**Das et al., 2022**
**J. Basic Appl. Res biomed 8(1): 4-7**

**10.51152/jbarbiomed.v8i1.217**

JBAAR
Journal of Basic and Applied Research in Biomedicine
ISSN 2413-7014

***Review Article***

# Silver Nanoparticles' Therapeutic Antibacterial, Antiproliferative, and Toxicological Effects.

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Received: 2-10-2022
Revised: 28-10-2022
Published: 30-10-2022

**Keywords:**
*AgNPs,*
*biosynthesized silver nanoparticles,*
*antimicrobial activity*

**Abstract**: Silver nanoparticles, among others, have broad-spectrum antimicrobial properties. Silver nanoparticles have suppressed dangerous microorganisms in medical and agricultural settings in several studies. Chemicals are harmful to humans and the environment, raising awareness of bioactive synthetic methods. These methods produce nanoparticles with better physicochemical qualities, stability, and toxicity. Biogenic nanoparticles can be made from bacterial and fungal byproducts that reduce and stabilize. Encapsulating these nanoparticles with biomolecules from the producing organisms may boost stability and biological activity. Nanoparticles' quick, clean, cheap, and ecological biologic manufacturing technique increases biocompatibility. Silver nanoparticles affect fish, algae, cell-based in vitro procedures, and microbes. Even though most of these studies were done quickly in well-regulated labs with much higher silver ion concentrations than in real life. Many silver types undergo long-term chemical transformation at extremely low levels (ng/L to g/L) in aquatic ecosystems. Thus, silver nanoparticles' environmental and health hazards need additional investigation. Recently detected antimicrobial silver at 10102 µg/mL. Multiple processes make silver nanoparticles dangerous. Basic (Ag0) and monovalent (Ag+) silver are most poisonous. Silver framework free ions affect silver toxicity. ROS damage DNA when elemental or zero-valent silver penetrates tissues. Packaged foods, contaminated water, swimming pools, antifouling, nasal and throat medicines, and other pharmaceuticals include silver nanoparticles. Consumption accumulates silver ions in subcutaneous fat. Prolonged exposure causes argyria-blue-gray skin. Silver inhibits Na+ and Cl absorption, disrupting electrolytes. Airborne silver nanoparticles may influence chronic pulmonary disease patients. Silver ions oxidize enzyme thiols, hindering electron transport and DNA replication. Ag+ rapidly damages DNA and RNA. Silver nanoparticle breakdown into silver ions creates germ-killing ROS. Silver nanoparticles are more hazardous than silver ions in the same atmosphere.

Cite this article as: Al-alwani, S.S. and Almashaleh, A.F. (2022). **Silver** Nanoparticles' Therapeutic Antibacterial**,** Antiproliferative**, and** Toxicological Effects. Journal of Basic and Applied Research in Biomedicine, 8(1): 8-15 **10.51152/jbarbiomed.v8i1.217**

## INTRODUCTION

Nanoscience is one of the most important branches of modern science, which deals with the knowledge, structure and properties of nanoparticles. Nano-technologies are considered among the modern and active branches of the sciences, as they are included in many disciplines such as medicine, pharmacy and engineering (Satalkar et al., 2016). Therefore, nanoscience and its techniques are considered one of the most important areas of research in the world today (Satalkar et al., 2016).

The word "nanoparticles" generally contains the prefix "nano," which denotes a particle that is one part per million of a millimeter in size. The second component of the name relates to the quality and origin of these molecules (Atul et al., 2010), which can be three-dimensional particles, two-dimensional threads, or one-dimensional plates (Calderón-Jiménez et al., 2017).

Nanotechnology is a large multidisciplinary field that has expanded rapidly during the last decade around the world. The term "nanoparticle" is derived from the Greek word "nanos," which refers to "dwarf" particles. The prefix "nano" refers to "one billionth." A nanoparticle, according to the American Society for Testing and Materials (ASTM), is a particle with a diameter of 1 to 100 nm ( Gomes, H.I.O et al ., 2021).

