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USE OF SILVER NANOPARTICLES IN PERIODONTAL TREATMENT

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Abstract

Purpose: *The present review is designed to investigate the efficacy of AgNPs as an adjunct treatment of antimicrobial therapy for periodontitis.*
Methodology: *A systematic review was done on electronic databases, including Google Scholar, Science Direct, and PubMed. Articles retrieved included in vitro, clinical, and cross-sectional studies with relevance. This further narrowed down the selection process by applying the PRISMA methodology.*
Results: *This study reveals that AgNPs possess robust antibacterial activity against periodontal pathogens. At the correct concentrations, they can halt bacterial multiplication and are equally effective as standard drugs like tetracycline. In vivo studies prove that AgNPs augmented traditional treatments for improvement in periodontal health.*
Conclusion: *Silver nanoparticles possess potential adjunctive therapies for periodontitis as they display an antimicrobial effect. Their long-term safety and efficacy have yet to be well established in many studies, however.*

INTRODUCTION

One of the main causes of all tooth loss diseases worldwide, periodontal disease is an idiopathic, chronic inflammatory condition that inflames the gingiva, the periodontal ligament, and the alveolar bone, which support teeth. It is also associated with numerous systemic diseases, such as diabetes mellitus, cardiovascular disorders, and respiratory infections.

Bacterial biofilms trigger an immune reaction that culminates in tissue destruction as the disease progresses in this pattern (Scannapieco & Gershovich, 2020). The initiated inflammatory response in the host by microbial dysbiosis results in the destruction of the periodontal tissues as well as an accelerated disease progression. The untreated disease will result in severe oral health issues such as mobility of the teeth, bone resorption, and loss of the teeth. The pathogenesis of periodontal disease is multifactorial; therefore, the treatment should comprise strategies that address both microbial and host factors (Fernandes et al., 2021).

Traditional periodontal diseases are treated as scaling and root planing: This tries to eliminate the biofilm and calculus in an attempt to decrease further the bacterial loads and inflammation. Although SRP is considered the "gold standard for non-surgical periodontal therapy", efficacy of SRP is usually minimal in deep pockets of periodontal and anatomy-based areas because biofilm could not be adequately eliminated in some regions. Instead, various adjunctive therapies have been used in combination with antimicrobial agents, including antibiotics and antiseptics. While highly effective, the use of antimicrobial therapy over long periods of time is complicated by a host of problems from drug resistance and compromise of the oral microbiome to adverse side effects (Qi et al., 2019). This is compounded by the issue of patient compliance with antimicrobial regimens and the potential for systemic effects, making routine use of antibiotics in periodontal management an even more formidable task. This has driven a quest for alternative therapeutic agents that can offer enough antimicrobial activity with minimal side effects (Mitra, Kang, and Neoh, 2021).

Such challenges have prompted researchers to adopt alternative antimicrobial methods, among which nanotechnology-based applications stand out. In terms of those alternative treatments, silver nanoparticles deserve the greatest attention as the most promising nanosized particles; high SA/Vol; being in size of 1-100 nm that allow reasonable interaction with the bacterial cells. Their mechanisms include the following:

- Disrupting bacterial cell membranes and altering cell permeability.
- It generates reactive oxygen species, which causes the death of bacterial cells.
- Inhibits bacterial DNA replication and enzyme activity, thus preventing bacterial growth (Mitra, Kang, & Neoh, 2021).

Nano-silver particles have already been utilized in several areas of dentistry, proving effective against oral microbe infections. Among them:

- **Dental Implants:** By coating the surfaces of implants with AgNPs, they reduce bacterial adhesion and biofilm formation thus further reducing any peri-implant infection risk.

- **Endodontics:** Silver Nanoparticles are used in root canal irrigants and sealers to enhance disinfection and prevent reinfection.

- **Periodontal Therapy:** AgNPs have been studied as an adjunct to SRP, applied in gels, mouth rinses, and dressings for the purpose of improving antimicrobial activity (Fernandes et al., 2021).

