



Evaluating the Effect of Metal Nanoparticles in the Treatment of Peri-implantitis: A Systematic Review and Meta-analysis

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ABSTRACT

Background and aim: Plaque-related pathological conditions such as peri-implantitis (PI) affect the tissues surrounding dental implants and affect the survival of implants. Hence, treatment of PI is of great importance, but bacterial resistance has been observed with antibiotics. Hence, the use of nanoparticles has been proposed. The present study aimed to evaluate the effect of metal nanoparticles (silver nanoparticles) in the treatment of peri-implantitis.

Material and methods: The international databases PubMed, EMBASE, and Web of Science were searched using keywords aligned with the study objective up to July 2025. Two blinded, independent authors reviewed all articles. STATA/MP. v17 (College Station, Texas, USA) was used to perform the analyses.

Results: In the present study, fifteen in vitro studies were included. Antibacterial activity of AgNPs in dental implants was 60% (ES: 0.60; 95% CI, 0.54, 0.67). The effectiveness of AgNPs for the treatment of peri-implantitis was 73% (ES: 0.73; 95% CI, 0.66, 0.81).

Conclusions: The present study showed acceptable effectiveness of silver nanoparticles' antibacterial activity and reduction of inflammatory factors in the treatment of PI.

1. Introduction

Dental implants have been a popular alternative to missing teeth for decades. Studies have shown that biological complications shorten the lifespan of implants. Clinical studies comparing the long-term survival rates of implants placed in augmented bone versus those in natural bone have yielded conflicting results.^[1] While some studies have reported comparable results in terms of marginal bone loss and implant survival rates, other studies have reported less than ideal results when placing implants in reinforced sites.^[2, 3] Based on available evidence, periodontal inflammatory disease (PID) can occur during implant treatment. Various studies have shown that peri-implantitis (PI) has a different prevalence in different populations. Several studies have also shown a strong correlation between poor oral hygiene and PI.^[4, 5] Biofilms are the primary cause of PIDs, characterized by the development of inflammatory conditions and tissue breakdown. The progression of PI leads to bone loss. However, studies have shown that the microbial profile of PI and the microbiome found in periodontitis lesions are not identical.^[6] Studies have shown that although surgical outcomes after PI

treatment help prevent further bone resorption and implant failure, they are still unpredictable in reducing inflammation. Evidence suggests that salvage care and implant removal are necessary in cases of further PI collapse.^[7] Additionally, the issue of disinfecting the rough and threaded surfaces of exposed implants in PI is challenging and requires the use of more complex treatment techniques.^[8] Research suggests that nanoparticles (NPs) may be a useful approach to addressing some of the challenges associated with dental implants. Their physical properties and sterilization could increase the survival rate of implants.^[9] Metal NPs, including copper (Cu), zinc (Zn), titanium oxide (TiO₂), silver (Ag), and gold (Au) NPs, can inhibit a variety of bacterial strains and treat oral health problems. Therefore, they are often used in nanoformulations to combine drug active ingredients with NPs, creating a synergistic effect.^[10, 11] Studies have shown that chitosan, metal NPs, and hybrid coatings with antibiotic agents can be used to prevent PI due to their antibacterial properties. Despite the promising results of these studies, further research is needed to evaluate their clinical behavior in humans before

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they can be widely marketed.^[12] Potential toxicity and slow metal accumulation are also major disadvantages of these approaches. In dental implant therapy, titanium is currently considered the most suitable biomaterial for connecting the implant abutment to the abutment.^[13-15] The large surface area and high charge density of NPs enable them to interact with the negatively charged surface of bacterial cells, thereby enhancing their antibacterial activity. Metal NPs help regenerate demineralized dental tissues by enhancing biomineralization.^[16] Effective management of biological complications that can compromise the long-term effectiveness of bone-integrated implant reconstructions can be challenging due to the widespread distribution of bone resorption.^[17] Titanium-containing silver NPs can increase bone mineral density, bone growth, and trabecular pattern without damaging the tissues surrounding dental implants.^[18] Nowadays, it is essential to treat PID with the latest advances in treatment and prevention. Therefore, metal NPs such as Cu, Zn, TiO₂, Ag, and Au have been proposed for the treatment of PID. For the treatment of PI, these NPs can serve as a promising alternative to antibiotics due to their antibacterial properties. Several studies have been conducted to reduce toxicity and increase the efficacy of these metal NPs in the treatment of PID. However, a consensus of findings could provide stronger evidence; hence, the present study aimed to evaluate the effect of AgNPs in the treatment of PI.

