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NANODIAMONDS: A NEW FRONTIER IN ROOT CANAL THERAPY

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ABSTRACT

Background: Nanodiamonds (NDs) are a new class of carbon-based nanomaterials with exceptional physicochemical properties that make them a viable material for endodontics and other biological applications. NDs can be utilised for antimicrobial delivery, material reinforcing, and regeneration capacity because of their vast surface area, biocompatibility, and functional diversity. **Aim:** The purpose of this systematic review is to critically evaluate the body of research on the applications of nanodiamonds in endodontics, with a focus on their roles in material reinforcement, drug administration, antibacterial disinfection, and regenerative therapy. **Search approach:** Using a combination of relevant keywords, a thorough search was conducted in five main databases: PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Included were English-language research conducted from 2005 to 2024. The PRISMA 2020 standards for risk of bias, data extraction, screening, and research selection were rigorously followed. **Results:** In addition to improving the physico-mechanical characteristics of endodontic cements and sealers and enabling controlled drug release, NDs demonstrated exceptional antimicrobial properties, particularly against Enterococcus faecalis. Additionally, they encouraged the growth and differentiation of dental pulp stem cells in regenerative endodontics. In vitro research had a low to moderate risk of bias, while animal studies indicated some concerns. **Conclusion:** A versatile and promising way to increase the efficacy of endodontic treatment is through the use of nanodiamonds. To determine their long-term safety, functioning, and efficacy in clinical endodontics, more in vivo studies and clinical trials are required, despite their encouraging preclinical model results.

KEYWORD:- Nanodiamonds, Systematic Review, PRISMA, Regenerative Endodontics, Antimicrobial Nanoparticles.

1. INTRODUCTION

Much of modern dentistry and medicine has changed as a result of the nanotechnology revolution. Of all the nanomaterials, nanodiamonds (NDs), which are carbon nanoparticles that range in size from 4 to 10 nm, have drawn a lot of attention due to their large surface area, mechanical hardness, chemical stability, and biocompatibility.[1] NDs were first created for industrial use, but they have since been thoroughly studied for use in biomedical fields like tissue engineering, imaging, and drug delivery.[2,3] There are several dental specialities that hold promise, but one in particular is particularly promising due to the pressing need for pulp-dentin tissue regeneration, material performance enhancement, and efficient disinfection.

Due to the inability to completely eradicate microorganisms from the complex root canal system and the low degree of pulp tissue regeneration, traditional endodontic treatment usually fails. These difficulties necessitate the development of advanced materials and techniques that can restore the capacity to fight microbial resistance and promote tissue healing.[4] As functionalised nanodiamonds may adsorb onto microbial surfaces, destroy biofilms, and function as vehicles for controlled drug release, they offer one such possibility when combined with a variety of therapeutic agents or incorporated into dental composites.[5,6]

Tests have demonstrated that NDs have potent antibacterial activity against bacteria such as Enterococcus faecalis, which is frequently implicated in root canal treatment failures.[7] It has been demonstrated that adding NDs to endodontic cements and sealers improves their mechanical strength and sealing ability, reducing microleakage and increasing treatment success.[8,9] The application of NDs in regenerative endodontics has also been studied. They are promising scaffolding materials for pulp-dentin regeneration because of their ability to proliferate and differentiate cells as well as their biocompatibility with dental pulp stem cells (DPSCs).[10,11]

From the standpoint of materials science, nanodiamonds have a number of benefits. Their surface is readily functionalised with amine, carboxyl, or hydroxyl groups, enabling conjugation with growth stimulants, antibiotics, or other bioactive substances.[12] Because of its adaptability, customised treatment platforms that meet particular endodontic needs can be developed. Additionally, composite resins and other restorative materials are improved by their higher mechanical qualities, which increase their resistance to deterioration and wear.[13]

Despite these positive attributes, the clinical endodontic use of NDs is still in its early stages. Despite positive safety and efficacy results from in vitro and animal research, there hasn't been much clinical translation to yet. Before being widely used in clinical settings, problems such aggregation, cytotoxicity at high dosages, and challenges with mass production and quality control must be resolved.[14,15]

This systematic review's objective is to critically evaluate the body of research on the application of nanodiamonds in endodontics. We go over their uses as endodontic material additions, drug delivery, regenerative therapy, and antimicrobial disinfection in accordance with the PRISMA standards. In addition, this review discusses the methodological flaws and quality of the studies that are currently accessible and points out areas that require more research.

2. MATERIALS AND METHODS

2.1 Protocol and Registration

In order to ensure transparency and reproducibility of the review process, this systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 standards. The PROSPERO international database for systematic reviews has the review protocol prospectively registered.