Various studies have revealed that AgNPs inhibit periodontitis-causing pathogens such as P. gingivalis, A. actinomycetemcomitans, and F. nucleatum. Additionally, their anti-inflammatory effects enhance wound healing and tissue regeneration. Thus, these nanoparticles have been considered an effective adjunct to periodontal therapy (Wong et al., 2023). AgNPs had been demonstrated also to enhance REPs efficacy within regenerative endodontic treatments through modulation of inflammatory cytokines and induction of tissue repair-an activity which contributed much to preservation of periodontal health. Some recent research works deal with immunomodulatory AgNPs-activity which exhibits suppression of such pro-inflammatory products as IL-6 and TNF-α production, which finally protects tissue damage due to inflammation caused in the periodontium (Nwankwo et al., 2023).

However, despite these potential benefits, reservations regarding the cytotoxicity of AgNPs and their long-term biocompatibility persist. It has been indicated that high concentrations of AgNPs can trigger oxidative stress, apoptosis, and DNA fragmentation in human cells. The prolonged exposure to AgNPs has also been associated with systemic bioaccumulation, raising a long-term safety concern. Optimization of concentration, size, and application methods are important for maximum therapeutic benefits and minimal adverse effects. Furthermore, interaction of AgNPs with host tissues, their resistance potential, and oral microbiome disruption also require more study. Future studies shall be conducted and standardized clinical practice guidelines shall establish the safe effective use of AgNPs so that their employment remains both effectual and bio-compatible (Moraes et al., 2021).

Research Question:

How effective are Silver Nano Particles (AgNPs) as antibiotic therapies towards periodontitis?

This study aims to explore the current evidence on AgNPs in periodontal treatment, including their efficacy, safety, and potential for clinical application. It will evaluate their antimicrobial properties, mechanisms of action, and integration into existing periodontal therapies to determine the viability of AgNPs as a sustainable and effective alternative in periodontal disease management.

2. Literature Review

2.1 Periodontal Disease and Its Treatment

It is actually an inflammatory condition where supporting structures of the tooth suffer chronic and multifactorial inflammation. These include the alveolar bone, cementum, gingiva and periodontal ligament. The disease is essentially considered one wherein microbial biofilms are developed, which leads to the inflammatory immune response with tissue destruction, as proposed by Hajishengallis in 2022. Untreated, periodontal disease progresses from gingivitis to severe periodontitis, potentially leading to loss of teeth and systemic conditions like cardiovascular disease, diabetes, and pregnancy complications. It's therefore crucial that the disease process be advanced based on the relationship between bacterial pathogens and host immune responses with a call to early intervention and holistic treatment approaches (Prapaipittayakhun et al., 2023).

Classification of periodontal disease has experienced massive change over time. The new EFP and AAP classification places the periodontal diseases under three broad headings, which encompass gingival diseases, periodontitis, and other conditions influencing the periodontium (Hernándes-Venegas et al., 2023). Periodontitis is further subclassified based on severity, extension, and the rate of progression, and calls for early detection and individualized treatment approaches. With the new classification and staging, and grading system introduced, the disease complexity could now be evaluated with risk factors so that the patient's treatment will be specifically guided (Prapaipittayakhun et al., 2023).

The more traditional approaches used in periodontal diseases mainly include the technique of mechanical debridement including scaling and root planing which removes plaque and calculus on both the surfaces and below the gums. Besides this, adjunctive therapies consist of systemic and locally delivered antibiotics, antiseptics, host-modulatory agents, and surgical interventions in advanced cases (Curtis et al., 2020). While SRP is considered the gold standard, anatomical challenges, persistence of bacterial biofilms, and patient-specific factors like an immune response and compliance with oral hygiene reduce its effectiveness. Though antibiotics are useful in specific situations, they have flaws such as antimicrobial resistance, dysbiosis of the oral microbiome, and side effects (Hajishengallis, 2022).

2.2 Properties of Silver Nanoparticles

Due to the peculiar physicochemical and biological properties of AgNPs, silver nanoparticles in dentistry have been greatly recommended. Having a size that ranges between 1 and 100 nm, they provide an extremely high SA/Vol and are, therefore, in higher contact with bacterial cells, thus more significantly conferring them with the antimicrobial property (Ahmed et al., 2020). AgNPs have been extensively researched to show anti-amoebic properties, inflammation response regulation, and tissue regeneration enhancement and have increasingly been applied as an adjunct in periodontal treatment (Hernándes-Venegas et al., 2023).

