



Silver Nanoparticles and Silver Ions as Potential Antibacterial Agents

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Abstract

Bacteria and superbugs have become more resistant to several antibiotics. Continuous and overuse of such antibiotics led to outbreaks of superbugs in both hospitals and communities. In recent decades, silver was used in medical treatment such as burns, wounds and bacterial infections. Silver metallic, silver nitrate and silver sulfadiazine were utilized for this treatment. Nowadays, silver nanoparticles and silver ions are effectively used as antibacterial agents in the medical field in the form of nanoparticles and ions, where silver ions proved an effective antimicrobial against active bacteria, viruses, and fungi than silver nanoparticles Ag NPs. However, modified or functionalized silver NPs are extremely active to kill bacteria than pure Ag NPs. Silver nanoparticle's size, shape, and concentration play an important role in their antimicrobial activities.

Keywords Silver nanoparticles · Silver ions · Antibacterial agent · Microorganisms

1 Introduction

The existence of new infections led to stimulating looking for new antimicrobial agents. Nevertheless, most of these agents are deadly/ poisonous and unsafe for people to use [1] as well the existence of such bacterial strains has resistivity to common antibacterial treatment and this presents the global community health issue loom. Therefore, the production of eco-friendly, efficient, irresistible, and natural-source/available antimicrobial agents is the main goal. By the combination of nanotechnology and microbiology, it can easily generate a novel type of antimicrobial agents [2–6], e.g., Carbon-based nanomaterial and its compounds can be used as a good antibacterial agent because of their high surface-to-volume ratio and unique physical and chemical properties [2, 3]. Also, metal oxide nanoparticles such as CuO NPs [4], NiO NPs [5], TiO₂ NPs [6], and CeO₂ [7] NPs can be utilized as antimicrobial agents because of their

effectiveness on resistant strains of microbial pathogens, low toxicity, heat resistance, and good compatibility nanostructured materials. Similarly, ZnO Nanoparticles and its compounds showed antibacterial potential against a great variety of bacterial species owing to their desirable properties such as non-toxicity, long-term stability, and strong activity even when given at low concentrations [8, 9]. Recently, bio-nanotechnology gains a tremendous impetus wherein the biosynthesis of nanoparticles is one mostly main area in bio-nanotechnology. These noble nanoparticles play a vital role in different fields such as optoelectronic applications, catalysis, and medicine applications [10–14]. For instance, in biomedicine applications, it serves gene delivery, as a platform for the drug, and cancer treatments. The properties and operation of such nanoparticles are tightly linked to their size, shape. The unique high surface area feature of nanoparticles can enhance the antimicrobial activity, enabling for a big interaction of such nanomaterial with the adjacent environment [15].

Nowadays, extensive studies on the metal nanoparticles have carried out as antimicrobial agents, which are considered as an alternative approach for figuring problems out and to meet challenges caused by multiple drug resistance in bacteria [15]. Among these nanoparticles, silver and its compound have currently gained renewed attention due to silver is extensively used as antimicrobial agents in earlier. This is because some of the bacterial strains have shown good resistance against antibiotics. In addition, the

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characteristics of antimicrobial of silver ions have been known in the ancient era, where they have extensively been used as a bactericide in medical treatment. For example, Ag NPs have been demonstrated to control bacterial growth, and have proved to be strong biocides against various bactericidal such as bacteria, fungi, and viruses [16–20]. Nano-silver has been documented/considered as a biocide material in USA since 1954, where it has been used for more than 150 years. Silver can take part in forming various organic complexes and inorganic complexes with the most stable oxidation states are 0 and 1. Silver nanoparticles exist in various shapes like spheres, rods, wires, triangles, and etc. with different size from few nm up to 100 nm. Several techniques have been reported for production silver NPs [21].

In the present state of the art, Ag NPs have shown as origin antimicrobial agents owing to their noble physico-chemical characteristics such as eco-friendly, low volatility and big thermal stability; Silver NPs with such unique properties can be simply employed in a varied spectrum of applications, especially medical and pharmaceutical. This has led to many studies comprising of the role Ag nanoparticles as a drug and as well as a promising antibacterial agent [21]. The silver nanoparticles combined antibiotics have shown the highest synergistic antibacterial activity. Silver can use in the form of creams or gel that can efficiently reduce bacterial infections in chronic wounds [22]. Antibacterial of Ag NPs has not only attributed to releasing metal ions in solution but to their nanosized and low surface/volume ratio that enables to interact with membranes. One of the noble silver nanoparticles features is the enhancement of biochemical activity, and thus, nanoparticles have higher antibacterial activity than bulk counterparts [21].

Nanomedicine is a fresh field; is relatively emerged from the combining of science and technology, by interacting such a nanoparticle with biological molecules, nanotechnology widens the analysis and application fields. Nanomedicine aims to understand the interactions of nanodevices with biomolecules within the living medium and within human cells. Operating at nanoscale permits the exploitation of physical properties which is totally unlike from those noticed at a small scale like the volume/surface magnitude relation [23, 24].

In nanotechnology, nanoparticles' function is the site-specific drug delivery, where a fixed medication dose has employed; which considerably reduces the side-effects because of the chemical agent deposits within the sick affected region only. This extremely selective approach will minimize prices and ache to the patients. This leads to widespread using of nanoparticles such as dendrimers and nonporous materials. Micelles are used for drug encapsulation. They are passing tiny drug molecules to the specified place. Similarly, nanoelectromechanical device systems are used for the active giving up of medicine. Fe nanoparticles

or Au shells are finding a vital application within cancer treatment. Target medicine decreases medication consumption and treatment cost, making patients treatment less expensive [25]. In this review, we are going to show the effects of the metallic and ionic silver nanoparticles against pathogenic bacteria. The goal of this work is to advance the knowledge of this field. The novelty of this review paper lies in the following two aspects: First, we show and compare the effects of both Ag NPs and Ag ions together in detail, as two antibacterial agents, against both gram-positive and gram-negative bacteria, which did not show and compare in pervious works. Second, we recognize particular objects of interest in antibacterial mechanism of both types of antibacterial agents. In addition, we are going to present the relationship between these two antibacterial agents in term of mechanism of action.

2 Silver Nanoparticles (Ag NPs) and Silver Ions (Ag⁺)

Ionic silver or silver ions are totally different from the metallic silver nanoparticles. Ionic silver is also known as monatomic colloidal silver and is water-soluble, unlike metallic silver. Scientifically speaking, when an electron is taken away from an Ag atom a silver ion will be produced which is water-soluble. It is worth mentioning that the Ag⁺ is highly reactive with the other elements that readily combine to produce compounds. In the case of ingestion of highly concentrated ionic silver about 100 ppm and more make a condition called Argyria [26].

Colloidal silver contains silver in two different forms: silver nanoparticles and silver ions. Sometimes they are known as colloidal silver nanoparticles and colloidal silver ions. Colloidal silver nanoparticles contain silver ions at the same time because silver metal could release silver ions at the surface of the metal which is considered the main source of its antimicrobial activities. It was reported that a typical colloidal silver product of 10 ppm (10 mg/L) of total silver has only 10% in Ag NPs and 90% of the Ag⁺ [18, 19]. In other words, you are getting only 1 ppm (1 mg/L) of Ag NPs in a product announced as 10 ppm that is assuming 10% of particles. The output that is only 1% NPs would produce only 0.1 ppm of nanoparticles. It can simply be seen that for the greatest effectiveness you have to look for a product that has most of the silver content in the form of nanoparticles rather than ions [26]. There are three different types of commercial silver products that consumers find labeled as “colloidal silver” are Ionic Silver Solutions, Silver Protein and True Colloidal Silver [27].

