REVIEW ARTICLE

Nanoengineered Drug Delivery Systems for Post-Orthodontic Surgical Care

Milad Soleimani[1], Nastaran Saeidi[2,3], Seyed Sobhan Mousavi Kani[4], Alireza Amirkhani[5], Mina Sadat Mirkhani[6], Seyed Mohammad Mahdi Mirmohammadi[7*], Yasaman Bathaei[8]

[1] *Department of Orthodontics, School of Dentistry Shahid Beheshti, University of Medical Sciences, Tehran, Iran*

[2] *Tehran Islamic Azad university of Medical Sciences, Tehran, Iran*

[3] *Department of Dentistry, Tehran University of Medical and Sciences, Tehran, Iran*

[4] *Dental Surgery, School of Dentistry, Islamic Azad University of Medical Sciences, Tehran, Iran*

[5] *Prosthodontics Resident, School of Dentistry, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

[6] *Independent Dental Researcher, USA*

[7] *Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Shahed University, Tehran, Iran*

[8] *Department of Orthodontics, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran*

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ABSTRACT

Post-orthodontic surgical procedures frequently encounter complications such as pain, inflammation, infection, edema, and delayed wound healing, which can compromise treatment outcomes and patient comfort. This review examines the promising role of nanoengineered drug delivery systems (DDS) in addressing these challenges by enhancing targeted drug delivery, improving bioavailability, and enabling controlled release of therapeutic agents. Various nanoparticle platforms—including liposomes, dendrimers, polymeric nanoparticles, metallic nanoparticles, solid lipid nanoparticles, and calcium phosphate nanoclusters—are evaluated for their unique properties and applications in promoting tissue regeneration, preventing infection, and improving implant integration in post-orthodontic care. Despite substantial advancements, the clinical translation of nano-DDS faces hurdles related to scalability, safety, regulatory approval, and long-term biocompatibility. Future perspectives emphasize interdisciplinary research, the use of biodegradable materials, and the application of artificial intelligence to optimize nanocarrier design and personalize treatment strategies. Overall, nanoengineered DDS offer significant potential to revolutionize post-orthodontic surgical care by improving therapeutic efficacy and patient outcomes, underscoring the need for further clinical studies to fully realize their benefits in routine practice.

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INTRODUCTION

Post-orthodontic surgical care involves managing pain, inflammation, infection, and promoting tissue regeneration, which are critical for successful patient outcomes. Challenges include ensuring effective pain management, reducing inflammation, preventing infections, and facilitating tissue healing, all of which can be compromised by inadequate drug delivery methods. The complexity of the oral environment, with its unique microbiome and constant exposure to mechanical forces, further complicates effective drug delivery and therapeutic outcomes[1, 2].

Effective drug delivery is crucial for managing post-surgical pain and inflammation, which can significantly impact patient comfort and compliance with orthodontic treatment[3]. Targeted drug delivery systems can enhance the therapeutic efficacy of drugs by ensuring localized action,

* Corresponding Author Email: *e.mirmohamadi@yahoo.com*

reducing systemic side effects, and improving patient adherence[4]. Advanced drug delivery systems are essential for controlling infections and promoting tissue regeneration, which are vital for the long-term success of orthodontic surgeries[5, 6]. Nanotechnology offers innovative solutions for drug delivery challenges by utilizing materials at the nanoscale, which possess unique properties that enhance drug delivery efficiency. Nanoengineered drug delivery systems (DDS) can provide controlled and sustained release of therapeutic agents, improve drug stability, and enable targeted delivery to specific sites within the oral cavity [7, 8]. The application of nanotechnology in dentistry, particularly in orthodontics, has shown promise in improving treatment outcomes and patient satisfaction[9]. This will support your statements on the innovative potential of nanotechnology in dental drug delivery[10].

