e-ISSN: 0974-4614
p-ISSN: 0972-0448

Review study in efficacy of silver nanoparticles in preventing and treating pediatric dental caries

Dr.Roaa Mohammad AlDomyati[1], Dr.Waleed Abdulrahim Aljehani[2], Dr.Hussam sultan Farrash[3], Dr.Anmar Essam Kattan[4], Dr.Rozan Sameer A Nasruddin[5], Dr.Omar Mohammed abo nawas[6], Dr.Wail Hisham Ragkhan[7], Dr. Abdullah Sameer Kaki[8], Dr. Maha Suliman Tayeb[9], Dr. Salwa Abdulmonem Mohammed Alsaid[10], Dr.Moayad Adnan Diwan[11], Dr.Rasha Abdulkarim Alshehri[12], Dr.Ali Hassan Assiri[13], Dr.Lugain Wadye Qari[14], Dr.Rasha Ali Alyafei[15]

[1]Consultant in pediatric dentistry, East Jeddah Hospital
[2]Dental department at Khulais General Hospital
[3]General dentist at Khulais general hospital
[4]Al Adel Primary Healthcare, Ministry of Health, Makkah, Saudi Arabia General dentist
[5]General Dentist at Dental Department Khulais General Hospital
[6]General dentist at Khulais General Hospital
[7]Dental department at Khulais general hospital
[8]Dental Department At Khulais General Hospital
[9,10]General Dentist at Alnaeem Primary Health Care Center
[11]General Dentist, Bahrah Primary Healthcare Center, Makkah Healthcare Cluster, Mecca, Saudi Arabia
[12]General Dentist, Nakhal Primary Healthcare Center, Makkah Healthcare Cluster, Mecca, Saudi Arabia
[13]General Dentist, Al-Jamum Primary Healthcare Center, Makkah Healthcare Cluster, Mecca, Saudi Arabia
[14,15]General Dentist, Almajed Primary Healthcare Center, Jeddah Healthcare Cluster, Jeddah, Saudi Arabia

Received: 16.08.2024 Revised: 19.09.2024 Accepted: 27.10.2024

ABSTRACT
Nanoscience and nanotechnology are nascent disciplines focused on the synthesis and utilization of nanoscale materials and structures. Metallic nanoparticles and metallic oxides are widely utilized in dentistry due to their ability to disrupt bacterial metabolism and inhibit biofilm development. Silver nanoparticles (AgNPs) represent a category of zero-dimensional materials characterized by unique morphologies. The metallic nanoparticles have considerable antibacterial action through ion release, oxidative stress induction, and non-oxidative processes. Metallic silver has been recognized for its antibacterial properties since antiquity. Over the years, silver-containing compounds have been utilized in many forms to address multiple medical ailments. The integration of silver nanoparticles into dental materials may improve their mechanical qualities and antibacterial efficacy. Consequently, a growing array of dental materials including silver nanoparticles is being created to enhance patients' overall oral health. This review paper is to examine the literature about the unique properties of silver nanoparticles and their applications in pediatric dentistry, as well as their effectiveness in the prevention and treatment of dental caries.

Keywords: induction, non-oxidative, Metallic, Nanoscience

INTRODUCTION
Dental caries is a disease induced by a particular biofilm that produces acid, initiating demineralization of the enamel surface, characterized by a white spot lesion, which appears as a white and opaque discoloration. The primary pathogens implicated in dental caries are Streptococcus mutans and Lactobacillus [1]. Despite advancements in dental treatment in recent decades, dental caries remains a global health issue that is both costly and detrimental to the health and quality of life of children and adults. The most effective interventions for the prevention and management of early-stage dental caries are predicated on the application of fluorides. Silver has been utilized in dentistry for more than a century as an antibacterial agent because of its wide efficacy, low toxicity, and lack of cross-resistance among microorganisms. Silver nitrate was employed to diminish the occurrence of caries in the primary dentition, serve as a caries preventative agent for permanent molars, act as a cavity sterilizing agent, and function as a dentine desensitizer [2,3].
Metallic silver has been recognized for its antibacterial properties since ancient times. Over the years, silver-containing compounds have been utilized in various forms for multiple medical diseases, including wound

healing, burns, and ulcer treatment, primarily based on practical experience prior to the understanding that microbes were the causative agents of infections. Silver possesses significant antibacterial capabilities effective against a diverse array of microorganisms [4]. In recent decades, the prevalence of antibiotic-resistant bacteria has risen, jeopardizing the effectiveness of antibiotics; therefore, it is essential to develop potent bactericides to manage bacterial illnesses.