Because of its numerous applications in science, nanoscience, and biotechnology, nanotechnology is a fast emerging discipline (Bayda S et al ., 2019). Nanobiotechnology is concerned with nanomaterials that have been synthesized or changed utilizing biotechnology. Metal nanoparticles are synthesized by fungi and have numerous applications including wound healing, disease detection and control, food preservation, textiles, materials, and so on (Khan et al ., 2017). Other physical and chemical techniques of producing AgNPs are costly and contain harmful chemicals. As a result, for the biosynthesis of AgNPs, which are particularly essential due to their decreased toxicity and ecologically benign behavior, green, simple, and effective techniques have been chosen. Fungi-derived AgNPs have been discovered (Halkai KR et al ., 2018).

Nanoparticles' physicochemical qualities influence their behavior, bio distribution, safety, and effectiveness. As a result, characterization of AgNPs is critical in order to assess the functional properties of the produced particles. UV-vis spectroscopy, X-ray photoelectron spectroscopy (XPS), dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), and atomic force microscopy are used for characterization (AFM) (Zhang XF et al ., 2016).

Due to their unique physical, chemical, and optical features, silver nanoparticles have received increased attention in this field (Krishnan et al ., 2020). Antibacterial and anticancer activities are inherent in silver nanoparticles (AgNPs) (Talapko et al ., 2020). The ability to combine the anticancer intrinsic feature of AgNPs with the pharmacological effect of anticancer medications could be the answer for treating malignancies that stop responding to chemotherapy or radiotherapy after a while. Thus, the use of AgNPs as simultaneous target-directed drug delivery systems, specifically for anticancer medicines, will be investigated (Lara et al.,2010a and b).

Silver nanoparticles are particles with diameters ranging from 1 to 100 nm, apart from antibacterial properties, the principal uses of silver nanoparticles in the medical area include diagnostic and therapeutic applications, because of their nanotoxicity, the biological procedure is being employed as a quick fix since it is less hazardous to the environment (Mathur P et al .,2018).

### Synthesis Mechanisms: How Does Extracellular Synthesis of Silver Nanoparticles by Fungi Occur?

While numerous research on the biogenic manufacture of silver nanoparticles employing fungus have been reported, the precise mechanisms implicated are still not fully understood. It is recognized that elemental silver (Ag0), which is produced at a nanometric scales by the enzymes found in the fungus filtrations, is produced during extracellular creation of nanoparticles. Following the reactions, the filtrate's color changes, and surfaces plasmons resonances bands indicating altered optical characteristics of the substance can be seen using UV-visible spectroscopy (Abd-Elsalam et al., 2021). These bands' absorption wavelengths extend between 400 and 450 nm, and an absorption maximum at a greater wavelengths denotes the existence of bigger nanoparticles (R. Liu et al., 2022). The size is dependent on the synthesizing circumstances, including the type of fungi, temperatures, pH, and dispersing media, as well as whether or not the nanoparticles have capping (Khan et al., 2022). The surfaces plasmons resonances, which differs depending on the size and absorption of the nanoparticles, is also clearly relevant to the color of the dispersions (Islam et al., 2021).

A wide variety of biomolecules can interact with silver ions and contribute to synthesis, including those involved in the intricate signaling pathways electrons transference during the transformation of NADPH/NADH to NADP+/NAD+ (Gole et al., 2022). In the biogenic manufacture of metallic nanoparticles, nicotinamides adenines dinucleotides (NADH) and NADH-dependent nitrates reductases enzymes are thought to be particularly significant ((Chadha et al., 2022); (Figure 1).

In recent research, nanoparticles production was accomplished without the nitrates reductases enzymes by the actions of NADPH. This is especially interesting because it opens the door to the potential of synthesizing nanoparticles utilizing various organisms without the requirement of reductases enzymes manufacturing (Akshhayya et al., 2022). Additional investigators, who created silver nanoparticles employing *Fusarium oxysporum*, hypothesized that the nitrates reductases enzymes and anthraquinones were responsible for the degradation of silver ions. In a different investigation, the same fungus' pure nitrates reductases and phytochelatins were used, and it was discovered that quinines and extracellular NADPH-dependent nitrates reeducates enzymes were in charge of producing nanoparticles (Nas & Calimli, 2021).

