

Antiseptic Effects of Silver Nanoparticles in Dental Practice: A Narrative Mini-Review

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Objectives The release of secretions and aerosols during dental procedures is a common way of transmitting viral infections in the dental environment. Therefore, the use of effective antiviral materials such as Silver-containing solutions at non-cytotoxic doses can be of great importance. The present study aimed to review the antiviral effects of silver nanoparticles on infectious viruses for the purpose of disease prevention.

Methods In this review, databases, including Web of Science, PubMed, Medline, and Google Scholar, were electronically searched for relevant articles, using the following keywords: “nano-silver”, “antiviral”, “virus”, and “disinfection”. A total of 291 relevant articles published during 2010-2022 were found; according to the inclusion criteria, only 20 studies were directly included in this study. Full-text articles written in English, which openly examined the cellular effects of silver nanoparticles on infectious viruses, were carefully selected.

Results Using nanoparticles such as silver nanoparticles for dental practice disinfection purposes is documented and can be advantageous for their antiviral effects.

Conclusion Incorporating nanoparticles into dental materials is the most common application of nanoparticles in dentistry, which leads to an increase in antimicrobial properties of dental materials. Cancer diagnosis and treatment, regeneration of alveolar bone defects, and treatment of tooth hypersensitivity are the other emerging applications of nanoparticles in dentistry.

Keywords Anti-Infective Agents; Nanoparticles; Dentistry; Nanotechnology; Nanostructures

Introduction

In recent years, the prevention of nosocomial infections in the elderly and patients with a compromised immune system has been recognized as a serious problem. The need for most dental treatments, especially in these groups, has attracted the attention of investigators to the health of the environment and water used in the tubes of dental units. Although the use of water during dental treatments is critical, dental unit waterlines (DUWL) are commonly polluted with microorganisms in the environments of dental clinics.^{1,2} Dissemination of these particles, from water and saliva in the oral cavity to the clinic air in the form of aerosols, leads to the spread of contaminants in the air.²

Besides common oral bacteria, aerosols may contain pathogenic bacteria and viruses, such as human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, herpes simplex virus, influenza virus, rhinovirus, coronavirus, and other infectious agents.³⁻⁶ Although conventional water cleansing measures, such as filtration⁷, flushing⁸, biocides and chemical disinfectants⁹, and ultraviolet light¹⁰, have been somewhat successful, efforts to find safer methods have led scientists to use the latest technologies, such as nanotechnology.¹¹

Materials signified as nanomaterials are smaller than 100 nm in at least one dimension. When reduced to this size, these materials show unique size-dependent properties which differ from those of their larger counterparts, many of which have been discovered for water and wastewater treatments. The scalable size-dependent properties which have been exploited are the properties of nanomaterials

related to a large specific surface area, such as fast dissolution, high reactivity, and strong sorption.¹² In this regard, nanoemulsions have been technologically advanced using nanoparticles (NPs) of materials, such as silver. These nanomaterials show prolonged biochemical activity against coated viruses, spores, fungi, and bacteria.¹³ A substantial reduction in live bacteria observed in DUWL tubes, treated with nanoemulsions, showed that these nanoemulsions effectively decreased DUWL Bacterial communities.¹¹

Materials and Methods

The Web of Science, PubMed, Medline, and Google Scholar databases were searched for relevant articles, using the following keywords: “nano-silver”, “antiviral”, “virus”, and “disinfection”. About 291 relevant articles published during 2010-2022 were found; according to the inclusion criteria, only 20 studies were directly used in this study. As the inclusion criteria of this study, full-text English studies directly examining the cellular effects of silver NPs (AgNPs) on infectious viruses were selected and reviewed. The exclusion criteria were non-English articles, case reports, and articles without full-text access.

Literature review

The use of nanotechnology is a relatively new and effective approach for disinfection. Nanotechnology, which refers to the targeted alteration of matter into particle size in the range of less than 100 nanometers, facilitates the development of newer materials and devices. This advantage of nanotechnology is attributed to the high reactivity of NPs due to their great surface-to-volume

ratio.¹² Nanomaterials are smaller than 100 nanometers in at least one dimension. When these materials are reduced to this size, they show exclusive size-dependent properties which differ from those of their larger counterparts. The exact properties of these materials are the general properties of nanomaterials related to a large specific surface area, such as fast dissolution, high reactivity, and strong adsorption.¹²

Nanoemulsions containing nano-silver are exclusive disinfectants with a uniform population of high-energy droplets.¹³ In 2010, Humberto H Lara et al.¹⁴ conducted an in vitro study on the results of pretreatment with silver nanoparticles on HIV-1. In this study, commercial 30-50 nm silver NPs, coated with 0.2% polyvinylpyrrolidone (PVP), were used. Stock solutions of silver NPs, silver sulfadiazine (Sigma-Aldrich®), and silver nitrate (Sigma-Aldrich®) were prepared in RPMI-1640 cell culture media. Next, cytotoxicity assays, HIV-1 viral inhibition assays, virus adsorption assays, and cell-based fusion assays were performed.

