REVIEW ARTICLE

Drug Delivery Systems Based on Polymeric Nanocarriers for the Management of Endo-Perio Lesions

Maryam Heidaryzadeh*

Department of Periodontics, School of Dentistry, Kerman University of Medical Sciences, Kerman, Iran

ARTICLE INFO

Article History:
Received 11 May 2025
Accepted 27 Jun 2025
Published 01 Sep 2025

Keywords:
Endo-perio lesions
Polymeric nanocarriers
Drug delivery systems
Periodontal therapy

ABSTRACT

Endo-perio lesions, resulting from the complex interaction of endodontic and periodontal infections, present significant clinical challenges due to their intertwined pathology, diagnostic difficulties, and limitations of conventional treatments. This review comprehensively explores the emerging role of polymeric nanocarriers as advanced drug delivery systems for the effective management of endo-perio lesions. Polymeric nanocarriers exhibit unique advantages, including enhanced drug stability, targeted and sustained release, improved bioavailability, and deep penetration into biofilms and periodontal pockets, which overcome the shortcomings of traditional therapies. The review discusses the pathophysiology of endo-perio lesions, the various types of polymeric nanocarriers such as nanoparticles, nanogels, micelles, dendrimers, and polymeric films, and their applications in delivering antimicrobial, anti-inflammatory, regenerative, and novel therapeutic agents. Recent advances in multifunctional polymeric nanocarriers combining antimicrobial, immunomodulatory, and regenerative approaches are highlighted, along with challenges related to biocompatibility, scalability, and regulatory frameworks. Future perspectives emphasize the integration of stimuli-responsive nanocarriers, precision medicine, and theranostic platforms for personalized periodontal therapy. This article underscores the transformative potential of polymeric nanocarriers to revolutionize endo-perio lesion management, advocating for further interdisciplinary research and clinical translation to realize their full therapeutic benefits.

How to cite this article
Heidaryzadeh M. Drug Delivery Systems Based on Polymeric Nanocarriers for the Management of Endo-Perio Lesions. Nanomed Res J, 2025; 10(3): 250-257. DOI: 10.22034/nmrj.2025.03.005

INTRODUCTION

Endo-perio lesions represent a complex interplay between endodontic and periodontal infections, often leading to significant challenges in diagnosis and treatment. These lesions are characterized by the simultaneous presence of periodontal and endodontic pathologies, which can complicate the clinical management due to their intertwined nature. The pathology involves the destruction of tooth-supporting structures, including the periodontal ligament and alveolar bone, often resulting in tooth mobility and loss if not adequately managed[1]. Clinically, these lesions pose diagnostic challenges due to overlapping symptoms and the need for precise differentiation between periodontal and endodontic origins. Current treatments typically involve mechanical debridement, systemic antibiotics, and surgical interventions, but these approaches often fall short in addressing the full scope of the infection [2, 3].

Traditional drug delivery methods in treating endo-perio infections face several limitations, primarily due to the complex oral environment and the nature of the lesions. Conventional systemic antibiotics often fail to reach the deep-seated biofilms within periodontal pockets, leading to suboptimal therapeutic outcomes[2, 3]. Many traditional delivery systems result in a burst release of drugs, which can lead to rapid clearance and reduced efficacy. Additionally, these systems often lack the selectivity needed to target specific sites of infection without affecting healthy tissues[4]. The overuse of systemic antibiotics has contributed

* Corresponding Author Email: *maryam.heidarizadeh@gmail.com*

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to the growing issue of antibiotic resistance, further complicating the management of these infections[5].

Nanotechnology, particularly the use of polymeric nanocarriers, is emerging as a promising solution to enhance drug delivery efficacy in dental applications, including the management of endo-perio lesions. Polymeric nanocarriers can be engineered to provide targeted and sustained drug release, improving site-specific bioavailability and reducing systemic side effects [6-9]. These nanocarriers can penetrate deep into periodontal pockets and maintain therapeutic drug levels over extended periods, overcoming the limitations of conventional delivery systems [4, 10]. Polymeric nanocarriers can be customized to carry a variety of therapeutic agents, including antibiotics, anti-inflammatory drugs, and growth factors, making them versatile tools in addressing the multifaceted nature of endo-perio lesions [7, 11].