### Optimization of Silver Nanoparticles Synthesis

However, in attempt to get optimal monodispersity, stabilities, and bio - compatibility of the particles, the procedure's variables should be tuned. This is true even if the silver nanoparticles are synthesized employing fungus is straightforward and efficient (Tan et al., 2021). Numerous fungus have the ability to be used in the synthesis, thus it's crucial to take into account their unique traits and adjust the synthesis settings accordingly (Ahuja et al., 2022).

According to the type of fungus utilized, variables including agitating, temperatures, lights, and cultures and synthesizing durations must be changed in order to achieve the necessary nanoparticles properties. The settings employed for both fungal growing and the synthesis processes must be adjusted in order to control nanoparticles sizes and form (Boonyeun et al., 2021). Studies have demonstrated that varied combinations of temperatures, metal precursors concentrations, pH, cultures medium, and biomass quantity may be used to produce nanoparticles with various physicochemical properties (Moghadam et al., 2022).

### Silver toxicity

According to a number of research studies, silver nanoparticles are hazardous to fishes, algae, cell-based in vitro techniques, and microbial contamination (Arora et al., 2021), both the human reproductive systems (Syafiuddin et al., 2017). Even though the majority of these investigations were conducted in strictly managed lab settings in a short amount of time with a substantially higher concentrations of silver ions than in actual life. In fact, the natural aquatics ecosystem has a complicated dynamics between its residents, the environment, other nanoparticles, and contaminants, as well as a long-term chemical transformation of the many types of silver at extremely low levels (ng/L to g/L). As a result, more work has to be done to fully understand the environmental and health dangers connected with silver nanoparticles in practical settings (Bharti et al., 2020). Latest evidence, though, demonstrates that silver at concentrations as low as 10 to 102 μg/mL has antimicrobial activity (Ghosh, 2022)