Silver nanoparticles have been recognized for decades for their broad medicinal applications, including antibacterial, antifungal, and anti-plasmodial properties. The antibacterial impact relies on the concentration and rate of ionic silver release. Silver nanoparticles, due to their nanoscale dimensions and significant surface area, can directly engage with bacteria, induce structural alterations, and result in cell death [5]. Silver nanoparticles exhibit antibacterial and anti-adherence characteristics against Streptococcus mutans, the primary pathogen implicated in tooth cavities. Silver nanoparticles measuring 1-10 nm exhibit considerable antibacterial and anti-adherence efficacy against S. mutans bacteria [6].

Review

Recent observations have noted new formulations that combine silver nanoparticles and fluoride. The silver nanofluoride suspension was evaluated in vitro for its effectiveness against cariogenic microorganisms and its cytotoxicity. The determined MIC was 33.54 µg/ml, and the MBC was 50.32 µg/ml. The values were comparable to those of Silver diamine fluoride (SDF). Nonetheless, this study did not assess the discoloration of the enamel surface [7].

A formulation comprising silver nanoparticles, fluoride, and a chitosan carrier was also assessed. A solitary application of this tailored varnish was administered on dental cavities and monitored at intervals of seven days, five months, and twelve months. During the seven-day period, 81% of the samples exhibited arrested cavities during the five-month evaluation, 72.7% demonstrated evidence of arrested carious lesions, and after 12 months, 66.7% of the carious teeth remained arrested. No dark or black stains were noticed on the enamel of the teeth [8].

In a similar manner, silver nanoparticles were included into a commercially available fluoride varnish and assessed for the remineralization of primary teeth exhibiting white spot lesions. The study included anterior primary teeth following inspection with the DIAGNOdent laser wand. A formulation of silver nanoparticle powder and fluoride varnish was created at a concentration of 0.1% weight. One tooth in each quadrant was treated with the experimental varnish, while the corresponding opposing quadrant received the standard control fluoride varnish. The medication was administered weekly for a duration of three weeks. Follow-up assessments were conducted with the DIAGNOdent after three months to assess alterations in remineralization. The remineralisation rate was seen to exceed that of ordinary water when treated with silver nanoparticles [9].

Silver nanoparticles attract public interest due to their remarkable antimicrobial efficacy coupled with minimal toxicity and affordability. They are utilized in minimal doses and do not induce bacterial resistance. Numerous antibacterial properties of silver nanoparticles have been suggested, while the precise mechanism behind their antibacterial activity remains incompletely understood. Silver nanomaterials emit silver ions that infiltrate microbial membranes, interfering with deoxyribonucleic acid replication and protein synthesis. Furthermore, silver ions can inhibit respiratory enzymes, ultimately leading to cell lysis. Silver nanoparticles derived from nanomaterials can aggregate in the cell wall pits, leading to membrane denaturation. They can also penetrate bacterial cell walls and cytoplasmic membranes, resulting in the denaturation of both structures [9,10].

Researchers examined the application of silver nanoparticles in dental materials as an antibacterial agent for clinical purposes. Silver nanoparticle-modified implants were created to avert peri-implant infections.12 A multitude of studies has examined silver nanoparticles for caries prevention. Silver nanoparticles are integrated into adhesives and orthodontic brackets to inhibit enamel caries, a frequent consequence of orthodontic therapy. Silver nanoparticles may be included into restorative materials to inhibit secondary caries, a prevalent factor contributing to restoration failure [11].

Dental caries is a prevalent condition globally, impacting 95% of individuals at various times of life. Numerous studies have developed formulations incorporating silver nanoparticles targeting cariogenic pathogens, particularly Streptococcus mutans, assessing their minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) as well as their efficacy in biofilm formation control. The findings indicate that these nanoparticles serve as effective oral antimicrobial agents, particularly at sizes ranging from 80 to 100 nm, as cytotoxicity escalates at dimensions below 20 nm [12].