Silver nanoparticles are regarded as one of the most promising materials in nanotechnology science applications. It possesses antimicrobial activity, which plays a vital role to

control conventional antimicrobial agents [28]. Antibacterial activity of silver ions has been recognized since ancient times, which was used to store water or liquids in silver vessels to prohibit it from any microbiological contamination [29]. Silver ions with micromolar concentrations (1 to 10 μM) are enough to damage bacteria in water. However, at high doses can be toxic to mammals and freshwater and marine organisms which are probably compromising the growth and shape of animal cells by damaging a different of biological functions [28]. Silver in the range of nanoscale has been largely employed in the coating of medical instruments, disinfection of medical apparatuses, water purification, and house appliances. This is due to their antibacterial, antiviral and antifungal characteristics [17]. Furthermore, silver and silver nanoparticles are not only utilized as antimicrobials in medical applications, but it is also used in different applications such as industrial and domestic applications [30, 31]. Integrating of silver nanoparticles into wound dressings and antimicrobial coating on medical equipment is typically used to inhibit biofilm formation. The clinic scope of silver nanotechnology is of explicit concern to the field of medical science, wherever infection of deep-seated apparatuses act a persistent threat [31].

The main goal of using silver ions is their toxicity against the membrane proteins which that cause a disruption of generic membrane integrity leading to an excess in its liquidity. It has been reported that the Ag ions are 1600 times more toxic against *Pseudomonas putida* mt-2 than that of the Ag NPs [29]. In contrast, it was reported that the Ag ions have a similar toxicity effect as silver nanoparticles on *E. coli* bacteria whilst it is larger than Ag NPs on *S. aureus* case. Kim and his group have attributed the reason for the toxicity impact of silver nanoparticles to the oxidative stress and not to the silver ions [32]. Nevertheless, it is not clear that to which amount the toxicity of silver nanoparticles causes from emitted silver ions and how much toxicity is related to the Ag NPs per each second.

The working mechanism of antibacterial Ag NPs has not yet been fully known and understood. It has been reported a release of the silver ions from Ag nanoparticles in aqueous solutions It was suggested that it takes part in attack the bacterial cell in different methods; causes cell damages [29]. Multiple levels interactions for silver ions with the bacterial cell have been stated for cell wall components, the cytoplasmic membrane, DNA, and proteins. From Proteomic studies of *E. coli* cells, adapting response of them against silver ions is shown through raising the term level of the three outer membrane protein precursors that happen after treating them with nano-silver to face an impact resulting from interactions of silver ions with the cell wall. It has been reported that both Ag^+ and Ag NPs possess a strong effect on the cis–trans isomerization of unsaturated membrane fatty acids which clearly provides proof that their mode of activity associates

to the destruction of membrane and breakdown of their function as a permeability barrier [29].

3 Antimicrobial Activities of Silver Nanoparticles (Ag NPs) and Silver Ions (Ag^+)

Ag NPs and Ag^+ have strong antibacterial activity against microorganisms. Their antibacterial activity has been studied together and separately. This is because silver nanoparticles in liquid solutions produce silver ions at the same time. However, pure silver ions can be produced by an electrochemical method. It was reported that the silver nanoparticles show effective antimicrobial activity against common pathogenic microorganisms [33]. The Ag NPs produce oxidative stress which is revealed by spectrophotometric assays [34]. In addition, the nanoparticles can be used to study ex-situ and in situ treatments and use in other applications such as health care, electronics, water treatment, and household appliances [35].

Many researchers reported that the silver ions have better antimicrobial activity than the silver nanoparticles. In other words, they have proved that almost all activity of Ag NPs is owing to the silver ions released from the silver nanoparticles in a solution. Swathy et al. [36] has shown that 50 parts per billion (ppb) (0.05 mg/L) of silver ions (Ag^+) released continuously from silver nanoparticles (Ag NPs). It was shown that the antibacterial and antiviral activities of the silver ions (Ag^+) can be enhanced one thousand-fold when the concentration of the carbonate ions is below the drinking water norms. In the case of using this method in antimicrobial activity, approximately 1,300 tons of silver can be saved each year. Akter et al. [37] showed that the Ag ions are more toxic than the Ag NPs to both; *Normal Human Dermal Fibroblasts (NHDF)* and *Normal Human Epidermal Keratinocytes (NHEKs)*. In addition, it was also shown that the neurotoxicity is furnished by Ag^+ more than Ag NPs. Salvioni, et al. [38] also concluded that the Ag NPs have stronger antibacterial activity, against *E. coli* and *S. aureus* bacteria, than the Ag^+ salts. Huang [39], reported differential behaviors of metallic silver nanoparticles and ionic silver towards cysteine (Cys), in the aspects of bioremediation and their toxicity to *Phanerochaete chrysosporium*, an amino acid representative of thiol ligands that coordinate to silver ions and graft to the surface of the nanoparticles were characterized. It was observed a significant reduction in the total Ag uptake, after adding about 5 to 50 mM cysteine in some groups treated with 1 mM Ag ions and 10 mM Ag NPs, particularly at a Cys:Ag molar ratio of 5.

Several organisms such as the human immunodeficiency virus (HIV), Hepatitis-B virus, Methicillin-resistant *Staphylococcus aureus* (MRSA), human immunodeficiency

virus HIV-1, and Ampicillin-resistant *E. coli* are difficult to treat. It has been shown that silver nanoparticles and silver ions function as broad-spectrum bactericidal and virucidal agents. In addition, it has been demonstrated that Ag nanoparticles can increase wound healing [40]. The clinical strains of bacteria are resistant to 80% of antibiotics, but one of the clinical strains was more sensitive to colloidal silver nanoparticles. In addition, Ag nanoparticles at 0.156 $\mu\text{g/ml}$ concentration have been found to be non-toxic in normal mouse fibroblasts 929, HepG2 cells and cellule tumoral HeLa [41]. The antibacterial activities of the nanoparticles are size- and dose-dependent; these contingencies are more pronounced against gram-negative bacteria than gram-positive bacteria [40].

Various studies [42, 43] have made to investigate the impact of the combination of Ag NPs with antibiotics; and the result has been a synergy. Fayaz et al. [42] used *Trichoderma viride* for the synthesis of silver NPs and additionally examined the antimicrobial action of such nanoparticles within the presence of antibiotics. They have found that activity against bacterium was inflated for ampicillin, kanamycin, erythromycin, and chloramphenicol. Dar et al. [43] has investigated the characteristics of Ag NPs that made victimization the plant gus *Cryphonectria sp.* They have fungally made Ag NPs which had found to possess supreme medication activity against *E. coli*, *S. typhi* and *S. aureus* compare to standard antibiotics streptomycin and amphotericin. It additionally exhibited antifungal activity against *Candida albicans* and hence increased the consequences of substitution antibiotics. It was also shown that the Ag NPs have better activity than the AgNO_3 and

standard antibiotics streptomycin and amphotericin at a concentration of 5 $\mu\text{g/ml}$.

