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Research Paper

Silver Nanoparticles – A New Era In Antimicrobials: A Review

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ABSTRACT: *With the introduction of nanotechnology, there has been a continually growing interest in its application in medicine and dentistry. Metallic nanoparticles have fascinated scientists for over a century and are now heavily utilized in biomedical sciences and engineering. Silver nanoparticles are one of the most vital and fascinating nanomaterials among the several metallic nanoparticles that are involved in biomedical applications. Because of its greater surface area and small particle size, silver nanoparticles possess excellent anti- microbial properties without affecting the mechanical properties of the material to which it is incorporated. This review aims to provide an overview of the antibacterial mechanism of silver nanoparticles and their uses in the various fields of dentistry, highlighting their applications in Conservative Dentistry and Endodontics.*
KEYWORDS: *Nanotechnology, Metallic nanoparticles, Silver nanoparticles, Biomedical applications Anti-microbial properties*

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I. INTRODUCTION

Nanotechnology is a science and engineering which involves the synthesis, characterization, and application of materials by controlling their shape and size at the nanoscale.[1] It has been applied as an innovative concept for the development of many dental materials with better properties and anticaries potential.[2]

Silver nanoparticles (AgNPs), or nano-silver, are nanoparticles of silver of between 1 nm and 100 nm in size containing 20 to 15,000 silver atoms. They have been one of the most popular topics of study in recent decades because of their outstanding antimicrobial activity even at low concentrations including antibacterial, antifungal, antiviral, and anti-inflammatory effects.[3] Due to their large surface area more atoms come in contact with the reactant providing better bio-availability and anti-microbial action without altering the mechanical properties of the material.[4] In addition, they are economical and have shown low cytotoxicity and favorable immunological response.[5] Therefore, silver nanoparticles are widely used in biomedical applications.

In dentistry, the anti-microbial action of silver nanoparticles is used to develop materials with improved quality for a better treatment outcome.[5]

This review aims to provide an overview of the antibacterial mechanism of silver nanoparticles and their uses in the various fields of dentistry, highlighting their applications in Conservative Dentistry and Endodontics.

II. ANTIBACTERIAL ACTION

The antimicrobial activity of Silver nanoparticles is very pronounced and, more significantly, has the advantage of having the ability to overcome the usual mechanisms of resistance formation.[3] Silver nanoparticles, at biocompatible concentrations, can also synergistically increase the antibacterial effectiveness of antibiotics against multiple bacterial species. Moreover, antibiotic resistance shown by some bacterial species tested could be overcome by the addition of silver nanoparticles, thus broadening the overall antibacterial potential.[6]

Silver nanoparticles can also continually release silver ions, which, owing to electrostatic attraction and their affinity to sulphur proteins, can in turn adhere to the cell wall and cytoplasmic membrane of microorganisms. This enhances the permeability of the cytoplasmic membrane, thereby leading to the disruption of the bacterial envelope.[5] Silver ions can also inhibit the synthesis of proteins by denaturing ribosomes in the cytoplasm.[5]

In addition to being able to release silver ions, silver nanoparticles can themselves kill bacteria. They can accumulate in the pits that form on the cell wall after they anchor to the cell surface.[7] Silver nanoparticles, due to their small size, also have the ability to penetrate bacterial cell walls and subsequently change the structure of the cell membrane.[7] The denaturation of cytoplasmic membrane can rupture organelles, and even result in cell lysis.[5]

Silver nanoparticles demonstrates varying activity in inhibiting the growth and production of biofilms of S. epidermidis, and this is related to the size of nanoparticles applied.[8] The highest efficacy against standard S. epidermidis strains was demonstrated by particles of size 10 nm and at a concentration of 5 µg/mL.[8] For the strains which form biofilms, the silver nanoparticles activity increased with increasing particle size.[8]

The antibacterial activity is more evident in Gram-negative bacteria than in Gram-positive and it was also observed that silver nanoparticles with a positive charge had the most potent antimicrobial activity against all tested bacterial species.[9] Silver nanoparticles should not be larger than 50 nm, and those of 10 and 15 nm have increased activity.[3] This is because smaller silver nanoparticles have a higher surface area-to-volume ratio, which permits them to associate more with cell membranes than larger nanoparticles. Silver nanoparticles in the range of 1 to 10 nm have shown the highest antimicrobial activity.[3]

Researchers have also demonstrated that silver nanoparticles release silver ions faster in acidic solution than they do in neutral solution and capping agents can be used to modify their surfaces to change their dissolution behavior.[5]

