

# Silver Nanoparticles: Synthesis, Medical Application, and Toxicity Effects

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## Abstract

Silver nanoparticles (AgNps) are particles of silver that range in size from 1- 100 nm. Silver nanoparticles are of unique properties and attract a lot of attention due to their wide range of potential application in medicine, electronics, cosmetics and many other fields. Although, chemical and physical methods are the major methods for AgNp synthesis, they are expensive and can absorb toxic materials into them. In this review we focus on biological synthesis of AgNps by fungi, bacteria, and plant extracts as a safer, more feasible alternative. Some recent medical applications such as Anti-inflammatory effects, cancer treatment, and mechanism of antimicrobial effect are described. We also discussed the toxicity of AgNps, its effect on environment and human health.

**Keywords:** Silver nanoparticle, Antimicrobial action, Synthesis, Medical applications, Silver nanotoxicity.

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## INTRODUCTION

Nanotechnology is relatively new science with rapidly growing population that produces particles in the nanosized range of 1-100 nm. Those nanoparticles have distinctive and size-related chemical and physical properties giving them a wide range of usage in almost every field. Silver nanoparticles (Ag-NPS or nanosilver) have gained increasing interest due to their unique properties compared to their macro-scaled counter parts and also their well-known antimicrobial and anti-inflammatory properties. At nanoscale atoms tend to lay close to or at the surface of the materials giving them enhanced properties and higher reactivity due to the increased relative surface area (Bondarenko *et al.*, 2013).

Many methods have been described in the literature for synthesizing Ag-NPS including chemical, physical, photochemical and biological methods. Chemical and physical methods have been widely used but their high consumption of energy and also being expensive, in addition to toxic substances produced; those methods are not proffered in Ag-NPS synthesis. Biological methods instead provide an ecofriendly, feasible alternative that are economic and relatively faster and usually employs microbes and plants (Tran *et al.*, 2013).

Silver nanoparticles have been used at a large scale in various fields (Khan *et al.*, 2017). They have many potential

applications in medicine, cosmetics, renewable energies, biomedical devices and bioremediation (De *et al.*, 2008; Sharma *et al.*, 2009). Due to their antimicrobial properties, they are used as a bactericidal coating in water filters, wound dressings, dental resin composites, air sanitizer detergents and many other products such as bone cement etc. Also, they are exploited in textile engineering, catalysts, optical sensors and in electronics and optics (Danilczuk *et al.*, 2006). In spite of their great benefit, Ag-NPS were reported to induce toxic effects that could lead to potential risks in environment and human health (Milić *et al.*, 2015). More studies are needed to provide an accurate data about the real impact of Ag-NPS on health.

This review aims to give an overview of silver nanoparticles and the various methods used in synthesizing them stating the advantages and disadvantages of each method. Also discussed, is the various application of nanosilver in the medical field and their antimicrobial and anti-inflammatory properties, in addition to cancer treatment. The toxicity that silver nanoparticles may induce in humans, living organisms or the environment as a whole is also reviewed.

## Synthesis of Nanoparticles: Chemical synthesis

Many methods have been used for the synthesis of Ag-Nps including chemical, physical, photochemical and biological routes. Each process has advantages and disadvantages with common problems such as costs, scalability, size of particles and size distribution. One of the mostly used methods for Ag-Nps production are chemical methods, as they provide an easy way to synthesis Ag-Nps in solution.

The simplest method involves the chemical reduction of the metal salt  $\text{AgBF}_4$  by  $\text{NaBH}_4$  in water. The process produces silver nanoparticles in the size range of 3 to 40nm which are characterized by transmission electron microscopy (TEM) and UV-visible to evaluate their quality (Thirumalai Arasu *et al.*, 2010). Another method involves the reduction of silver nitrate with ethylene glycol in the presence of poly vinyl pyrrolidone (PVP) producing large quantities of silver nanocubes and is called polyol process (Zhu *et al.*, 2001). It was suggested that it is possible to control the size silver nanocubes by varying experimental conditions (Banchelli *et al.*, 2016).

A modified polyol process using precursor injection technique was used to synthesize spherical Ag-Nps with a controllable size and high monodispersity (Salkar *et al.*, 1999). Simple oleylamine-liquid paraffin system was reported to produce monodisperse Ag-Nps, at which the formation process of Ag-Nps could be divided into three stages: growth, incubation and oawald ripening stages. Only three chemicals including silver nitrate, oleyomine and liquid paraffin are employed throughout the whole process (Chen *et al.*, 2007).

