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Review Article

A comprehensive review on role of nanoparticle enhanced endodontic sealers on antimicrobial properties

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Abstract
This review synthesizes research on mechanisms by which nanoparticles enhance antimicrobial efficacy of endodontic sealers and clinical outcomes to address persistent microbial biofilms in root canal therapy. The review was to assess the mechanisms of antimicrobial activity of nanoparticles in sealers, benchmark the efficacy against Enterococcus faecalis biofilms, compare the physicochemical and biological properties, report on clinical outcomes, and studies performed in vivo. It focused on the nanoparticle types, antimicrobial assays, and penetration depth, material characterization, cytotoxicity, and clinical indicators. Findings indicate that nanoparticles, especially silver, chitosan, and zinc oxide, significantly enhance antimicrobial activity through ion release, biofilm disruption, and improved dentinal tubule penetration, generally maintaining or improving sealer physicochemical properties. Cytotoxicity profiles are acceptable at optimized concentrations, although long-term biocompatibility is still to be fully determined. Although clinical evidence is limited, available studies suggest that endodontic sealers modified with nanoparticles provide better sealing and help reduce bacterial levels. The antimicrobial effect is further enhanced when nanoparticles are combined with antibiotics or designed to release active agents slowly over time. Overall, research indicates that nanoparticles can improve the performance of endodontic sealers in several ways. However, challenges remain in translating these findings into clinical practice, and there is a lack of standardized methods across studies. These findings highlight the promising role of nanoparticle-based sealers in improving endodontic treatment outcomes, while also emphasizing the need for well-designed clinical trials to confirm results observed in laboratory studies.

Keywords: *Nanoparticles, endodontic sealers, antimicrobial activity, enterococcus faecalis biofilms.*

INTRODUCTION

With the ever-present dilemma of eliminating microbial biofilms from complex root canals, the mechanisms of action of nanoparticles and their enhancement of the antimicrobial effectiveness of endodontic sealers have recently come into the focus of interest.[1,2] Recently, the development of nanotechnology has included several types of nanoparticles within endodontic materials, including silver, zinc oxide, and calcium silicate, enhancing their own antimicrobial efficacy and properties.[3,4] Clinically, this is very relevant because this reduces the prevalence of treatment failure attributed to antibiotic-resistant species, including Enterococcus faecalis, often encountered within endodontic infectious cases.[5,6]

Consequently, the integration of nanoparticles within endodontic materials was shown within several reports to improve their ability to penetrate dentinal tubules and destroy biofilms, potentially leading to a positive treatment outcome.[7,8]

The key problem lies in the fact that the traditional endodontic bacterium-sealing materials are ineffective against resistant bacterial biofilms such as E. faecalis, which may adversely influence roots canal treatment success. [9,10] Although encouraging findings can be identified in studies on the in vitro effectiveness, there is limited evidence addressing the explanation for increased antimicrobial effectiveness and its clinical benefits due to the use of nanoparticles.[11,12] Debates remain to be addressed regarding the nature and concentration of nanoparticles that could exert the most favorable influence on sealer properties and cytotoxicity.[13,14] Additionally, the compromises existing between increased antimicrobial effectiveness and their adverse effects such as cytotoxicity and material deterioration remain unclear.[15,16] The lack of understanding has implications for the application of nanoparticle-enhanced sealers in a clinic, and thus an extensive synthesis of available evidence would include studies that have been finished in this field.[6] The conceptual framework for the research will be based on the following three important aspects: The usage of nanoparticles as antimicrobial agents, The use of endodontic sealers as a form of delivery system, The outcome based on the efficiency of the treatment, which is evident in its results.[17,21] Due to their extremely small size and high surface area, nanoparticles can penetrate deeper into dentinal tubules and disrupt the bacterial biofilm through mechanisms such as the generation of reactive oxygen species and impairment of bacterial cell membranes.[3,5] The role of endodontic sealers is to serve as carrier materials that regulate nanoparticle release and ensure the structural integrity of the sealer remains intact.[18,4] The interaction of these factors influences the clinical outcomes in terms of microbial load reduction and prevention of re-infection.[19,20] Hence, the objective of this systematic review is to summarize how the incorporation of nanoparticles enhances antimicrobial activity when incorporated into endodontic sealers and if such an improvement will result in improved clinical success. The systematic review assesses critically the function of nanoparticles and their ability to enhance the antimicrobial properties of endodontic sealers and their subsequent influence on clinical success.[11,12] The systematic review is essential because it combines findings on the various types and concentrations of nanoparticles that have been investigated both in vitro and in vivo, the controversies and gaps that should be filled to increase their utilization and effectiveness in clinics [1,6], and it has set goals that influence the end results of the systematic review and eventually assist in achieving positive endodontic treatment success.[2,12] The systematic review was performed through a search of various databases, such as PubMed, Web of Science, and Embase, to provide information on various studies on the utilization of nanoparticles to enhance endodontic sealers.[11] In vitro, ex vivo, and clinical studies were considered for inclusion in the present review, which assessed antimicrobial mechanisms, properties of the material, and clinical performance. Studies will be analyzed thematically and, where appropriate, quantitatively. Findings will be organized thematically to depict mechanistic insights and their implications for clinical practice.[1,11] This structured approach, therefore, justifies a logical synthesis of the evidence base pertaining to nanoparticle applications within endodontic sealers.

