

SYNTHESIS, ROLE IN ANTIBACTERIAL, ANTIVIRAL, AND HAZARDOUS EFFECTS OF SILVER NANOPARTICLES

Mohamed Jamal Saadh^{1*}

¹Faculty of Pharmacy, Middle East University, Amman, Jordan

* msaadeh@meu.edu.jo

Abstract

Viral pathogen infections pose a major global health challenge: the emergence of bacteria and strains of viruses that are resistant to conventional antibiotics and antivirals, and undesirable side effects due to their long-term use, are slowing the use of many antiviral therapies. As a potentially useful tool in the prevention of various pathogens, silver nanoparticles have already demonstrated their potential as an effective antiviral agent thanks to their unique physical and chemical properties. Silver nanoparticles offer an excellent opportunity for new antiviral therapies as they can attack a wide variety of viruses. It has been suggested that AgNPs induces reactive oxygen species and free radicals that induce apoptosis, which leads to cell death and prevents cell replication and cell wall destruction, and smaller nanoparticles have also been shown to be more toxic than larger particles. The toxicity of AgNP depends on the size, concentration, pH of the medium and the duration of exposure to the pathogen. This review examines the antimicrobial mechanisms, deleterious effects, and synthesis of AgNPs.

Keywords: *Silver nanoparticles, virus infection, antibacterial, antimicrobial mechanism.*

Introduction

The elemental metal silver (Ag) has a broad antimicrobial spectrum of activity against various bacteria, fungi, and viruses, due to its versatility, silver nanoparticles (AgNPs) have currently established themselves as microbicides for biological surfaces in various forms as wound dressings, medical devices, aerosol deodorants, and tissue.

Antimicrobial mechanism of silver nanoparticles

The antibacterial mechanism of silver Nanoparticles (AgNPs) is described by several researchers. Bacterial cell membranes contain sulfur-containing proteins and sulfur-containing amino acids; Silver can interact with them inside and outside the cell membrane, which leads to inactivation of bacteria. In addition, the silver ion released from AgNPs interacts with phosphorus in the DNA as well as with sulfur-containing proteins, which leads to an inhibition of enzyme activities. Also, other parameters to determine the antimicrobial activity. In the size-dependent study, it can be shown that an NP size of less than 20 nm can have a higher adhesion of the sulfur-containing membrane protein, which leads to a maximum permeability through the membrane and ultimately to bacteria cell death [1].

The exact mechanism by which AgNPs exert their destructive effects on viruses is not yet clear; however, it has consistently been observed that AgNPs interact with structural proteins on the surface of extracellular viruses to inhibit early phase infection, either by preventing the binding or entry of viruses or by damaging surface proteins to cause viral infection influence [2]. It has been shown that AgNPs preferentially bind to sulfhydryl-rich viral surface proteins and cleave disulfide bonds in order to destabilize the protein, which affects viral infectivity [3]. It has also been suggested that AgNPs have intracellular antiviral effects by interacting with viral nucleic acids [4]. The AgNPs with zinc has antiviral activity against the influenza virus H5N1, H9N2, SARS-Cov2 and PPRV [5-9].

This must be taken into account due to the high surface-to-volume ratio that nanomaterials usually have. The smaller the particles, the larger the exposed metal surface and

therefore a stronger microbicidal effect can be expected [10]. The shape is the rest of the parameters of the nanocrystals that are responsible for interacting with the bacterial cell wall. Truncated triangular silver nanoplates showed higher antibacterial activity against *E. coli* bacteria than spherical and rod-shaped nanoparticles [11]. Recently, AgNPs less than 10 nm in size have created pores in the cell wall due to these pores; the amount of cytoplasm released into the medium to control cell death, without interacting with proteins and nucleic acids inside and outside the bacterial cell. The interaction of AgNP with some cells can lead to programmed cell death (apoptosis) [12]. In addition AgNPs induces reactive oxygen species and free radicals that induce apoptosis [12], as shown in figure 1, and figure 2.

Thus, AgNPs is an effective antiseptic in a variety of products such as Acticoat™ for wound dressings, Silverline® for intraventricular polyurethane catheters, SilvaSorb® for hand gels, wound dressings and dental fillings. ONQ SilverSoaker™ for drug catheter [13]. In addition to using in various products such as shirts, wipes, and medical masks, toothpaste, hand washing, shampoo, toys, laundry detergents, and humidifiers. However, the use of AgNPs in a consumer product is safe or not the current topic of discussion.