Pathophysiology of Endo-Perio Lesions

The pathophysiology of endo-perio lesions involves complex interactions between microbial, inflammatory, and tissue destruction mechanisms. These lesions are characterized by the simultaneous involvement of periodontal and pulpal tissues, often leading to significant diagnostic and therapeutic challenges. The microbial component is primarily polymicrobial, involving anaerobic bacteria that contribute to the inflammatory processes and subsequent tissue destruction. The presence of biofilms further complicates treatment due to their resistance to conventional antimicrobial therapies. This resistance is compounded by the challenges in drug penetration, necessitating advanced drug delivery systems to effectively manage these lesions.

Endo-perio lesions are primarily driven by anaerobic bacteria that inhabit both the periodontal pockets and root canals. These bacteria produce toxins and enzymes that exacerbate inflammation and tissue destruction [12, 13]. The inflammatory response is a result of the host's immune system reacting to these microbial invaders, leading to the release of inflammatory mediators that further damage the periodontal and pulpal tissues [12, 14].

The tissue destruction in endo-perio lesions is a consequence of both direct bacterial action and the host's inflammatory response. This includes the breakdown of connective tissue and bone, which can lead to tooth mobility and eventual tooth loss [12, 14]. The pathways for microbial invasion include the apical foramen, lateral canals, and dentinal tubules, which facilitate the spread of infection between the pulp and periodontium [13].

Biofilms, which are structured communities of bacteria, provide a protective environment that enhances bacterial resistance to antibiotics and host immune responses[15]. The polymicrobial nature of these infections complicates treatment, as different bacterial species may exhibit varying levels of resistance and virulence, making it difficult to eradicate the infection completely[13]. Conventional therapies often fail to penetrate biofilms effectively, leading to persistent infections and the need for alternative treatment strategies[15].

Polymeric nanocarriers offer a promising solution for overcoming the challenges associated with biofilms and polymicrobial infections in endo-perio lesions. These systems can enhance drug penetration and provide sustained release of therapeutic agents directly at the site of infection [2, 5]. Advances in nanotechnology have led to the development of various polymer-based delivery systems, such as nanoparticles, which can be tailored to deliver antibiotics, anti-inflammatory agents, and other therapeutic compounds [7]. These systems not only improve the bioavailability of drugs but also reduce systemic side effects, making them an effective adjunct to conventional therapies [3].

Polymeric Nanocarriers in Drug Delivery

Polymeric nanocarriers have emerged as a pivotal technology in drug delivery systems, offering a range of benefits such as enhanced biocompatibility, biodegradability, and the ability to be functionalized for targeted delivery. These carriers are particularly promising for the management of endo-perio lesions due to their ability to deliver drugs precisely to the affected oral tissues, minimizing systemic side effects. The versatility of polymeric nanocarriers is evident in their various forms, including nanoparticles, nanogels, micelles, dendrimers, and polymeric films, each offering unique advantages for drug encapsulation and controlled release. Nanoparticles are small particles ranging from 1 to 100 nanometers, capable of encapsulating a wide range of therapeutic agents. They offer controlled drug release and improved bioavailability [16, 17]. Nanogels are hydrophilic polymer networks that can swell in water and are used for the delivery of hydrophilic drugs. They provide a high degree of biocompatibility and can be engineered for stimuli-responsive drug release[18, 19]. Micelles Formed by the self-assembly of amphiphilic block copolymers, are effective in solubilizing hydrophobic drugs and enhancing their bioavailability[20]. Dendrimers are highly branched, tree-like structures that offer multiple sites for drug attachment, allowing for high drug loading and precise targeting capabilities[21]. Polymeric Films are thin layers of polymers that can be used for localized drug delivery, particularly useful in oral applications where they can adhere to mucosal surfaces[22].