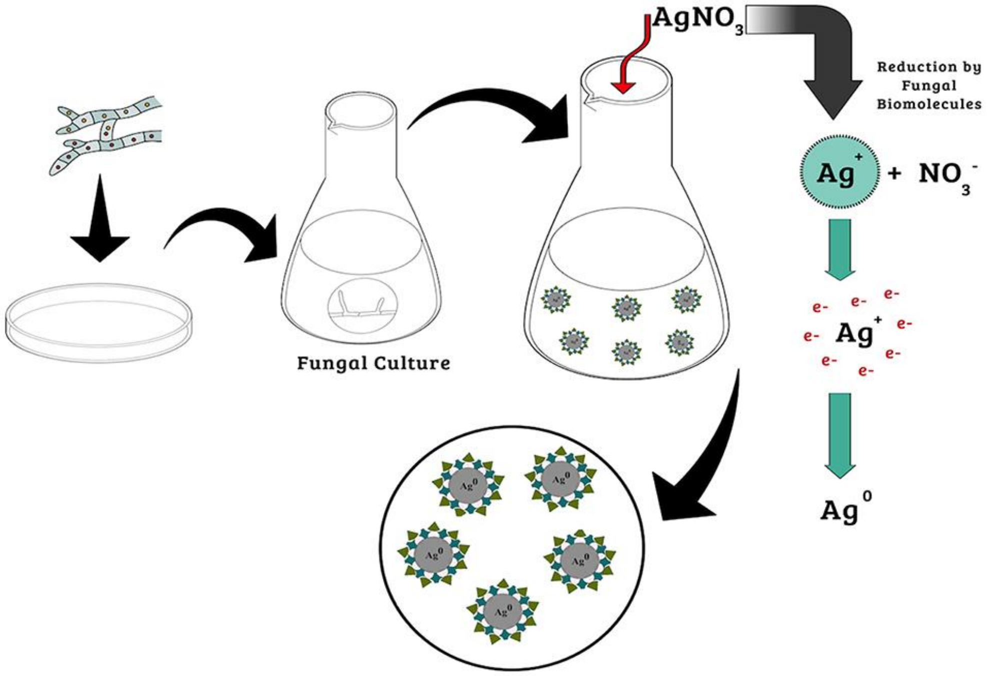

**Figure 1.** Silver nanoparticles biogenic production processes (Chadha et al., 2022).

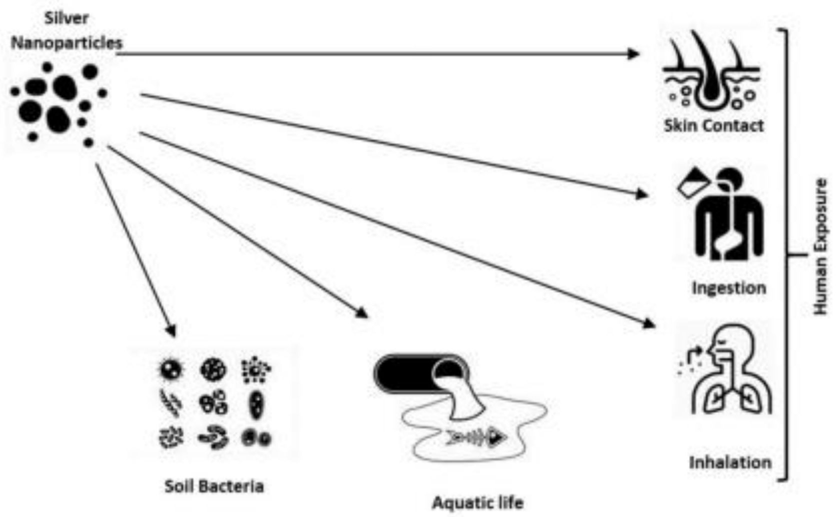

**Figure 2.** Irradiation path for silver nanoparticles (Soni, 2017).

Several processes can be used to account for the toxic effects of silver nanoparticles. The bulk of investigations on the toxicology of silver have found that the most hazardous forms of silver are basic silver (Ag0) and monovalent silver (Ag+). The quantity of free silver ions generated from the silver frameworks, though, determines the poisonous action of silver (F. Ali et al., 2022). When elemental or zero-valent silver enters tissues, this could combine with oxygens to form reactively oxygens species (ROS), which could also damage DNA (Kamal et al., 2021).

Silver nanoparticle exposures in humans may happen by skin contacts with items containing silver nanoparticles, packaged foods containing silver nanoparticles, contaminated drinking water, swimming pools, antifouling, nasal and throats medications, and other medications (Laraib et al., 2022). When a human consumes the silver ions, it is stored in the subcutaneous fatty tissues (Yilmaz et al., 2022). Prolonged exposures can result in argyria, a condition where a person's skin turns blue-grey (R. Li et al., 2022). Additionally, silver can prevent the absorption of Na+ and Cl, which could result in electrolytes imbalance in bodily fluids (Ghorbani et al., 2020). When individuals have underlying disorders like chronic lung disease disorder, airborne silver nanoparticles may create chronic health issues that could become severe (Carter et al., 2019).

Enzymes thiols groups are oxidized by silver ions, which disrupts the electrons transportation chains and DNA replication. Additionally, DNA and RNA can be immediately interacted with by Ag+, damaged (Bhattacharyya et al., 2022). But occasionally, the breakdown of silver nanoparticles into silver ions could result in reactive oxygen species (ROS) that can render bacteria inactive (Soni, 2017). As a result, in the same atmosphere, silver nanoparticles are typically more hazardous than silver ions. The various ways that silver nanoparticles are exposed to the environment, involving exposures in humans, are summarized in Fig. 2.

## CANCER

Cancer is the largest cause of mortality in the globe , accounting for over 10 million fatalities in 2020, or roughly one in every six deaths (Ferlay J et al.,2020). Cancer develops from the change of normal cells into tumor cells throughout a multi-stage process that typically goes from a precancerous lesion to a malignant tumor (Ferlay J et al.,2020). These modifications are the consequence of a person's hereditary elements interacting with three types of external agents, including physical carcinogens, such as ultraviolet ; chemical carcinogens, such as components of tobacco smoke; and biological carcinogens, such as infections from certain viruses, bacteria, or parasites (de Martel C et al.,2020). Cancer is the second greatest cause of mortality in Jordan, after cardiovascular disease, as it is globally (Mattiuzzi and Lippi,2019) .