III. APPLICATIONS IN CONSERVATIVE DENTISTRY

3.1 Resin Restorations

Silver nanoparticles can be added to adhesive systems and composite resins for the prevention of secondary caries by bringing notable antimicrobial properties at low concentration.[10] Restorative adhesives containing silver nanoparticles show widespread inhibitory action against cariogenic bacteria which in turn interfere with the biofilm formation.[5] Moreover, no significant adverse effects were seen on fibroblasts by the action of composite resin with silver nanoparticles because the silver ions released per day are very low.[5]

Silver nanoparticle incorporation in dental materials can cause cosmetic changes of tooth-colored materials. However, 0.5– 1.0% concentrations have shown to present the antibacterial properties of silver while having a less detrimental effect on the color of composite resins.[2] In vitro studies on the effects of a composite containing 2.7 nm silver nanoparticle well-dispersed in the resin matrix showed a high antibacterial efficacy without significantly compromising composite color or mechanical properties.[2] Strong antibacterial properties were obtained using a silver nanoparticle filler level of 0.05% in primer and adhesive without decreasing the microtensile dentin bond strength nor causing any noticeable change in the color of primer and adhesive.[11]

Silver nanoparticle-containing infiltrant resin can hamper the re-formation of microbial biofilms, thus increasing the durability of the infiltrated lesion without compromising its mechanical properties and preventing development of recurrent or secondary caries.[12]

More recently, the novel NACP (nanoparticles of amorphous calcium phosphate) nanocomposites containing silver nanoparticles is promising for caries-inhibiting restorations due to their antibacterial action along with the Ca and PO4 release and acid neutralization capability.[13]

3.2 Dentin Hypersensitivity

Dentinal hypersensitivity is one of the most common complaints from patients in dental clinics. The dentinal tubules of a hypersensitive tooth have twice the diameter and eight times the surface density of those in non-sensitive teeth.[14] Dental nanorobots could selectively and precisely close damaged tubules thus offering a quick and permanent cure.[14]

3.3 Biofilm

A biofilm is an assemblage of surface-associated microbial cells that is enclosed in an extracellular polymeric substance matrix. Dental plaque is a structurally and functionally organized biofilm.

Cariogenic bacteria, such as S. mutans and lactobacilli, in the dental plaque can metabolize carbohydrates to acids, causing demineralization of the tooth and the tooth-restoration margins beneath the biofilm. Incorporation of silver nanoparticles into composites containing amorphous calcium phosphate nanoparticles can cause a reduction in the biofilm Colony Forming Unit (CFU) counts, metabolic activity, and lactic acid production.[13] In vitro studies have shown the application of silver nanoparticles as a useful antimicrobial against S. mutans adhesion, growth, and subsequent biofilm formation in dentine lesions.[15]

However, due to its complicated architecture, biofilm is relatively tolerant to silver nanoparticles. Silver nanoparticles' diffusion coefficients, which are generally related to size and physicochemical characteristics, determine their mobility and bioavailability in biofilm.[5]

3.4 Bond Strength

Pre-treatments of dentin and enamel with Silver nanoparticles, Titanium nanoparticles, and Zinc nanoparticles do not have any adverse effect on the bond strength values of composite resin to coronal dentin, with Silver nanoparticles showing the best results.[16] Silver nanoparticle solution, when used as an irrigation agent in post space prior to fiber post cementation process, also show no negative effect on the interface permeability and bond strength values of fiber posts to intra-radicular dentin.[17] Moreover, dentin pre-treatment with Silver nanoparticles have shown to positively affect the bond strength of etch-and-rinse and self-etch adhesives.[18] Silver nanoparticles pre-treatment might provide wettable surface and improve infiltration of adhesive resin into dentin surface and increase bond strength to coronal dentin.[19]

NACP and silver nanoparticles can also be incorporated into bonding agents to combine the Ca and P ions from NACP with the antibacterial activity from Nag, leading to the inhibition of biofilms and caries while maintaining a strong dentin bond strength.[20]

3.5 Glass Ionomer Cement

Increase in the amounts of silver nanoparticles in Glass Ionomer have shown to decrease the number of colonies of S. mutans and S. sanguinis bacterial species.[21] In addition, both bacterial species exhibit comparable sensitivity to silver nanoparticles.[21]

A new Nanosilver-Glass ionomer cement was developed and proved to have an antibacterial effect by diffusion, suggesting silver ions undergo oxidative dissolution from the cement matrix.[22] This in turns leads to the assumption that they are efficient in arresting caries and preventing the development of oral biofilms on their surface.[22]

3.6 Dental Porcelain

Dental porcelains are brittle in nature due to their low tensile strength. This commonly results in the fracture or chipping of ceramic restorations necessitating their replacement.