A typical tissue-like cell is a human mesenchyme stem cell (hMSCs); were implanted in the existence of Ag ions and Ag NPs, and the viability of such cells was investigated by fluorescence microscopy. Figure 1 shows the influence of both forms of silver on the viability of the cell at different concentrations for 24 h, under the same cell culture conditions. It can be seen that the toxicity of Ag ions and Ag NPs increased with concentration [44].

Ag nanoparticles and Ag ions have different effects on *E. coli* and *S. aureus* implanted in RPMI/10% FCS circumference (see Table 1). It can be calculated that increases in both minimum inhibitory concentration (MIC) and the minimum bactericidal concentration (MBC) of the silver preparations occurred by increasing the inoculated cell number [44].

In comparison with the other types of the nanoparticles, Ag NPs and Ag ions have better antibacterial activity against both gram- positive and negative bacteria. For example, Hamad et al. [45, 46] compared the antibacterial activity of the Ag NPs with the pure TiO_2 and Ag- TiO_2 nanoparticles at 12.5 $\mu\text{g/ml}$ concentration, prepared by laser ablation in ice water. It was concluded that the antibacterial activity of the pure Ag NPs is significantly higher than that of the pure TiO_2 and Ag- TiO_2 NPs.

Morales-Avila et al. [47], concluded that the antibacterial activity of the functionalized Ag NPs with the cationic antimicrobial peptide ubiquicidin 29–41 (UBI) against both *E. coli* and *P. aeruginosa*, was significantly increased. While, with pure Au NPs and conjugated Au NPs with the UBI (182 $\mu\text{g/ml}$), no inhibition of bacterial growth was observed. Furthermore, Njue [48] produced silver and gold

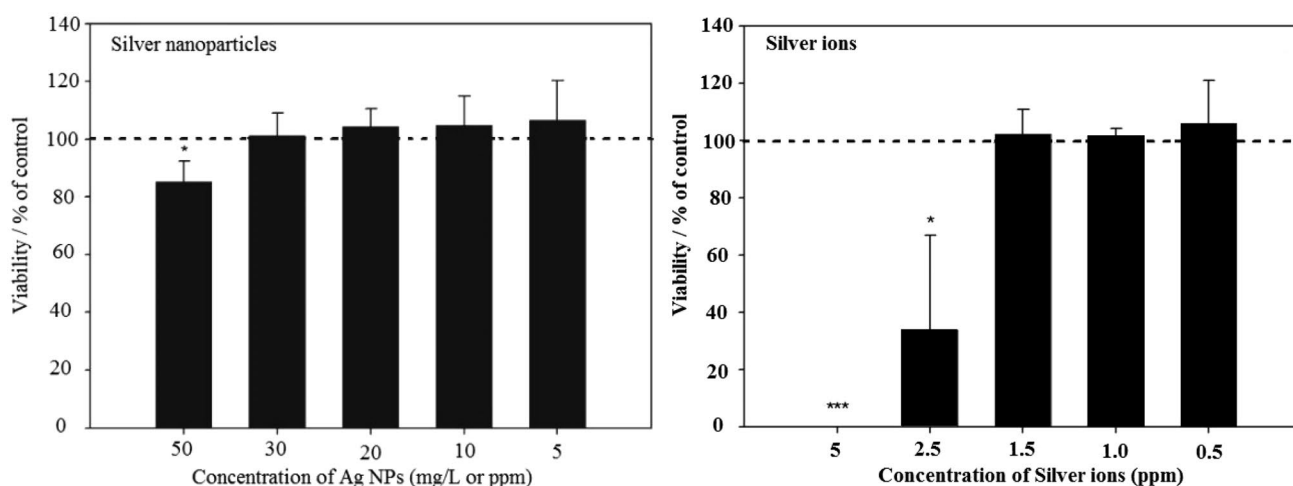


Fig. 1 Influence of Ag NPs and Ag^+ on the viability of human mesenchymal stem cell (hMSCs) at different concentrations for 24 h, under the same cell culture conditions. The output data are expressed as mean \pm standard deviation (N=3) given as the percentage of

the control (cells cultured without silver). An asterisk (*) referred to considerable differences compared to the control (* $p < 0.05$, *** $p < 0.001$)

Table 1 Influence of Ag NPs and Ag⁺ on *E. coli* and *S. aureus* implanted in RPMI/10% FCS medium. Impossible measuring MIC for Ag NPs because of scattering (turbidity) of the Ag NPs in this medium [44]

Cell density (ml ⁻¹)	<i>E. coli</i>			<i>S. aureus</i>		
	Silver ions (acetate) (N=9)		Ag NPs (N=6)	Silver ions (acetate) (N=9)		Ag nanoparticles (N=4)
	MIC (ppm) Silver	MIC (ppm) Silver	MBC (ppm) silver	MIC (ppm) Silver	MBC (ppm) Silver	MBC (ppm) silver
1 × 10 ³	0.5–1	0.5–1.25	12.5–20	0.5	1.25	20
1 × 10 ⁴	0.75	1–1.25	20	0.75	2.5	0
1 × 10 ⁵	1–1.25	2.5	50	1.25	2.5	> 50
1 × 10 ⁶	1.25–2.5	2.5–5	> 50	2.5	5	> 50

Table 2 Antibacterial activities of Ag NPs and Au NPs against *E. coli* and *S. aureus* bacteria [48]

Samples	Inhibition Zones (mm)	
	<i>E. coli</i>	<i>S. aureus</i>
Ag NPs	15.5 ± 0.09	13.3 ± 0.14
Au NPs	14.510 ± 0.35	13.3 ± 0.50
<i>G. lucidum</i> extract	7.0 ± 0.00	6.75 ± 0.15
Vancomycin	N/A	22.1 ± 0.12
Ciprofloxacin	33.4 ± 0.542	N/A
Distilled water	6	6

nanoparticles via a green method and then their antibacterial activity were compared against *E. coli* and *S. aureus*. It was concluded that the inhibition zones method shows that the antibacterial activity of the Ag NPs is a little higher than that of the Au NPs (see Table 2). The positive controls (distilled water), ciprofloxacin and Vancomycin are also shown for comparison.

4 Mechanisms of Antibacterial Activity of Silver Nanoparticles (Ag NPs) and Silver Ions (Ag⁺)

The antibacterial mechanism of NPs or nanoparticles' toxicity against various bacteria is not yet fully understood. The antibacterial activities of the nanoparticles depend upon two main factors: physicochemical properties of nanoparticles and type of bacteria [49]. The antibacterial mechanisms of Ag NPs are quite similar to those of Ag⁺ because the silver ions are released from silver nanoparticles when the nanoparticles contact with a solution. In other words, when we talk about silver nanoparticles as a solution (or colloidal Ag NPs), we automatically talk about silver ions. The antibacterial mechanism of the silver nanoparticles involves the nanoparticles attaching to the bacteria membrane by electrostatic interaction which leads to disruption of the integrity

of the bacterial membrane [50]. In general, nanotoxicity is triggered by the “induction of oxidative stress by free radical formation, that is, the reactive oxygen species ROS, following the administration of NPs” [51, 52]. In addition, it is also activated cytochrome b while the ions combining the sulfhydryl group [53]. On the other hand, silver ions are absorbed by a membrane which deactivates adenosine triphosphate (ATP) generation and deoxyribonucleic acid (DNA) replication and produces reactive oxygen species (ROS), effectively leading in suppressing and controlling bacterial growth [54].