Hazardous effects of Silver nanoparticles

AgNP are used in various industries for their excellent antibacterial properties and effectiveness; Researchers and policymakers have raised awareness of the negative impacts of AgNPs on the environment and human health. Therefore, it is necessary to consider its health hazards and understand the associated long-term risks, which fill the knowledge gap on toxicity. As we know about AgNPs are an efficient material that is used in various fields such as food, health and fitness, cleaning, electrical devices, toys and medical devices [14].

Due to their physicochemical properties, silver NPs show signs of certain *in vivo* or *in vitro*. Another form of environmental toxicity is observed in the release of AgNPs, which are readily ingested by aquatic species. In addition, the widespread use of AgNPs as disinfectants may pose a risk of microbial resistance, which reduces its applicability. A bluish-gray discoloration of the skin is referred to

as argyria due to the toxicity of the AgNPs. Indeed, the toxicity of silver is low, but a different consequence than that of Argyria has been observed. In a higher concentration; Data from the available literature show that the cutoff of 0.9 g is the lifetime threshold for Argyria diseases [15]. The drinking water limit value is also 100 µg / L for nanosilver components. The toxicity of nanosilver or dissolved silver is much debated, but recent research reports show that the toxicity arises from the release of silver into the environment in both particulate and nano-sized rather than dissolved silver. The sensitivity of the toxicity of silver NPS is higher in aquatic species with a concentration of 1 to 5 µg / L³ than in humans and mammals [16]. In the environment, nanosilver toxicity is introduced in sequential manner, e.g. B. by release, emission, distribution, and impact on aquatic life. AshaRani et al. reported that Agnp has the likely cause of toxicity for the human cell line as determined by cytotoxicity, genotoxicity, and antiproliferative parameters [17]. A review analyzes the various aspects of the transformation of the surface properties of silver NPs such as phase transformation, aggregation, and sulphidation in the environment, which lead to toxicity for living aquatic organisms. In addition, it showed the toxicity of silver NPs for the skin of the aquatic, land, plant, algae, fungal, vertebrate, and human cells (keratinocytes, lung fibroblast cells, and glioblastoma cells) [18]. Gliga et al. reported that detailed nanotoxicological studies of silver NPs with particle agglomeration in cell medium, cell uptake, intracellular localization, and silver release were investigated; and the disclosed intracellular release of silver is responsible for the toxicity to human lung cells [19]. Although knowledge about the dangerous effects of silver NPs is enriched, it is necessary to evaluate and optimize the toxicity limit, dose, and concentration for living aquatic organisms, and human, after that, it can be safely and effectively used in various functions.

Synthesis of silver nanoparticles

Ag-NPs have received a lot of attention because they also have the properties of LSPR, which makes them important for medical applications. They also have unique broad-spectrum

antimicrobial properties against fungi, viruses, and bacteria [20]. Optical, electrical, and thermal properties that make them indispensable for the industrial application of electronics, catalysis, and photonics. They have been used in surface-enhanced Raman spectroscopy (SERS) in chemical and biological sensors, and in biomedical materials used. In addition to biomarkers. The main uses of AgNPs are targeting cells and treating diseases such as interacting with the HIV₁ virus and preventing it from binding to host cells in vitro [7,8, 21].

The antimicrobial activity of AgNPs has benefited various applications such as (1) coatings; for example, coating vegetable oil with AgNPs shows excellent antimicrobial properties; (2) Ag NPs deposited on carbon filters reduced waterborne diseases; and (3) nanocrystalline Ag has been used in wound dressings to treat ulcers [22]. Chemical reduction is the most widely used method for the chemical synthesis of AgNPs. This method is believed to be simple, inexpensive, and powerful. Chemical reduction depends on these components: metal precursors; a reducing agent such as ethylene glycol, glucose, NaBH₄; and stabilizing/protecting agents such as sodium oleate, polyvinylpyrrolidone (PVP), polyvinyl acetate. However, the shape and size of chemically synthesized AgNPs depend on the reaction components, in addition to adjusting reaction parameters such as temperature and pH [22]. As shown in figure 3.

The physical synthesis of AgNPs can be achieved by various methods, such as condensation, evaporation, and thermal decomposition methods [8,22]. The ceramic heating process is used to produce the monodisperse AgNPs of uniform size. The physical techniques used for the synthesis of AgNPs resulted in a uniform shape and size of the AgNPs [24]. However, the primary cost of equipment investment, the time required, and the high energy demand must be taken into account [24].

