

Targeted Intracanal Drug Delivery Systems in Endodontics: Current Advances, Challenges, and Future Perspectives

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ABSTRACT

Background: Endodontic infections are biofilm-mediated and persist due to the complex anatomy of the root canal system, limiting the effectiveness of conventional intracanal medicaments.

Objective: This review aims to critically analyze current and emerging targeted intracanal drug delivery systems and their potential in improving endodontic disinfection.

Methodology: This review was conducted following a structured narrative approach. A comprehensive literature search was performed using PubMed, Scopus, and Google Scholar databases for articles published between January 2010 and December 2025. Search keywords included: “intracanal drug delivery,” “nanoparticles in endodontics,” “controlled drug release,” “biofilm targeting,” and “regenerative endodontics.”

Inclusion criteria comprised in vitro studies, in vivo studies, and relevant review articles focusing on drug delivery systems in endodontics. Exclusion criteria included non-English articles, case reports, and studies not directly related to intracanal drug delivery. A total of approximately 120 articles were identified, of which 55 relevant studies were included based on relevance and scientific quality.

Results: Nanoparticle-based systems (silver, chitosan, and polymeric nanoparticles), liposomes, hydrogels, and bioactive materials demonstrate enhanced dentinal penetration, sustained drug release, and improved antimicrobial efficacy. However, most evidence remains limited to laboratory studies with minimal clinical validation.

Conclusion: Targeted intracanal drug delivery systems represent a promising paradigm shift in endodontics. Future research should focus on clinical trials, standardization, and translational applicability for routine clinical use.

Keywords: Intracanal drug delivery, Nanocarriers, Biofilm targeting, Controlled release, Regenerative endodontics, Smart drug delivery

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1. Introduction

Successful endodontic therapy depends on effective elimination of microorganisms from the root canal system and prevention of reinfection. However, the intricate anatomy of root canals, including lateral canals, isthmuses, apical ramifications, and dentinal

tubules, makes complete disinfection challenging. Microorganisms organized as biofilms within dentinal tubules are particularly resistant to conventional antimicrobial strategies and are a major cause of persistent apical periodontitis and treatment failure [1,2].

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Traditional intracanal medicaments such as calcium hydroxide and triple antibiotic paste are widely used for microbial control. Although these agents reduce bacterial load, they exhibit important limitations. Their diffusion into dentinal tubules is often inadequate, antimicrobial concentrations decline rapidly over time, and prolonged exposure may induce cytotoxic effects or bacterial resistance [3–5]. Additionally, conventional delivery systems lack mechanisms for sustained and controlled release.

Targeted intracanal drug delivery systems have emerged as advanced therapeutic strategies aimed at overcoming these challenges. By integrating principles of nanotechnology, polymer science, and biomaterials engineering, these systems allow localized delivery of antimicrobial agents at therapeutic concentrations for extended durations while minimizing systemic exposure [6].

Nanoparticle-based carriers, liposomes, polymeric micro- and nano-systems, injectable hydrogels, and bioactive scaffold platforms are increasingly being explored for intracanal application. These emerging technologies enhance penetration into dentinal tubules, improve biofilm disruption, and enable sustained antimicrobial release [7–9].

This review critically examines current and emerging targeted intracanal drug delivery technologies and discusses their translational potential in contemporary endodontic therapeutics.

2. Rationale for Targeted Intracanal Drug Delivery

Endodontic infections are biofilm-driven. Biofilms provide structural protection to bacteria, limiting antimicrobial penetration and increasing resistance to disinfectants [10]. Microorganisms such as *Enterococcus faecalis* can penetrate deeply into dentinal tubules and survive under harsh conditions [11].

Targeted drug delivery systems aim to:

- Enhance dentinal tubule penetration
- Provide sustained antimicrobial release
- Reduce cytotoxicity
- Minimize systemic side effects
- Prevent development of resistance

Localized controlled-release systems maintain effective antimicrobial concentration within the canal for prolonged periods, thereby improving microbial eradication [12].

3. Nanotechnology-Based Intracanal Drug Delivery Systems

3.1 Silver Nanoparticles

Silver nanoparticles (AgNPs) exhibit broad-spectrum antimicrobial activity through membrane disruption, generation of reactive oxygen species, and interference with DNA replication [13]. Due to their nanoscale size, AgNPs penetrate dentinal tubules more effectively than conventional irrigants.

Studies demonstrate enhanced antibacterial action against *E. faecalis* biofilms when silver nanoparticles are incorporated into irrigants or medicaments [14]. However, concerns regarding cytotoxicity and dosage control require further investigation.

3.2 Chitosan Nanoparticles

Chitosan is a natural biopolymer with intrinsic antimicrobial properties and excellent biocompatibility. Chitosan nanoparticles improve drug stability and allow sustained release of antimicrobial agents [15].

They demonstrate effective biofilm disruption and deeper penetration into dentin [16]. Their mucoadhesive properties enhance retention within the canal system, improving therapeutic efficiency.