2. Material and methods

Search strategy and selection criteria

The present study was conducted in accordance with the PRISMA 2020 checklist^[19] by conducting a targeted search of the PubMed, EMBASE, and Web of Science databases up to July 2025 using relevant keywords. References of reviews and related articles were reviewed to identify additional relevant articles. Only articles published in English were considered. After conducting separate literature searches, two blinded and independent authors reviewed the titles, abstracts, and full texts of the studies.

The following Mesh terms were used to retrieve literature:

((((((((((((((("Dental Implants"[Mesh] OR "Dental Implantation"[Mesh]) AND "Periodontal Diseases"[Mesh]) OR ("Periodontal Diseases/classification"[Mesh] OR "Periodontal Diseases/complications"[Mesh] OR "Periodontal Diseases/diagnosis"[Mesh] OR "Periodontal Diseases/drug therapy"[Mesh] OR "Periodontal Diseases/etiology"[Mesh] OR "Periodontal Diseases/prevention and control"[Mesh] OR "Periodontal Diseases/surgery"[Mesh] OR "Periodontal Diseases/therapy"[Mesh])) OR "Peri-Implantitis"[Mesh] OR ("Peri-Implantitis/classification"[Mesh] OR "Peri-Implantitis/complications"[Mesh] OR "Peri-Implantitis/diagnosis"[Mesh] OR "Peri-Implantitis/drug therapy"[Mesh] OR "Peri-Implantitis/etiology"[Mesh] OR "Peri-Implantitis/microbiology"[Mesh] OR "Peri-Implantitis/prevention and control"[Mesh] OR "Peri-Implantitis/surgery"[Mesh] OR "Peri-Implantitis/therapy"[Mesh])) OR "Mucositis"[Mesh] AND "Nanoparticles"[Mesh] OR "Metal Nanoparticles"[Mesh] OR ("Metal Nanoparticles/administration and dosage"[Mesh] OR "Metal Nanoparticles/adverse effects"[Mesh] OR "Metal

Nanoparticles/classification"[Mesh] OR "Metal Nanoparticles/microbiology"[Mesh] OR "Metal Nanoparticles/statistics and numerical data"[Mesh] OR "Metal Nanoparticles/therapeutic use"[Mesh] OR "Metal Nanoparticles/toxicity"[Mesh])) OR "Magnetic Iron Oxide Nanoparticles"[Mesh] OR "Gold"[Mesh] OR "Silver"[Mesh] OR "Iron"[Mesh] OR "Copper"[Mesh] OR "Zinc"[Mesh] OR "Aluminum"[Mesh] OR "titanium dioxide" [Supplementary Concept]) AND ("Bacteria"[Mesh] OR "Microbiology"[Mesh] OR "microbiology" [Subheading])) AND "Anti-Bacterial Agents"[Mesh] AND "Contraceptive Effectiveness"[Mesh].

Studies were included if they met the PICO strategy criteria. Population (P): Patients with implants, Intervention (I): metal nanoparticles, Comparison (C): not defined; Outcome (O): treatment outcome. Exclusion criteria include: reviews, case report studies, and literature studies; studies with unavailable or incomplete data; articles written in a language other than English.

Data extraction

Two investigators independently and blindly extracted data from each selected study using a standard "primary and secondary data extraction" form; a third reviewer resolved any disagreements between investigators. Data related to study characteristics, including the name of the first author, year of publication, sample size, methodology, and results, were selected as demographic and clinical data. The original data were then entered into the meta-analysis after extraction.