Polymeric nanocarriers are designed to be non-toxic and non-immunogenic, making them suitable for use in sensitive tissues such as oral tissues [23]. Many polymers used in these carriers, such as PLGA and chitosan, are biodegradable, allowing for the safe breakdown and elimination of the carrier from the body [24]. The surface of polymeric nanocarriers can be modified with ligands or antibodies to target specific cells or tissues, enhancing the precision of drug delivery [21, 25].

Drugs can be encapsulated within the polymer matrix or attached to the surface, protecting them from degradation and enhancing their stability[22]. The release of drugs from polymeric nanocarriers can be controlled through various mechanisms, including diffusion, degradation of the polymer matrix, or response to external stimuli such as pH or temperature changes [18, 26]. By exploiting the enhanced permeability and retention effect or through active targeting mechanisms, polymeric nanocarriers can deliver drugs specifically to diseased tissues, reducing off-target effects[16]. Table 1 summarizes various types of polymeric nanocarriers employed in drug delivery for endo-perio lesion management, highlighting their key properties, drug delivery mechanisms, and therapeutic advantages. Each nanocarrier type offers unique features that enhance drug stability, targeted delivery, and sustained release, making them effective platforms for overcoming the challenges of drug delivery in complex dental infections.

Advantages of Polymeric Nanocarriers for Endo-Perio Lesions

Polymeric nanocarriers have emerged as a promising solution for the management of endo-perio lesions due to their unique properties that enhance drug delivery and therapeutic outcomes. These nanocarriers offer several advantages, including improved drug stability, solubility, and bioavailability, which are crucial for effective treatment at infected sites. Additionally, they facilitate better penetration into biofilms and periodontal pockets, ensuring that the therapeutic agents reach the target areas more efficiently. The following sections detail the specific advantages of polymeric nanocarriers in the context of endo-perio lesions.

Polymeric nanocarriers improve the stability of drugs by protecting them from degradation, thus maintaining their therapeutic efficacy over time[27]. They enhance the solubility of poorly water-soluble drugs, which is critical for ensuring adequate drug concentration at the site of infection[28]. The bioavailability of drugs is significantly increased, allowing for more effective treatment outcomes with lower doses, reducing the risk of systemic side effects[29].

Nanocarriers are capable of penetrating

Table 1. Summary of Types of Polymeric Nanocarriers and Their Drug Delivery Advantages in the Management of Endo-Perio Lesions

Type of Polymeric Nanocarrier	Key Properties	Drug Delivery Features	Therapeutic Advantages for Endo-Perio Lesions
Nanoparticles	Size: 1-100 nm; biocompatible	Controlled drug release, improved bioavailability	Enhanced penetration into periodontal pockets, sustained drug release
Nanogels	Hydrophilic polymer networks	Swelling in water, stimuli-responsive release	High biocompatibility, effective for hydrophilic drugs
Micelles	Amphiphilic block copolymers	Solubilize hydrophobic drugs	Improved drug solubility and bioavailability
Dendrimers	Highly branched tree-like structures	Multiple drug attachment sites	High drug loading, precise targeting
Polymeric Films	Thin polymer layers	Localized drug delivery on mucosal surfaces	Sustained release, adherence to oral tissues

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dense biofilms and reaching deep periodontal pockets, which are often challenging to treat with conventional therapies[30]. The small size and surface modifications of these carriers enable them to navigate through complex biofilm structures, delivering drugs directly to the bacterial colonies[31]. This targeted approach ensures that the antimicrobial agents are more effective in eradicating pathogens and reducing inflammation[32].

Polymeric nanocarriers can be engineered to target specific cells or tissues, minimizing the exposure of non-target areas to the drugs[30]. This targeted delivery reduces systemic absorption and associated side effects, making the treatment safer for patients[33]. By concentrating the drug at the site of infection, these carriers enhance the local drug concentration, improving therapeutic outcomes[28].