3.3 Polymeric Nanoparticles

Biodegradable polymers such as poly(lactic-co-glycolic acid) (PLGA) are widely used for controlled drug delivery [17]. PLGA nanoparticles enable gradual and predictable release of encapsulated antibiotics, maintaining therapeutic concentration over extended periods.

Antibiotic-loaded PLGA systems have shown improved antimicrobial efficacy with reduced cytotoxicity compared to conventional paste formulations [18].

4. Liposomal Drug Delivery Systems

Liposomes are phospholipid vesicles capable of encapsulating hydrophilic and hydrophobic drugs. Their structural similarity to bacterial membranes enhances interaction with biofilms [19].

Liposomal formulations improve drug stability, penetration, and sustained release. Liposomal chlorhexidine and calcium hydroxide systems have demonstrated superior antimicrobial efficacy compared to conventional preparations [20].

5. Hydrogel-Based Intracanal Delivery Systems

Hydrogels are three-dimensional polymer networks capable of retaining large amounts of water. Injectable hydrogels serve as scaffolds for sustained drug release

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and can be engineered to exhibit temperature- or pH-sensitive behavior [21].

In regenerative endodontics, hydrogels act as carriers for antibiotics and growth factors, supporting cell proliferation and tissue regeneration [22]. Their biocompatibility and customizable release kinetics make them promising platforms.

6. Stimuli-Responsive Smart Delivery Systems

Advanced drug delivery research has introduced stimuli-responsive systems that release drugs in response to environmental triggers such as pH, temperature, or bacterial enzymes [23].

In infected root canals, acidic pH and enzymatic activity can activate targeted release. Such systems improve specificity and reduce unnecessary drug exposure, representing a step toward precision endodontic therapeutics.

7. Bioactive Materials as Drug Carriers

Calcium silicate-based materials such as mineral trioxide aggregate (MTA) and bioceramic sealers exhibit bioactivity and can serve as drug delivery platforms [24].

Incorporation of antimicrobial agents into sealers allows dual functionality—mechanical sealing and sustained antimicrobial release [25]. These bioactive carriers may enhance periapical healing while providing local drug action.

8. Drug Delivery in Regenerative Endodontics

Regenerative endodontic procedures require elimination of infection while preserving stem cell viability. Controlled-release systems reduce cytotoxic effects associated with high antibiotic concentrations [26].

Scaffold-based delivery platforms facilitate gradual release of growth factors and antimicrobial agents, supporting tissue regeneration and pulp-dentin complex formation.

Table 1: Comparison of Intracanal Drug Delivery Systems

System	Advantages	Limitations	Clinical Status
Silver nanoparticles	Strong antimicrobial, deep penetration	Cytotoxicity concerns	Experimental
Chitosan nanoparticles	Biocompatible, bioadhesive	Limited stability	Emerging
PLGA nanoparticles	Controlled release	Cost, complex synthesis	Preclinical
Liposomes	Improved drug stability	Limited shelf-life	Experimental
Hydrogels	Sustained release, regenerative use	Technique sensitive	Emerging
Bioactive materials	Dual function (sealing + drug delivery)	Limited drug loading	Clinical use evolving

Critical Analysis

Despite promising in vitro findings, the majority of studies remain laboratory-based, with limited clinical trials evaluating long-term safety and efficacy.

Variability in drug concentration, delivery mechanisms, and outcome measures further limits direct comparison across studies.

Standardization of protocols and large-scale randomized clinical trials are essential for successful clinical translation.

Challenges and Translational Barriers

Despite encouraging laboratory evidence, several practical challenges hinder clinical translation...”

- Standardization of drug concentration
- Long-term biocompatibility evaluation
- Regulatory approval processes
- Manufacturing scalability
- Cost considerations

Large-scale clinical trials are necessary to validate safety and therapeutic superiority.

Future Perspectives

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Future research should focus on:

- Multifunctional nano-platforms
- Biofilm-targeted smart systems
- Personalized intracanal drug delivery
- Integration with digital navigation systems

The convergence of nanotechnology, biomaterials science, and clinical endodontics may redefine infection control strategies.

Clinical Implications

Targeted intracanal drug delivery systems have the potential to significantly improve disinfection outcomes in endodontic practice. Enhanced penetration into dentinal tubules and sustained antimicrobial release may reduce treatment failures associated with persistent infections.

These systems may be particularly beneficial in retreatment cases, regenerative endodontics, and infections involving resistant microorganisms such as *Enterococcus faecalis*.

However, before routine clinical adoption, issues related to cost, ease of application, and long-term safety must be addressed.

Conclusion

Targeted intracanal drug delivery represents a transformative advancement in endodontic therapeutics. Nanoparticle-based systems, liposomal carriers, hydrogels, and bioactive materials demonstrate enhanced penetration, sustained antimicrobial release, and improved biofilm disruption. Although promising, further translational research and well-designed clinical trials are essential before routine clinical adoption.

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