bioadhesive platforms to enhance the precision, stability, and therapeutic efficacy of vitamin delivery systems in dentistry. These innovations may contribute to the development of more effective and patient-friendly treatment strategies[28].

Conclusion

Recent advances in polymer-based delivery systems demonstrate substantial potential for enhancing vitamin stability, solubility, mucosal retention, and controlled release within the oral environment. Among these platforms, mucoadhesive nanoparticles, biodegradable hydrogels, nanofibrous scaffolds, and polymer–lipid hybrid systems appear promising due to their ability to improve site-specific delivery, prolong residence time, and protect vitamins from premature degradation. Hydrogel-based systems such as chitosan have shown notable advantages for mucosal adhesion and biofilm interaction, whereas PNP systems such as PLGA carriers provide sustained release profiles suitable for periodontal and regenerative applications. In addition, polymer–lipid hybrid formulations may offer improved encapsulation efficiency and permeability for lipophilic vitamins such as vitamins A, D, and E.

The effectiveness of these systems is influenced by the physicochemical properties of the polymer, including molecular weight, crystallinity, hydrophilicity, degradation behaviour, and surface charge. These factors collectively regulate encapsulation efficiency, biofilm penetration, mucosal permeation, and release kinetics. In addition, the design of vitamin delivery systems should consider the distinct characteristics of hydrophilic and lipophilic vitamins, including differences in solubility, stability, and absorption mechanisms. These differences affect carrier selection and therapeutic performance.

Despite encouraging preclinical findings, major translational challenges remain. The oral cavity presents a highly dynamic environment characterized by continuous salivary washout, enzymatic degradation, pH fluctuations, microbial biofilms, and complex periodontal pocket dynamics, all of which may compromise delivery efficiency and local retention. Furthermore, most currently available evidence is derived from in vitro and animal studies, while robust clinical trials

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evaluating long-term safety, efficacy, dosage optimization, and patient-centered outcomes remain limited. Additional concerns related to large-scale manufacturing reproducibility, storage stability, polymer degradation by-products, immunogenicity, and regulatory standardization must also be addressed before widespread clinical implementation can be achieved.

Future research should prioritize multifunctional, stimuli-responsive polymeric systems capable of site-specific targeting and adaptive release within the oral environment. Greater emphasis should also be placed on clinically relevant outcomes, including periodontal regeneration, caries prevention, mucosal healing, and modulation of oral biofilms. Standardized comparative studies evaluating encapsulation efficiency, release kinetics, particle size–permeability relationships, and long-term biocompatibility are needed to facilitate meaningful translation from laboratory research to clinical dentistry. In addition, the development of clear regulatory frameworks and standardized evaluation protocols will be critical for facilitating clinical translation.

Overall, polymer-based vitamin delivery systems represent a rapidly evolving field with strong translational potential for preventive, regenerative, and therapeutic oral healthcare applications.

Conflict of Interest:

None

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Figure 1 Physicochemical factors governing the performance of polymer-based vitamin delivery systems

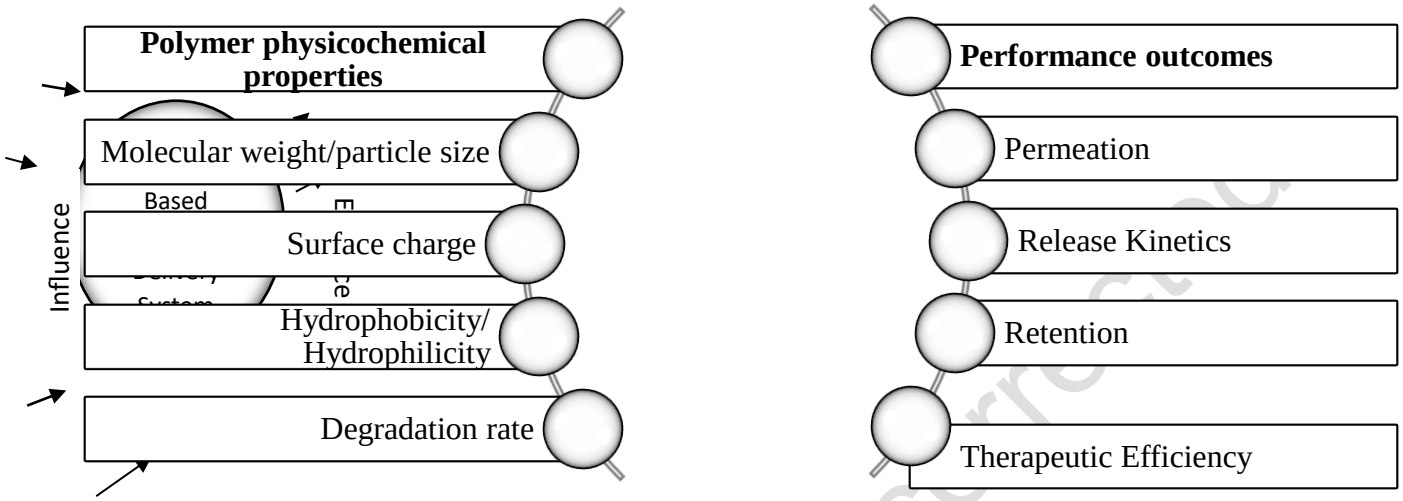


Figure 2 Translational challenges and future perspectives of polymer-based systems for oral vitamin delivery