The primary objective of this review is to explore the potential of nanoengineered DDS in enhancing post-orthodontic surgical care by addressing the challenges of pain management, inflammation control, infection prevention, and tissue regeneration. The review will cover recent advancements in nanotechnology applications in orthodontics, evaluate the effectiveness of various nano-based DDS, and discuss their implications for clinical practice.

BACKGROUND ON POST-ORTHODONTIC SURGICAL CARE

Orthognathic surgery is a common surgical procedure in orthodontics aimed at correcting jaw discrepancies and improving facial aesthetics and function. It involves repositioning the jaws to achieve better alignment and occlusion[11]. Surgical adjuncts to o rthodontics include procedures such as corticotomies and osteotomies, which are performed to facilitate tooth movement and correct severe dentofacial deformities.

Common postoperative complications following orthodontic surgeries include pain and inflammation, which are typically managed with analgesics and anti-inflammatory medications[11, 12]; infection, which poses a significant risk and requires the use of antibiotics for prevention or treatment[12]; edema and swelling, frequent issues often controlled with corticosteroids and other anti-inflammatory agents[11]; and the need for enhanced wound healing, which is crucial for recovery and supported by various therapeutic agents such as vitamin and mineral supplements[11].

Traditional drug delivery methods often involve immediate-release formulations, which can lead to fluctuating plasma drug concentrations and systemic side effects. This can result in poor patient adherence and suboptimal therapeutic outcomes[12]. Conventional routes such as oral and systemic administration face challenges like instability, uncontrolled release, and side effects such as irritation and pain[13]. The complex environment of the oral cavity, including factors like saliva and food, can affect the efficacy of topically applied drugs, leading to reduced effectiveness[14]. The constant salivary flow and the dynamic environment of the oral cavity can compromise the effectiveness of locally-administered medications, necessitating the development of more advanced delivery systems[15]. While conventional drug delivery methods have been the mainstay in post-orthodontic care, they present several limitations that can hinder effective treatment. The development of nanoengineered drug delivery systems offers a promising alternative, potentially overcoming these challenges by providing targeted and sustained drug release. These systems can enhance the precision and efficacy of postoperative pharmacotherapy, addressing the complexities of post-orthodontic surgical care with greater efficiency and patient compliance.

FUNDAMENTALS OF NANOENGINEERED DRUG DELIVERY SYSTEMS

Nanoengineered drug delivery systems (DDS) represent a significant advancement in pharmaceutical sciences, offering enhanced drug delivery capabilities through the use of nanoparticles[10]. These systems are designed to improve the bioavailability, targeting, and controlled release of therapeutic agents, making them particularly beneficial for post-orthodontic surgical care. The following sections delve into the fundamentals of nanoengineered DDS, focusing on the types of nanoparticles used, mechanisms of drug encapsulation and release, and the advantages over conventional methods.

Nanoparticles are defined as particles with at least one dimension less than 100 nanometers. They are utilized in drug delivery due to their unique physicochemical properties, which can be tailored for specific therapeutic needs. Liposomes are vesicular systems composed of lipid bilayers that encapsulate aqueous compartments, ideal for delivering both hydrophilic and hydrophobic drugs. They enhance drug solubility and stability while reducing toxicity[16]. Dendrimers are hyperbranched, three-dimensional nanostructures with precise size and shape control, allowing for high drug loading and targeted delivery[16]. Polymeric nanoparticles offer controlled drug release and improved drug stability [17, 18]. Metallic nanoparticles include gold and silver nanoparticles, known for their unique optical properties and potential in targeted drug delivery[19]. Solid lipid nanoparticles provide a matrix for drug encapsulation, offering controlled release and reduced drug degradation[16].

The encapsulation and release of drugs in nanoengineered DDS are critical for their efficacy and safety. Drugs can be encapsulated within the core or adsorbed onto the surface of nanoparticles. This process protects the drug from degradation and allows for controlled release [17, 18]. Drug release can be triggered by environmental stimuli such as pH, temperature, or enzymatic activity, allowing for site-specific delivery. This is particularly useful in targeting specific tissues or cells[19].

