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Application of Silver Nanoparticles in Dentistry: Review Article

Sangeeta Mahendrakar[1], Mahesh Patange[2]

[1]Sr. Lecturer, Public Health Dentistry, Al-Badar Dental College and Hospital, Kalaburgi
[2]Asst. Professor, Department of Chemistry, Reshmi UG and PG Degree College, Kalaburgi

ABSTRACT

There are a number of papers available that highlight nanoparticle uses in a variety of fields, including biology, biotechnology, and biomedicine. Researchers have recently become interested in nanoparticles owing to their structure-dependent chemical and physical properties. These nanoparticles have been shown to improve the diagnosis, prevention, and treatment of a variety of oral illnesses, particularly in dentistry. Furthermore, shape, biocompatibility, charge, colour, stability, and chemical reactivity are all physicochemical and biological characteristics that make nanoparticles suitable for use in dentistry. This research, which covered investigations from 2010 to 2022, examined the application of silver (Ag) nanoparticles in dentistry.

Keywords: Biomedicine, dentistry, oral diseases, silver nanoparticles

1. INTRODUCTION

Recently, nanotechnology has attracted the attention of the scientific community due to its applications in various fields such as optics [1], electronics [2], drug delivery [3], catalysis [4], environmental health [5], cosmetics [6], biomedical sciences [7], healthcare [8]. Nanotechnology has made a significant contribution to dentistry in recent years. However, among metallic nanoparticles, silver nanoparticles have shown great applications in the field of dentistry [9-12]. Because of their antibacterial qualities and biological activities, Ag nanoparticles have been identified as a possible contender against fungi, bacteria, and viruses [9-12]. Ag nanoparticle's antibacterial action is mostly accompanied by the release of Ag^+ ions and their oxidative potential [13,14]. It has been reported that when Ag^+ ions enter a bacterial cell wall, the structure of the cell membrane changes, causing the bacterial envelope to be damaged [11,15,16]. As a result, the change in structure and morphology of the bacterial cell wall can be noticed. However, Ag nanoparticles have the ability to kill 650 different types of disease-causing germs [10,17]. There are several reports on the synthesis method of Ag nanoparticles including autoclave [18], gamma ray radiation [19], chemical reduction [20], micro emulsion [21], laser ablation [22], electrochemical method [23], and microwave [24]. Metallic nanoparticles generally have a high surface energy that causes agglomeration hence to avoid this issue capping agents are used [25,26]. Furthermore, in dentistry the most common synthesis is the chemical method [27]. The shape, size, and synthesis processes of Ag nanoparticles, on the other hand, have a big impact on their antibacterial properties [10,27]. The composition, morphology, surface chemistry and particle size distribution of the nanoparticles can be tuned to achieve improve properties. Because of their tiny size (10 nm), Ag nanoparticles behave differently than bulk materials chemically, biologically, and physically [11,28,29]. These improved properties are usually linked to nanoparticles with a high surface-to-volume ratio. However, high surface to volume ratio plays a major role to exhibit remarkable antibacterial activities even at lower filler concentration without affecting mechanical properties of composites [10,30].

Apart from their antibacterial characteristics, Ag nanoparticles have several advantages, including low toxicity, high biocompatibility with human cells, and low bacterial resistances [21,28,31]. As a result, Ag nanoparticles are now commonly employed in dentistry to develop antibacterial materials that extend the life of dental equipment and enhance oral health through treatments [32,33]. Ag nanoparticles-methyl polymethylmethacrylate (PMMA) [34,35], amorphous calcium-Ag nanoparticles-phosphate [36], chitalac-Ag [37], and nano Ag fluorides [38] are among the biomaterials developed by some researchers. Endodontics [39,40], implantology [41,42], restorative dentistry [43,44], and dental prosthetics [28,45] are some of the dental specializations that allow the use of Ag nanoparticles.

2. APPLICATIONS OF SILVER NANOPARTICLES IN DENTISTRY

Research on the Ag nanoparticles has been opened a new platform for the scientific community owing to their characteristic properties. These properties are generally responsible for performing the antibacterial activities with Ag nanoparticles.

A. Orthodontic treatment

The Ag nanoparticles can be used to treat the prevention of enamel caries in orthodontic patients. Some adhesive materials, such as resin-modified glass ionomers and composite adhesives containing Ag nanoparticles, can be used to prevent biofilm growth. To prevent enamel caries, orthodontic elastomeric modules such as ligatures can be combined with silver nanoparticles [46]. In such cases, streptococcus mutans attached to the materials gets affected after interaction with bacteria. However, by releasing Ag^+ ions, bacterial action around the brackets and wires can be prevented [47]. Additionally, the long-term antibacterial action of these materials can be sustained by the release of Ag^+ ions. As a result, these stand out as biocompatible. However, in such materials, delayed type hypersensitivity and negligible irritation are observed. Their mechanical characteristics, such as shear bond strength, are unaffected. [48].