It was also reported that the antibacterial mechanism of nanoparticles that it starts when the nanoparticles adhere to the surface of bacteria and irreversibly damage the structure of the membrane. This process leads to penetrating cells by NPs, preventing protein activity, and finally causing the death of the bacteria [55]. About the silver ions (Ag⁺), when they contact the wall of the bacteria, it breaks through the cell wall, and then it links to the phospholipid layer of the cytoplasmic membrane cause inactivation of membrane-bound proteins. Furthermore, the Ag ions will bind with the DNA with subsequent disrupting DNA replication. Ions will also reduce the capability of ribosomes to translate messenger RNA to the disruption of the cell wall [56]. Figure 2 describes the antibacterial activity of silver ions against a bacteria cell.

It was also reported that the antimicrobial mechanism of the Ag ions relies on; (a) damage proteins of the membrane, (b) discrepancy with the system of electron transport, and (c) inhibiting the respiratory enzymes to enhance the production of reactive oxygen species (ROS). Moreover, oxidative stress considers one of the signs that allow controlling the toxic impacts of heavy metals on microorganisms. It is worth mentioning that the toxic impacts are based on the incorporation of Ag⁺ into the wall of the bacteria and the plasma membrane followed an inhibition of the respiratory process of the microorganism. Oxidative stress can be increased by increasing the concentration of the Ag⁺ [57, 58].

TEM images of the bacteria cells after treated with the silver ions showed a significant change in the bacterial cell

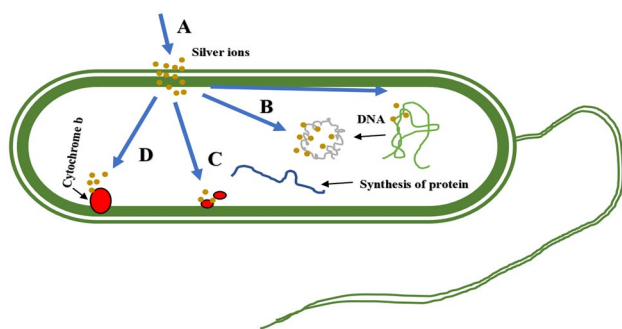


Fig. 2 Antibacterial mechanisms of the Ag ions against a bacteria cell

membranes when being treated by silver ion, which might be the cause of cell death. It was suggested that Ag ions may cause *E. coli* and *S. aureus* bacteria to reach an active but nonculturable (ABNC) state and eventually die [58]. Silver ions (Ag^+) result in the suppression of respiration, membrane hurt, and destruction of the nucleon driver. The reaction of ions with thiol teams in membranes is supposed to be a serious toxicity process, with research proposing that the key toxicity case comprises interactions between Ag^+ and metabolic process chain enzymes [59]. Several proteomic studies showed that ionic and metallic Ag caused to the instability of the outer membrane, collapsing of the protoplasm membrane potential and thereby, depletion of intracellular adenosine triphosphate levels in *E. coli*, according to overlapping with the chains of the metabolic process [60–63]. Other studies suggested that though still cytotoxic to microorganisms below anaerobic conditions, intracellular Ag^+ conjointly results in reactive oxygen species (ROS) bring out and interference with DNA replication [64], enhanced membrane porosity and enhanced sensitivity to antibiotics. It is worth mention that there is some disagreement concerning whether ROS is necessary during this mechanism of Ag ion mediated injury. Gordon et al. [65] counseled the emergence of OH ions via unharnessing of iron from proteins through bind Ag^+ with thiol teams, leading indirectly to the formation of hydroxyl. Other work was shown that low amounts of silver ions cause the breakdown of the nucleon driver and nucleon flow, and therefore the membrane of protoplasm is the main goal for the lower amounts of Ag ions [67]. Silver cations conjointly cause speedy and intensive loss of membrane integrity in *S. aureus* [66]; has good broad activity against germs including Gram-positive and Gram-negative microorganisms, fungi and viruses [67]. Vitro studies showed that silver Ag release active ions biologically from its surface. The free Ag^+ connects to various cell structures of microorganisms, as well as the membrane of peptidoglycan plasma and, cell wall, the microorganism deoxyribonucleic acid and microorganism proteins [68]. This generates three different mechanisms by

which Ag applies its violent influence. Connecting of Ag^+ to the plasma membrane destroys the outer layers of the cell, inflicting the removal of cell contents and creating structural distortions [69]. As Gram-positive bacterium possesses a thick cell wall, a higher concentration of Ag is essential to stop microorganism growth than Gram-negative bacterium [70]. Furthermore, interaction with sulfhydryl (SH) teams in microorganism proteins and enzymes weakens several of main cell functions, like breathing and porosity, relating to nucleic acids in deoxyribonucleic acid [71].

There is an additional toxicity mechanism through the assembling of reactive oxygen species (ROS) by Ag^+ . The latter ROS generation likely acts naturally with the SH group in the interaction process. The proof of the latter case; is the inflated activity of antimicrobial which be seen in the aerobic versus anaerobic conditions [64]. This action causes the de-configuration of proteins, cells, and resultant biofilms (surface species) which successively enhances long-term exposure to the surface Ag NPs and their relating antimicrobial impacts [72]. Part of this impedance appears to be associated with genetic which is manage to eject silver out of the cell [73]. Taglietti et al. [74] showed that a self-constructed mono-layer of Ag NPs on a glass surface was obtained by amino-salinization of the glass surface. From their results, there was a long-term unleashing of Ag^+ , while the Ag NPs still connected to the underlying substrate, and a potent anti-biofilm activity versus the biofilm-formed *Staphylococcus epidermises* was found out. Structure make-up of silver has a consequence for its antimicrobial performance. Choi et al. [75] performed a comparative study between metallic Ag NPs with the Cl^- , and NO^- ions. They outcome that Ag NPs have larger effectiveness against bacteria, this is may be due to silver nanostructure along with a secondary mechanism of action.

Li and his group reported that there are three antibacterial approaches of Ag NPs. Firstly, strong adhesion of such nanoparticles to the surface of bacteria has correlated to a surface zeta potential of the nanoparticles, thus altering the bacteria membrane properties. As Cao et al. [76] studied the antibacterial properties of Ag NPs that included with titanium "Ag-PiII-originated surface". All the examined Ag-PiII surfaces showed a reduction in the proliferation of both types of studied bacteria (Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*). Secondly, silver nanoparticles can breakthrough inside the bacterial cell, causing damage in DNA. As stated, by Choi and Hu [77] in their study, the suppression of nitrifying organisms has attributed to the Ag NPs of less than 5 nm; wherein their toxicity was being higher than the other shapes of silver "silver ions, AgCl colloids" [21]. Thirdly, in the case of using a dissolution of Ag NPs, it releases Ag ions for antimicrobial and, these ions may interact with sulfur-containing proteins in the cell wall of bacteria which may cause compromised

their function. The latter mechanism is at most regarded as the major approach of the antimicrobial activity for Ag NPs [21].

Cao et al. [78] has also proposed that dissolved such Ag ions interact the wall of the cell and proteins of the cytoplasmic. They have highlighted the fact that the interaction of silver ions with the group of thiols of vital enzymes; probably leads to poor their function or disable. Ions exchange of silver between the complexes of inorganic sulfur and thiols was also suggested [79, 80]. It has been proposed by Lee [81], that silver ions prevent enzymes from working in the phosphorus, sulphur, and nitrogen cycles of nitrifying bacteria [29].