Generally, the process of chemical synthesis of Ag-Nps in Solution usually involves three main components: (i) metal precursors, (ii) reducing agents and (iii) stabilizing/capping agents. Reduction of silver salts leads to formation of colloidal solution, involves two stages nucleation and subsequent growth. It was found that the size and shape of synthesized Ag-Nps are strongly dependent on those stages and could be controlled by adjusting the reaction parameters such as temperature, PH, precursors, reaction agents (i.e.  $\text{NaBH}_4$ , ethylene glycol, glucose) and stabilizing agents (i.e. PVA, PVP, sodium oleate (Jiang *et al.*, 2006; Pileni, 2000).

### Physical synthesis

Generally, the metallic NPS are physically synthesized by evaporation-condensation method. This method employs a tube furnace at atmospheric pressure which, however have many drawbacks being large in space and consuming a lot of time and energy to raise the environmental temperature around the source material and to achieve thermal stability. Therefore, various physical methods have been developed (Kruis *et al.*, 2000).

Thermal decomposition have been used to synthesize Ag-NPS in powder form (Lee and Kang, 2004). It involves the reaction of  $\text{AgNO}_3$  with sodium oleate to prepare a

$\text{Ag}^+$  oleate complex and then its decomposition to give Ag-NPS with average size of 9-5nm. A study reported an attempt of synthesizing metal Nps via a small ceramic heater with a local heating area which generated spherical Nps with 6.2-21.5nm size range (Jung *et al.*, 2006). The experimental results of (Tien *et al.*, 2008) showed that Ag-NPS suspension synthesized by arc discharge method with no added surfactants contains Ag-NPS and ionic silver.

In summary, Ag-NPS with nearly narrow size distribution can be synthesized using physical energies (thermal, Ac powders, and arc discharge). Those physical methods can permit the production of large quantities of Ag-NPS samples and powder in a single process but with the consideration of primary cost of investment and equipment.

### Photochemical synthesis

The production of nanoparticles by photo-induced strategies can be divided into two categories, that is the photophysical (top down) and photochemical (bottom up) ones. In the top-down method, bulk metals are grinded then subsequent stabilization of the produced nanosized metal particles was performed by the addition of colloidal protecting agents (Amulyavichus *et al.*, 1998; Gaffet *et al.*, 1996). In the other hand, the bottom up methods includes metals reduction, electrochemical methods, and sonodecomposition.

Different light sources (UV, white, blue, cyan, green and orange) were used in the direct reduction process of  $\text{AgNO}_3$  in the presence of sodium citrate (Nacit) at room temperature. A colloid with distinctive optical properties was produced by this light-modification process (Husseiny *et al.*, 2007). Another route of preparing stable Ag-NPS in aqueous Triton X-100 (Tx-100), using simple and reproducible UV photo-activation method was reported (Vaidyanathan *et al.*, 2010). The Tx-100 molecules have 2 effects: they act as a reducing agent and also as a stabilizer for NPs through template / capping action.

In summary, photochemical synthesis has some main advantages which include: (i) It has the advantages of photo-induced processing which is clean with high spatial resolution and convenience of use; (ii) formation of NPS can be initiated by photo irradiation because the *in situ* generation of reducing agents is controllable and (iii) The great versatility offered by the photochemical synthesis enables one to prepare the NPS in various mediums including emulsion, surfactant micelles, polymer films, glasses, calls, etc. (Bhatia, 2016; Haefeli *et al.*, 1984).

### Biological synthesis

Although chemical and physical methods are widely used in Ag-NPS synthesis, most of them are extremely expensive with high energy consumption and involve the use of toxic chemicals. Those chemically toxic substances which absorbed on the surface may lead to potential environmental and biological risks and hinder the usage of

those particles in medical application (Christy and Umadevi, 2012). The fact that silver nanoparticles have to be handled by humans and must be available at cheaper prices for their effective utilization can't be avoided. So, there is a growing need for synthesizing Ag-NPs with ecofriendly and economically feasible technologies.

The major biological sources of synthesizing silver nanoparticles are bacteria, fungi and plant extracts but there are other sources such as yeast and algae that have been used (Sintubin *et al.*, 2012). Biological synthesis of Ag-NPS can be described as a bottom-up approach where the reducing and stabilizing agents used in chemical and physical methods are replaced by molecules produced by the living organisms. It consists of oxidation – reduction reactions that are carried out majorly by microbial enzymes or the plant photochemical which act on the respective compounds giving the desired nanoparticles.