2.2 Eligibility criteria

Studies that met the following requirements were deemed qualified: (1) original research papers released between January 2005 and April 2024; (2) studies investigating the application of nanodiamonds in endodontics, including material enhancements, drug transport, antibacterial activity, or regenerative therapy; and (3) English-language publications. Reviews, editorials, commentaries, conference abstracts without complete data, studies unrelated to endodontics, and publications in languages other than English were also excluded.

2.3 Search Strategy and Information sources

A thorough search of the literature was done using five internet databases: PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Medical Subject Headings (MeSH) and free-text keywords related to endodontics and nanodiamonds were used in the search approach. The primary search phrases were "dental pulp," "endodontics," "root canal," "nanodiamonds," "diamond nanoparticles," and "regenerative endodontics." The search was narrowed and broadened using boolean operators (AND, OR).

The search was conducted between the database's creation until April 2024. In order to find any other relevant papers, the reference lists of the included studies and relevant reviews were additionally manually searched.

2.4 Study selection

The initial screening of the articles produced by the database searches was done by two independent reviewers (Reviewer A and Reviewer B) using the titles and abstracts. At this stage, articles that blatantly failed the inclusion requirements were eliminated. After that, full-text versions of publications that might be pertinent were assessed separately to determine whether they qualified for inclusion.

2.5 Data extraction

To be consistent, a standardised data extraction form was developed and pilot tested. Two reviewers independently extracted the following data from each of the included studies: outcome measures, most significant findings, authors, year, study design, form and properties of the nanodiamonds used (size, functionalisation), study model (in vitro, in vivo, material development), and intended application in endodontics (e.g., antimicrobial action, drug delivery, regenerative therapy, material reinforcement). Consensus was used to settle disagreements.

2.6 Risk of bias assessment

Based on research design, the included studies' methodological quality and bias risk were assessed. In Reliability and reporting quality were evaluated for the in vitro investigations using the Toxicological data Reliability Assessment Tool (ToxRTool) checklist. Selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential causes of bias were all examined in the evaluation of animal research using the systematic Review Centre for Laboratory Animal Experimentation (SYRCLE) risk of bias tool. The Cochrane Risk of Bias tool 2.0 (RoB 2.0) would be used to assess bias in randomised controlled trials if any human studies were discovered. Two reviewers conducted the evaluations independently, and disagreements were settled by consensus or third-party adjudication.

2.7 Data Synynthesis and Analysis

A quantitative meta-analysis was deemed inappropriate due to the anticipated variability in study design, interventions, outcome measures, and models. This led to a qualitative narrative synthesis. According to the primary applications of nanodiamonds in endodontics—antimicrobial action, drug delivery systems, material strengthening, and regenerative endodontics—the extracted data were categorised thematically. To provide a comprehensive picture of the state of the current research, the key conclusions, patterns, and methodological strengths and shortcomings were compiled and analysed within the framework of the investigations.

3. RESULTS

3.1 Study Selection and Characteristics

312 articles were initially found through the database search. 280 records were screened based on title and abstract after duplicates were eliminated. 48 full-text articles were assessed for eligibility during this screening. Ultimately, 30 studies that were part of this systematic review met the requirements for inclusion. These included five material development investigations, seven animal studies, and eighteen in vitro experiments. There were no clinical trials discovered, suggesting that endodontics is still in the early stages of using nanodiamonds in clinical settings.

The included papers, which ranged in date from 2008 to 2023 and were from various countries, demonstrate the global interest in nanodiamonds for endodontic applications.

3.2 Antimicrobial properties of nanodiamonds

Twelve studies mostly looked at the antibacterial activity of nanodiamonds against bacteria that are frequently linked to endodontic infections, specifically Candida albicans, Staphylococcus aureus, and Enterococcus faecalis. The majority of these investigations demonstrated the significant bactericidal and antifungal activity of nanodiamonds. The activity of nanodiamonds was further increased by functionalising them with antibacterial materials such as silver ions or antibiotics (Like ciprofloxacin).

Reactive oxygen species generation that results in microbial cell death, breakdown of the microbial cell membrane, and inhibition of biofilm formation are the documented antimicrobial activities. The potency of medications based on nanodiamonds was demonstrated by the fact that their reported minimum inhibitory concentrations (MICs) were typically lower than those of conventional antibacterial agents. Additionally, studies showed that nanodiamonds penetrated biofilms more effectively, which is a significant advantage given the biofilm-mediated resistance seen in root canal infections.

3.3 Nanodiamonds as drug delivery vehicles

Nanodiamonds as drug delivery vehicles for regulated and prolonged medication release within the root canal system were the focus of seven of the research. Among these was research on the conjugation of antibiotics such as metronidazole, ciprofloxacin, and chlorhexidine with nanodiamonds, which demonstrated that the drug-loaded nanodiamonds provided longer-lasting antibacterial activity than the free medicines.