Some of the significant properties of AgNPs which result in outstanding efficiency in treating diseases against periodontal infection are:

- **Antibacterial Activity:** AgNPs have broad-spectrum antibacterial properties that work against important periodontal pathogens like Porp as well as Gram-positive and Gram-negative bacteria. AgNPs' primary mode of antimicrobial action involves breaking down bacterial cell membranes, producing reactive oxygen species, and interfering with bacterial DNA replication, all of which ultimately result in bacterial death. (Mitra, Kang, & Neoh, 2021). Ag nanoparticles could also prevent quorum sensing, an adaptive communication amongst bacteria for biofilm formation, thereby restricting their proliferation (Hernándes-Venegas et al., 2023).

- **Anti-Inflammatory Effects:** The AgNPs control host immune reactions through the suppression of pro-inflammatory mediators such as tumor necrosis factor-alpha, IL-6 and IL-8. The AgNPs provide a mode to facilitate tissue repair and healing pathways that are the backbone of periodontal therapy (Hernándes-Venegas et al., 2023). This property is particularly advantageous for chronic inflammatory conditions, wherein sustained activation of the immune response leads to tissue destruction and bone loss (Curtis et al., 2020).

- **Biofilm Disruption:** The greatest treat in the treatment procedure of periodontal therapy is biofilms that serve as the 'safe' environment of pathogenic bacteria to survive. AgNPs have been shown to be able to penetrate biofilms very effectively and disrupt their structure by preventing bacterial adhesion to tooth surfaces and periodontal tissues (Ahmed et al., 2022). That's why AgNPs are one of the major tools in fighting the recolonization and consequent re-infection of a treated periodontal pocket.

- **Osteoinductive Potential:** AgNPs have recently been reported to possess osteoinductive potential and their use results in the improvement of bone regeneration due to osteoblast differentiation and mineralization. This property is very relevant to periodontal regeneration therapies and implantology. AgNPs are also explored in the role they play in augmenting the bioactivity of grafting materials and scaffolds utilized in periodontal and implant regenerative procedures (Curtis et al., 2020).

Despite all these bright prospects, several concerns remain with regard to the cytotoxicity and long-term biocompatibility of AgNPs. At high concentration, AgNPs can provoke oxidative stress and apoptosis in human cells, therefore, further investigation is needed for safe use in clinical fields. The behavior of AgNPs with host tissues and their systemic implications along with the long-term stability should be addressed before their common clinical usage (Brun et al., 2020).

2.3 AgNPs in Periodontal Treatment

AgNPs, as an adjunct to periodontal therapy, have been significantly explored. AgNPs incorporation into dental materials and various other therapeutic modalities has been researched in many studies. The principal uses of AgNPs in periodontal therapy are summarized as follows:

- **AgNP-Loaded Mouthwashes and Gels:** AgNP-loaded mouthwashes and gels have been studied for the reduction of periodontal pocket depth, formation of plaque, and inflammation of gingiva. These formulations are non-invasive; thus AgNPs do reach the periodontal tissues, which improves the antimicrobial action while controlling the systemic exposure. The sustained release of AgNPs in these preparations ensures extended antibacterial effects, which limits the need for frequent applications (Fernandes et al., 2021).

- **AgNP-Coated Dental Implants and Membranes:** This has been one of the significant problems in implantology, that is the risk of developing peri-implantitis-an inflammatory process leading to the failure of an implant. Coating dental implants with AgNP stops the formation of bacteria colonization which restricts infection, and that will be very useful for improvement in the success of placing an implant (Bharkhavy et al., 2022). Authors claimed that the GBR membrane coated with AgNPs has supported healing in surgical sites, avoiding microbial contamination.

- **AgNP-Based Root Canal Sealers:** Sealers with AgNPs have better antimicrobial activity against pathogenic microorganisms in the root canal, with a lesser tendency to cause secondary infections and improved long-term follow-up results (Espinosa-Cristóbal et al., 2019). These sealers can also enhance obturation material sealability by stopping bacterial penetration through the obturated canal wall.