Breast cancer is Jordan's most prevalent cancer and the third largest cause of cancer mortality, after only lung and colorectal cancers. Although the incidence of breast cancer in Jordan is lower than in developed countries, the number of new cases has been steadily growing. Women in Jordan are diagnosed with breast cancer at a younger age and at a later stage than women in Western nations ( Abdel-Razeq H et al .,2020).

Pancreatic adenocarcinoma is a deadly disorder with an increasing prevalence that is expected to become the second biggest cause of cancer mortality in some places, ranking last among all cancer sites in terms of patient prognosis. A better knowledge of the risk factors and symptoms of this disease is required to advise both health professionals and the general public about potential preventative and/or early detection methods (McGuigan A et al .,2018).

## Classification and types of nanomaterial’s

Nanomaterial’s are naturally occurring things in nature that are created by plants, oceans , dust and other bodies of water (Calderón-Jiménez et al., 2017). They can also be caused by human activity such as combustion, construction, industrial processes, and cars. Meanwhile, engineered nanomaterial’s are chemical compounds or materials with particle sizes ranging from one to one hundred nanometers. Engineered nanomaterial’s are classified into four types based on the materials employed in their synthesis (Calderón-Jiménez et al., 2017): Carbon-based nanomaterial’s (nanomaterial’s containing carbon), inorganic-based nanomaterial’s (metal and metal oxide NPs and NMs), organic-based nanomaterial’s (nanomaterial’s mostly composed of organic substances), and composite-based nanomaterial’s (multiphase NPs and NSMs)

Nanoparticles are particles with sizes ranging from one to one hundred nanometers. Nanoparticles are defined as follows by ISO, an international standardization organization(Shah et al., 2015; Khan et al., 2017). According to the International Organization for Standardization (ISO), a nanoparticle is a nano-level and distinct object with all three Cartesian dimensions less than one hundred nm. Nanoparticles, both one-dimensional and two-dimensional, have also been detected(Shah et al., 2015). The presence of a surrounding interfacial region, which might be organic molecules, ions, or inorganic, influences the majority of the features of these nanoparticles in terms of size(Nguyen et al., 2014). In general, the bulk of a given element has consistent physical properties regardless of size, but at the nanoscale, the same materials react differently, resulting in changes in the properties of the materials as the size exceeds the nanoscale limit (Shah et al., 2015; Khan et al., 2017). The fast mobility and high surface area of nanoparticles are important physical properties (Navya and Daima, 2016).

Nanoparticles are often classed according to their size, shape, and the nature of the substance used to create them. They can be classed as organic or inorganic nanoparticles, for example. Organic nanoparticles can take the form of dendrimers, liposomes, and polymeric particles. In the meantime, fullerenes, quantum dots, and metal nanoparticles are examples of inorganic nanoparticles. In another approach, they might be classed as carbon-based, ceramic, semiconducting, or polymeric based on the material employed in their synthesis. They are also divided into hard nanoparticles like titania, silica nanoparticles like silica dioxide and fullerenes, and soft nanoparticles like liposomes, vesicles, and nano-droplets based on their texture. Others categorize them based on their uses (diagnostics, antifungal, antimicrobial,etc) (Mody et al., 2010; O'Brien et al., 2018; Nguyen et al., 2018; Navya and Daima, 2016).

However, because of their large surface area to size ratio, nanoparticles have been widely employed in practical studies and fundamental research as an outstanding and highly significant medium in addition to their many other chemical and physical characteristics. However, their microscopic nanoscale can cause toxicity and severe consequences if released without environmental management. It can, for example, become extremely damaging to human health if it penetrates water and soil and interferes with the food chain, or if it is inhaled by living species. As a result, its hazards should be minimized by constantly analyzing its potential negative impacts (Wilson, 2018; Reidy et al., 2013; Tolaymat et al., 2010).