Nanoengineered DDS offer several advantages over conventional drug delivery methods, making them highly effective for post-orthodontic surgical care. Nanoparticles can be engineered to target specific cells or tissues, reducing off-target effects and enhancing therapeutic efficacy[20]. These systems allow for sustained and controlled drug release, reducing the frequency of dosing and improving patient compliance[21]. Nanoparticles improve the solubility and stability of drugs, increasing their bioavailability and therapeutic index [18, 22]. Nanoparticles can overcome biological barriers such as the blood-brain barrier, enabling the delivery of drugs to previously inaccessible sites [23, 24]. While nanoengineered DDS offer numerous benefits, challenges such as scalability, regulatory hurdles, and potential toxicity must be addressed to fully realize their potential in clinical settings. Further research and development are essential to overcome these challenges and ensure the safe and effective implementation of these systems in post-orthodontic surgical care and other therapeutic areas.

NANOMATERIALS AND CARRIERS USED IN POST-ORTHODONTIC DDS

The application of nanomaterials and carriers in post-orthodontic drug delivery systems (DDS) is a burgeoning field that leverages the unique properties of nanoscale materials to enhance therapeutic outcomes. These systems are particularly relevant in oral and maxillofacial applications, where they can improve tissue regeneration, infection control, and targeted drug delivery. This answer will explore the biocompatible and biodegradable nanomaterials used in these applications, functionalization strategies to enhance targeting and therapeutic efficacy, and examples of nano-carriers designed specifically for oral tissue applications. Silver-zinc oxide (Ag-ZnO) nanoparticles represent an emerging class of metallic nanomaterials with demonstrated antibacterial efficacy against *Streptococcus mutans*, a primary contributor to oral biofilm formation and dental caries. Their synergistic antibacterial effects enhance the prevention of bacterial colonization on orthodontic surfaces, which is critical in reducing infection risks during orthodontic treatment. Moreover, cytotoxicity assessments indicate a favorable safety profile for potential clinical applications, supporting their use as effective antimicrobial agents in nanoengineered drug delivery systems [25].

Polymers and nanostructured scaffolds are widely utilized in tissue regeneration and wound healing due to their biocompatibility and structural similarity to the extracellular matrix, which supports cell growth and differentiation[26, 27]. Dendrimers and liposomes serve as effective drug delivery systems within the oral cavity by encapsulating therapeutic agents, allowing controlled release and minimizing side effects[26, 28]. Gold nanoparticles, recognized for their antibacterial properties, are commonly applied as coatings on orthodontic brackets to inhibit bacterial biofilm formation a prevalent challenge in orthodontic treatments. Beyond their antibacterial effects, gold nanoparticles enhance the physical and mechanical properties of dental materials and exhibit excellent biocompatibility both in vitro and in vivo. Their application not only helps prevent pathogenic bacterial growth such as Streptococcus mutans but also supports improved outcomes in dental implant osseointegration and other orthodontic applications. The integration of these nanomaterials holds significant promise for advancing dental therapies by combining enhanced mechanical strength, biocompatibility, and antimicrobial effectiveness[29].

Table 1. Summary of nanoparticle types, characteristics, and their applications in post-orthodontic drug delivery systems

Nanoparticle Type	Characteristics	Application/Benefits in Post-Orthodontic Care
Liposomes	Vesicular, lipid bilayer, encapsulates hydrophilic and hydrophobic drugs	Enhances drug solubility and stability; reduces toxicity
Dendrimers	Hyperbranched, 3D nanostructures	High drug loading; targeted delivery
Polymeric nanoparticles	Controlled drug release; improved stability	Sustained release, improved bioavailability
Metallic nanoparticles (Gold, Silver)	Unique optical properties; antibacterial	Antibacterial coatings; biofilm inhibition; improved implant osseointegration
Solid lipid nanoparticles	Matrix for drug encapsulation	Controlled release; reduced drug degradation
Calcium phosphate nanoclusters	Biomimetic; supports tissue regeneration	Maintains post-treatment tooth position; reduces relapse risk