Silver in the form of ions has an impact on the process proliferation of cells. It has used in the dermatology application to aid the healing of wounds [34, 82]. Furthermore, an approach of modifying antimicrobial characteristics of silver ions was performed by the preparation of Ag NPs, which can effectively be modified their surface. The nanoparticles can be applied to broad kinds of therapeutic usage. In addition, silver nanoparticles exhibit an improvement of antimicrobial impact in comparison with silver ions [57]. Silver nanoparticles may, therefore, be further interacting because of their catalytic properties and being more toxicity to the bacteria than Ag ions [34].

Several mechanisms are correlated to the anti-bactericidal of Ag NPs, wherein it has suggested that the Ag NPs may alter the permeability of the membrane for the bacterium, leading to a drift of the Ag NPs toward the cell, and then mainly interacts with intracellular proteins “membrane proteins and microbial DNA” which probably intervene with the division of the cell, thereby to kill cell. On the other hand, the bacterial replication breakthrough is owing to releasing of silver ions from the silver nanoparticles [83]. However, the science behind Ag NP mediated membrane damage that leads to cell death is not fully understood yet [84].

One of the mechanisms for antibacterial toxicity of nanosilver ions correlates with their reacting with the structural proteins and functions proteins, particularly with thiol groups (–SH) [83]. Exposing to Ag NPs causes an increase in the level of intracellular reactive oxygen species (ROS), which leads to oxidative stress, destroys protein, DNA strand fraction, and thereby, kills the cell. Protein S2 is the main target inside the cell which centers on in the tiny branch units on the ribosome of the bacteria. Connecting of Ag⁺ to the proteins of ribosome leads to change of the original structure of ribosome and suppression of protein biosynthesis [83].

The antimicrobial mechanism of Ag nanoparticles was studied; it [85] suggested that it is related to the forming of the free roots which results in damage to the membrane. This free root is probably derived from the surface of silver NPs and be in charge of the antibacterial action [22].

In contrast of the above results, it has been proved that silver ions and silver nanoparticles possess the same formula of action. But the antibacterial activity for silver ions is more potent than Ag NPs. This antibacterial function of Ag ions is linearly proportional to the surrounding environmental concentration of Ag⁺, the latter exhibits high antibacterial activity even in low concentrations owing to the oligodynamic effect. Silver ions prepared in electrolytic method showed a supermom antibacterial agents than one produced via dissolve the Ag compounds [83].

Several reports suggest that the similarity of antibacterial toxicity mechanism of Ag NPs and silver ions, because of the life cycle of Ag NPs and their turning to Ag ions. The interaction of nanoparticles with cells can be explained as follows: (i) with the envelope of the cell for example membrane, pep membrane, (ii) with the big structures of molecules such as proteins and nucleic acids and (iii) in the pathways of biochemical [83].

The interaction of ions with the inner membrane of bacterial considers one of the most important mechanisms of Ag⁺ toxicity [83]. It has been proved that the aggregation, of Ag⁺ on the cell film of the bacterial, is subsequent by the detachment of membrane of the cytoplasmic (CM) from the cell wall in bacteria [58]. Sütterlin et al. [86] has shown that a minimal bactericidal concentration (MBC) of Ag⁺ for Gram-positive bacteria was more than 32 times higher than the MBC values for the Gram-negative bacterial cells. It was reported that (–COOH) groups in both glutamic acid and phosphate groups in teichoic acid are mainly in charge of binding of silver ions [83]. Table 3 shows some more mechanism action of Ag NPs against different bacteria.

5 Effects of Size, Shape and Concentration of Silver Nanoparticles on Their Antimicrobial Activity

In the agreement with the results that have been reported by various researchers, characteristics of nanoparticles such as size, shape, and concentration play an important role in each application. To date, many scientists and academic researchers have paid great attention to a find different ways of optimizing nanomaterial production, which is mostly preferred and utilized in healthcare, medicines, protective textiles and other fields [99]. The special features of NPs of a large surface to volume ratio and crystallographic surface structure make them a strong candidate to fight and inhibit microbes owing to revealing chemical activity [21].

The properties and functionality of silver nanoparticles are closely correlated to their size, shape, and concentration. Synthesizing Generation of nanoparticles and manipulating of their size is one of the important factors that play a key role in determining the biocides activity [100, 101].

Table 3 Details of Ag NPs and their mechanisms of action against bacteria

Method of generation	Size	Density or concentration of Ag NPs	Shape	Bacteria	Mechanism of action	Ref
Purchased	5 nm (average)	1000 ppm		<i>E. coli</i>	“The combined results suggested that SNPs may damage the structure of bacterial cell membrane and depress the activity of some membranous enzymes, which cause <i>E. coli</i> bacteria to die eventually”	[87]
Purchased	30–130 nm	Ag% (5–25%)		<i>E. coli</i>	“The strong bactericidal activity of the Ag composites based on bacterial cellulose is attributed to the action of silver nanoparticles obtained when a combination of hydroxylamine as reducing agent and gelatin as protective colloid was employed”	[88]
Lycopersicon esculentum extract	10–40 nm	1, 2, 5, 10, 20, 50, 100, and 200 µg/ml)		<i>E. coli</i>	“The electrostatic attraction between negatively charged bacterial cells and positively charged Ag nanoparticles was crucial for the antibacterial activity”	[89]
green methods	85.07 ± 12.86 nm	10 µL		<i>E. coli</i>	“The mechanism of action involves the inactivation of enzymes and the DNA damage of microorganisms”	[90]
Chemical reduction	below 20 nm	1600 ppm			The received antimicrobial agents of silver can be considered as an adopted strategy to reduce adhesion of bacteria and to inhibit the formation of bacterial biofilm	[91]
Chemical reduction	12 nm	N/A		<i>S. basillus</i> , <i>S. aureus</i> , and <i>P. aureginosa</i>	“It is believed that cellular proteins become inactive after treatment with silver nanoparticles. Ag NPs are toxic and react with proteins, therefore they bind protein molecules; as a result, cellular metabolism is inhibited causing death of microorganism”	[92]
Biosynthesis	20–50 nm	N/A		<i>B. subtilis</i> and <i>K. pneumoniae</i>	“Possible mechanism of metal and microbes interaction which may be due to structural specificity of the cell of microbes and how metal availability influences microbial resistance”	[93]

Table 3 (continued)

Method of generation	Size	Density or concentration of Ag NPs	Shape	Bacteria	Mechanism of action	Ref
Manufactured by Thermolon Korea, Inc. (Busan, Korea)	N/A	0, 50, 100, 150, 250, and 500 µg/ml		<i>S. aureus</i> and <i>E. coli</i>	“Ag-NPs have potent antibacterial activities against bacteria”. “The inactivation of lactate dehydrogenase LDH and increased protein leakage observed with Ag-NPs treatment decreased the growth and reproduction of bacterial cells”	[94]
Purchased (chemically produced)	5–10 nm	10 µg/ml	Near spherical	<i>P. aeruginosa</i>	After Ag NPs touching on <i>P. aeruginosa</i> , the wall of the cell will be thin after that, the cell membrane crushed and broken, thereby the cell constituents leaked out. Furthermore, as Ag NPs damped the function of CAT and POD, the extreme ROS such as H ₂ O ₂ and peroxides cannot be eliminated in time. This could lead to weak DNA and ribosome and, reduced the synthesis of the macromolecules. All of the above facts may do together for the death of bacteria	[95]
Chemically	5 nm	0.1 µg/ml		<i>P. aeruginosa</i>	“Analysis of the protein profiles showed that the cell membrane was the main target of Ag NPs and cellular oxidative stress was induced by ROS generation. The release of silver ions and particle-specific effects synergistically achieve the antibacterial action of Ag NPs”	[96]
Inert gas condensation (IGC) method	16 nm	60 µg/ml		<i>E. coli</i>	“Silver nanoparticles adhered to the cell wall of bacteria and penetrated through the cell membrane. This resulted into inhibition of bacterial cell growth and multiplication”	[97]