Silver nanoparticles can be added to porcelain to enhance its mechanical properties such as hardness and fracture toughness. This reinforcement can be attributed to the residual compressive stress generated by an ion-exchange reaction and differential thermal expansion of silver nanoparticles.[23] It was observed that the addition of silver nanoparticles to Noritake Super (NS) porcelain significantly increased its fracture toughness and Vickers hardness.[24]

Addition of silver nanoparticles to dental porcelain can also increase the fatigue parameter which characterized its subcritical crack growth (SCG) behaviour.[25] This parameter grew as the concentration of silver nanoparticles added increased, suggesting that it might be effective in inhibiting the fatigue fractures of dental porcelains in the oral cavity.[25]

3.7 Caries Inhibition

Dentin treated with silver nanoparticles showed shallower lesion depth and less mineral loss than dentine in groups without silver nanoparticles ($p < 0.01$).[26] In addition, caries in groups treated with Silver nanoparticles also underwent more effective remineralization.[26] Sodium fluoride (NaF) solutions that incorporate silver nanoparticles have shown to remineralize artificial dentine caries without significant staining and silver nanoparticles when adjunctively applied with sodium fluoride on carious dentine surfaces do not influence the remineralizing effect of sodium fluoride nor the anti-biofilm effect of silver nanoparticles.[26]

Polyethylene glycol-coated silver nanoparticles (PEG-Silver nanoparticles) were shown to be stable at a 2.5% sodium fluoride solution.[27] Because it has antibacterial activity against S. mutans and no tooth-staining effect, fluoridated PEG-Silver nanoparticles can be used as an anti-caries agent.[27] The use of sodium fluoride solution with PEG-Silver nanoparticles can remineralize artificial dentin caries and inhibit collagen degradation.[28] It may be a better anti-caries agent than silver diamine fluoride due to its non-staining ability.[28]

IV. APPLICATIONS IN ENDODONTICS

Complete elimination and prevention of bacteria from the root canal system is an essential element for the successful endodontic treatment. However, it has been shown that, even after meticulous root canal instrumentation, thorough root canal disinfection, and obturation, bacteria still persist in the root canal system.[29] Enterococcus faecalis is commonly associated with persistent peri-radicular lesions.[30] It possess certain virulence factors which makes it the most resistant microbe such as cytolysin, lytic enzymes, aggregation substance, pheromones, and lipoteichoic acid.[31] Moreover, it can invade dentinal tubules and cementum, resist most of the root canal disinfectants and survive longer periods in dentinal tubules even in nutrient depleted conditions such as an obturated canal.[30] Therefore, newer advancements to control and eliminate such resistant microbes have to be developed to prevent reinfection and achieve a successful treatment. Nanoparticle antimicrobial agents can be used as an alternative disinfection method against intracanal infections due to their ability to disrupt biofilm and prevent bacterial adhesion to dentin.[32]

Sodium hypochlorite is regarded as the gold standard for chemical disinfection of root canals in endodontic treatment. However, sodium hypochlorite reduces the elastic modulus and flexural strength of dentine and causes toxic damage to the periapical tissues.[5] A study found that root canal irrigation with silver nanoparticle solution did not significantly affect the mechanical properties of dentine.[33]

The use of silver nanoparticles as a medicament, in the form of a gel, and not as an irrigant has been suggested to disrupt E. faecalis biofilm.[32] Dong et al. reported 0.1% and 0.2% nanosilver gel is more effective on E. faecalis biofilm compared to other disinfectants such as CHX and camphorated phenol.[30]

Gutta-percha, which is most commonly used in root canal obturation, has limited antibacterial properties. However, gutta-percha coated with silver nanoparticles was found to have antibacterial and antifungal properties and was as effective as conventional gutta-percha in preventing bacterial leakage.[34] In addition, there is no difference in the cytotoxicity of fibroblasts and subcutaneous tissue reaction or inflammation between gutta-percha-coated silver nanoparticles and conventional gutta-percha.[5]

Due to its many advantages such as low solubility, low cytotoxicity, biocompatibility, and the ability to induce hard tissue formation, the mineral trioxide aggregate (MTA) has been used in many indications including sealing perforations, repair of external or internal root resorption, retrograde filling, pulp-capping agent in vital pulp therapy procedures, apexification, and as intraorifice barrier. A study done to evaluate the antimicrobial properties of Angelus white mineral trioxide aggregate (MTA) and the mixture of MTA with silver nanoparticles (1% weight; MTA/SN) shows that the antimicrobial activity of MTA improved with incorporation of silver nanoparticles without altering its biocompatibility.[35] The addition of silver nanoparticles to white MTA increased the pH, lowered the solubility and the initial and final setting times.[36] Silver nanoparticles, being an excellent radio-opacifier, can also incorporated be as a radio-opacifier for MTA to overcome the latter's disadvantage of having low radiopacity, which makes it difficult for any radiographic observation.[37]

