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Perspective

Antibacterial efficacy of nanocarrier-assisted antimicrobial photodynamic therapy (nano-apdt) against enterococcus faecalis in root canals: key findings and perspectives

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Background

Persistent *Enterococcus faecalis (E. faecalis)* infection remains a primary cause of endodontic treatment failure due to its strong biofilm-forming ability, nutrient tolerance, and penetration into dentinal tubules and root canal isthmuses.[1,2] Conventional irrigants such as sodium hypochlorite (NaOCl) remain the gold standard, exhibiting strong antibacterial and tissue-dissolving effects.[3] However, high NaOCl concentrations are cytotoxic, reduce dentin microhardness, and risk periapical tissue injury, underscoring the need for safer and more biocompatible alternatives.[4]

Antimicrobial photodynamic therapy (aPDT) has emerged as an adjunctive disinfection strategy that uses photosensitizers activated by light to produce reactive oxygen species (ROS) capable of killing microorganisms.[5] Yet, conventional aPDT suffers from limited tissue penetration, hydrophobic photosensitizer aggregation, and suboptimal ROS generation in deep biofilm layers. Incorporating nanocarriers—such as liposomes, polymeric nanoparticles, and metallic nanostructures—into PDT systems (Nano-aPDT) has shown potential to overcome these shortcomings by enhancing photosensitizer solubility, stability, and targeted delivery.[6]

Objectives and Methods

This systematic review and meta-analysis comprehensively evaluated the antibacterial efficacy of Nano-aPDT against *E. faecalis* biofilms, compared with conventional aPDT and NaOCl irrigation, and synthesized evidence-based insights for clinical translation.

Following PRISMA guidelines (PROSPERO: CRD42021214056), systematic searches across PubMed, Embase, Web of Science, Scopus, and Cochrane Library (through June 2025) identified nine eligible in vitro studies. Eleven datasets compared Nano-aPDT with NaOCl, and nine compared Nano-aPDT with conventional aPDT. Pooled risk ratios (RR) were calculated using the Mantel–Haenszel random-effects model.

Results

Meta-analysis demonstrated that Nano-aPDT achieved significantly higher antibacterial efficacy than conventional aPDT (pooled RR=1.41; 95% CI: 1.11–1.78; p=0.004), confirming that nanocarrier incorporation enhances photosensitizer activity and ROS generation. Compared with NaOCl, Nano-aPDT exhibited slightly lower antibacterial performance (RR = 0.85; 95% CI: 0.74–0.97; p = 0.01).

Subgroup analysis revealed that curcumin-based Nano-aPDT systems achieved the most consistent antimicrobial outcomes (RR = 0.53; 95% CI: 0.39–0.72; $p < 0.0001$), while methylene blue and indocyanine green subgroups showed variable results due to differences in nanocarrier composition and irradiation parameters.[7] Despite substantial heterogeneity (I^2=99%), sensitivity analyses confirmed that overall trends remained robust, validating Nano-aPDT's enhanced efficacy over conventional PDT and near-equivalence to NaOCl.

Mechanistic Insights

The improved antibacterial activity of Nano-aPDT arises from three key mechanisms:

Enhanced Photosensitizer Delivery and Stability–Nanocarriers prevent hydrophobic photosensitizer aggregation, prolong stability, and facilitate deep dentinal penetration.[6]

Microenvironmental Modulation–Oxygen-generating nanocomposites (e.g., Ce6/CaO_2/ZIF-8) alleviate hypoxia within canals, sustaining ROS production for effective bacterial eradication.[8] Physical and Magnetic Synergy–Activation methods such as ultrasound, SWEEPS, and magnetically guided nanoparticles improve drug diffusion and mechanical disruption of biofilms.[9,10] Collectively, these advancements transform PDT from a surface-level disinfection tool into a precision-targeted, multi-mechanistic antimicrobial strategy suitable for complex root canal systems.

Clinical relevance and potential

Although NaOCl retains superior immediate bactericidal activity, Nano-aPDT offers distinct advantages in biocompatibility, selective action, and preservation of dentin integrity. Notably, combining low-concentration NaOCl (1–2%) with Nano-aPDT may achieve comparable disinfection efficacy while reducing cytotoxicity by up to 80%.[11] This complementary approach leverages NaOCl's ability to degrade the biofilm matrix and Nano-aPDT's capacity for localized ROS-mediated bacterial killing.Beyond endodontic disinfection, Nano-aPDT shows translational potential in treating periodontal disease, peri-implantitis, oral precancerous lesions, and soft-tissue infections due to its controllable, non-invasive antimicrobial action.[12]

Limitations and future directions

Despite encouraging findings, several limitations persist. Considerable heterogeneity in nanocarrier types, photosensitizer concentrations, and irradiation parameters complicates cross-study comparison. Standardized Nano-aPDT protocols remain lacking, and most current evidence derives from in vitro models with limited clinical extrapolation.

Future research should emphasize

a. Standardization of Nano-aPDT parameters (wavelength, dose, carrier type).

b. Multicenter in vivo and clinical studies to verify efficacy and long-term safety.

c. Integration of multifunctional nanoplatforms combining antimicrobial, anti-inflammatory, and regenerative effects.

d. Exploration of synergistic protocols integrating Nano-aPDT with optimized NaOCl irrigation.

Conclusion

Nanocarrier-assisted antimicrobial photodynamic therapy represents a significant evolution in endodontic disinfection. Although slightly less potent than NaOCl, Nano-aPDT achieves superior penetration, precision targeting, and biocompatibility. Continued optimization and clinical validation could establish Nano-aPDT as a cornerstone of precision endodontic therapy, offering a safer, more effective alternative to conventional chemical irrigation.

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Conflict of interest

None.

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