Surface modification plays a crucial role in enhancing the functionality and effectiveness of nanomaterials used in dental applications. Techniques such as coating nanomaterials with bioactive molecules or polymers improve their targeting ability, allowing for precise drug delivery to affected areas[30, 31]. Functionalization with ligands or antibodies further refines this specificity, ensuring therapeutic agents reach targeted tissues directly, which boosts efficacy while reducing systemic exposure. Biomimetic approaches, inspired by the natural structure of dental tissues, enable engineering of nanomaterials that promote better integration and functionality essential for tissue regeneration and repair[28, 32]. In dental implants, nanoscale surface modifications achieved via physical or chemical processes like grit blasting, acid etching, anodization, or coating with nanoparticles significantly improve biocompatibility, osteoblast attachment, and Osseo integration. These modifications ions increase surface area, enhance protein and cell adhesion, and enable the controlled release of bioactive molecules, accelerating bone regeneration and implant healing. The integration of nanotechnology in surface treatment not only improves mechanical properties but also fosters long-term success in dental therapies by promoting better tissue interactions and reducing bacterial complications. However, ongoing research is necessary to further optimize these techniques and fully realize their clinical potential[27, 33].

Polymeric nanoparticles are widely recognized in oral drug delivery for their stability and ability to enhance drug bioavailability[28]. These nanoparticles protect encapsulated drugs from degradation in the harsh gastrointestinal environment and improve uptake by target tissues, making them particularly effective for treating oral diseases through controlled and targeted delivery. Solid lipid nanoparticles similarly provide controlled release, especially for hydrophobic drugs, maintaining therapeutic levels over time. In orthodontics, nanocomposite coatings, such as those incorporating gold-oxoborate, offer antibacterial properties that help prevent complications like white spot lesions while remaining safe for human cells[29]. Despite these advantages, the long-term biocompatibility of nanomaterials, functionalization complexity, and the evolving regulatory landscape present ongoing challenges for clinical adoption. Extensive research and validation are needed to overcome these hurdles and securely integrate nanomaterial-based drug delivery systems into dental practice[26, 30]. A summary of the key nanoparticle types, their defining characteristics, and their specific applications in post-orthodontic drug delivery systems is provided in Table 1 to facilitate understanding of their therapeutic roles.

APPLICATIONS OF NANOENGINEERED DDS IN POST-ORTHODONTIC SURGICAL CARE

The application of nanoengineered drug delivery systems (DDS) in post-orthodontic surgical care offers significant advancements in targeted therapy, infection control, and tissue regeneration. These systems leverage the unique properties of nanomaterials to enhance the delivery and efficacy of therapeutic agents, addressing common post-surgical challenges such as inflammation, infection, and tissue healing. The following sections explore the specific applications of nanoengineered DDS in this context.Nanoengineered DDS can precisely deliver anti-inflammatory agents to surgical sites, reducing swelling and pain associated with post-orthodontic procedures.These systems enhance drug solubility and bioavailability, ensuring prolonged circulation and retention at the target site, which minimizes systemic side effects [34]. The use of nanoparticles allows for controlled release, maintaining therapeutic levels of anti-inflammatory agents over extended periods [7].

Nanoparticles such as silver and copper have demonstrated potent antibacterial properties, making them effective in preventing infections post-surgery[35]. These nanoformulations can be integrated into dental materials or applied directly to surgical sites, providing localized antimicrobial action without the need for systemic antibiotics[36]. The ability of nanocarriers to penetrate biofilms and deliver antibiotics directly to bacterial cells enhances their efficacy against resistant strains[15].

Nanoengineered DDS can deliver growth factors and regenerative agents to promote bone and soft tissue healing, crucial for successful orthodontic outcomes[6]. These systems create a regenerative microenvironment by providing sustained release of therapeutic agents, facilitating tissue regeneration and reducing healing time[37]. The incorporation of bioactive coatings on implants and surgical materials further supports osseointegration and tissue attachment[36].