Statistical analysis

Statistical heterogeneity among studies was evaluated with the use of the I² statistic and Q test p-value < 0.05: No heterogeneity: 0.0% < I² < 24.9%; low heterogeneity: 25.0% < I² < 49.9%; Moderate heterogeneity: 50.0% < I² < 74.9%; High heterogeneity: 75.0% < I² < 100%. STATA/MP.v17 (College Station, Texas, USA) was used to perform the analyses. The effect size, as determined by the random effect model and the Restricted Maximum Likelihood (REML) method, was used to assess efficacy.

3. Results

Literature search

After a thorough keyword search in international databases, a significant number of articles were found, totaling 227 articles, as shown in Figure 1. After reviewing the titles, 89 of these articles were excluded based on duplication and inconsistency with the inclusion and exclusion criteria; the abstracts of 138 articles were reviewed and studies that did not meet the study selection criteria were excluded at this stage (n=106), and two blind and independent authors reviewed the full text of 32 articles. Finally, after removing irrelevant articles, 15 articles were included in the study (Fig. 1).

Study characteristics

Fifteen in vitro studies assess the effect of Ag NPs in the treatment of peri-implantitis. Table 1 shows a summary of the study data.

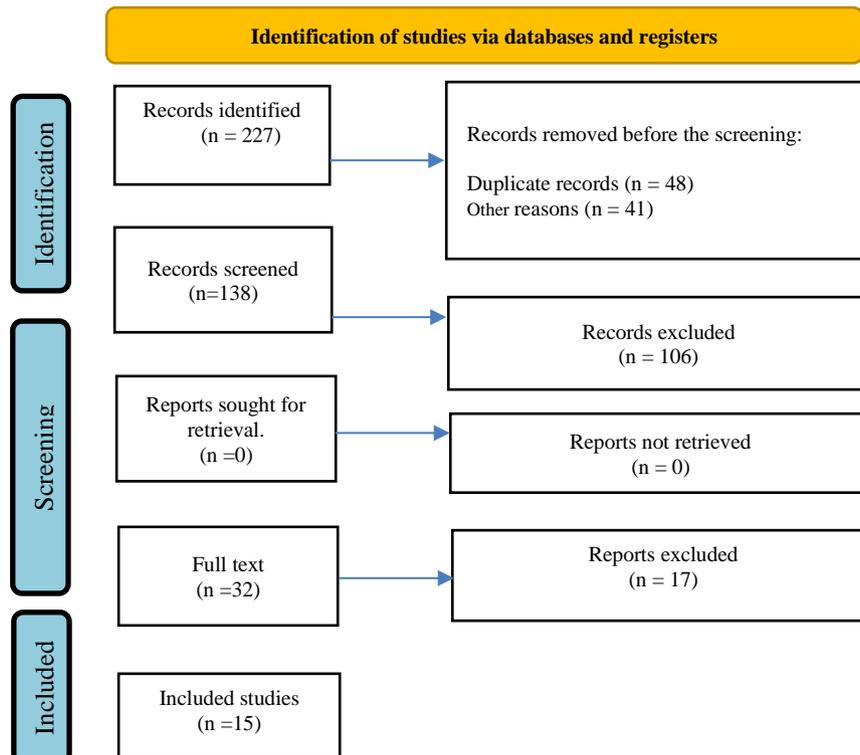


Fig. 1. PRISMA 2020 Checklist.

Table 1. Study characteristics of the included studies.