B. Prosthetic treatment

Acrylic resins are widely used for the prosthodontic purposes because of their optical properties, biocompatibility and aesthetics. Long-term polymethylmethacrylate (PMMA) wearers have low fatigue resistance and microbial adhesion [49]. To improve the mechanical properties of PMMA, researchers are interested in incorporating nanoparticles such as zirconium oxide (ZrO) and titanium oxide (TiO_2), Silver (Ag) [50]. It is reported that removable dentures are extensively manufactured by acrylic resins. However dental infection such as denture stomatitis can occur as a result of opportunistic oral pathogens colonizing acrylic materials [32]. To inhibit the growth of bacteria such as Streptococcus mutans, Escherichia coli, and Staphylococcus aureus, Ag nanoparticles can be added to acrylic resin. Acrylic resin infused with silver nanoparticles has antifungal properties against Candida albicans adhesion, which is one of the most common opportunistic pathogens on denture bases, in addition to antibacterial properties [51]. In this context, different shapes and concentration of Ag nanoparticles were used to study the antimicrobial properties. These studies reported the significant decrease in microbial count and reduction in tensile bond strength of resins, hardness and liners. Vimbela et al [52] performed the antimicrobial study with different types of Ag concentration where significant reduction of *C albicans* were observed. Similarly, reduction in flexural strength and elastic modulus of Ag incorporated PMMA resins with 0.8 and 1.6 wt% were reported by Habibzadeh et al [53]. However, mechanical properties of the resin can be enhanced with incorporation of Ag nanoparticles. The concentration of Ag nanoparticles plays an important role in influencing the mechanical properties, the type of resin and the polar interactions between the PMMA chains and Ag nanoparticles [54]. The flexural strength and elastic modulus of the resin can also be increased with Ag nanoparticles. Moreover, they can increase the thermal conductivity and compressive strength of the acrylic base [55].

C. Restoration treatment

Resin composites play an essential role in dental restorations due to their excellent aesthetics, vivid translucence like natural teeth, good manoeuvrability, and acceptable biocompatibility [56]. However, secondary dental caries develops due to the uneven surface of restorative materials which are mainly responsible to accumulates the biofilm and plaque. It has been observed that most of the restorations failed due to the appearance of caries at the margins [57]. To solve this problem, a resin composite with specialized antibacterial properties and long-term durability is required. Several researchers have tried a number of different techniques to make the antimicrobial resin composites. In order to develop such materials, Ag nanoparticles can be added into resin composites and adhesive systems [58]. However, antimicrobial properties of these reinforced materials can be manifested even at very low concentrations, and hence these are helpful in preventing secondary dental caries [59]. In addition to their numerous inhibitory effects, the Ag nanoparticle containing restorative adhesives also interfere with biofilm formation due to cariogenic bacteria. The composite containing silver nanoparticles showed no measurable negative effects on fibroblasts, despite constantly releasing very low levels of silver ions [60]. Furthermore, the maximum lethal effect on microbial cell can be achieved by dispersing the Ag nanoparticles in biocompatible polymers. It is reported that the mechanical properties of porcelain can be improved by dispersing Ag nanoparticles in it. It has been found that the residual compressive stress generated by an ion-exchange reaction and differential thermal expansion of silver nanoparticles enhances porcelain's hardness and fracture toughness [61].

D. Endodontic treatment

A variety of materials have been used to treat endodontic diseases, but the success of these treatments is highly limited to biomaterials [11]. The removal of the complicated resistant polymeric biofilm structure is the primary objective of endodontic treatment. Biofilms are a major cause of root canal failure and secondary infection [62]. In order for root canal treatment to be successful, endodontic biofilms must be removed from canal walls, microorganisms must be eliminated, and thick, leak-proof fillings must be used [63].