- **Periodontal Dressings and Regenerative Scaffolds:** AgNPs have been added to the bioactive scaffold and wound dressings to encourage periodontal tissue regeneration. Such materials provide cells with scaffolding for their proliferation and differentiation, thus enabling healing in the periodontal defects (Oana Craciunescu et al., 2018).

3. Methodology

A systematic approach has been adopted for the review of silver nanoparticle utilization in periodontal therapy. The study considers that it does very well in all relevant search strategies, data selection, and quality assessment criteria in order to contain studies of high quality.

3.1 Research Design
This systematic literature review was aimed to critically evaluate and synthesize any existing scholarly literature on the efficiency and safety profiles of AgNPs in the therapy of the periodontals. Therefore, this study resorts to a qualitative research design towards reviewing primary studies that have appraised the possible antimicrobial activity, anti-inflammation activities, and ability to regenerate effects of AgNPs in periodontics.

3.2 Literature Search Strategy
Peer-reviewed studies are accessed through multi-database search with Google Scholar, ScienceDirect, and PubMed, using keyword combined with the Boolean operators. It was achieved with a wide scope of key research articles: Key search terms:
- Silver nanoparticles OR AgNPs or nanosilver.
- Periodontal treatment or periodontitis or gum disease.
- Antimicrobial efficacy or biofilm disruption or inflammation reduction
- "Tissue regeneration" OR "periodontal healing" OR "dental applications"

The systematic approach adopted was by means of the PRISMA framework towards ensuring transparency in the study selection processes and reproducibility. This accordingly involved the usage of PRISMA checklist and flow diagram in tracking the identification, screening, eligibility, and inclusion of studies.

3.3 Inclusion and Exclusion Criteria
To maintain the calibre and relevance of the research included in this review, specific inclusion and exclusion criteria were applied.

Inclusion Criteria:
- In vitro or primary clinical research examining the application of AgNPs in the management of periodontal disease.
- Research released in the past ten years to keep the review current with new findings.
- Full-text articles available in English to ensure clarity and comprehensive analysis.
- Studies assessing AgNPs for antimicrobial, anti-inflammatory, or regenerative activity.
- Researches adopting standardized techniques, including RCTs, cohort studies, and lab-based experiments.

Exclusion Criteria:
- Review articles, meta-analyses, and opinion pieces were excluded to focus on original experimental and clinical data.
- Studies conducted exclusively on animal models or in vivo studies without direct application to human periodontal treatment.
- Conference abstracts, editorials, and short communications were excluded due to the lack of comprehensive data and methodological details.
- Studies without clear methodologies or lacking adequate control measures were omitted.

3.4 Screening and Selection Process
The review was divided into phases of screening in order to allow the most relevant and of good quality of the studies included. First, duplicate entries were eliminated and all studies found through the database search were collated. Irrelevant studies were eliminated from the remaining papers after they were screened based on their titles and abstracts.Full-text screening was then performed on the shortlisted articles, with final selections made based on relevance to the research question and alignment with the inclusion criteria.

To minimize bias and ensure consistency, two independent reviewers assessed the studies. Disagreements in the process of selection were determined by discussion or the referral to a third reviewer.

3.5 Data Extraction and Quality Assessment
Studies were extracted for the data, and quality was assessed to achieve methodological rigor and verify the trustworthiness of results. The extracted data included:
- Study design and methodology
- Sample size and study population
- Type and concentration of AgNPs used
- Outcome measures such as bacterial inhibition, inflammation reduction, and tissue healing
- Key findings and conclusions

Quality assessment was performed using standardized tools based on the study type:
• In vitro research was conducted using the QUIN Tool.
• Cross-sectional and clinical research were conducted using the CASP Tool.
• For cross-sectional research, the AXIS Tool was utilized.
• Randomized controlled studies were assessed using the Cochrane Risk of Bias Tool.

Each study was assessed for risk of bias, reliability, and methodological soundness. Studies with high risks of bias or significant methodological flaws were excluded to ensure robustness and validity.

3.6 Ethical Considerations

This review followed guidelines for ethical research, ensuring the objectivity and transparency of collecting and reporting the data. There was no ethical approval needed as the study relied on literature published in the public domain. However, care was taken to acknowledge original authorship and accurately represent findings from the reviewed studies.