Study. Years	Study Design	Concentration of Nanoparticles ($\mu\text{mol/L}$)	Microorganisms	Antibacterial Efficacy Tests
Memon et al., 2025 ^[20]	In vitro	0.5	<i>p. aeruginosa</i>	NR
Sanhueza et al., 2024 ^[21]	In vitro	0.5	<i>Pseudomonas aeruginosa</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus mutans</i>	NR
Madiwal et al., 2024 ^[22]	In vitro	0.5	<i>Streptococcus oralis</i> , <i>Streptococcus sanguinis</i> , <i>Aggregatibacter actinomycetemcomitans</i> , and <i>Porphyromonas gingivalis</i>	NR
Pérez-Tanoira et al., 2022 ^[23]	In vitro	0.5	<i>Staphylococcus aureus</i> or oral mixed bacterial flora composed of <i>Streptococcus oralis</i>	NR
Cotton et al., 2019 ^[24]	In vitro	0.5, 2.25, 5	<i>Escherichia coli</i> , <i>Streptococcus mutans</i> , <i>Streptococcus Mitis</i> , and <i>Staphylococcus aureus</i>	MIC, MBC
Xu et al., 2019 ^[25]	In vitro	NR	inflammatory parameters	NR
Prasetyo et al., 2018 ^[26]	In vitro	NR	inflammatory parameters	NR
Dong et al., 2017 ^[27]	In vitro	0.5	peri-implant infection	SEM
Diniz et al., 2016 ^[28]	In vitro	0.5	<i>Aggregatibacter actinomycetemcomitans</i>	SEM
Franková et al., 2017 ^[29]	In vitro	0.5	peri-implant infection	ELISA
Shen et al., 2017 ^[30]	In vitro	10, 4, and 2	<i>Staphylococcus aureus</i> , <i>Streptococcus mutans</i>	SEM
Godoy-Gallardo et al., 2016 ^[31]	In vitro	0.5	peri-implant infection	SEM
Habiboallah et al., 2014 ^[32]	In vitro	NR	Inflammatory factors	SEM
Munger et al., 2014 ^[33]	In vitro	NR	Inflammatory factors	SEM

Vargas-Reus et al., 2012 ^[34]	In vitro	0.5	Prevotella intermedia, Porphyromonas gingivalis, Fusobacterium nucleatum, and Aggregatibacter actinomycetemcomitans.	MIC, MBC
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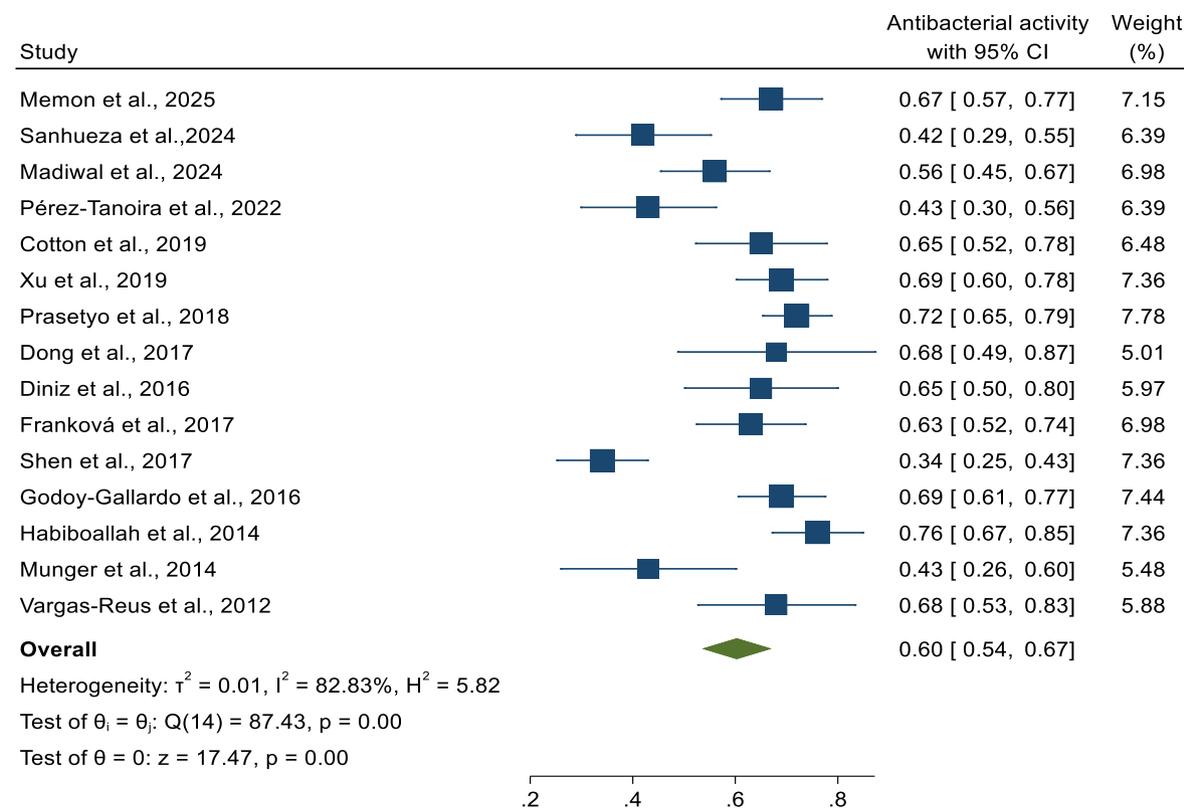
Aa: Aggregatibacter actinomycetemcomitans; MIC: Minimum inhibitory (bacteriostatic) concentration; MBC: minimum bactericidal concentration; SEM, scanning electron microscopy; ELISA: enzyme-linked immunosorbent assay.