Novel formulations have been assessed for their efficacy against cariogenic infections and their cytotoxic effects via hemolytic activity at various doses, provisionally designated as silver nanofluoride (NSF). The MIC and MBC were around 33.54 µg/ml and 50.32 µg/ml, respectively. Silver diamine fluoride (SDF) exhibited comparable values. NFS demonstrated antibacterial properties akin to silver diamine fluoride, but with less cytotoxicity; however, its effect on enamel staining was not evaluated [13].

Dentin discs were produced from previously demineralized premolars in one investigation. Sodium fluoride (SDF) (38%), nano-silver fluoride (NSF) (3.16%, 3.66%, and 4.16%), and propolis fluoride (PPF) (3%, 6%, and

10%) were administered and subjected to pH cycling with a demineralization solution (pH 4.4) for 30 minutes and a remineralization solution (pH 7) for 10 minutes, repeated six times daily over a period of eight days. The concentrations of calcium, phosphate, and fluoride ions on the surface of the dentine discs were analyzed using energy dispersive X-ray spectroscopy. The findings indicated that the concentrations of calcium ions, phosphate, and fluoride in the NSF and PPF groups were significantly elevated in comparison to SDF [14]. Based on prior findings and consistent methodologies, fluorapatite crystals were identified on the dentine surface in both SDF and NSF, alongside enhanced hardness and superior intensity and quality of apatite crystal compounds. Additionally, optical coherence tomography imaging revealed a more pronounced remineralization effect of NSF compared to sodium fluoride (NaF) in deciduous teeth [15].

A controlled clinical research was conducted on decaying teeth in vivo. The experimental group consisted of a formulation of nanoparticle silver, fluoride, and chitosan (NSF), while the control group utilized water. Caries was identified clinically, and a single application was performed, followed by evaluations after seven days, five months, and twelve months. On the seventh day, 81% of the teeth in the treatment group exhibited arrested cavities, whereas 0% in the control group did. After five months, 72.7% of the treatment group exhibited arrested caries, compared to 27.4% in the control group. At 12 months, 66.7% of the carious lesions treated with NSF remained arrested, whereas the control group exhibited a rate of 34.7%. No discolorations were noted on the teeth [16].

A comparable study assessed the impact of silver nanoparticles (AgNPs) incorporated into a commercial fluoride varnish on the remineralization of deciduous teeth. The research was performed on children exhibiting white spot lesions in anterior deciduous teeth, diagnosed using a laser cavity detection pen to assess tooth demineralization. A 0.1% wt combination of silver nanoparticles and fluoride varnish was formulated. Each hemi-arc was allocated one tooth for the experimental treatment, which involved fluoride varnish containing 0.1% AgNPs, and one tooth for the control treatment, which utilized commercial fluoride varnish. Each tooth underwent these treatments weekly for three weeks, with measures reassessed at three months to evaluate changes in remineralization, which were significantly greater in the AgNPs therapy ($p=0.001$) [17]. Another study assessed the effectiveness of silver nanoparticles incorporated into a pit and fissure sealant in permanent molars to evaluate the demineralization of this formulation compared to a control group. The conventional sealant exhibited an average microleakage of 30.6%, while the sealant included with silver nanoparticles demonstrated 33.6% (P = NS). A drop in fluorescence that was three times larger was seen in the AgNPs group compared to the conventional group ($p < 0.05$). No correlations were identified concerning sex or age, leading to the conclusion that the sealant containing silver nanoparticles markedly diminished tooth demineralization and likely enhanced remineralization relative to the traditional sealant [18].