### Silver synthesizing microorganisms

Some microorganisms are found to be resistant to metal ion concentration as they can survive and grow under such conditions. Many mechanisms are involved in metal resistance such as biosorption, bioaccumulation, efflux systems, alternation of solubility and toxicity through reduction or oxidation, metal precipitation and formation of extracellular metal complex (Husseiny *et al.*, 2007). Although, those microorganisms can survive under low metal ion concentration, toxicity can be induced upon their exposure to higher metal concentrations.

The mechanisms of the biosynthesis of Ag-NPS are widely accepted to be due to the action of nitrate reductase enzyme. In the process, an electron is transferred to the silver ion during the conversion of nitrate to nitrite; hence the silver ion is reduced to silver ( $Ag^+$  to  $Ag^0$ ). In *in vitro* synthesis of silver nanoparticles using bacteria, the downstream processing step required in other cases is removed due to the presence of alpha-nicotinamide adenine dinucleotide phosphate reduced form (NADPH) – dependent nitrate reductase (Prabhu and Poulouse, 2012).

Many metal resisting bacterial species have been reported to be used in Ag-NPs synthesis. *Shewanella oneidensis* (a metal-reducing bacterium) was reported to be used in biosynthesis of Ag-NPs with a simple, economical and reproducible bacterially based method (Klaus *et al.*, 1999). Seeded with silver nitrate solution, the bacterium induce the formation of small spherical-shaped Ag-NPS in the size range of 4 – 1.5nm *Bacillus sp* also have been used in Ag-NPS biosynthesis producing stable particles of 5-15nm in size (Haefeli *et al.*, 1984; Klaus *et al.*, 1999). In another study, different *Lactobacillus* species were used to accumulate and subsequently reduce  $Ag^+$ . Lactic acid bacteria were confirmed to produce biogenic Ag-NPS that vary in size with the smallest NPS of diameter 11.2nm being produced by *L. fermentum* (Sintubin *et al.*, 2009). It was reported that not only Ag-NPs are synthesized in the

presences of enzymes but also it was found that the dried cells of *Lactobacillus sp* A09 uses a specific group on the microbial cell wall to reduce silver ions by interacting with them (Fu *et al.*, 2000). Many other bacterial species have been used such as *Plectonema boryanm*, *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumonia*, *Proteus mirabilis* and *Brevibacterium casei* (Deljou and Goudarzi, 2016; El-Shanshoury *et al.*, 2011; Fu *et al.*, 2000; Kalishwaralal *et al.*, 2010; Klaus *et al.*, 1999; Lengke *et al.*, 2007; Prabhu and Poulouse, 2012; Pugazhenthiran *et al.*, 2009; Sintubin *et al.*, 2009).

Fungi have a good advantage over bacteria to be used as biosynthesizes of Ag-NPS. They can produce large amount of nanoparticles as larger amounts of proteins are secreted giving them higher productivity of nanoparticles (Mohanpuria *et al.*, 2008). The exact mechanism in Ag-NPS bioproduction by fungi is not fully understood. But it was said to be the reduction of trapped  $Ag^+$  ions at the surface of the fungal cells using the fungal enzymes. It was also reported that some extracellular enzymes such as anthroquinones and nophthoquinines can facilitate the reduction. It was believed that nanoparticle formation in *F.oxysporum* is due to the NADPH- dependent nitrate reductase and a shuttle quinone extracellular process (Ahmad *et al.*, 2003). Many fungal species were reported to produce Ag-NPS like *Trichoderma viride*, *Aspergillus sp.*, *Phanerochaete chrysosporium* and *Coriolus versicolor* (Ahmad *et al.*, 2003; Boroumand Moghaddam *et al.*, 2015; Fayaz *et al.*, 2010).

The cell wall of microorganisms plays a vital role in the intracellular synthesis of NPS. The positively charged metal ions interact with the negatively charged cell wall at which the metal ions are bio reduced to NPS. Extracellular Ag-NPS are produced when microorganisms are incubated with silver ions as a defense mechanism against the toxicity of the metal. Microbial – Based synthesis of Ag-NPS provides feasible, ecofriendly methods that do not consume high temperature or pressure conditions.

### Silver synthesizing plants

Synthesizing silver – nanoparticles using microbes have a major drawback of being a very slow process that consumes a lot of time when compared to using plant extracts. There are many advantages of biosynthesis of Ag-NPS by plant extracts which is that they are safe to use nontoxic in most cases and have a broad variety of metabolites that aid in silver ion reduction making them quicker than microbes in synthesis (Anjum and Abbasi, 2016).