## Biological and biomedical applications of silver nanoparticles

Silver is one of the rare elements that occur naturally on our planet. The presence of silver in nature in the form of a metal, it is not soluble in water, while in the salty state of silver becomes soluble in water as silver nitrate and silver chloride. Silver salts, Bothe forms and metallic silver have been used in the treatment of various types of medical conditions such as burns, fungicides, mental and physical diseases, as well as infectious diseases (Lara et al., 2011). Finally, silver salts have been exploited in the synthesis of silver nanomaterials in the form of nanoparticles and films.

Silver nanoparticles are three-dimensional particles (SNPs/AgNPs) ranging from 1 to 100 nm and, depending on size and shape, have unique and varying physical properties (optical, electrical and magnetic) when compared to their larger counterparts. So, they are nanoparticles of distinct importance, as they have been combined into a variety of ways according to the possibility of their medical applications, whether as anti-inflammatory agents, fungi, bacteria, viruses, anti-cancers, or in the treatment of blood vessels (Zhang et al., 2016).

Silver nanoparticles show high antifungal activity against both endogenous and exogenous fungi and have been utilized to treat a variety of fungal illnesses in both humans and plants. It has been demonstrated to be highly effective against Trichophyton mentagrophytes and other kinds of Candida. The biosynthetic AgNPs shown inducible antifungal efficacy against Phoma and Trichoderma species, Fusarium, and Candida species when combined with fluconazole (Vahabi et al., 2011).

When compared to standard antifungal treatments, silver nanoparticles stabilized by sodium dodecyl sulfate showed greater antifungal activity against Candida albicans. White and colleagues (2002) Fusarium oxysporum , Sclerotinia sclerotiorum ,Rhizoctonia solani, Botrytis cinerea, Macrophomina phaseolina, Curvularia lunata, Alternaria alternata, and other plant diseases have been listed as being cured by silver nanoparticles (Salem et al., 2011; Perez, 1990; Pfaffl, 2001; Park et al., 2011; Osman et al., 2022).

Silver nanoparticles (AgNPs) have become one of the most researched and explored nanotechnology-derived nanostructures in recent years, owing to the fact that nanosilver-based materials have proven to have interesting, challenging, and promising properties suitable for a variety of biomedical applications (Burdușel et al .,2018). Among the modern biomedical potential of AgNPs, there is a great deal of interest in therapeutically enhanced personalized healthcare practice (Burdușel et al .,2018). AgNPs demonstrated genuine properties and significant potential for the development of novel antimicrobial agents, drug-delivery formulations, medical device coatings and , biomaterial detection and diagnosis platforms, performance-enhanced therapeutic alternatives, regeneration materials and tissue restoration , complex healthcare condition strategies. Given AgNPs' impressive biomedical-related potential applications, significant efforts have been made to understand the intricate mechanisms of their potential toxic effects and biological interactions (Burdușel et al .,2018).

The small size of silver nanoparticles allows for a wide range of novel uses in a variety of industries. The synthesis of noble metal nanoparticles for applications such as catalysis, electronics, optical, environmental, and biotechnology is a growing field of study. The physical and chemical approaches are the two basic methods for producing silver nanoparticles. The issue with these technologies is that harmful compounds absorb onto them. This constraint is overcome by green synthesis approaches. The small size of silver nanoparticles allows for a wide range of novel uses in a variety of industries (Abbasi E et al .,2016).

Because of its demonstrated capabilities as an antibacterial, antiviral, and antifungal agent, silver nanoparticles (AgNPs) have been used in a variety of biotechnology disciplines. AgNPs are typically manufactured using a variety of chemical, physical, and biological processes (Naganthran et al .,2022). Because each approach brings its own set of benefits and limitations, a trend analysis of literature for AgNPs synthesis utilizing various forms of synthesis was also conducted using a bibliometric approach. AgNPs are a great, dependable, and successful solution for seven primary concerns: antiviral , antibacterial, anticancer, dental applications, bone healing, bone cement. AgNPs have been used in biological applications in recent years due to their antibacterial, antiviral, and anticancer characteristics (Naganthran et al .,2022).