There is significant interest in using nanoparticles for endodontic disinfection because of their clinically effective antimicrobial properties. Metallic nanoparticles are very effective in preventing the growth of bacteria. Many studies have shown that Ag nanoparticles can eliminate biofilm layers, which are the most common cause of secondary infections [59]. It was found that Ag nanoparticles and NaOCl (sodium hypochlorite) had similar bactericidal effects in an irrigation solution against E. faecalis when tested them against NaOCl at 5.25 % and Ag nanoparticles at low concentrations [11]. It is reported by Hiraishi et al [64] that those biofilms were completely eliminated after administered 3.8 % sodium diamine fluoride. In a different study measured the effectiveness of antibacterial solutions according to the application strategy and found that Ag nanoparticles solutions killed fewer bacteria and dissolved more biofilm than chlorohexidine (CHX) solutions [65]. Ag nanoparticles medicament gel with 0.02 % was found to be more effective than 0.01 % Ag nanoparticles gel, 0.01 % Ag nanoparticles irrigation solution or calcium hydroxide for treatment of biofilm structure [66]. Here, the anionic biofilm bacteria and cations of Ag nanoparticle of medicament interact with each other at an extended level. In another report it has been observed that Ag nanoparticles were effective against the *E. faecalis*, *Klebsiella pneumoniae,* and *Candida albicans* [67]. However, recently it has been found that the mixture of calcium hydroxide with Ag nanoparticles is more effective against the biofilm. However, gutta-percha is often used as filling materials in root canal treatment [68]. In order to investigate of leakage in obturated teeth, Shantiaee et al [69] developed gutta-percha coated Ag nanoparticles which shown less leakage. Furthermore, mineral trioxide aggregates (MTA) are widely utilised in dentistry for pulp capping, apexification, and perforation sealing. However, antimicrobial properties of MTA can be enhanced by adding antimicrobial agents in it. It has been noticed that Ag nanoparticles combined with MTA are very effective against anaerobic endodontic pathogens. The antifungal activity of Ag-containing MTA (i.e., modified MTA) against *C. albicans* was tested, and the results were found to be superior than unmodified MTA [32].

E. Periodontal treatment

Periodontal disorders are mainly associated with various types of microorganisms which can cause the inflammation and infection and damage the tissues that support the teeth, including gums, periodontal ligaments, and the alveolar bone [70]. However, control over inflammation can be managed through periodontal treatment, which disrupts the biofilm and suppresses inflammation [71]. This biofilm is made up of a mixture of aerobic and anaerobic bacteria that cause tooth cavities, periodontal disease, and abscesses. It is necessary to avoid further periodontal infections and tooth decay by eliminating biofilms. However, these biofilms have their own integrated structure that resists the microbials. In such cases, Ag nanoparticles, owing to their antimicrobial activities, can emerge as potential candidates to work against gram negative organisms. In order to this, Frankova et al [72] studied the effect of Ag nanoparticles on the normal human dermal fibroblasts (NHDFs) and normal human epidermal keratinocytes (NHEKs). These cells have a key role in wound healing, particularly in terms of inflammation, proliferation, and tissue remodeling. It has been found that the production of inflammatory cytokines (TNF- and IL-12) and growth factors (VEGF) by NHDFs and NHEKs, as well as the expression of COX-2, were reduced by Ag nanoparticles after 24 and 48 hours, but only at the maximal concentration of Ag nanoparticles (25 parts per million). As a result of the findings, it's assumed that NHEKs are more responsive to Ag nanoparticles than NHDFs, and that Ag nanoparticles might be useful in medical applications like wound treatment. In another study, it was revealed that antibacterial activity worked synergistically when Ag nanoparticles were combined with selected antibiotics. When coupled with Ag nanoparticles at concentrations below 1 mg/L, the synergistic impact resulted in a decrease in antibiotic MICs of at least one order of magnitude [73]. Similarly, cellulose-capped Ag nanoparticles inhibited gram-negative bacteria better than gram-positive bacteria, whereas sodium alginate Ag nanoparticles inhibited gram-positive bacteria better than gram negative bacteria. Indeed, these Ag nanoparticles may be useful in the treatment of periodontal diseases caused mostly by gram-negative bacteria [74]. It has been reported that antibacterial activity of Ag nanoparticles against oral anaerobic bacteria is a function of particle size [75]. In another report, Ibrahim et al [76] studied the nanoparticle's antimicrobial effect on human pathogenic organisms. Ag nanoparticles shown more activity towards the gram negative bacteria (*E. coli and P. aeruginosa*) than the positive bacteria (*B.subtilis and S. aureus*). In vitro study was performed by Rani et al [77] to evaluate the colonization and penetration of specific bacteria on Ag nanoparticle impregnated guided tissue regeneration membrane. The obtained results are very useful to further conduct the study on periodontal pathogens. Recently, Steckiewicz et al [78] developed novel Ag nanoparticles in conjugation with chlorhexidine (CHL) or metronidazole (PEG-MET). Both these compounds show effective antimicrobial activity against bacteria and fungi. However, it has been found that the Ag-CHL composite has more potential antimicrobial activity than the Ag-PEG-MET composite.