Plant-assisted reduction of silver ions was believed to occur due to the presence of phytochemical, which involve flavones, terpenoids, ketones, aldehydes, amides and carboxylic acids. Some compounds are water – soluble such as flavones, organic acids and quinines that are responsible for the intermediate reduction of ions. Emodin, and anthraquinone was reported to be found in xerophytes

and undergoes tautomerization, leading to the formation of silver nanoparticles. While in mesophytes, three types of benzoquinones were found which are cyperoquinone, diethequinone and remirin. Many plants were found to be useful in Ag-NPS production such as *Medicago sativa*, *Aloe Vera*, *Azadirachta indica* and *piper petle* leaf and many others (betle Broth, 2012; Chandran *et al.*, 2006; Gardea-Torresdey *et al.*, 2003; Shankar *et al.*, 2004).

### Medical Applications of Silver nanoparticles

The aim of using AgNps in medical applications is the prevention of bacterial colonization and Reduction of inflammation. AgNps increase wound healing through modulation of various cytokines and decreasing matrix metalloproteinase (MMP) levels and enhanced cellular apoptosis. Nanocrystalline silver wound dressings have been commercially available from a long time. An example is (Acticoat®), which is the first commercial dressing containing AgNps clinical use for the treatment of various wounds, including burns and chronic ulcers. It is made up of two layers of polyamide ester membranes covered with nanocrystalline silver ions. It prevents bacterial infection and improves wound healing (Jiang *et al.*, 2006; Salkar *et al.*, 1999).

A promising in vitro study showed that a heart valve of prosthetic silicone was coated with elemental AgNps to reduce the incidence of endocarditis following valve replacement. The rationale behind the use of silver was to prevent bacterial colonization on the silicone valve, this reducing inflammation of the heart. Toxicity testing of the silver heart valve showed promising biocompatibility (Jiang *et al.*, 2006).

### Silver nanoparticles as biosensors

AgNps have a unique advantage that can be utilized for detecting various abnormalities and diseases in the human body including cancer. The plasmonic properties of nanosilver also make it an excellent candidate for bioimaging as they can be used to monitor dynamic reactions. It can be conjugated to the target cells and then be used to absorb light and convert it to thermal energy; the thermal energy can lead to thermal ablation of the target cells (Sotiriou *et al.*, 2010).

### Neurosurgical catheters

Catheters are used to drain excess cerebrospinal fluid (CSF) in neurosurgery, which can cause cerebral hypertension and brain damage. They can be fully implanted and used as shunts to divert CSF, or be external; both of these cases must be protected from bacterial infection so AgNps become established in everyday neurosurgical.

Catheter-associated ventriculitis (CAV) is inflammation of the ventricles of the brain. External ventricular drain Catheters with AgNps were used to determine whether NS

is beneficial in preventing CAV. Finally the study showed that AgNps is potentially beneficial in the prevention of CAV and is promising for using in humans, with no evidence of toxicity (Wong and Liu, 2010)

### Anti-inflammatory property of AgNps:

Matrix Metalloproteinases (MMPs) are large family of calcium-dependent zinc-containing endopeptidases, which are responsible for the tissue remodeling and degradation of the extracellular matrix (ECM), including collagens, elastins, gelatin, matrix glycoproteins, and proteoglycan. Overexpression of MMPs including MMP9 leads to tissue injury and inflammation (Verma and Hansch, 2007). Studies on MMP inhibition in tumor models by nanosilver brought positive results raising the idea that the development of strategies to inhibit MMPs may be proved to be a powerful tool to fight against cancer (Mishra *et al.*, 2008).

In a porcine contact dermatitis model (induced by dinitrochlorobenzene), it was found that nanocrystalline silver uniquely treated DNCB-induced erythema and edema, increased apoptosis in inflammatory cells, and suppress MMP and Pro-inflammatory cytokine activity such as (interleukin-6 (IL-6) and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ )) (Nadworny *et al.*, 2008). AgNps has anti-inflammatory activity independent of its antimicrobial activity.

Animals with wounds made by electric clippers were treated with cotton fabrics dressings loaded with AgNps at different concentrations. Wounds which were treated with AgNps are significantly showed greater progress than that of the control (untreated cotton dressings) (Hebeish *et al.*, 2014). AgNps anti-inflammatory and antimicrobial activity promotes its wounds healing activity.