Antibacterial activity of AgNPs in dental implants

The antibacterial activity of AgNPs in dental implants was 60% (ES: 0.60; 95% CI, 0.54-0.67). The I² coefficient of 82.83% indicates high heterogeneity between studies (p < 0.001) (Fig. 2).

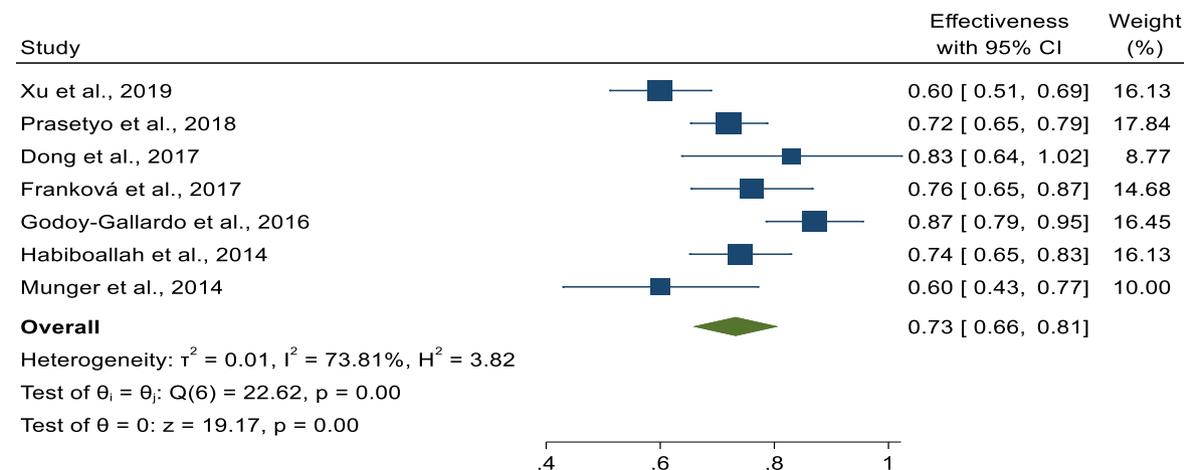
Inflammatory factors

The effectiveness of AgNPs for treating peri-implantitis was 73% (ES: 0.73; 95% CI, 0.66-0.81). The I² coefficient of 73.81% indicates high heterogeneity between studies (p<0.001) (Fig. 3). AgNPs exhibit acceptable effectiveness in reducing inflammation in the surrounding area of the implant.



Random-effects REML model

Fig. 2. The forest plot showed the Antibacterial activity of AgNPs in dental implants.



Random-effects REML model

Fig. 3. The forest plot showed the Effectiveness of AgNPs for inflammatory factors.