In green chemistry, traditional reducing and stabilizing agents have been replaced by biomolecules. In biological engineering, AgNPs are produced using bacteria, yeast, fungi, algae, and plants as reducing and stabilizing agents, for

example, the fungus *Trichoderma* Ride was used as a precursor for the synthesis of AgNPs from AgNO₃ [7,8]. In addition, the mixture of *Fastia japonica* leaf extract with AgNO₃ produced AgNPs with excellent antimicrobial activity [24].

Acknowledgments

The author is grateful to the Middle East University (MEU), Amman, Jordan, for the financial support granted to cover the publication fee of this research article.

References

1. Morones JR, Elechiguerra JL, Camacho A, et al., The bactericidal effect of silver nanoparticles. *Nanotechnology* 2005; 16: 2346.
2. Woodward RL. Review of the bactericidal effectiveness of silver. *J Am Water Works Assoc* 1963; 55: 881–886.
3. Lal HM, Uthaman A, Thomas S. 2021. Silver Nanoparticle as an Effective Antiviral Agent. In: Lal H.M., Thomas S., Li T., Maria H.J. (eds) *Polymer Nanocomposites Based on Silver Nanoparticles*. Engineering Materials. Springer, Cham. https://doi.org/10.1007/978-3-030-44259-0_10
4. Lu L, Sun RWY, Chen R, et al. Silver nanoparticles inhibit hepatitis B virus replication, *Antivir Ther* 2008; 13: 253e262.
5. Saadh MJ, Almaaytah AM, Alaraj M, et al. Punicagin and zinc (II) ions inhibit the activity of SARS-CoV-2 3CL-protease in vitro. *Eur Rev Med Pharmacol Sci* 2021; 25: 3908-3913.
6. Saadh MJ, Almaaytah AM, Alaraj M, et al. Sauchinone with zinc sulphate significantly inhibits the Activity of SARS-CoV-2 3CL-Protease. *Pharmacologyonline*. 2021. 2: 242-248.
7. Saadh MJ, Aggag MM, Alboghdady A, et al. Silver nanoparticles with epigallocatechin gallate and zinc sulphate significantly inhibits avian influenza A virus H9N2. *Microb Pathog* 2021; 158: 105071. 13.
8. Saadh MJ, Aldalaen SM. Inhibitory effects of epigallocatechin gallate (EGCG) combined with zinc sulfate and silver nanoparticles on avian influenza A virus subtype H5N1. *Eur Rev Med Pharmacol Sci* 2021; 25: 2630-2636.
9. Saadh MJ, Epigallocatechin gallate (EGCG) combined with zinc sulfate inhibits Peste des petits ruminants virus entry and replication, *Saudi Journal of Biological Sciences*, 2021. <https://doi.org/10.1016/j.sjbs.2021.07.035>.
10. Wigginton NS, De Titta A, Piccapietra F, et al. Binding of silver nanoparticles to bacterial proteins depends on surface modifications and inhibits enzymatic activity. *Environ Sci Technol* 2010; 44: 2163–2168.
11. Pal S, Tak YK, Song JM. Does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? A study of the gram-negative bacterium *Escherichia coli*. *Appl Environ Microbiol* 2007; 73: 1712–1720.
12. Sondi I, Salopek-Sondi B. Silver nanoparticles as antimicrobial agent: a case study on *E. coli* as a model for Gram-negative bacteria. *J Colloid Interface Sci* 2004; 275: 177–182.
13. Chaloupka K, Malam Y, Seifalian AM. Nanosilver as a new generation of nanoparticle in biomedical applications. *Trends Biotechnol* 2010; 28: 580–588.
14. Pulit-Prociak J, Banach M. Silver nanoparticles – a material of the future...? *Open Chem* 2016; 76.
15. Height MJ. Nanosilver in Perspective, Presentation “Health Risk Assessment of Nanosilver” Workshop. 2011.
16. Nowack B, Krug HF, Height M. 120 years of nanosilver history: implications for policy makers. *ACS Publications* 2011; 45: 1177–1183.
17. AshaRani P, Low Kah G, Mun MP, et al. Cytotoxicity and genotoxicity of silver nanoparticles in human cells. *ACS Nano* 2008; 3: 279–290.
18. Levard C, Hotze EM, Lowry GV, G.E. Brown. Environmental transformations of silver nanoparticles: impact on stability and toxicity. *Environ Sci Technol*. 2012; 46: 6900–6914.
19. Gliga AR, Skoglund S, Wallinder IO, et al. Size-dependent cytotoxicity of silver nanoparticles in human lung cells: the role of cellular uptake, agglomeration and Ag release. *Part Fibre Toxicol* 2014; 11: 11.