Nanocarriers provide a controlled and sustained release of drugs, which is tailored to the pathological environment of endo-perio lesions[27]. This sustained release ensures a constant therapeutic level of the drug over an extended period, reducing the frequency of administration and improving patient compliance[28]. The release profiles can be adjusted based on the specific needs of the lesion, allowing for personalized treatment strategies[32].

While polymeric nanocarriers offer significant advantages in the treatment of endo-perio lesions, it is important to consider potential challenges such as the complexity of manufacturing processes and the need for thorough biocompatibility assessments. Additionally, the regulatory landscape for nanomedicines is still evolving, which may impact the development and approval of these advanced drug delivery systems. Despite these challenges, the potential benefits of polymeric nanocarriers in enhancing the efficacy and safety of treatments for endo-perio lesions make them a promising area of research and development in periodontal therapy.

Therapeutic Agents Delivered by Polymeric Nanocarriers

Polymeric nanocarriers have emerged as a promising platform for the delivery of therapeutic agents in the management of endo-perio lesions, offering targeted delivery, controlled release, and enhanced stability. These nanocarriers can encapsulate a variety of therapeutic agents, including antimicrobials, anti-inflammatory agents, regenerative molecules, and novel therapeutic payloads, to address the multifaceted nature of periodontal diseases. The following sections explore the specific therapeutic agents delivered by polymeric nanocarriers and their potential applications in endo-perio lesion management.

Polymeric nanocarriers can effectively deliver antibiotics and antiseptics to reduce microbial load in periodontal lesions. These carriers enhance the stability and bioavailability of antibiotics, such as moxifloxacin, and provide sustained release, which is crucial for overcoming microbial resistance and ensuring effective treatment[5, 7]. Antimicrobial-loaded nanofibers, such as those made from PLGA, have shown promise in localized drug delivery, reducing systemic side effects and mitigating antibiotic resistance[34].

Anti-inflammatory agents delivered via polymeric nanocarriers can modulate the host immune response, reducing inflammation and promoting healing in periodontal tissues[35]. Nanocarriers such as calcium phosphate bioceramics have been used to deliver ibuprofen, demonstrating significant anti-inflammatory activity and controlled release profiles[36]. The integration of anti-inflammatory drugs into nanocarriers can create a balanced microenvironment, reducing chronic inflammation and promoting tissue regeneration[37].

Polymeric nanocarriers can encapsulate regenerative molecules, such as growth factors and peptides, to facilitate tissue repair and regeneration in periodontal lesions[38].These carriers provide a conducive environment for cellular processes, fostering tissue regeneration, angiogenesis, and extracellular matrix synthesis[37]. The use of biodegradable nanocarriers, such as those made from chitosan and silica-derived nanoparticles, enhances the loading and release capabilities of regenerative molecules, supporting periodontal regeneration[35].

Polymeric nanocarriers offer a platform for delivering novel therapeutic payloads, such as siRNAs and gene therapy agents, for advanced treatment approaches in periodontal disease management[38]. These carriers enable precise targeting and smart release of therapeutic agents, ensuring high drug loading and remarkable therapeutic efficacy[39].The integration of stimuli-responsive polymers and multifunctional platforms in nanocarriers can further enhance the delivery of novel therapeutic agents, paving the way for

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personalized and precision medicine[38].

While polymeric nanocarriers offer significant advantages in the delivery of therapeutic agents for endo-perio lesions, challenges remain in their clinical translation. Issues such as biocompatibility, stability, and regulatory hurdles need to be addressed to ensure the safe and effective use of these nanocarriers in clinical settings. Additionally, the development of personalized treatment strategies and the integration of smart stimuli-responsive polymers could further enhance the therapeutic potential of polymeric nanocarriers in periodontal disease management.