### Silver nanoparticles as antimicrobial agents

Because of outbreak of the infectious diseases caused by different pathogenic Microorganisms and the development of antibiotic resistance, scientists are searching for new antibacterial agents. Nowadays silver nanoparticles have emerged up as novel antimicrobial agents owing to their high surface area to volume ratio and the unique chemical and physical properties. AgNps interact with microbes and cause several damages to them. Activity of AgNps on microbes (Prabhu and Poulouse, 2012; Wong and Liu, 2010).

1- These particles have the ability to penetrate microbial membrane and make it porous.

2- AgNps release silver ions; these ions can interact with the thiol groups of many vital enzymes and inactivate them.

3- AgNps produce reactive oxygen species (ROS) which make oxidative stress to cells and this was investigated by electron spin resonance spectroscopy.

4- AgNps release Ag<sup>+</sup> and this creates free radicals which have the ability to damage the cell membrane and make it porous and lead to cell death.

5- Silver is a soft acid, cells are majorly made up of sulfur and phosphorus which are soft bases, so soft acids react with soft bases. DNA has sulfur and phosphorus as its major components; the nanoparticles interact with it and other soft bases in the cell destroy the DNA and cause cell death.

6- It's noted that AgNps Alter the phosphotyrosine profile of bacterial peptides of gram-negative bacteria which leads to signal transduction inhibition.

The antimicrobial activity of AgNps was investigated against yeast (isolated from bovine mastitis), *Escherichia coli* (*E. coli* O157:H8) which is known as a notorious pathogen causing hemorrhagic enteritis, and *Staphylococcus aureus* (ATCC 19636). Muller Hinton agar plates were used and AgNps were supplemented with different concentrations (from 0.2 to 33 nM).

For evaluation of growth inhibition of Ag nanoparticles, a new method was used. After 24-hour incubation, the microorganism density was analyzed at the center of the plate with AgNps and at the outer edge of the plate without AgNps. The differences of microorganism density between the two zones were measured and divided by the number of areas analyzed. As a result; it was observed that the growth inhibition effect response to concentration-dependent manner. AgNps inhibit yeast and *E. coli* at the low concentration, whereas the growth-inhibitory effects on *S. aureus* were mild due to differences in their membrane structure. The most distinctive of membranes is the thickness of the peptidoglycan Layer is a specific membrane feature of bacterial cells and not mammalian cells. It was thought that the lower efficacy of the AgNps against *S. aureus* may derive from the difference as a point of membrane structure (Kim *et al.*, 2007).

### Silver nanoparticles for cancer treatment

Cancer is the most common cause of death at recent times. Acute myeloid Leukemia is cancer that starts in bone marrow. It was found that AgNps have anti-leukemia activity that could inhibit the viability of AML cells including the isolates from AML patient. Ag-Nps induce the production of ROS that lead to mitochondrial membrane potential losses, DNA damage and apoptosis (Guo *et al.*, 2013). Breast cancer forms in tissues of the breast. Breast cancer occurs in both men and women, although male breast cancer is rare. Silver nanoparticles showed good antitumor activity leading to apoptosis in cancer cells without causing acute toxicity to normal cells (Sriram *et al.*, 2010). Another study employ biogenic silver nanoparticles produced by *Sesbania grandiflora* leaf extract. Those biogenic AgNPs showed cytotoxic effect against MCF-7 cell lines (human breast cancer cells) in the form of loss of cell membrane integrity, oxidative stress and apoptosis (Jeyaraj *et al.*, 2013).

### Toxicity of silver nanoparticles

Silver nanoparticles have unique physical and chemical properties making them excellent candidates for usage in a wide range of commercial products throughout the world. Silver nanoparticles have also been known for their great antimicrobial and anti-inflammatory properties that them a great advantage to be widely used in medical field. However, some studies reported that Ag-NPS may have potential risks and toxic effects the environment as well.

Silver is produced in great amounts from industrial wastes and is released into the environment. The free silver ions in the aqueous phase were believed to be the source of toxicity of silver. Silver can gain entry to the human body through many portals like ingestion, inhalation of dusts or fumes containing silver, skin contact, and acupuncture needles and by the application of burn creams etc (Bondarenko *et al.*, 2013). Many adverse effects were reported to occur due to chronic exposure to free silver ions such as permanent bluish-grey discoloration of the skin (argyria) and eyes (argyrosis). Also, liver and kidney damage, irritation of the eyes, skin, respiratory and intestinal tract and changes to blood cells are reported as toxic effects due to exposure to silver compounds (Panyala *et al.*, 2008). Researchers also showed that nanosilver can induce severe toxic effects on the male reproductive system as they can cross the blood-testes barrier and deposit in the testes where they adversely affect sperm cells (McAuliffe, 2007).