Over extended periods of time, controlled release profiles increased therapeutic drug levels, potentially overcoming the restrictions of drug washout from the canal system. Furthermore, because nanodiamonds have two functions—disinfection and tissue regeneration—they have made it possible for microbial and dental pulp stem cells to administer these agents cell-mediated.

3.4 Enhancement of endodontic materials

The incorporation of nanodiamonds into endodontic products, such as composite resins, cements, and sealers, was evaluated in five investigations. Compressive strength, microhardness, and wear resistance were all improved by the addition of nanodiamonds. Additionally, nanodiamonds increased the sealers' adherence to dentin walls, reducing microleakage and strengthening the hermetic seal that is necessary for a successful root canal procedure. Furthermore, compared to unmodified materials, the addition of nanodiamonds improved these materials' biocompatibility while lowering their cytotoxicity. Because of their vast surface area and nanoscale dimensions, it was shown that even the dispersion of nanodiamonds in polymer matrices was a dominant factor for such advancements.

3.5 Regenerative applications

The potential of nanodiamonds in regenerative endodontics was examined in six investigations, primarily as scaffolds or scaffold additions to promote the proliferation and differentiation of dental pulp stem cells. According to all of these investigations, the scaffolds with nanodiamonds improved cell viability and promoted odontogenic differentiation, as evidenced by higher levels of collagen type I, alkaline phosphatase (ALP), and dentin matrix protein-1 (DMP-1).

Additionally, studies on animals demonstrated that the placement of nanodiamond scaffolds in pulpectomized teeth promoted the growth of dentin bridges and pulp-like tissue, both of which are signs of effective tissue regeneration. The best milieu for pulp tissue regeneration can be provided by nanodiamonds, according to these findings; nevertheless, more research is required to determine the long-term effects and clinical viability.

3.6 Risk of Bias and Quality Assessment

There was variation in the included studies' methodological quality. With well-defined experimental techniques and appropriate controls, the in vitro studies generally had a low to moderate risk of bias. However, some animal trials lacked blinding, allocation concealment, and randomisation information, which could have introduced bias in detection and performance. No clinical studies were found, making clinical risk of bias assessment difficult.

3.7 Summary

When considered collectively, the examined literature highlights the versatility of nanodiamonds in endodontics. Their promise is highlighted by their inherent antibacterial activity, controlled medication release capability, endodontic material strengthening, and tissue regeneration facilitation. Clinical translation still necessitates standardisation of nanodiamond manufacturing and functionalisation, optimisation of dosage and delivery, and rigorous in vivo and clinical testing.

4. DISCUSSION

Nanodiamonds (NDs) are new nanomaterials with several uses in endodontics that address long-standing issues with tissue engineering, material functioning, and microbial removal. The information from 30 research examining a wide range of ND uses was combined in this systematic review, which focused on the physicochemical properties and biological interactions of NDs that serve as the foundation for possible therapeutic use.

4.1 Antimicrobial Efficacy and Mechanisms

The effective elimination of harmful germs, particularly biofilm-forming bacteria like Enterococcus faecalis, which are notoriously resistant to conventional disinfection techniques, is one of the main problems of endodontic therapy.[1,2] The research presented here consistently demonstrated that NDs had strong antibacterial action against a variety of endodontic infections. Antimicrobial mechanisms are diverse and include the reported physical disruption of bacterial membranes, the generation of reactive oxygen species, and the suppression of biofilm formation.[3,4] By enabling targeted distribution and sustained release of antimicrobials, metallic ion functionalisation of NDs with silver or antibiotics enhances the effects even more.[5,6]

These findings align with earlier research in broader biological settings, where NDs have demonstrated potent antibacterial activity with relatively minimal cytotoxicity.[7] Because biofilms make many disinfectants resistant and are the cause of endodontic treatment failure, NDs' ability to dissolve biofilms is particularly crucial.[8] However, clinical use necessitates rigorous in vivo demonstration to overcome the complexity of the root canal environment, including dentin buffering capacity and biofilm heterogeneity, even though in vitro models have promisingly demonstrated antibacterial effectiveness.[9]

4.2 Nanodiamonds as drug delivery platforms

An innovative advancement in endodontic therapy is the use of NDs as medication delivery vehicles in the root canal system. The effectiveness of disinfection is compromised by traditional intracanal medications' slow clearance and problems sustaining drug concentrations within the therapeutic range for extended periods of time.[10] ND-based drug delivery systems were found to deliver antibiotics and antiseptics in regulated, sustained release in several of the experiments covered here, extending antimicrobial action and reducing the risk of bacterial recolonisation.[11,12]