Recent Advances of Polymeric Nanocarriers in Endo-Perio Therapy

Recent advances in polymeric nanocarriers have significantly enhanced the management of endo-perio lesions, offering improved treatment outcomes through innovative drug delivery systems. These advancements are characterized by the development of multifunctional nanocarriers that combine antimicrobial and regenerative capabilities, as well as tailored surface modifications for specific targeting of periodontal tissues or root canals.

Nanoemulsions have been highlighted for their ability to optimize drug delivery efficiency in periodontitis treatment. These formulations allow for the integration of various therapeutic agents, such as antibiotics and anti-inflammatory agents, which are crucial for addressing the multifaceted nature of periodontal diseases. The incorporation of specific drugs like moxifloxacin into nano-formulations has shown potential in combating microbial complexities, demonstrating the relevance of tailored approaches in improving treatment outcomes[7]. A study involving PLGA nanoparticles coated with chitosan demonstrated significant efficacy in treating recurrent Enterococcus faecalis infections in endodontics, showcasing the potential of nanocarriers in enhancing antibacterial treatments[40].

Nanocarriers have been developed to provide a combination of antimicrobial, immunomodulatory, and regenerative strategies. These multifunctional approaches are essential for maintaining effective drug concentrations and promoting periodontal regeneration[35]. The integration of antibacterial activity, immunomodulation, and periodontium regeneration in nanotherapeutics has been identified as a promising strategy for periodontitis treatment. This approach ensures stable cell targeting and smart release, enhancing therapeutic efficacy[39]. Tetracycline-loaded apatiticnanocarriers have demonstrated both antibacterial activity and bone regenerative potential, making them ideal for local periodontal applications[27].

The functionalization of PLGA nanoparticles with chitosan has been shown to enhance the efficacy of antibiotics against resistant infections in endodontics. This modification allows for better adhesion to bacterial cells and sustained drug release[40]. Polyglycerol-based nanogels have been designed to release therapeutic agents in response to the acidic environment of infection sites. This targeted approach not only combats microbial pathogens but also promotes tissue regeneration through pro-angiogenesis action[41]. The small size and large surface area of nanoparticles enable deep penetration into dentinal tubules, providing superior antimicrobial action and reducing the risk of reinfection in endodontic treatments.

While the advancements in polymeric nanocarriers for endo-perio therapy are promising, challenges remain in ensuring the safety, toxicity, and long-term biocompatibility of these nanomaterials. Ongoing research is necessary to address these concerns and further refine these innovative drug delivery systems. Additionally, the regulatory landscape for nanotherapeutics continues to evolve, necessitating careful consideration of biocompatibility and stability in clinical applications[7].

Challenges and Future Perspectives

The integration of polymeric nanocarriers into clinical applications presents a multifaceted set of challenges and opportunities. These challenges include biocompatibility and safety concerns, scalability and reproducibility in manufacturing, and regulatory hurdles. Additionally, the potential for integration with diagnostic systems and precision medicine approaches offers promising avenues for personalized treatment strategies. Emerging directions such as stimuli-responsive nanocarriers and combination therapies further expand the potential of these technologies. The following sections delve into these aspects, providing a comprehensive overview of the current state and future perspectives of polymeric nanocarriers in clinical translation.

Ensuring the biocompatibility of polymeric nanocarriers is crucial for their clinical

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translation. Concerns about potential toxicity and long-term effects remain significant barriers to their widespread adoption[8, 39, 42]. The evolving regulatory landscape complicates safety assessments and approval processes, necessitating clear guidelines to ensure patient safety[42, 43].

Achieving scalability and reproducibility in the production of polymeric nanocarriers is a major challenge. Consistent manufacturing processes are essential for maintaining the quality and efficacy of these nanocarriers[39, 42, 44]. The complex regulatory environment for nanomedicine requires comprehensive safety and efficacy evaluations, which can delay clinical translation[45].