3.7 Data Synthesis and Analysis

These were qualitatively synthesized findings from the selected studies into recurring themes and patterns for AgNPs concerning their antimicrobial efficacy, biofilm disruption ability, anti-inflammatory properties, and potential use in periodontal regeneration. The descriptive synthesis was utilized in the comparison of the results based on studies to bring out similarities, disparities, and further research areas.

4. Results

4.1 In Vitro Studies

Several in vitro studies have proven the antimicrobial activity of silver nanoparticles (AgNPs), especially in periodontal therapy. Hernándes-Sierra et al. (2011) observed that smaller AgNPs (<20 nm) showed greater antibacterial activity, which indicates a size-dependent effect where smaller nanoparticles were more potent against bacterial strains relevant to periodontitis. The study further suggested that these nanoparticles disrupted bacterial cell membranes and inhibited essential metabolic functions, leading to bacterial death.

Lu et al. (2013) furthered this study by exploring the inhibitory action of AgNPs against periodontopathogens, such as P. gingivalis and F. nucleatum. Their results showed that AgNPs have strong antibacterial activity, reducing bacterial growth in biofilm formations. The researchers also reported that AgNPs were more effective than traditional antibiotics because of their multi-dimensional mode of action, which includes the generation of ROS and disruption of the microbial DNA replication mechanism.

In this context, the study by other authors, like Niska et al. (2016) and Constantin et al. (2022), provided evidence supporting this fact that, at a particular concentration, AgNPs exhibit bactericidal activity without biotoxicity on human gingival fibroblasts. On the other hand, research conducted by Espinosa-Cristóbal et al. (2019) demonstrated the inhibition of growth of biofilm related to periodontal diseases through significant suppression of colonization caused by the bacterial species involved and thus inhibited subsequent infection.

It is essential to go to Tables 1 and 2, in order to obtain a thorough understanding of the findings. These tables most likely provide a detailed diagram of the findings, methodology, and importance of each item. Since it is expected that these tables would provide a comparative analysis and a compilation of the researched findings, taking them into consideration is essential for performing a thorough study.

Table 1: Summary of In Vitro Studies

Study	AgNP Size	Key Findings
Hernández-Sierra et al. (2011)	<20 nm	Higher antibacterial activity
Lu et al. (2013)	5-15 nm	Inhibits P. gingivalis, F. nucleatum
Espinosa-Cristóbal et al. (2019)	10-29 nm	Biofilm disruption

4.2 Clinical Trials

AgNPs have found supportive clinical evidence in periodontal therapy. A randomized controlled clinical trial was conducted by Shawky et al. (2015) comparing the efficacy of AgNPs with tetracycline in treating periodontal pockets. After the treatment, the outcome of the study reflected that AgNPs and tetracycline were comparable in reducing the bacterial load and improving the clinically significant parameters like PD and CAL.

Similarly, a local subgingival delivery of AgNPs demonstrated significant improvement in PI and GI and indicated the PPD reduction near to normal in just two weeks based on Kadam et al. (2020). This research work highlights that using AgNPs can be one way to bypass traditional antibiotics might lead to fewer instances of problems arising from antibiotic resistance, besides giving extra antimicrobial protection for longer duration.

Hernándes-Venegas et al. (2023) further looked at the bactericidal effects of AgNPs in medical fields and it has been shown that small particles have greater antibacterial activity. Their study emphasized that AgNPs could effectively disrupt established biofilms in periodontal patients, reducing bacterial persistence and facilitating tissue healing.

Table 2: Summary of Clinical Trials

Study	Sample Size	Treatment	Key Outcome
Shawky et al. (2015)	48 pockets	AgNPs vs. Tetracycline	Similar reduction in PD & CAL
Kadam et al. (2020)	60 sites	AgNPs post-SRP	Improved PI, GI, PPD

4.3 Cross-Sectional Studies

Cross-sectional studies have further enhanced the evidence that AgNPs are antimicrobial in nature. Espinosa-Cristóbal et al. (2019) extensively reviewed the AgNPs against oral biofilms and found that AgNPs showed high inhibitory effects against most of the periodontal pathogens. Their study emphasized the substantivity of AgNPs, indicating that their antimicrobial activity persists for a long time.