Numerous studies have examined the application of silver nanoparticles in caries prevention. Eighteen participants reported the creation of silver nanoparticles and silver nanocomposites, which may be effective in managing caries. A study employed silver nanoparticles in toothpaste. A study indicated the application of silver nanoparticles on orthodontic brackets to inhibit enamel caries.Thirteen investigations indicated the application of nano silver fluoride solution for the remineralization of early enamel caries and the cessation of dentin caries [19]. Thirty-one research employed resins containing silver nanoparticles to inhibit caries formation. Silver nanoparticles were included into restorative products, including filling resins and adhesives, to inhibit secondary caries. Silver nanoparticles were integrated into the resin of orthodontic products, including adhesives, elastomeric ligatures, and detachable retainers, for the prevention of caries [20]. A clinical trial indicated that a dental sealant containing silver nanoparticles was superior to a conventional sealant in reducing enamel cavities in first permanent molars. Seven research investigated the efficacy of glass ionomer cements including silver nanoparticles for caries prevention. Six individuals employed glass ionomer containing silver nanoparticles as orthodontic cements to inhibit enamel caries. The subsequent study utilized it as a restorative substance to inhibit secondary caries [21].

Furthermore, enamel exhibiting fake caries can be treated with silver nanoparticles to enhance microhardness. A silver nanoparticle-coated orthodontic bracket reduced the caries incidence on the surface of an incisor in a rat's oral cavity. Moreover, resin containing silver nanoparticles can enhance the microhardness of dentin caries following an acid (pH-cycling) challenge. A dental sealant containing silver nanoparticles decreased mineral loss in children's first molars during a clinical experiment. Six research examined the remineralizing properties of nano silver fluoride. Enamel treated with nano silver fluoride has a microhardness comparable to that of enamel treated with sodium fluoride. The microhardness of enamel caries treated with nano silver fluoride surpasses that of enamel caries treated with sodium fluoride. Nonetheless, the disparity in mineral composition between nano silver fluoride– and sodium fluoride–treated decaying enamel is undetectable with optical coherence tomography. Nano silver fluoride effectively halted dentin caries in children throughout two clinical trials [22,23].

CONCLUSION

This review categorizes silver nanomaterials utilized for caries prevention into silver nanoparticles, resin containing silver nanoparticles, glass ionomer with silver nanoparticles, and nano silver fluoride. Silver nanoparticles can impede the proliferation of cariogenic bacteria and the formation of biofilm adhesion. They additionally impede collagenase action and maintain the collagen matrix. Furthermore, they impede the demineralization of enamel and dentin. Research in laboratory and clinical studies has demonstrated the efficacy of silver nanoparticle compounds in preventing and halting dental caries, without causing tooth pigmentation. This therapy is user-friendly and more economical than SDF. The interaction of AgNPs with oral tissues, along with the perfect concentrations, optimal sizes of AgNPs, delivery vehicles, dosages linked to cellular toxicity, and potential side effects, must be investigated to assess the advantages of their combination with other components.