Silver nanoparticles have been shown to inactivate viruses such as hepatitis B virus, human immunodeficiency virus, herpes simplex virus (HSV), human parainfluenza virus type 3 and influenza virus (Sun et al., 2005; Shanmukh et al., 2006; Panyala et al., 2008; Lu et al., 2008; Galdiero et al., 2008; Mehrbod et al., 2009; Lara et al., 2010b). Furthermore, silver nanoparticles have anti-inflammatory effects via regulating inflammatory factors and so decreasing the inflammatory effect (Ahmed et al., 2000; Nahrendorf et al ., 2008). Furthermore, silver nanoparticles serve as antiangiogenic agents, controlling angiogenesis-related disorders and thereby preventing their occurrence (Jo and Kim et al., 2015). According to a research team, silver nanoparticles play a significant role on a wide scale as alternative anti-cancer therapies that selectively target and select cancer cells. They discovered that AgNPs induce apoptosis while also sensitizing tumor cells in their research (Gopinath et al., 2008).It has been observed that AgNPs are mostly taken up by cells via endocytosis, and starch-coated AgNPs have been shown to trigger changes in human glioblastoma (U251) cells, culminating in DNA damage (Hahm, 2004). Other research suggests that biosynthetic AgNPs can cause considerable cell death (Morones et al ., 2005). These silver-embedded magnetic nanoparticles have also been utilized to specifically target floating breast cancer and leukemia cells (Jun et al., 2010). AgNPs biosynthesized by fungi have significantly stronger anti-cancer properties than AgNPs produced by bacteria due to the type of reducing agents used (Gurunathan et al ., 2013).

Huge efforts have been achieved regarding the use of silver nanoparticles against many bacteria that are resistant at least to a wide range of antibiotics, thus overcoming the problem of bacterial resistance to antibiotics, and at the same time using these nanoparticles as an alternative to traditional antibiotics. It has been concluded that the mechanism by which AgNPs can effectively kill germs is by contact killing and by surface-mounted nanoparticles when compared to colloidal AgNPs. AgNPs that accumulate in the cell wall cause the formation of pits in the cells of Escherichia coli so that, the components of the cell get leaked outside and eventually lead to cell death (Gurunathan et al., 2009). This was evident by the loss of an amount of reducing sugars and proteins from Escherichia coli cells as a result of the ability of AgNPs to destroy the permeability of bacterial membranes through the formation of pits and vacuoles on the surface of the cell (Sondi and Salopek-Sondi, 2004). While, Morones et al. They suggested in 2005 that AgNPs can inhibit bacteria by more than one mechanism. For example, AgNPs adhere to the surfaces of the cell membrane, disrupting the permeability and respiration in the event that the size of the nanoparticles is small and ranging between 1 to 10 nanometers, or by penetrating the nuclear particles into the cells and then interacting with compounds containing sulfur and phosphorous groups, causing further damage and destruction to the cell. Finally, by releasing silver ions from AgNPs, this promotes further damage and thus cell death. We must not forget that dosage, size and shape factors are also determinants of their activity against bacteria (Morones et al ., 2005; Montes-Burgos et al ., 2010).

Historically, silver in all of its forms has been employed as an antibacterial agent either alone or in combination with other technologies (Silva L.P et al ., 2017). This metal has been researched for its ability to inhibit bacterial growth by incorporating it as silver nitrate or silver sulfadiazine in creams and dressings to treat burns and ulcers, in food packaging to prevent contamination, in home appliances such as refrigerators and washing machines, and in several industrial applications (Tong, 2009).Because of the existing knowledge and evidence of silver's antibacterial activity (Kędziora A et al.,2018), the research of the antibacterial potential of AgNPs was an obvious path with the rise of nanotechnology.