Table 3 (continued)

Method of generation	Size	Density or concentration of Ag NPs	Shape	Bacteria	Mechanism of action	Ref
Chemically	11 nm	0, 1, 5, 10, 25, or 50 ppm	Near spherical	<i>B. subtilis</i>	The findings confirmed the silver species in silver nanoparticles-treated the cells of <i>B. subtilis</i> as Ag ₂ O referring that toxicity of the Ag-NP is probably mediated by freed Ag ⁺ ions from Ag NPs, which penetrate bacterial cells and have been then oxidized intracellularly to Ag ₂ O. These outcomes offer decisive evidence for the function of Ag ⁺ ions in Ag-NP microbial toxicity, and it was also proposed that the effect of improperly disposed Ag NPs to soil and water ecosystems may have to be further investigated	[98]

For instance, Marambio-Jones and Hoek [102] have been reported that smaller particles have a larger surface area to volume ratio and thereby more efficient antimicrobial activity. Along with particle size, Ag NPs concentration also plays a key role to determine antimicrobial power.

In addition to the Ag⁺ released by Ag NPs, in the fact that for further studies; that the size and shape of the Ag NPs can also play an important role in their toxicity, that becomes the main concern of several researchers [29]. Morones et al. [103] reported that particle shape has a great effect on the antibacterial activities. It has shown that the Ag NPs with facets shapes $\langle 111 \rangle$ have a promising antibacterial activity. This is due to their possessing powerful antibacterial characteristics; where $\langle 111 \rangle$ contain larger atom densities for better interaction. In the line of the published reports, several factors of Ag NPs (such as shape, size, surface charge, composition, and stability) have a powerful toxic impact on the antibacterial activity [15].

The intrinsic properties of metal nanostructures depended on their size, shape, composition, crystallite which is strongly correlated to their preparation conditions. From the acknowledge in the researches, size and specific area of Ag NPs affect their antimicrobial activity. It has found that smaller sized silver nanoparticles possess a greater antimicrobial characteristic in comparison to larger-sized Ag NPs. This is because of the higher intracellular bioavailability of silver caused by better cell-particle contact and increased the release of silver ions [85].

Sondi and Salopek-Sondi [104] have studied the antibacterial activity of Ag NPs on the Gram-negative bacteria; they have found that it relied on Ag nanoparticle concentration and which is tightly linked to forming of ‘pits’ in the bacterial cell wall and then Ag NPs aggregated on the membrane of bacteria penetrate the cell wall, thereby the death of a cell and they are also confirmed that there was a deterioration of the structure of membrane of microorganism with Ag NPs [22].

Nanoparticle size is inversely linked to the surface area and the radius of the particle, consequently increasing of surface area to volume accelerated reactions; thereby nanoparticles are used as a catalyst. A dramatic increase in the ratio of surface area to volume results in a smaller size of the nanoparticle [101]. Small size particles have a great influence on the bactericidal activity, where the small size gives them the ability to interact with the external microbial membrane, releasing metal ions in a solution that will kill it [101, 105]. According to this consideration, several scientists have utilized antimicrobial additives like silver nanoparticles in different textiles such as clothing, medical and hospital sheets, seeking a way to inhibit humans from viruses, and bacterial infections. The dimension and morphology of the nanoparticles plays a vital role in all applications, therefore significant attention has been focused on this field [100].

Numerous studies have been proven that antibacterial activity depends on the special features of the nanoparticles. Several metal nanoparticles have a positive bactericidal effect on different types of bacteria. The bactericidal effect of Ag NPs depends on various factors. Although the shape and the surface charge of the particles affect the antibacterial activity, smaller sized particles have been demonstrated to have a greater antibacterial activity which correlated to gain Ag NPs two benefits: One is that nanoparticles could simply have entered bacteria reaching its nuclear content because the structure of bacteria cell wall, especially in gram-negative ones. Other benefits include their large surface area enhancing bactericidal interactions [106]. Unlike bulk material, nanoparticles with a larger surface area to volume ratio have been shown to have a more active tendency against microbes which reveals a novel biological activity [105]. It was shown that the nanoparticles collect on the cellular surface compromise cellular penetration, while nanoparticles smaller than 10 nm pass through the bacteria cell wall, affecting DNA and the enzymes, and thus leads to cellular death [106]. The phenomena of antibacterial activities have been observed with nanoparticles of sizes less than 100 nm. However, it has proven that Ag NPs around 20 nm have a threshold biological effect [105]. The effect of Ag NPs size on the microbial activity has been demonstrated. Where has found that a 10 nm Ag NPs were revealed to have higher cytotoxic and antimicrobial activity than 100 nm Ag NPs with the identically control concentration [107]. On the other hand, the shape of the nanoparticles also has a great impact on antimicrobial activity. The interaction of nanoparticles with bacteria is not only dependent on their size but also dependent on their shapes. Several investigations have reported the impact of the silver NPs morphology on their function of antibacterial. It was reported that the Ag NPs which possess a similar surface area can reveal various microbial activity depending on their shape effect. This influence can be attributed to the difference in their active facets [106]. Different shapes of silver nanoparticles such as spherical, rod-shaped, and truncated triangular Ag NPs were prepared using chemical methods. It has been shown that truncated triangular nanoparticles overcome spherical particles in the retardant growth of *E. coli* at a given concentration, while spherical nanoparticles confirmed better antibacterial activity than AgNO_3 [80]. Truncated triangular silver NPs with 1 μg of dose hindered bacterial growth while spherical nanoparticles with content above 12.5 μg reduced the number of colonies dramatically and caused 100% inhibition of bacterial growth with a total of 50 to 100 μg of silver. On the other hand, rod-shaped nanoparticles and AgNO_3 had shown a poor antibacterial efficiency. It has been demonstrated that when was used the same dose (100 μg) of rod-shaped particles and AgNO_3 ,

rod-shaped particles have shown some colonies grew on the plate which fewer as compared than AgNO_3 [81].

Similar investigations have shown the role of silver nanostructures on antibacterial activates. Chemical reduction methods have been used to produce Nano-silver of different forms structure (such as spheres, flat nanoplates, nanoprisms, polygonal nanoparticles, and hierarchical structures). The effects of these different shapes of the Ag NPs on the antibacterial activity has been examined where cotton fabrics were treated with these various shapes of Ag NPs. Growth prohibition examines were imposed on the cotton cloths which was showed fluctuated antimicrobial functions against gram-negative bacterium *E. coli* and gram-positive *S. aureus* [100]. It has been found that among all shapes of Ag NPs, a hierarchical morphology displayed stronger antimicrobial activity over 91% after five washing cycles as compared with the other Ag NPs morphologies. This effect was correlated not only to the quantity and the contact of Ag NPs carried out on the surface of the fiber but also the calculation parameter of the Ag NPs specific surface area on the consideration. Nanoparticles of spherical shapes were showed a weak contact in the cotton fibers thereby they are more easily detached than other morphologies. For the same reason, there was no growth inhibitory effect of disc silver nanoparticles against both bacteria of *S. aureus*, and *E. coli* after a repeatable washing process (five-time) which can be simply removed from the cotton fibers surface due to the poor connection of the disc particles to the fibers surface [93].