4. Discussion

Currently, 28% to 56% of patients lose their implants due to PI.^[35] Therefore, the effective prevention, control, and successful treatment of PI can have a positive impact on improving the quality of life of patients.^[36] Surgery, local irrigation, and antimicrobial therapy are typically treatment options to prevent implant failure.^[37] Antibiotics are generally recommended for PI along with surgical procedures. However, studies have shown that antibiotics are not effective and have not been successful in treating PI. Research suggests that nanoparticles are promising options for the treatment of PI; however, there is insufficient evidence, and most of the studies conducted are in vitro and in-vivo. The findings of these studies have shown significant antibacterial effects of nanoparticles. Metal nanoparticles have demonstrated a broad spectrum of antibacterial activity and also prevent the development of bacterial resistance.^[38, 39] Study findings have shown that using silver as an antibacterial agent can be a good option in healthcare settings to prevent infections. Studies have also reported low toxicity and high antimicrobial properties for silver. Some studies have shown that silver can prevent bacteria from adhering to dental implants. AgNPs have been used as biocompatible coatings for dental implants, and it has been demonstrated that adding an appropriate amount of Ag to the surface exhibits acceptable antibacterial properties.^[40, 41] Therefore, in the present study, the effectiveness of AgNPs in treating PI was investigated.

Based on the present meta-analysis, high antibacterial activity was observed for AgNPs. Other studies, consistent with the present results, have shown that the addition of AgNPs at different concentrations exhibits antibacterial activity against a variety of bacteria.^[30] Recently, the use of 3D printers to create personalized and precisely dimensioned implants has received considerable attention. However, evidence has shown that these implants have poor bone bonding potential and lack antibacterial properties, often causing implant loosening and microbial infections, which can lead to PIDs.^[42] Therefore, it has been suggested that the use of nanoparticles may yield good results in preventing PIDs, thereby increasing the survival rate of implants and reducing the risk of implant failure.^[43, 44] The homogeneous PDA-AgNPs nanocomposite coating promoted optimal soft tissue healing and bone formation around implants, achieving a balance between cell compatibility and antibacterial activity, as indicated by the results of subcutaneous implantation, osteogenesis, cytotoxicity, and antibacterial tests. A study demonstrates that the method for synthesizing antibiotic-containing surfaces with favorable cytocompatibility and excellent antibacterial activity can be easily applied to other surfaces with similar properties. This development is expected to increase the therapeutic efficacy of silver composite-coated dental implants.^[45] A green synthesis technique was used to create AgNPs in a study. The findings demonstrated that Ag-PVP nanocomposites at varying concentrations were applied to implants using a deep coating technique, exhibiting high antibacterial activity. These findings indicated that the prevalence of infection around implants could be effectively reduced by AgNPs.^[46] In a review study, the potential advantages and disadvantages of using metal nanoparticles in clinical settings for the management of PID were examined to advance future therapeutic strategies for this condition, and promising results were presented.^[47]

The present study had some limitations. First, the number of articles that examined effectiveness using a similar methodology and the same tools was very small, which was considered inconsistent across the above studies. Also, the antibacterial activity was examined at different concentrations of AgNPs, which in the present study was considered at a concentration of 0.5 µmol/L.

Therefore, this factor can cause heterogeneity. On the other hand, not all studies provided sample sizes or were very small, which requires more robust studies. The citation and interpretation of the results from the present study should be done with caution due to the high heterogeneity of the studies. Additionally, clinical trial studies and in vitro studies with similar methodologies and more appropriate methods are needed to confirm the evidence.

5. Conclusion

Using modern methods to prevent the growth of microorganisms inside the mouth is crucial because it prevents bacterial resistance to treatment. Therefore, the present study demonstrated the acceptable effectiveness of AgNPs' antibacterial activity and reduction of inflammatory factors in the treatment of PI. AgNPs have the potential to inhibit bacterial growth and can be used as effective antibacterial and anti-inflammatory scaffolds for the treatment of PI.

Conflict of Interest

The authors declared that there is no conflict of interest.

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