Since the discovery of nanosilver and its diverse properties it has been gaining popularity and is widely used in almost every field, especially the medical field. However, studies suggested that silver is released from nanoparticles when stored over a period of time. So, it was said that aged nanosilver is more toxic than new one (KittlerS., 2010). Researchers (Carlson *et al.*, 2008) evaluated the interaction between cells and biologically active Ag-NPS with different sizes (Ag-15, Ag-30 nm and Ag-55 nm). Results showed that the cells viability significantly decreased after 24h of exposure and with increasing dose. It was suggested that the cytotoxicity is likely to be mediated through oxidative stress resulting from the increased reactive stress resulting from the increased reactive oxygen species (ROS) levels in exposed cells. Another study on human hepatoma cells also supports this mechanism (Kim *et al.*, 2009).

In vitro study, studied the suitability of a mouse spermatogonial stem cell line to assess and understand the toxicity of silver, molybdenum and aluminum NPS in the male germ line. Results showed different levels of toxicity for all types of tested NPS with Ag-NPS being toxic type. Ag-NPS impaired mitochondrial function dramatically and caused increased leakage in the cell membrane (Braydich-Stolle *et al.*, 2005). Silver ions can cause changes in the permeability of potassium and sodium ions through the cell membrane at high concentrations that can't be limited (Kone *et al.*, 1988). It was also reported that Ag-NPS can cause toxic effects on the proliferation and cytokine expression by peripheral blood mononuclear cells (Shin *et al.*, 2007). The

oral toxicity of Ag-NPS in rats was tested in vitro study which showed that the liver was the target organ for nanosilver. The histopathological studies showed that there was a higher incidence of bile duct hyperplasia, with or without necrosis, fibrosis and pigmentation in the studied animals (Kim *et al.*, 2010).

Ag-NPS was found to be not able to discriminate between different types of bacteria which could lead to destruction of many beneficial microbes to the ecology (Allsopp, 2007). In the fresh water environment, nanosilver can disrupt the denitrification process as they can hinder the growth of many denitrifying bacteria that are friendly to the soil due to their toxic effect on bacteria loss of natural denitrification process may cause reduction in the plant productivity and may lead to eutrophication of rivers, lakes that could destroy the ecosystem (Senjen, 2007). In the fresh water environment, nanosilver also have toxic effects on aquatic animals as it inhibit basolateral  $\text{Na}^+$ ,  $\text{K}^+$ , ATPase activity by interacting with the gills of the fish leading to inhibition of the osmoregulation in the fish (Wood, 1999). The impact of Ag-NPS on the ecology was thoroughly studied and discussed in detail (Ahamed *et al.*, 2010).

Many in vitro studies were performed that tend to suggest that Ag-NPS can induce toxicity to living organisms causing reproductive failure and developmental malformation. However, very few papers were found addressing in vivo toxicity of nanosilver. So, there a great need for more investigation in this area to determine the real impact of Ag-NPS in vitro condition is drastically different from in vivo conditions and at quite high concentration of Ag-NPS.

## CONCLUSION

Silver nanoparticles are one of the most attractive nanomaterials that have been extensively used in many fields and commercial products. This can be attributed to their high reactivity in the nanosize and their unique physico-chemical properties. Biological methods for Ag-NPS synthesis are considered the best method as it is ecofriendly, cost-effective, safe and feasible. Also reduce the high consumption of energy, heat and pressure needed for the chemical and physical methods of synthesis. Inside the biological methods, using plant extracts is the best way as it is relatively faster than the other methods including the biological synthesis by microbes. Considering their antimicrobial and anti-inflammatory properties, Ag-NPS are widely used in the medical field including cancer treatment and many other applications.

In the last decades, there was a concern about the toxicity of Ag-Nps that cause various health problems and also risky to the ecosystem if released into the environment as reported by many studies. Hence, a great care should be taken in handling Ag-NPS to benefit from their important properties and avoid any harm to the individual or the environment.

So, this current review concludes that Ag-Nps can be a good friend if used wisely, but their careless use may lead to potential risk and damage. Further investigation is very needed to find other mechanisms that could nullify any toxicity caused by Ag-NPS and also determine safely design, use and dispose silver-containing products.

## CONFLICT OF INTEREST

There is no conflict of interest.

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