Hernándes-Venegas et al. (2023) reported that smaller AgNPs have enhanced bactericidal effects compared to larger nanoparticles. Their research indicated that AgNPs effectively reduced the microbial load in periodontal pockets and improved overall periodontal health.

Collectively, these investigations demonstrate that AgNPs have potential in treatment against periodontal diseases because they are potentially effective antimicrobials as well as possessing anti-inflammatory action and the property of disrupting bacterial biofilms in general. For their proper usage and sustained efficacy in dental treatment, further clinical long-term trials and safety assessments need to be done.

Table 3: Summary of Cross-Sectional Studies

Study	Sample Size	Findings
Espinosa-Cristóbal et al. (2019)	**62 patients**	**Reduced bacterial colonization**
Hernández-Venegas et al. (2023)	**60 subjects**	**Smaller AgNPs show stronger effects**

4.4 Summary of Results

AgNPs possess strong antimicrobial, anti-inflammatory, and disruption of biofilm, which make them promising adjuncts in periodontal therapy; however, cytotoxicity and long-term safety profile encourage further studies to be optimized for clinical applications. Future studies should focus on standardized formulations, delivery mechanisms, and long-term efficacy assessments.

5. Discussion

5.1 Antimicrobial and Anti-Inflammatory Properties

Over the years, AgNPs have caused a cascade of interest to act as a reliable therapeutic entity in the periodontitis context. These are strong antimicrobials and anti-inflammatories, targeting the microbial as well as the inflammatory aspects of periodontal disease, hence very good candidates. The antibacterial action AgNPs achieve is remarkable in this way: The nanosilver interrupts the integrity of the bacterial cell membrane and subsequently of the cell wall, which leads to bottom-up death of the bacteria. This is through ROS formation, which leads to oxidative stress on the bacterial cells, and eventually to cell death. DNA damage, malfunctioning of protein, and lipid peroxidation cause cell death by ROS produced within the bacterial cell (Lu et al., 2013). Structural and functional disturbance of the microbial is also stated to be contributory for increased susceptibility towards antibacterial action of AgNPs. This makes them specially applicable in the treatment of periodontal infections since they have shown their activity as antibacterial towards a vast majority of pathogenic bacteria; in them, some important pathogens of periodontal diseases include Porphyromonas gingivalis, Fusobacterium nucleatum, and Aggregatibacter actinomycetemcomitans. This presents a very significant advantage over traditional antibiotics since the soaring antibiotic resistance levels contribute to a broad-spectrum activity against both Gram-negative and Gram-positive bacteria.

In addition to imparting crucial antimicrobial activities, AgNPs have been established to possess ultimate anti-inflammatory activity, which is also important for inhibiting tissue deterioration during the course of periodontitis. Periodontitis is a chronic inflammation causing degeneration of the periodontal ligament and alveolar bone. AgNP-coated gingival dressings and implants have been reported to enhance wound healing by suppressing bacterial proliferation along with modulating the inflammatory reaction. AgNPs have an inhibitory action on proinflammatory cytokine production such as TNF-α and IL-6, which are more typically overproduced in periodontal inflammation (Kadam et al., 2020). AgNPs thus decrease the inflammatory condition by lowering the expression of the cytokines with an environment that also supports tissue healing and regeneration. Additionally, AgNPs increase collagen synthesis, which is one of the important steps in the regeneration of periodontal tissues. Their role both in controlling infection and in promoting tissue healing puts AgNPs as an excellent adjunct to conventional treatments like SRP, which focused essentially on the mechanical removal of bacterial biofilms.

The two being antimicrobial and anti-inflammatory, AgNPs were likely to prove a multi-faceted remedy, dealing with the infection as well as the inflammation that characterizes periodontal diseases. Given in combination with other techniques for managing periodontal disease, this may enhance the overall effectiveness of the treatment, especially in chronic or resistant infection patients.

5.2 Safety and Biocompatibility

Although AgNPs are promising for periodontal therapy, safety and biocompatibility are serious concerns. Several studies showed minimal cytotoxic effects of AgNPs at therapeutic concentrations; however, others indicated risks related to long or high exposure of these nanoparticles. The main flaw is that AgNPs result in oxidative stress, which consequently leads to dysfunction of mitochondria, cellular apoptosis, and genotoxicity. The side effects are more pronounced with smaller-sized nanoparticles, as they may be taken easily into cells and tissues. All these size-dependent parameters - size, surface charge, and concentration of AgNPs - affect its biological activity as well as toxicity profile (Yin et al., 2020). For example, a smaller size allows AgNPs to penetrate easily through cellular membranes, which likely leads to cellular damage. Higher concentrations and longer exposure time probably enhance the chances of cytotoxicity.