For the treatment of HIV-1 cell-associated virus, chronically HIV-1-infected peripheral blood mononuclear cells (PBMC) and the human lymphoid cell line (H9 cells) were incubated with serial two-fold dilutions of AgNPs for one minute for PBMCs and 60 minutes for H9 cells. It was found that after five minutes of exposure to the virus, the infection of viral particles decreased; this effect was enhanced after 60 minutes of exposure. The results showed that AgNPs acted directly on the virion and inactivated it. AgNPs were effective against HIV-1 transmission due to the chronic contamination of PBMC and H9 cells and reduced the transmission rate by 50%. Moreover, silver ions have been shown to be less effective than AgNPs, as AgNPs inactivate HIV particles in a short period and show antiviral activities in the early stages of viral replication.¹⁴

In an in vitro study in 2018, Park et al.¹⁵ investigated the effects of AgNPs, as suitable antiviral agents against influenza virus A (IVA), which is one of the main causes of seasonal flu. In this study, Ag₃₀-SiO₂ particles with a diameter of 400 nm were used, which contained silver NPs with a diameter of 30 nm. It was observed that Ag₃₀-SiO₂ particles could prevent IVA which was dependent on the dose of Ag₃₀-SiO₂. However, when the RT-PCR method was used, only a reduction of 0.5-10 log in IVA was detected at 5°C and 20°C. The results showed that interaction with viral components in the membrane was the main antiviral mechanism of Ag₃₀-SiO₂ particles. Therefore, these particles can cause nonspecific damage to various components of IVA and be used to passively control the virus.¹⁵

In 2014, an in vitro study by R.L. Hu¹⁶ evaluated the interaction of nano-silver with HSV-2 to determine whether nano-silver could cause a major reduction in

progeny viruses with poor cytotoxicity for the host cells. According to their findings, although an AgNP concentration of 100 µg/mL or higher was toxic to Vero cells, 50 and 25 mg/mL of AgNPs could significantly inhibit the generation of HSV-2 progeny. Even at a lower concentration, such as 6.25 µg/mL, nano-silver showed a significant preventive effect on the titer of progeny viruses. At a higher concentration, such as 100 µg/mL, nano-silver exerted more significant toxic effects on the Vero cells. Coating of cells with polysaccharides or other substances could successfully protect the cells against toxicity of AgNPs. However, this coating significantly affected the interaction between AgNPs and HSV-2. Regardless of coating with polysaccharides, AgNPs had limited toxic effects on the Vero cells. Virus replication was inhibited with 100 µg/mL of AgNPs, while the virus progeny significantly reduced using 6.25 µg/mL of AgNPs.¹⁶

In an in vitro study by Wang et al.¹⁷ in 2021, a zero-valent nano-silver/titania-chitosan (nano-Ag⁰/TiO₂-CS) filter bed, whose broad-spectrum antimicrobial efficacy had been previously proven, was applied to remove viral aerosols and minimize the risk of airborne transmission. The photochemical deposition technique was used to synthesize the antiviral component of nano-Ag⁰/TiO₂-CS. The surface morphology, essential composition, and microstructure of nano-Ag⁰/TiO₂-CS were analyzed by scanning electron microscopy/energy dispersive X-ray spectroscopy and transmission electron microscopy, respectively. The MS2 bacteriophages were used as surrogate viral aerosols.

The antiviral efficacy of nano-Ag⁰/TiO₂-CS was estimated by the MS2 plaque reduction assay (PRA) and filtration experiments. In the filtration experiments, the MS2 aerosols passed through a nano-Ag⁰/TiO₂-CS filter, and the MS2 aerosol exclusion efficiency was evaluated using an optical particle counter and the culture method. In the MS2 PRA, 3 g of nano-Ag⁰/TiO₂-CS inactivated 97% of MS2 bacteriophages in 20 mL of liquid culture (2±0.5×10¹⁶ PFU/mL) within two hours. The removal competence of nano-Ag⁰/TiO₂-CS filter (thickness, 6 cm) for MS2 aerosols reached up to 93%. More than 95% of MS2 bacteriophages on the surface of nano-Ag⁰/TiO₂-CS filter were inactivated within 20 minutes.¹⁷