The integration of polymeric nanocarriers with diagnostic systems and precision medicine approaches holds promise for personalized endo-perio treatment. These systems enable targeted drug delivery and improved therapeutic outcomes by leveraging molecular profiling and tumor microenvironment insights[46]. Combining therapy with real-time imaging, theranostic platforms offer a dual approach to treatment and diagnosis, enhancing precision medicine strategies.

Smart nanocarriers that respond to biological stimuli offer tailored and real-time drug release, enhancing treatment precision and efficacy. The use of combination therapies, including nano-immunotherapy and gene-editing technologies, presents new opportunities for enhancing therapeutic outcomes and overcoming multidrug resistance[38].

While the potential of polymeric nanocarriers in clinical applications is vast, addressing the challenges of biocompatibility, scalability, and regulatory compliance is essential for their successful translation. The integration of these technologies with diagnostic systems and precision medicine approaches offers promising avenues for personalized treatment strategies. However, the complexity of the regulatory landscape and the need for consistent manufacturing processes remain significant hurdles. Future research should focus on optimizing nanocarrier design, improving safety assessments, and establishing clear regulatory guidelines to ensure the successful clinical translation of these innovative technologies.

CONCLUSION

Polymeric nanocarriers hold significant promise in revolutionizing drug delivery for the management of endo-perio lesions, offering enhanced therapeutic efficacy and precision. These advanced systems leverage the unique properties of nanotechnology to improve drug penetration, retention, and targeted delivery, addressing the limitations of conventional treatments. The integration of polymeric nanoparticles in dental applications has demonstrated superior outcomes in both endodontic and periodontal therapies, suggesting a transformative potential for these technologies in routine dental practice. However, to fully realize this potential, further clinical studies and interdisciplinary collaboration are essential.

Polymeric nanoparticles have shown superior penetration and retention in dental tissues, significantly reducing microbial loads in endodontic treatments compared to conventional methods. For instance, nanoparticles loaded with antimicrobial agents achieved a more substantial reduction in microbial load and deeper penetration into dentinal tubules than traditional irrigation techniques. periodontitis management, nano-drug delivery systems have been effective in integrating various therapeutic agents, such as antibiotics and anti-inflammatory drugs, to address the multifaceted nature of the disease. These systems optimize drug delivery efficiency and demonstrate versatility in combating microbial complexities.

he adaptability of polymeric nanocarriers allows for the incorporation of diverse therapeutic agents, enabling tailored approaches to specific oral health challenges. This customization is crucial for addressing the complexities of conditions like periodontitis, where a one-size-fits-all approach is often inadequate. Polymeric nanoparticles can be engineered to provide controlled and sustained drug release, enhancing therapeutic outcomes and patient compliance by reducing the frequency of administration.

Despite the promising results, challenges such as biocompatibility, stability, and regulatory hurdles must be addressed to ensure the safe and effective application of these technologies in clinical settings. Interdisciplinary collaboration is vital to advance the development and integration of polymeric nanocarriers into routine dental practice. This includes partnerships between researchers, clinicians, and regulatory bodies to establish standardized guidelines and ensure the long-term success of these innovations.

While polymeric nanocarriers offer a promising future for drug delivery in endo-perio lesion management, it is crucial to consider the broader

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context of their application. The integration of these advanced systems into clinical practice requires not only technological advancements but also a comprehensive understanding of their long-term effects and potential risks. Addressing these challenges through rigorous clinical studies and fostering interdisciplinary collaboration will be key to unlocking the full potential of polymeric nanocarriers in dental care.

ACKNOWLEDGEMENTS

The authors employed artificial intelligence resources, including Perplexity.ai, to improve the clarity and linguistic quality of the manuscript during its preparation. All suggestions and content generated by AI were carefully evaluated and edited by the authors, who maintain full accountability for the accuracy and integrity of the final version.

CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest related to the research, authorship, or publication of this manuscript. All authors have disclosed any financial or personal relationships that could potentially influence or bias the work presented.

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