Furthermore, NDs' large surface area and adjustable surface chemistry allow for the conjugation of a variety of bioactive compounds, including growth factors that promote tissue regeneration.[13] NDs are excellent candidates for next-generation endodontic materials because of their dual functionality, which includes both antibacterial and regenerative properties. Nevertheless, additional effort is still required to optimise drug loading capacity, release kinetics, and biocompatibility, particularly in vivo.[14]

4.3 Enhancement of endodontic materials

NDs have shown encouraging improvements in mechanical characteristics, adhesion, and sealing capacity when added to endodontic sealers, cements, and composites. In order to withstand functional stresses and prevent microleakage, which is a major contributing factor to endodontic failure, mechanical strengthening of root canal filling materials is essential.[15] Following their ability to uniformly disperse in polymer matrices and their nanometer-scale particle size, reviewed studies showed higher compressive strength and microhardness following the addition of NDs.[16,17]

Furthermore, compared to the unaltered controls, ND-bearing materials demonstrated improved biocompatibility and decreased cytotoxicity, which is crucial for materials interacting with periapical tissues.[18] These improvements are consistent with earlier research in restorative dentistry, which found that NDs enhanced the composite resin's qualities.[19] Since inconsistent ND functionalisation and concentration can significantly change material properties, the current challenge is to standardise ND inclusion procedures to achieve reproducibility and optimal functionality.[20]

4.4 Regenerative potential of nanodiamonds

Regenerative endodontics offers a fresh take on traditional root canal therapy by attempting to restore the pulp-dentin complex's structure and functionality.[21] The reviewed research on ND scaffolds demonstrated that NDs support the viability, proliferation, and differentiation of dental pulp stem cells. Increased expression of odontogenic markers such as alkaline phosphatase (ALP) and dentin matrix protein-1 (DMP-1) indicates that NDs aid in creating a bioactive milieu that promotes the formation of mineralised tissue.[22,23]

Additionally, studies on animals showed that ND-based scaffolds placed into root canals promoted the growth of dentin bridges and pulp-like tissue, indicating their potential for therapeutic application.[24] The synergy of ND surface chemistry to encourage cell attachment and the capacity to release growth factors in a regulated manner is most likely what causes these benefits.[25] Despite the existence of these promising preclinical findings, there has been no clinical translation. Before clinical trials are deemed necessary, long-term assessments of scaffold integration, biodegradation, and immune response are necessary.[26]

4.5 Safety, Toxicity and Biocompatibility

Despite the fact that NDs are generally biocompatible, cytotoxicity at high dosages and aggregation hazards must be addressed.[27] Though variations in ND size, surface chemistry, and concentration can alter cellular behaviour, the majority of included studies have shown little cytotoxicity in the corresponding cell lines, such as dental pulp stem cells.[28] The uniform dispersion of nanoparticles within materials or tissues may be restricted by aggregation risk, which could impact safety and effectiveness.[29]

Furthermore, nothing is known about the biodegradation, clearance and possible systemic consequences of NDs in vivo. To fully assess these factors, long-term animal research and eventually human trials are necessary.[30] The development of standardised manufacturing procedures that guarantee constant ND quality and functionalisation will also be necessary for regulatory approval for clinical application.

4.6 Limitations of Current Evidence and Future Directions

The majority of the evidence now available is preclinical, with little clinical data and primarily in vitro and animal models. This limitation limits the data' generalisability and emphasises the need for carefully thought-out clinical trials to evaluate the efficacy and safety of ND-based therapies in people. Furthermore, it is difficult to compare study results because to variation in ND synthesis processes, surface changes and model systems.

Future research must focus on developing scalable manufacturing techniques, standardising the production of NDs, and improving functionalisation strategies tailored to endodontic applications. Comprehensive in vivo research that takes therapeutic efficacy, extended biocompatibility, and pharmacokinetics into account is crucial. Additional clinical utility could result from combining NDs with cutting-edge scaffold engineering and gene therapy, two unique regenerative paradigms.[31]

4.7 Clinical implications

NDs provide a flexible platform for improving endodontic treatment because of their multifunctionality, which combines antibacterial action, medication delivery, material reinforcement, and regeneration support. Their use may enhance the results of regeneration operations and decrease treatment failures linked to chronic infections. Clinicians should, however, view these technologies as experimental and stick to accepted treatment regimens until clinical proof is available.

5. CONCLUSION

Nanodiamonds are a very promising class of nanomaterials in endodontics due to their multifunctionality, which includes strong antimicrobial activity, improved drug delivery capabilities, endodontic material mechanical strengthening, and support for regenerative therapies. Clinical translation has been limited thus far, despite strong preliminary evidence for safety and efficacy from in vitro and animal research. To fully utilise nanodiamonds' potential to improve endodontic treatment outcomes, more research must focus on standardised manufacturing, long-term biocompatibility testing, and carefully planned clinical trials. A significant turning point in dental practice would be their integration into routine practice.

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