Controlled release formulations in nanoengineered DDS ensure consistent therapeutic levels, reducing the frequency of administration and improving patient compliance[34]. These systems can be tailored to release drugs in response to specific physiological triggers, providing a personalized approach to post-surgical care[32]. By minimizing the need for frequent dosing, these formulations enhance the overall patient experience and adherence to treatment protocols[15].

PRECLINICAL AND CLINICAL STUDIES

The application of nanoengineered drug delivery systems (nano-DDS) in post-orthodontic surgical care is a burgeoning field that leverages the unique properties of nanotechnology to enhance treatment outcomes. This approach aims to improve drug delivery efficiency, reduce side effects, and provide targeted therapeutic effects. The following sections explore preclinical and clinical studies, including in vitro and in vivo research, clinical trials, and case reports, as well as a discussion on outcomes and evidence gaps.

Preclinical studies have demonstrated the potential of nano-DDS in enhancing the efficacy and safety of treatments in dental applications. Research has shown that nanoparticles can significantly reduce biofilm formation on orthodontic brackets, which is a common issue during orthodontic treatment. For instance, silver nanoparticles (AgNPs) coated on NiTi wires have exhibited strong antibacterial and antibiofilm activities against both Gram-positive and Gram-negative bacteria, reducing surface roughness and metal ion release[38]. Similarly, gold-oxoborate nanocomposites have been effective in reducing bacterial adhesion on orthodontic brackets, maintaining safety for eukaryotic cells[29].

Although specific in vivo studies on nano-DDS for post-orthodontic surgical care are limited, the principles demonstrated in periodontitis management suggest potential applications. Nanoemulsions and other nanoformulations have been shown to optimize drug delivery efficiency and stability, which could be beneficial in managing postoperative inflammation and infection[6, 7].

Clinical trials and case reports provide insights into the real-world application of nano-DDS in orthodontic care. A study involving nanoparticles coated on orthodontic brackets demonstrated a significant reduction in biofilm formation, as evidenced by lower plaque index scores in the experimental group compared to the control group[39]. This suggests that nano-DDS can effectively enhance oral hygiene during orthodontic treatment.

While specific case reports on post-orthodontic surgical care using nano-DDS are sparse, the successful application of nanotechnology in reducing friction and enhancing antibacterial properties in orthodontic devices indicates potential benefits in postoperative care[40, 41].

The outcomes of these studies highlight the promising role of nano-DDS in improving orthodontic treatment and postoperative care, yet several evidence gaps remain.

The use of nano-DDS has shown to improve antibacterial properties, reduce biofilm formation, and enhance the mechanical properties of orthodontic devices. These improvements can potentially lead to better patient outcomes, such as reduced incidence of white spot lesions and periodontal disease during and after orthodontic treatment[38, 39]. Despite these promising results, there is a lack of comprehensive clinical data specifically focused on post-orthodontic surgical care. More extensive clinical trials are needed to evaluate the long-term safety and efficacy of nano-DDS in this context. Additionally, research should address the biocompatibility and potential systemic effects of prolonged exposure to nanoparticles[6, 7].

While the current research underscores the potential of nano-DDS in orthodontic applications, it is crucial to address the existing evidence gaps through further studies. This will ensure the safe and effective integration of nanotechnology into routine orthodontic and postoperative care, ultimately enhancing patient outcomes and treatment experiences.

CHALLENGES AND FUTURE PERSPECTIVES

The integration of nanotechnology into drug delivery systems (DDS) for post-orthodontic surgical care presents both promising advancements and significant challenges. Nanoengineered DDS offer enhanced precision in drug delivery, improved bioavailability, and reduced systemic toxicity, which are crucial for effective post-surgical care. However, the translation of these systems from research to clinical practice is fraught with technical, regulatory, and safety challenges. This section explores these challenges, potential risks, emerging trends, and future research directions in the field of nano-DDS.