20. Franci G, et al. Silver nanoparticles as potential antibacterial agents. *Molecules* 2015; 20: 8856_8874.
21. Tran QH, Nguyen VQ, Le AT. Silver nanoparticles: synthesis, properties, toxicology, applications and perspectives. *Adv Nat Sci.: Nanosci. Nanotechnol* 2013; 4: 033001.
22. Naeem, H, et al. Facile synthesis of graphene oxide silver nanocomposite for decontamination of water from multiple pollutants by adsorption, catalysis and antibacterial activity. *J Environ Manage* 2019; 230: 199-211.
23. Iravani S, et al. Synthesis of silver nanoparticles: chemical, physical and biological methods. *Res Pharm Sci* 2014; 9: 385-406.
24. Saleh TA. A strategy for integrating basic concepts of nanotechnology to enhance undergraduate nanoeducation: statistical evaluation of an application study. *J Nano Educ* 2013; 4: 1-7.
25. Zhang J; et al. Antimicrobial effects of silver nanoparticles synthesized by *fatsia japonica* leaf extracts for preservation of citrus fruits. *J Food Sci* 2017; 82: 1861-1866.

FIGURE 1. The effect of silver nanoparticles on the microbe.

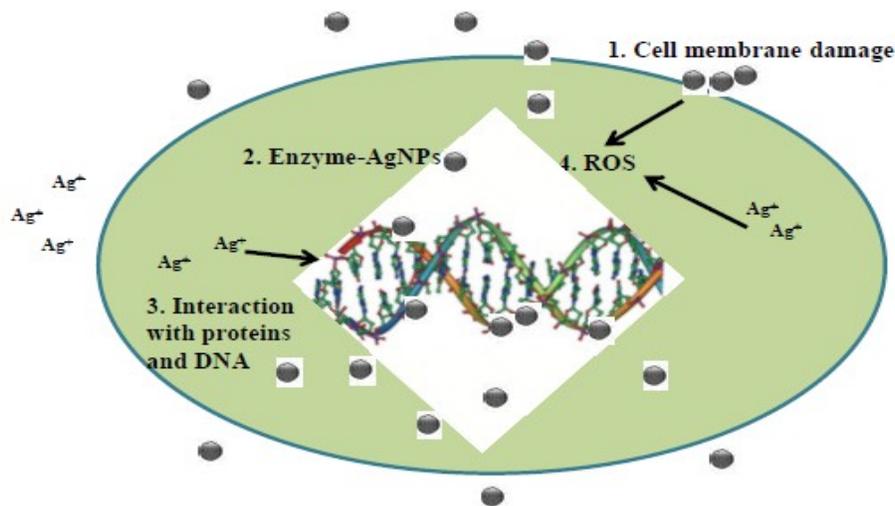
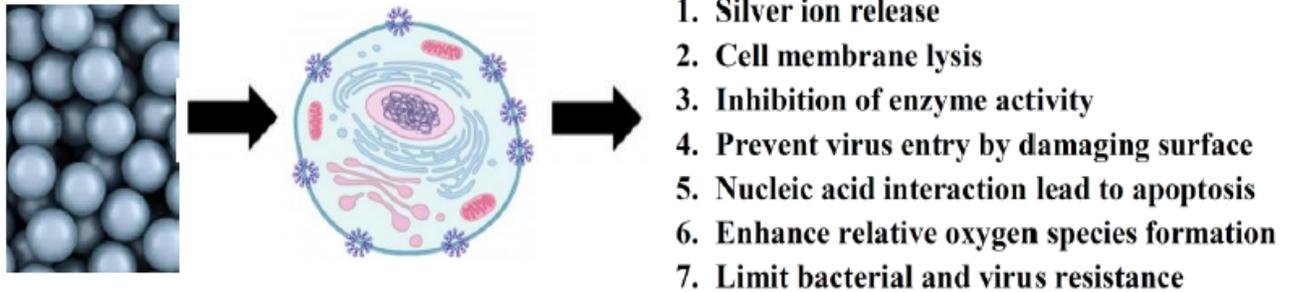


FIGURE 2. Antimicrobial mechanism of silver nanoparticles.

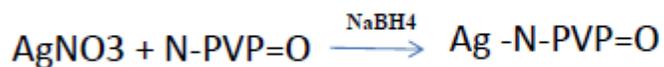


FIGURE 3. Representation of the synthesis of (a) PVP-AgNPs and (b) drug loaded AgNPs.