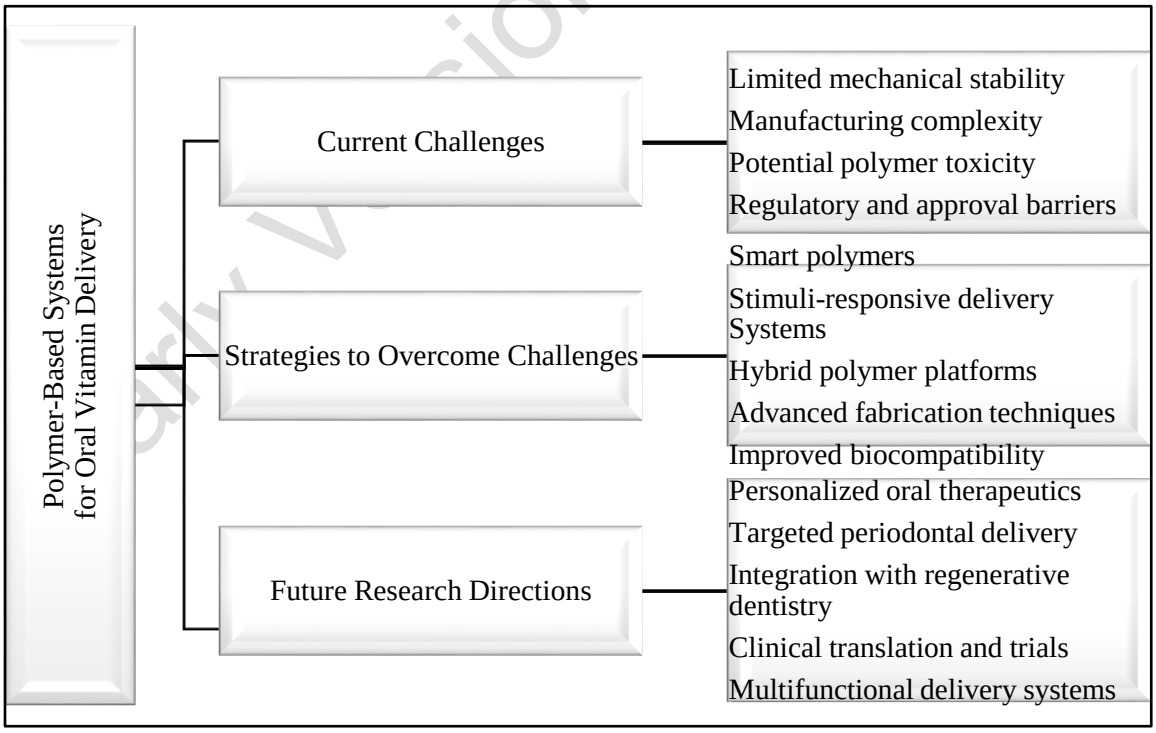


Table1 Comparative characteristics of polymer-based delivery systems and their key characteristics

Parameter	Polymeric Nanoparticles (PNPs)	Hydrogels	Polymer–Lipid Hybrid (PLH) Systems
Structural Characteristics	Nanoscale solid or colloidal carriers composed of nanospheres or nanocapsules [9].	Three-dimensional hydrophilic polymer networks with high water absorption capacity[28].	Core–shell hybrid nanocarriers combining lipid cores with polymer shells[9].
Common Polymers	PLA, PLGA, PEG, PCL.	Alginate, chitosan, gelatin, collagen, hyaluronic acid, HPMC, PVA, PVP, PAM, PHEMA, PEG.	PLGA, PEG with phospholipids or lipid–polymer conjugates[7].
Typical Particle Size / Structure	Typically 50–500 nm.	Macroscopic or injectable crosslinked matrix[28].	Commonly 80–300 nm[16].
Oral Applications	Periodontal therapy, biofilm-targeted delivery, regenerative dentistry, antimicrobial therapy[47].	Buccal delivery, wound healing, periodontal pockets, oral mucosal regeneration[48,49].	Mucosal delivery, poorly soluble vitamin delivery, anti-inflammatory therapy[50].
Loading Capability &	Loading both hydrophilic and lipophilic vitamins; higher	Suitable loading for hydrophilic vitamins and bioactive molecules[28]. Moderate	High loading efficiency for both hydrophilic and hydrophobic agents [7].