The effect of the Nanomolar concentrations of Ag NPs on the bacteria has been reported. It is found that the Ag NPs caused the death of *E. coli* cells within minutes might be due to the instant dissipation of the motive force of the proton [60] which is similar to that found for the antibacterial action of the Ag^+ ions [67]. For instance, the minimal concentration of Ag^+ ion causes a huge proton infiltration within the membrane of *Vibrio cholera*. The latter action might occur from either any Ag^+ -modified membrane protein or any Ag^+ -modified phospholipids bilayer. This process results in inactivation of the membrane and thus cell death [67].

Syu et al. [108] demonstrated the effect of size, shape and concentration of Ag NPs on microbial activity. In their studied, they found that 80% of silver NPs with the smallest size (8 ± 2) nm has the highest microbial activity compared with the 80% Ag NPs triangular and decahedral with size (47 ± 7) nm (45 ± 5) nm respectively. In addition, the microbial activity enhanced by an increase in the concentration of the Ag NPs, but it also has various effects for different shapes but the same size of the Ag NPs.

Overall, particles in the range of nano-size have a larger impact on microbial activities. This effect is considered as a fingerprint for the particles of a tiny size which can be attributed to their ratio of surface area to volume of the

nanoparticles. One of the major reasons that nanoparticles are more active is their high surface area to volume ratio which offered the possibility of NPs to anchor the external surface of the bacteria wall and then penetrates within it and then kills it [109, 110].

Nano-scaled size of silver nanoparticles is one of the main issues that influence the extent of the action of antimicrobial. It was shown that smaller particles less than 10 nm are considered most effective, as there is a bigger expanse for the ejection of Ag^+ [78]. The size of the particle, therefore, could be of greater importance than the concentration or mass of the nanoparticles [72]. The activity amount is additionally showed to be associated with the size of nanoparticle and, the kind of NPs functionalizing part. It has been confirmed that the concentration of particle for simplest antibiotic impacts vary 10 nM to 10 μM [86].

It was shown that the different sizes and Shapes of the Ag and Au NPs have different effects on their antimicrobial activities. Osonga [111], focused on characterization of the effects of luteolin tetraphosphate (LTP) derived Ag NPs and Au NPs as a therapeutic agent on the growth and expression of plant-based fungi and bacteria. It was reported that the shape and size of Ag and Au NPs have different capabilities against the gram positive and gram negative bacteria. Smaller sized quasi-spherical (21 nm) and spherical Ag NPs (9 nm) show 100% inhibition of the bacteria and fungi used their study. In comparison with the LTP-Au NPs, it was concluded that the smaller sizes of LTP-Ag NPs have stronger antibacterial activity [111].

6 The Impact of Surface Modification and Functionalization of Silver Nanoparticles

One major drawback with the exploitation of antibiotics and pesticides is the development of their resistance. As mentioned above, one in every of the foremost vital properties of nanoparticles is their high area to volume ratio. For several totally different nanoparticle varieties, this specific property leads to high surface reactivity [112–116]. Metal-based nanoparticles, like silver, are distinctive as a result of the fact that they provide the likelihood of sterilized their surfaces so as to introduce specific functionalities for environmental applications [117–120].

Cotton fibers are used for mainly analyze the functionality of silver with textile materials. There has been a fixed exchange of normal fibers with fabricated fibers in the medical/health care field, cotton fibers remain too desirable to a good expanse within the production of not implantable medical tissue materials and health care/hygiene creates [121]. One in each of the primary studies has shown that cotton fabrics added via an ethanol-solution (25- and 50-ppm) of

Ag NPs have the good activity of antibacterial against *S. aureus* and *K. pneumonia* [122], which indicated that the fascinating stage of medicament function has completed, notably once the filling of silver nanoparticles is distributed when coloring before the print of cotton fabrics. The identical trend has ascertained in the woven of cotton fabrics that were treated with a 20-ppm solution of Ag NPs. The surface of silver nanoparticles has been modified or functionalized through covalent and non-covalent bonds to ligands and thiol groups [123, 124] (see Fig. 3a, b).

Durán et al. [125] reported that silver ions could be reduced extracellular mistreatment via fungus *Fusarium oxysporum* to produce stable Ag NPs in water imaging maps of the elemental spectroscopy analyze discovered the existence of Ag, N, and S on the produced Ag NPs. It assumed that the proteins of fungal stabilize the silver nanoparticles. The inputting of silver NPs (size of only 1.6 nm) to cotton fabrics caused to a brilliant antibacterial efficiency against *S. aureus*. Thomas et al. [126] exhibited that amino and CHOO groups of biopolymer Chitosan tied to cotton fabric can be usefully employed for the connecting of Ag ions. The result oxidation in the cotton fabric from periodic acid led to the production of cellulose dialdehyde that enables the coupling of amino teams of Chitosan to organic compound teams of cellulose. Silver ions have efficiently high connected to the amino teams of the attached Chitosan, and they have been reduced via sodium citrate wherein the existences of silver NPs have changed cotton fabric. These fabrics of cotton presented honest medicament function against *E. coli*. Plasma treatment has performed to cotton fibers surface for

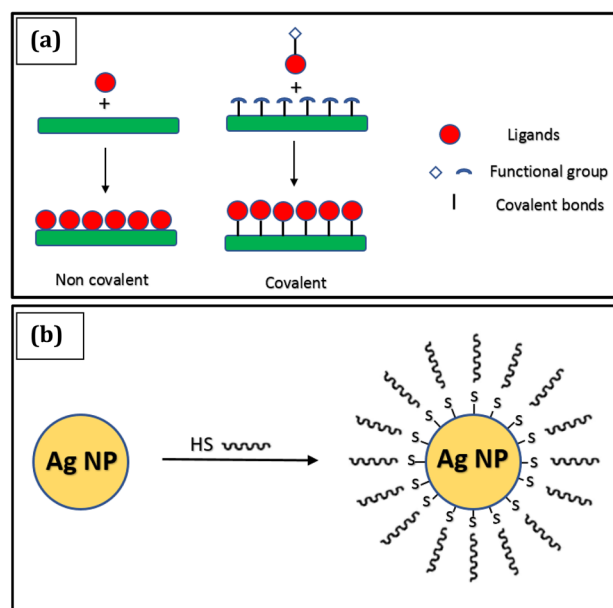


Fig. 3 Surface modification of Ag NPs through covalent and non-covalent bond with ligands (a) and thiol groups (b)