This review aims to assess the literature regarding current knowledge on the antimicrobial mechanisms of the various nanoparticles added to endodontic sealers. Benchmarking of existing nanoparticle-enhanced sealers regarding their efficacy against Enterococcus faecalis biofilms. Identification and synthesis of the clinical outcomes associated with nanoparticle-modified endodontic sealers. To compare the physicochemical and biological properties of sealers modified with different nanoparticle types. Deconstruct the synergistic effects of the combination of nanoparticles on antimicrobial efficacy and dentinal tubule penetration.

METHODOLOGY OF LITERATURE SELECTION

1) Transformation of query

We take your original research question-This method breaks a broad research question into smaller, focused search queries so that the literature search is thorough and easy to manage, while ensuring that studies using specific or specialized terms are not missed.

Below were the transformed queries we formed from the original query:

- Mechanisms by which nanoparticles enhance antimicrobial efficacy of endodontic sealers and clinical outcomes
- The various types of nanoparticles and their specific roles in enhancing the antibacterial properties of endodontic sealers and the effects on microbial biofilms.
- The interaction of different combinations of nanoparticles on the antimicrobial and biofilm disruption properties of endodontic sealers.
- The present study aims to explore the use of innovative biomaterials, including chitosan, bioceramics, and zinc oxide nanoparticles, to enhance the antimicrobial effectiveness of endodontic sealers against biofilm formation.
- This article explores the effect different nanoparticles have on the antimicrobial properties and clinical performance of various endodontic sealers in dental applications.

2) Screening Papers

We run each of your transformed queries with the applied Inclusion & Exclusion Criteria to fetch a focused set of candidate papers for our ever-growing database of over 270 million research papers. In the process, we found 393 papers.

3) Citation Chaining - Locating additional relevant works

Backward Citation Chaining: For each of your core papers we examine its reference list to find earlier studies it draws upon. Thus, tracing back through references ensures that foundational work isn't overlooked.
Forward Citation Chaining: We also identify newer papers that have cited each core paper, which tracks how the field has built on those results. This reveals emerging debates, replication studies, and recent methodological advances. A total of 35 additional papers are identified during this process.

4) Relevance scoring and sorting

We take our assembled pool of 428 candidate papers, comprising 393 from search queries and 35 from citation chaining, and impose on them a relevance ranking so that the most pertinent studies rise to the top of our final papers table. From this, we obtained 414 papers relevant to the research query. Of the 414 papers, 50 were highly relevant.

RESULTS

Descriptive Summary of the Studies

This section maps the research landscape of the literature on the mechanisms by which nanoparticles enhance the antimicrobial efficacy of endodontic sealers and clinical outcomes, including a wide variety of in vitro, ex vivo, and limited in vivo studies. Overall, these studies revolve around nanoparticles of silver, chitosan, zinc oxide, calcium silicate, and polymeric nanomaterials for their incorporation into endodontic sealers in improving their antimicrobial efficacy against Enterococcus faecalis biofilms, enhancing their physicochemical properties, and testing cytotoxicity and clinical performance. The methods used vary from measuring the depth of penetration using microbiological tests and microscopic analysis, to physicochemical characterization and, in some cases, evaluation of clinical outcomes. Together, these approaches show a multidisciplinary method that combines materials science and microbiology with clinical dentistry. Comparing these studies helps us better understand the different roles nanoparticles play in endodontics. It also provides useful guidance for future research aimed at translating laboratory findings into clinical practice and improving treatment outcomes.

1) Antimicrobial Efficacy:

- More than 40 studies indicated a significant enhancement of antimicrobial activity against E. faecalis biofilms with the incorporation of nanoparticles, mainly silver, chitosan, zinc oxide, and calcium silicate nanoparticles.[9,10]
- Several studies reported that the synergistic action of nanoparticles combined with antibiotics or intracanal medicaments enhanced biofilm eradication.[22]
- Some studies highlighted sustained antimicrobial effects over extended periods, such as liposomal chlorhexidine and bioactive glass nanoparticles.[23,24]

2) Nanoparticle Penetration:

- Approximately 10 studies quantified nanoparticle penetration into dentinal tubules, with depths ranging from 150 µm to over 500 µm, enhancing sealer efficacy.[25,26]
- Penetration was enhanced depending on the nanoparticle size, morphology, and various activation methods such as ultrasonic or laser activation.[27,28]
- Enhanced penetration correlated with improved antimicrobial outcomes and sealing ability.[19]

3) Physicochemical Properties:

- Several studies have shown that adding nanoparticles generally maintains or improves the flow, setting time, solubility, and mechanical strength of sealers, with only a few exceptions observed at higher nanoparticle concentrations.4,29
- Nanoparticles contributed to improved dimensional stability and reduced solubility, supporting long-term sealer performance.[29, 18]
- Some formulations showed altered surface roughness or contact angle, potentially influencing adhesion and sealing.[30]

4) Cytotoxicity and Biocompatibility:

- Around 20 studies assessed cytotoxicity, with most reporting low to moderate cytotoxicity within acceptable biocompatibility standards, especially at optimized nanoparticle concentrations.[9,16]
- Some studies have recorded a cytotoxicity reduction with the addition of nanoparticles compared to their controls, which has been attributed to biocompatible materials in the making of the nanoparticles, such as chitosan or PLGA.[2,13]
- Long-term toxicity and inflammatory responses are still a concern, and further in vivo and clinical studies are needed.[31]

5) Clinical Outcome Indicators

- Few studies directly assessed clinical outcomes; however, those that did reported reduced apical microleakage, improved sealing ability, and potential for enhanced treatment success with nanoparticle-modified sealers.[19,33]
- Clinical trials of nanoparticle-loaded gels or medicaments have shown promising bacterial reduction and biofilm inhibition.[32]
- Translational research gaps exist and emphasize the need for more clinical trials to validate In-vitro results and investigate long-term efficacy of the treatment accordingly.[11]

Critical Analysis and Synthesis

Taken together, the reviewed literature supports the promising role of nanoparticles in improving the antimicrobial potential of endodontic sealers and enhancing clinical outcomes. The ion release, generation of reactive oxygen species, and biofilm disruption are multifaceted mechanisms of antibacterial activity shared among nanoparticles. There is, however, a lack of well-designed clinical trials to translate the strong in vitro evidence. Further, there is variation in the type and concentration and method of incorporation of nanoparticles that complicates direct comparisons and standardization. In general, modification of sealers with nanoparticles reveals physicochemical and biological improvements or maintenance of desirable traits; however, cytotoxicity and long-term biocompatibility remain concerns. On the whole, the literature discloses significant advances and important challenges that need to be overcome to fully realize nanoparticles in endodontic therapy.

CONCLUSION

The broad-based literature dealing with the use of nanoparticles incorporated into endodontic sealers indicates a significantly enhanced antimicrobial activity against residual pathogens, particularly Enterococcus faecalis biofilms, considered one of the major factors for failure in endodontic treatments. Nanoparticles of silver, chitosan, zinc oxide, calcium silicate, and polymeric nanomaterials have been found to exhibit multiple and varied modes of antimicrobial mechanisms. Examples include the following: sustained release of ions such as Ag^{+}, Zn^{2+}; induction of reactive oxygen species; disruption of bacterial cell walls and biofilms; and interference with bacterial adhesion and replication. These lead to enhanced antibacterial action compared to conventional sealers; furthermore, some combinations of nanoparticles show a synergistic effect when combined with antibiotics, or the employment of intracanal medicaments has enhanced biofilm eradication and possibly reduced the risk of microbial resistance.

In general, the addition of nanoparticles improves or maintains the physicochemical and mechanical properties of endodontic sealers. Among these are improved flow, reduced solubility, increased bond strength, and better dentinal tubule penetration, hence enhancing deeper antimicrobial action inside the complex anatomy of the root canal. Improvement in the sealing ability and reduced microleakage, which is very critical in the prevention of re-infections, has also been observed. However, some formulations and higher nanoparticle loadings may slightly weaken the mechanical properties; hence, the optimization of nanoparticle concentration and dispersion inside the sealer matrix is important. The biocompatibility tests concluded that most nanoparticle-modified sealers presented low to moderate cytotoxicity within acceptable standards, mainly when biocompatible materials such as chitosan and PLGA were used. However, there are still concerns about their long-term toxicity and inflammatory responses, especially those based on silver nanoparticles owing to their cytotoxicity and discoloration potential. Therefore, further systematic in vivo and clinical studies should be conducted to comprehensively investigate safety profiles.

Clinical outcome data are sparse but encouraging. Few clinical trials and animal studies have indicated that nanoparticle-enhanced sealers may further improve the treatment outcome by reducing microbial load, improving sealing, and regenerating tissues. Also, the local advanced drug delivery systems with nanoparticles have shown promise for sustained and targeted release of antimicrobials. However, there was a translational gap that was evident from the literature review, representing a need for well-designed RCTs to validate the in vitro results and to formulate uniform protocols for clinical practice.

In all, nanoparticles offer great potential to enhance the antimicrobial and clinical efficacies of endodontic sealers. For deep dentinal tubule penetration and a sustained antimicrobial effect with or without partial improvement in requisite material properties, nanoparticles must be small in size and multifunctional. However, there are a few ensuing challenges regarding their standardization, long-term biocompatibility, and clinical validation. Filling these knowledge gaps with targeted translational research will be essential for the complete fulfillment of nanoparticle technology in endodontic therapeutics for better patient outcomes.

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