In another study in 2021, Merkl et al.¹⁸ examined nanoparticle coatings of three antimicrobial materials (Ag, CuO, and ZnO) deposited on both solid smooth surfaces and porous filter media, and their activities against SARS-CoV-2 viability were compared using a viral plaque assay. These nano-coatings were manufactured by self-assembly of aerosol NP during flame synthesis. Of the three studied nanomaterials, AgNPs showed the strongest antiviral activity as coatings, while copper oxide exhibited moderate activity, and zinc oxide did not significantly reduce the virus infectivity. Therefore, nano-silver and copper oxide showed potentials as antiviral coatings on solid surfaces

and filter media to reduce the transmission and superspreading events, while providing important information for any current or future pandemic mitigation efforts.²⁵

According to our review of previous studies, AgNPs exert adequate antiviral effects on infectious viruses, including AIDS (HIV-1), IAV, herpes simplex virus, and coronavirus. The findings of the reviewed articles are summarized in Table 1.

Results

Table 1- Summary of reviewed articles

Authors	Year	Type of procedure	Type of examined virus	Results
Lara et al. ⁽¹⁴⁾	2010	In vitro	HIV-1	After five minutes of exposure of nano-silver particles to the virus, the infection of viral particles decreased.
Park et al. ⁽¹⁵⁾	2018	In vitro	IVA	The main antiviral mechanism of Ag30-SiO ₂ particles was interaction with viral components located on the membrane.
Hu et al. ⁽¹⁶⁾	2014	In vitro	HSV-2	Nano-silver caused a significant reduction in progeny viruses with poor cytotoxicity for host cells; viral replication was inhibited using 100 µg/mL of AgNPs, while the virus progeny was significantly reduced using 6.25 µg/mL of AgNPs.
Wang et al. ⁽¹⁷⁾	2021	In vitro	MS2 bacteriophages in viral aerosols	In the MS2 PRA, 3 g of nano-Ag ⁰ /TiO ₂ -CS inactivated 97% of MS2 bacteriophages in 20 mL of liquid culture within two hours. The removal efficiency of nano-Ag ⁰ /TiO ₂ -CS filter for MS2 aerosols reached up to 93%. More than 95% of MS2 bacteriophages on the surface of nano-Ag ⁰ /TiO ₂ -CS filter were inactivated within 20 minutes.
Merkl et al. ⁽¹⁸⁾	2021	In vitro	SARS-CoV-2	Nano-silver showed potentials as an antiviral coating material on solid surfaces and filter media to minimize transmission and superspreading events, while providing critical information for any current or future pandemic mitigation efforts.

Discussion

AgNPs are highly effective particles, which inactivate viruses in a short period and show antiviral activity in the initial stages of viral replication. These NPs have a high surface area-to-volume ratio, as well as characteristic chemical features. They directly inactivate virions and are active against HIV-1 transmission. Regarding IAV, the main antiviral mechanism of c in the form of Ag30-SiO₂ is the interaction with viral components located on the virus membrane. These particles have been also shown to affect HSV-1 and cause a significant reduction in progeny viruses with poor cytotoxicity for the host cells.

It has been reported that nano-gold and nano-silver accelerate the treatment of herpes disease, and nano-silver shows antimicrobial activity against a broad spectrum of viruses, including HSV. Regarding the antiviral mechanism, inhibition of viral replication is attributed to a combination of attached NPs, facilitating capsid degradation, and more importantly, blockade of cell attachment, cell entry, and protein/genome injection. Using the nano-Ag⁰/TiO₂-CS filter, the removal efficiency for MS2 aerosols reached up to 93%, and more than 95% of MS2 bacteriophages on the surface of nano-Ag⁰/TiO₂-CS filter were inactivated within 20 minutes.

Given the proven antiviral effects of AgNPs, further studies are suggested to evaluate the clinical application of these NPs in the form of mouthwash before dental procedures to reduce the risk of infection transmission in dental clinics. Infection can be transmitted from a patient to a dentist and also from one patient to another patient through the spread of aerosols in the treatment space. Additionally, AgNPs can be used as strong disinfectants with running water in the water unit system. It is recommended to perform further laboratory studies to confirm the safety and possibility of using nano-silver with running water in the unit.

Conclusion

Based on the results, AgNPs exhibited acceptable antiviral properties. The synthesized nano-silver solutions were highly stable and had significant disinfecting effects on HIV, IAV, herpes simplex type 2, and coronavirus. They affected viruses in the early stages of viral replication, with low toxicity for the host cells.

Conflict of Interest

Non Declared ■

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