activation of fibers surface before deposition of silver NPs [127, 128]. In contrary to cotton fibers, the modified wool fibers with NPs have been considerably less discovered. Hadad et al. [129] has reported that the deposition of tiny Ag NPs on wool fibers can be successfully performed via the sonochemical method. The deposition of silver NPs on wool fibers was conducted using ultrasound irradiation in a liquid of nitrate, ammonia, and ethanediol; it works as a reducer. The system has been cleaned with argon and argon/hydrogen for different periods of time before sonication to take out dissolved oxygen/air. The particular surface area of fibers was magnified (from 1 to 4.6 m²/g) because of the insert of silver NPs to the surface of wool fiber. It was shown that the interaction between silver nanoparticles and sulfur atoms appeared due to the S–S bonds divide in the wool fiber. The modified nanocomposite has shown outstanding stability without any variation of Ag content even after it is washing for several cycles [130], treated the wool fibers with the sulfur nanosilver ethanol mixture by standard pad dry-cure technique. The treatment properties of the fibers were investigated against *S. aureus* and *K. pneumonia*. In the case of the *S. aureus* bacteria, modified wool fibers exhibited a bacteria reduction of 99.9% of the used mixture concentration (5–30 ppm). On the other hand, the colloids of incorporated wool fibers with silver NPs (from 5- to 10-ppm) showed a rather reduced *K. pneumonia* (99.70%). But, the higher concentration of such colloids (20 and 30 ppm) achieved the most bacterium reduction. Additionally, treated fabrics of wool woven with 20 ppm mixture fully have suppressed the expansion of each bacterium.

Major mind analyzes of applying the silver nanoparticles to the fibers of polyester (PES) and polyamide (PA) is aimed to activate the surface of fiber through applying a chemical or physical–chemical treatment which results in enhancing the binding efficiency of Ag NPs. Dubas et al. [131] developed a fascinating methodology for the deposition of silver NPs to PA fibers; supported the layer-by-layer approach. The film with antibacterial activity on the PA has formed in which fibers via organizing the dipping of fibers in a mixture of poly (diallyl dimethylammonium chloride)-PDADMAC and silver NPs covered with poly (methacrylic acid)-PMA. Layer deposition after layer was achieved resulting from the electrostatic interaction between anionic Ag NPs capped with PMA and cationic PDADMAC. It was advised that pre-treatment of fibers would possibly significantly amend surface chemistry and would possibly significantly amendment, improve deposition method, so as to obtain permanent antibacterial activity. Dastjerdi et al. [132] has adopted a method to treated PES fabrics at the same time or one by one with the emulsion of a poly compound and commercial colloidal Ag NPs at totally various concentrations. This method depends on the inclusion of silver nanoparticles in a cross-linkable

polysiloxane layer. It was shown that applying low concentrations of Ag NPs was enough to achieve satisfying biological processes against *S. aureus*, while the opposite trend has shown in the case of *K. Pneumoniae*. In the latter case, a higher concentration of such nanoparticles has been needed for an equivalent result. A cross joined polysiloxane layer supply a control releasing of Ag and therefore, a prolonged antimicrobial activity has expected. It has been reported that coinciding curing of PES with polysiloxane and silver nanoparticles led to higher medicament potent as compared with independent finishing. Biogenic silver nanoparticles were modified to improve their antibacterial activity and to have synergistic effects with antibiotics such as ampicillin, erythromycin and kanamycin against Gram-positive and Gram-negative bacteria [133].

The surface-modified of silver nanoparticles are able to bind with a particular target of drugs or other biomolecules. However, a straight coupling of AgNPs with medicament is also possible, in which it was observed that a conjugate of a metal NPs with antibiotics offer a superior outcome in the treating infections inside cells [134].

Ag NPs conjugation with an antibiotic enhances the performance to deliver the drug to target some cases. In general, the precise dosage is wanted to cause to death of the pathogens. However, the number of used antibiotics in the treatment has always too higher than the required dosage which can cause harmful impacts. In that direction, conjugation of an antibiotic with silver NPs will being useful to refine antibiotic effectiveness. The conjugation of Ag NPs with antibiotics or other medicament molecules can be directly carried out by ionic/covalent bonding or the physical absorption [22]. Table 4 shows some modified Ag nanoparticles with the other materials for antimicrobial activities.

7 Conclusions

This review can be used to answer the matters of whether silver nanoparticles or silver ions have the most marked antimicrobial activity, the exact antibacterial mechanism of silver nanoparticles and silver ions, and the impact of surface area, size, and concentration of the silver nanoparticles on their bactericidal activity. Mostly, silver ions are more effective to kill bacteria in comparison to the silver nanoparticles. However, modified and functionalized silver nanoparticles are more efficient as an antibacterial agent to kill microorganisms in comparison to non-functionalized and non-modified silver nanoparticles. The size, shape, and concentration of the nanoparticles are also having a crucial effect on their antibacterial activity.

Table 4 Antibacterial activity of modified Ag NPs

Ag modified or functionalised	Sizes	Concentrations	Methods	Purpose	Conclusions	References
Ag-TiO ₂ compound	Aver. 31 nm	20 µg/ml	Picosecond laser ablation in DIW	Antibacterial activity against <i>E. coli</i>	Antibacterial activity of the Ag-TiO ₂ compound NPs was better than the laser produced pure TiO ₂ NPs and chemically generated Ag NPs	[45]
Ag-TiO ₂ NPs	Aver. 38.33 nm	20 µg/ml	Laser ablation in ice water	Antibacterial activity against <i>E. coli</i>	Efficiency of the Ag-TiO ₂ NPs to kill <i>E. coli</i> bacteria was better than laser-generated pure TiO ₂ NPs	[46]
PEG/CTS-g-PAAm@Ag NP	The size of the PEG stabilized Ag NPs was 38 ± 4 nm	Ag NPs = 1 mg/ml 1:1, 2:1, 4:1, 6:1, 8:1 and 10:1; AgNP/pDNA weight ratio)	AgNPs were synthesized by one-pot, facile green method via a water soluble CTS-g-PAAm copolymer	For gene delivery	Efficiency of the Ag NPs was significantly increased by immobilization of the RGDS peptide	[124]
RGDS decorated PEG/CTS-g-PAAm@Ag NP	68 ± 5 nm and 7 ± 4 nm					
TiO ₂ -Ag core-shell	Aver. 27 nm	20 µg/ml	Sequential laser and ultrasonic wave	Antibacterial activity against <i>E. coli</i>	Antibacterial activity of the TiO ₂ @Ag core-shell NPs was slightly better than that of the Ag-TiO ₂ compound NPs under the same light conditions and at the same concentration. In addition, both types have better antibacterial activity in comparison with the pure laser produced TiO ₂ NPs	[135]
Ag doped TiO ₂ -chitosan (STC)	5–35 nm at 1%(v/v), 5–45 nm at 1.5%(v/v), 5–55 nm at 2%(v/v) and 5–45 nm at 2.5%(v/v)	1.0, 1.5, 2.0, and 2.5% (v/v)	inverse emulsion cross-linking reaction	Antibacterial activity against <i>E. coli</i> , <i>S. aureus</i> and <i>P. aeruginosa</i>	Optimal antibacterial activity of the STC with particle size in the range of 1–10 µm was observed against <i>E. coli</i> , <i>S. aureus</i> and <i>P. aeruginosa</i> under visible light	[136]
Ag-TiO ₂ NPs	N/A	80 µg/ml	Sol-gel	Antibacterial activity against <i>S. aureus</i> , <i>P. aeruginosa</i> and <i>E. coli</i>	Ag-ZnO NPs and Ag-TiO ₂ NPs can kill all the three types of bacteria at the concentration of 60 µg/ml and 80 µg/ml of culture, respectively	[137]
Ag-ZnO NPs		60 µg/ml				

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