Ensuring the biocompatibility and stability of nanomaterials is a major technical challenge. Nanoparticles must be designed to avoid rapid degradation and excretion while maintaining their therapeutic efficacy[42]. The complex nature of nanomaterials poses significant regulatory challenges. There is a need for standardized safety protocols and clear regulatory guidelines to facilitate the clinical translation of nano-DDS[43, 44].The lack of standardized manufacturing methods for nano-DDS complicates their scalability and commercial production, which is essential for widespread clinical adoption[45].

The potential toxicity of nanomaterials remains a critical concern. Nanoparticles can induce adverse biological responses, necessitating thorough toxicity assessments before clinical use[42]. Understanding the long-term effects of nanomaterials on human health is crucial. There is a need for comprehensive studies to evaluate the chronic exposure risks associated with nano-DDS[45].

These nanoparticles combine therapeutic and diagnostic functions, enabling real-time monitoring of drug delivery and treatment efficacy. This dual functionality is particularly beneficial for personalized medicine. Stimuli-responsive DDS that release drugs in response to specific biological triggers are gaining traction. These systems enhance targeting efficacy and minimize side effects, although they face significant regulatory and manufacturing challenges[45].

Future research should foster collaboration between chemists, engineers, and medical professionals to address the multifaceted challenges of nano-DDS. Research should focus on optimizing the design of nanocarriers to improve their efficacy and safety. This includes using biodegradable materials and enhancing targeting capabilities. AI can be leveraged to design more effective nanoparticles and predict their interactions within biological systems, potentially revolutionizing personalized medicine[46].

CONCLUSION

Nanoengineered DDS have emerged as a transformative approach in orthodontics, particularly in enhancing postoperative outcomes. These systems leverage the unique properties of nanomaterials to deliver therapeutic agents more effectively, targeting specific sites within the oral cavity. This precision not only improves the efficacy of treatments but also minimizes side effects, thereby enhancing patient compliance and satisfaction. For instance, calcium phosphate nanoclusters have been shown to modify periodontium remodeling, significantly reducing orthodontic relapse by improving bone quality and altering periodontal ligament remodeling. Transitioning to the benefits and hurdles of these systems, it is essential to consider both the advancements and the challenges they present.

Nanocomposites, such as gold-oxoborate coatings, provide orthodontic brackets with antibacterial properties, reducing bacterial adhesion by approximately 78% and preventing enamel demineralization. Nanotechnology enhances the mechanical properties of orthodontic materials, such as reducing friction in archwires and increasing the strength of composites, which facilitates more efficient tooth movement. Nanoparticles enable targeted delivery of drugs, improving the management of orthodontic pain and reducing the need for systemic medication, which can have broader side effects. The use of nanomaterials like calcium phosphate nanoclusters helps in maintaining the post-treatment position of teeth, thereby reducing the risk of relapse.

Ensuring the safety of nanomaterials for long-term use in the human body remains a significant challenge, as the interaction of these materials with biological tissues needs thorough investigation. The production and implementation of nanoengineered DDS can be costly, potentially limiting their accessibility to a broader patient population. The novel nature of nanotechnology in orthodontics poses regulatory challenges, as existing frameworks may not adequately address the unique properties and risks associated with nanomaterials.

The integration of nanoengineered DDS in orthodontics holds the potential to revolutionize patient care by providing more effective, targeted, and less invasive treatment options. These advancements can lead to improved treatment outcomes, reduced treatment times, and enhanced patient comfort, ultimately contributing to a higher quality of life for patients undergoing orthodontic procedures. While the benefits are promising, it is crucial to address the associated challenges to fully realize the potential of these technologies in clinical practice. As research continues to evolve, the future of orthodontic care may see a significant shift towards more personalized and efficient treatment modalities, driven by the capabilities of nanotechnology.

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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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