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Encapsulation Efficiency	encapsulation efficiency for hydrophobic compounds[17].	encapsulation efficiency (~55% and 60%)[51].	High encapsulation efficiency (~70–80%)[16,44].
Release Kinetics	Sustained release from hours to several days through diffusion and polymer degradation[19].	Swelling-controlled and diffusion-mediated release[12].	Controlled and prolonged release via combined lipid diffusion and polymer erosion mechanisms[12].
Mucosal Permeability	High due to nanoscale dimensions and enhanced surface interactions[28].	Moderate; dependent mainly on mucoadhesion rather than deep penetration[52].	High; lipid components improve membrane interaction and permeability[53].
Biofilm Penetration	Superior penetration, particularly for particles <200 nm[54].	Limited penetration through dense extracellular polymeric substance matrix[52].	Moderate to high depending on lipid composition and particle size[12].
Drug Release Mechanisms	Surface desorption, diffusion through polymer matrix, polymer degradation or erosion[47].	Diffusion-controlled release, swelling-induced release, and polymer degradation[28].	Diffusion, polymer erosion, membrane fusion, and lipid exchange mechanisms[53].
Advantages	Enhanced mucosal permeation, improved biofilm penetration, controlled and sustained release, protection of bioactive compounds	High biocompatibility, strong mucoadhesion, localized and prolonged drug release, tissue-like mechanical properties[28].	Combines polymer stability with lipid biocompatibility; improved permeability and retention, improved drug encapsulation and delivery efficiency[7,8].

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	from degradation, improved bioavailability[28,47].		

PLA, poly(lactic acid); PLGA, poly(lactide-co-glycolide); PEG, poly(ethylene glycol); PCL, polycaprolactone; PVA, poly(vinyl alcohol); PVP, polyvinylpyrrolidone; PAM, polyacrylamide; PHEMA, poly(hydroxyethyl methacrylate); HPMC, hydroxypropyl methylcellulose.

Table 2 Translational and regulatory challenges of polymer-based delivery systems for oral vitamin delivery

Parameter	**Polymeric Nanoparticles (PNPs)**	**Hydrogels**	**Polymer–Lipid Hybrid (PLH) Systems**
Stability	Generally high (rigid matrix) [55]; however, susceptible to particle aggregation, Ostwald ripening, and variable polymer degradation that may alter release kinetics and storage stability[47].	Moderate, it influenced by swelling behaviour, hydration, and crosslinking density. Excessive swelling may compromise structural integrity and release predictability[29,56].	High (rigid polymer core) [12]. However, may affect by lipid phase separation and lipid–polymer incompatibility during storage or physiological exposure[16].
Scalability & Manufacturing	Established with moderate challenges[55]. Large-scale production remains difficult because of batch-to-batch variability and sensitivity of nanoparticle fabrication	Scaling up is complicated by sensitivity to gelation and crosslinking variability,	Still emerging with more difficult challenges[55]. Manufacturing is technically demanding because of multilayer assembly and coordinated control of lipid

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Parameter	Polymeric Nanoparticles (PNPs)	Hydrogels	Polymer–Lipid Hybrid (PLH) Systems
	parameters; microfluidic methods improve uniformity[18]	particularly with natural polymers[56].	and polymer phases; industrial-scale production remains limited[16,57].
Biocompatibility & Toxicity	Moderate biocompatible (depending on the polymer nature) [55]. However, nanoscale interactions may induce cytotoxicity or inflammatory responses[34].	Typically highly biocompatible, although degradation products or unreacted crosslinkers may induce inflammatory responses[56].	Excellent biocompatible (lipid shields polymer) [55], however, long-term safety of hybrid structures and degradation products requires further evaluation, and potential cellular interactions may occur [16].
Regulatory Challenges	Requires extensive characterization of physical and chemical properties, degradation behaviour, residual solvents, and release reproducibility to meet regulatory standards[47].	Variability of natural polymers complicates standardization, reproducibility, and regulatory approval processes[33,56].	Structural complexity increases regulatory burden and challenges reproducibility across manufacturing batches[16].
Translational Status (Oral Tissue & Vitamin Delivery)	Mainly preclinical; limited clinical translation for oral tissue and oral vitamin delivery[58].	Most clinically advanced among current systems for mucositis, oral wound healing, and periodontal applications; oral	Primarily in the early preclinical stage for oral vitamin delivery, with promising results for poorly soluble vitamins[57].

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Parameter	Polymeric Nanoparticles (PNPs)	Hydrogels	Polymer–Lipid Hybrid (PLH) Systems
		vitamin delivery remains in early clinical development[59].	
Key Limitations	Salivary washout, nanoparticle aggregation, limited long-term retention, inconsistent penetration through mature oral biofilms, and manufacturing complexity	Rapid dilution by saliva, reduced penetration into dense biofilms, limited mechanical durability in dynamic oral environments, and lower stability for lipophilic compounds.	Formulation complexity, possible lipid instability, phase separation risk, process sensitivity, and limited clinical validation.

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