REFERENCES

1. Ancient and novel forms of silver in medicine and biomedicine. Ebrahiminezhad A, Raee MJ. J Adv Med Sci App Tech. 2016;2:122–128.
2. The antibacterial mechanism of silver nanoparticles and its application in dentistry. Yin IX, Zhang J, Zhao IS, Mei ML, Li Q, Chu CH. Int J Nanomedicine. 2020;15:2555–2562.
3. Antiadherence and antimicrobial properties of silver nanoparticles against Streptococcus mutans on brackets and wires used for orthodontic treatments. León Francisco Espinosa-Cristóbal, Natalie López-Ruiz. J Nano. 2018:1–11.
4. The bactericidal effect of silver nanoparticles. Morones JR, Elechiguerra JL, Camacho A, Holt K, Kouri JB, Ramírez JT, Yacaman MJ. Nanotechnology. 2005;16:2346–2353.
5. Synthesis of silver nanoparticles from Phenerochaete chrysosporium (MTCC-787) and their antibacterial activity against human pathogenic bacteria. Saravanan M, Arokiyaraj S, Lakshmi T, Pugazhendhi A. Microb Pathog. 2018;117:68–72.
6. Bactericidal activity of silver nanoparticles: A mechanistic review. Ahmad SA, Sabya SD. Materials Science for Energy Materials Science for EnergyTechnologies. 2020;3:756–769.
7. An innovative approach to treating dental decay in children. A new anti-caries agent. Targino AG, Flores MA, dos Santos Junior VE, de Godoy Bené Bezerra F, de Luna Freire H, Galembeck A, Rosenblatt A. J Mater Sci Mater Med. 2014;25:2041–2047.
8. A new "silver-bullet" to treat caries in children--nano silver fluoride: a randomised clinical trial. Santos VE Jr, Vasconcelos Filho A, Targino AG, Flores MA, Galembeck A, Caldas AF Jr, Rosenblatt A. J Dent. 2014;42:945–951.
9. Effect of silver nanoparticle-added pit and fissure sealant in the prevention of dental caries in children. Salas-López EK, Pierdant-Pérez M, Hernández-Sierra JF, Ruíz F, Mandeville P, Pozos-Guillén AJ. J Clin Pediatr Dent. 2017;41:48–52.
10. The effect of bioactive glasses on enamel remineralization: A systematic review. Taha AA, Patel MP, Hill RG, Fleming PS. J Dent. 2017;67:9–17.
11. Smith D. J. Dental Caries vaccines:prospects and concerns. Critical Reviews in Oral Biology & Medicine. 2002;13(4):335–349.
12. Ghorbani H. R. The study of anticariogenic effect of silver nanoparticles for dental applications. International Journal of Nano Dimension. 2017;8(4):361–364.
13. Ten Cate J. M. Novel anticaries and remineralizing agents. Journal of Dental Research. 2012;91(9):813–815.
14. Soekanto S. A., Marpaung L. J., Ushohwah H., Djais A., Darwita R. R. Efficacy of propolis fluoride and nano silver fluoride for inhibition of Streptococcus mutans and Enterococcus faecalis biofilm formation. International Journal of Applied Pharmaceutics. 2017;9(2):51–54.
15. Hernández-Sierra J. F., Galicia-Cruz O., Salinas-Acosta A., et al. In vitroCytotoxicity of silver nanoparticles on human periodontal fibroblasts. Journal of Clinical Pediatric Dentistry. 2011;36(1):37–42.
16. Scarpelli B. B., Punhagui M. F., Hoeppner M. G., et al. In vitro evaluation of the remineralizing potential and antimicrobial activity of a cariostatic agent with silver nanoparticles. Brazilian Dental Journal. 2017;28(6):738–743.
17. Butrón-Téllez Girón C., Mariel-Cárdenas J., Pierdant-Pérez M., Hernández- Sierra J. F., Morales-Sánchez J. E., Ruiz F. Effectiveness of a combined silver nanoparticles/fluoride varnish in dental remineralization in children: in vivo study. Superf. Vacío. 2017;30(2):21–24.
18. Salas-López E., Pierdant-Pérez M., Hernández-Sierra J. F., Ruiz F., Mandeville P., Pozos-Guillén A. Effect of silver nanoparticle-added pit and fissure sealant in the prevention of dental caries in children. Journal of Clinical Pediatric Dentistry. 2017;1(41):48–52.

19. Soekanto S. A., Rosithahakiki N., Sastradipura D. F. S., Sahlan M. Comparison of the potency of several fluoride-based varnishes as an anticariogenic on calcium, phosphate, and fluoride ion levels.International Journal of Applied Pharmaceutics. 2017;9(2):55–59.
20. Dias HB, Bernardi MIB, Marangoni VS, de Abreu Bernardi AC, de Souza Rastelli AN, Hernandes AC. Synthesis, characterization and application of Ag doped ZnO nanoparticles in a composite resin. Mater Sci Eng C Mater Biol Appl. 2019;96:391–401.
21. Espinosa-Cristóbal LF, Martinez-Castanon GA, Martínez-Martínez RE, et al. Antimicrobial sensibility of Streptococcus mutans serotypes to silver nanoparticles. Mater Sci Eng C. 2012;32(4):896–901.
22. Lu Z, Rong K, Li J, Yang H, Chen R. Size-dependent antibacterial activities of silver nanoparticles against oral anaerobic pathogenic bacteria. J Mater Sci Mater Med. 2013;24(6):1465–1471.
23. Abbaszadegan A, Ghahramani Y, Gholami A, et al. The effect of charge at the surface of silver nanoparticles on antimicrobial activity against gram-positive and gram-negative bacteria: a preliminary study. J Nanomater. 2015;2015.