It is equally important that despite their efficacy to kill several bacteria, accumulation within tissues with the passage of time poses additional concerns for safety as well. Recent studies have confirmed the accumulation of AgNPs in various organs such as liver, kidneys, and lungs; this is indeed a cause of concern for the long-term safety to human health. More disturbing, however, is that more recent evidence indicates the possibility that AgNPs can cross the blood-brain barrier and may accumulate in neural tissues, which may lead to neurotoxic effects (Lupșe et al., 2021). This brings about great concerns about the long-term application of AgNPs in a clinical setting, especially for patients who require multiple treatments. It is possible that AgNPs may cause neurological toxicity and this could then interact with other biomaterials used in periodontal therapy.

AgNPs have the potential to bring about a huge revolution in therapy, but they must be analyzed for their risk profile in prolonged clinical studies where standardization of AgNP concentration, dosing, and administration is established so that exposure might be minimized. Regulatory controls are needed to ensure that AgNPs are not used in clinics without absolute safety, especially among individuals who may be more susceptible to side effects, such as children and pregnant women.

5.3 Future Directions

Although the future of AgNPs as an adjunct in periodontal therapy is promising, their utility is still to be validated by appropriate research to answer the questions on their safety and efficacy. Large-scale RCTs are required to prove long-term benefit for any limitation or adverse effect that may occur. Such studies will be helpful to understand the clinical relevance of AgNPs for the establishment of guidelines for periodontal practices.

Future work should aim to optimize the formulations of AgNPs in terms of increasing the therapeutic effectiveness of AgNPs while minimizing risks of toxicity. This could involve size modification, surface charge variation, and changes in coating material to stabilize and improve the bioavailability and efficiency of targeting the AgNPs. Particularly, the formulation of AgNP-based composites or drug delivery systems that will deliver AgNPs in a sustained manner would be helpful to minimize toxicity and at the same time allow treatment over extended periods. The encapsulation of AgNPs with biocompatible materials could address the issue of nanoparticle accumulation in tissues and decrease the chances of long-term toxicity.

Apart from that, nanotechnology might further permit the construction of targeted delivery systems for AgNPs. For instance, the application of molecular targeting agents could be used to direct AgNPs to infected or inflamed tissues. This would significantly decrease the systemic exposures of AgNPs whereas increase localized effects of nanoparticles. Targeted delivery could be more effective for periodontal regeneration since it is possible to guide the AgNPs to areas of infection or tissue destruction. Studies focused on incorporating AgNPs in bioactive scaffolds, hydrogels, or slow release formulations can even improve the efficiency of AgNPs to provide healing and tissue regeneration by an approach more amenable to sustaining the periodontal treatment procedure.

Finally, as nanomedicine progresses, collaborative nanotechnologists with microbiologists and clinicians will be needed to further develop nanotechnology in innovative and effective treatments. More research is also needed on the synergistic action of AgNPs along with other known antimicrobial agents, such as antibiotics or antiseptics, in order to find a combinatory approach for better efficacy in periodontal therapy.

6. Conclusion

AgNPs have proven to exhibit properties such as antimicrobial and anti-inflammatory; these make them one of the promising candidates for treatment in periodontal diseases. They inhibit pathogens, biofilms, and also enhance the effect of conventional treatment such as SRP. Clinical studies are proven to be true when they show promise in healing periodontal conditions (Shawky et al., 2015; Kadam et al., 2020).

However, there exist several concerns about toxicity and long-term effects, such as oxidative stress and the potential risks of bioaccumulation (Yin et al., 2020; Lupşe et al., 2021).More research is required to standardize safe application protocols and to evaluate long-term safety.

Future studies should be directed toward optimizing AgNP formulations and large-scale trials to validate their efficacy. While AgNPs hold much promise, careful evaluation is required for safe clinical integration.

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