V. APPLICATIONS IN PROSTHODONTICS

Opportunistic oral pathogens can colonize acrylic materials, which are commonly used to fabricate removable dentures, causing dental infections such as denture stomatitis. Silver nanoparticles can be added to acrylic resin to inhibit the growth of bacteria such as Streptococcus mutans, Escherichia coli and Staphylococcus aureus.[5] Inhibition of the growth of Candida albicans by Silver nanoparticles (10–200 ppm) in denture liner material and silver nanoparticles (20.0–30.0%) in denture acrylic disks have been demonstrated.[38] Moreover, it has been observed that the impact strength, transverse strength, deflection and modulus of elasticity of acrylic denture base were also improved by adding silver nanoparticles to the light-cured acrylic material.[39]

Incorporation of silver nanoparticles to alginate have shown a time-dependent limited release of silver through biofilm structures, which is a desirable feature for persistent antimicrobial effects.[40] Significant cell killing on biofilms of Gram positive and negative bacteria was observed from the silver nanoparticle alginate gel.[40]

VI. APPLICATIONS IN ORTHODONTICS

The use of antibacterial release materials such as silver nanoparticles may help to maintain good oral hygiene[41] and for the prevention of enamel caries (white spot lesion), which is a common complication during orthodontic treatment.[1]

Effective antibacterial properties have been described for silver nanoparticle adhesives and association of orthodontic ligatures with silver nanoparticles have shown decreased enamel demineralization caused by the accumulation of bacterial plaque, without affecting the mechanical characteristics of the material itself.[41] It has also been observed that the modification of the surface of orthodontic brackets with silver nanoparticles can prevent the development of dental plaque and dental caries during orthodontic treatment.[42] The release of silver ions can affect the adhesion of Streptococcus mutans to the materials, thereby inhibiting bacterial action around brackets and wires.[5]

VII. APPLICATIONS IN DENTAL IMPLANTS

Peri-implantitis is an infectious disease that causes inflammation of the gum and the bone structure around a dental implant ultimately leading to implant failure.

This can be prevented by the application of nano-silver coating, which is a promising material that can be used for implant abutments and prostheses.[43] Additionally, titanium embedded with silver nanoparticles can enhance bone mineral density, bone formation and trabecular pattern, with no harm to tissues adjacent to dental implants.[5]

VIII. APPLICATIONS IN PERIODONTOLOGY

Silver nanoparticles have a better bacteriostatic and bactericidal outcome when used at five times lower concentration than chlorhexidine.[3]

Guided tissue regeneration membrane with silver nanoparticles, for the treatment of intrabony defects, have shown reduced adherence and penetration of bacteria, hence improving the clinical success of the treatment.[44]

IX. APPLICATIONS IN OTHER BIOMEDICAL FIELDS

Silver nanoparticles are used for drug delivery, medical imaging and molecular diagnostics as well as in therapeutics, such as surgical mesh, fabrication of artificial joint replacements, wound dressing and medicament for promotion of wound healing.[5]

Silver nanoparticles have also been used in cancer therapeutics to kill drug-resistant tumor cells.[1]

Moreover, due to their impressive anti-microbial properties, they are widely used in the medical field for sterilization of wound sutures, endotracheal tubes, surgical instruments, bone prosthesis, etc.[4]

X. CONCLUSION

The enhanced anti-microbial properties of silver nanoparticles have resulted in their widespread application in different biomedical and dental fields. In addition, incorporating silver nanoparticles into dental materials may even improve their mechanical properties.

In Conservative Dentistry, silver nanoparticles have shown to increase the antimicrobial properties of restorative materials without adversely affecting their mechanical features like bond strength and color. Studies have shown significant evidence of their effect in caries inhibition and dentin hypersensitivity reduction.

Tolerance to silver nanoparticles have been demonstrated by biofilms due to their unique and complex structural arrangement.

In Endodontics, incorporating silver nanoparticles in intracanal irrigants and medicaments have been suggested for intracanal disinfection. Antimicrobial action of nano-silver gel against E. faecalis biofilm, which is an intracanal bacteria commonly associated with reinfections and persistent peri-radicular lesions, has been observed. Addition of silver nanoparticles to gutta-percha and MTA has also shown favorable results.

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