F. Implant treatment

In dental surgery, implants are frequently used to replace missing teeth. However, achieving and maintaining osseointegration and the gingival epithelial interface with implants is a challenging task. The long-term success of implant treatment is dependent on mechanical, functional and biological factors [79]. It has been seen that titanium (Ti) and zirconium dioxide (ZrO_2) -based implants are being used for implant treatments [80]. However, peri-implantitis is a severe complication that can result in bone loss around the implant, eventually leading to implant failure. Thus, to resolve this issue, the Ti surface can be modified by using some antibacterial agents which is able to eliminate the peri-implant diseases [11]. In this context, the coating of Ag nanoparticles has been suggested by several researchers for implantation since Ag is a bioactive source for implant surfaces. In literature, it is reported that Ag nanoparticles embedded in Ti can be developed by a one-step silver plasma immersion ion implantation process for the biomedical applications. As reported there, Ag nanoparticles embedded in Ti has more potential to inhibit the *S. aureus and E. coli* strains. However, it simultaneously increases the proliferation of the osteoblast-like cell line MG63. This may be attributed to the interaction of the attached cells under the influence of the Ag and Ti matrix, which causes the formation of micro-galvanic couples [81]. Similarly, Ag-filled hydrogen titanate ($H_2Ti_3O_7$) was developed by Wang et al [82] to study the bactericidal effect. In this study, it has been observed from the results that Ag-filled hydrogen titanate ($H_2Ti_3O_7$) nanotube-layered titanium foils have a high bacteriostatic rate (>99%) and long-term release capability of Ag^+ ions. At same time, their excellent cytocompatibility and high osteogenic potential compared to pure Ti make them implantable biomaterial. In another report, the antimicrobial potential of Chitlac–nAg system has been investigated by Marsich et al [83]. Moreover, the

Chitlac–nAg coating was tested for its potential to prevent the growth of biofilms on BisGMA/TEGDMA samples when compared to samples that were uncoated. Additionally, the potential antimicrobial activity was also evaluated for measuring the durability of the release efficiency of Ag^+ ions. According to the study, the novel class of material is biocompatible, which makes it suitable for clinical applications where metallic implants are required. Zhu et al. [84] developed Ag nanoparticles that were fabricated in situ and immobilized on titanium surfaces. Specifically, the antibacterial study has been conducted on *F. nucleatum* and *S. aureus*, commonly suspected pathogens causing peri-implant infections. Ag nanoparticles on titanium surfaces inhibit pathogen growth, regardless of Ag^+ ion release. The fact that *F. nucleatum* was more susceptible to Ag nanoparticles is most likely due to its less rigid cell wall structure. In addition, a rat bone marrow mesenchymal stem cell (rBMSCs) model was also used to test their biocompatibility. Ag nanoparticles immobilised on acid-etched titanium surfaces did not exhibit cytotoxicity. In conclusion, the study indicates that Ag nanoparticles that were fabricated in situ and immobilized on titanium surfaces could provide balanced antibacterial and osteogenic performance, showing promise for safe, long-term clinical application. Zhong et al [85] investigated the antibacterial activity and long-term biocompatibility of Ag nanoparticles coated with lysozyme-primed phase transited titanium surfaces. The authors proposed that their strategy of coating titanium surfaces with phase-transited lysozyme (PTL) can give an incredibly simple, green, and strong alternative to standard time-consuming chemical production and costly titanium surface preparation strategies. Thus, the scientists concluded that using the layer of PTL method, it is possible to build multilayers loaded with osteogenic growth factors, cytokines or functional components, and antibacterial agents on titanium surfaces. This, in turn, helps to avoid implant-associated infection and promotes early osseointegration of an implant. This also facilitates in the fabrication of Ag nanoparticles coatings on various medical devices by using the substrate-independent PTL as the base layer.

CONCLUSION

Ag nanoparticles shows excellent biological activities such as antibacterial, antifungal and antiviral because of their high surface to volume ratio. In order to make them applicable in the field of dentistry as dental materials, Ag nanoparticles can be added in various types of resins. Such types of dental materials exhibit improved mechanical strength and antimicrobial properties. Despite the lack of evidence of the exact mechanism of antimicrobial effect, researchers believe that the antimicrobial properties of Ag nanoparticles may be associated with the continuous release of Ag^+ ions to kill microbes. The growing number of studies in the field of dentistry with Ag nanoparticles has made them potential candidates for prosthetic, periodontic, endodontic, restorative, and implant treatments.

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