Numerous studies have shown that AgNPs have high antimicrobial activity against Gram-positive and Gram-negative bacteria, including those strains that are highly resistant such as methicillin-resistant Staphylococcus aureus and methicillin-resistant Staphylococcus aureus (Feng et al., 2000; Sondi and Salopek-Sundy, 2004; Moronis et al., 2005; Song  et al., 2006). Moreover, synergistic activity against different pathogenic bacteria appeared between the antibiotics and the AgNPs when compared to each one separately. Examples of such nanoparticles, silver and titanium dioxide versus the disinfectant routine chlorhexidine in Streptococcus mutans, AgNPs had the strongest antibacterial activity (Besinis et al., 2014). Rapid improvement in nanotechnology and incorporation of silver nanoparticles (AgNPs) in huge variety of client merchandise inflicting the good sized launch of those NPs on the environment, main worries for environmental protection and plant health. Exposure of vegetation to AgNPs by myself decreased the foundation and shoot length, biomass production, chlorophyll contents, photosynthesis associated physiological parameters in addition to macro-and micronutrients in a dose-structured method.

## Biological synthesis of silver nanoparticles

It is thought that there are biological, physical and chemical strategies which might be used in the synthesis of silver nanoparticles. For example, physical strategies consist of condensation, evaporation, and laser ablation (Magnusson et al ., 1999; Mafune et al ., 2000; Mafune et al ., 2001; Dolgaev et al., 2002; Kabashin, 2003; Sylvestre et al ., 2004; Jung et al ., 2006). Physical strategies are recognized for his or brief at the same time as manufacturing . In physical strategies, radiation is used as a lowering agent without out unsafe chemicals. Their principal drawbacks are that they're characterised by their brief yield, loss of uniform distribution, solvent infection and occasional yield ( Mafune et al ., 2002 ; Dolgaev et al ., 2000; Kabashin, 2003 ; Sylvestre et al ., 2004 ; Jung et al ., 2006). As for the chemical strategies, it consists of 3 principal factors which might be metallic precursors, lowering sellers and stabilizing / capping sellers dissolved in both water or natural solvents (Link et al ., 2000; Kim et al ., 2005; Kawasaki., 2006; Tarasenko et al ., 2006). Chemical strategies yield excessive quantities of manufacturing in comparison to bodily strategies. Like physical strategies, they are afflicted by numerous negative aspects as the result of a low-purity, expensive, risky and poisonous product, or related to many poisonous and perilous byproducts (Wiley et al ., 2005).

Therefore, green synthesis has been proposed as an alternative to physical and chemical methods for the synthesis of silver nanoparticles as an efficient and environmentally friendly method consisting of natural reducing, stabilizing  and capping agents (Ahmad et al., 2003; Ankamwar et al., 2005). Green nanoparticles from silver salts are biologically synthesized based on the activity of biomolecules including enzymes/proteins, amino acids, sugars and vitamins in a simple, effective, inexpensive and environmentally safe manner. In this approach, different microorganisms such as bacteria, fungi, biological molecules including plant extracts and small biomolecules such as vitamins and amino acids are used (Ahmad et al., 2000; Ghosh et al., 2003). The synthesis of biological nanoparticles has three characteristics, including the use of aqueous solvents, reducing agents, and their freedom from toxic substances. It also meets the most important requirement of its medical and biological applications (Mafuné et al., 2001; Magana et al., 2008; Lehmann and Joseph, 2009; McGuigan et al., 2018; Mathur et al., 2018; Mattiuzzi and Lippi, 2019). For example, the shape and size of the biosynthetic silver nanoparticles can be adjusted with the least degree of particle aggregation with stability, well dispersion and at the same time high solubility in water (Anacek et al., 2006).

Monitoring the nanosynthesis process by adjusting the amounts of silver precursors, reducing agents, pH and temperature enables the process to control the distribution and size of the produced nanoparticles. Many studies mentioned the diverse use of bacteria and fungi in addition to many biomolecules and plant extracts. One of the important studies that used bacteria isolated from silver mines such as Pseudomonas stutzeri AG259, which showed its ability to synthesize silver nanoparticles by nitrate reduction enzyme, which is the most widely accepted and widely proposed mechanism (Duran et al., 2005). However, although the mechanism of silver nanoparticle synthesis by fungi is not fully understood, the fungi showed their ability to produce a greater amount of reducing agents compared to bacteria, and thus their ability to produce a greater amount of silver nanoparticles. It was reported that fungi synthesize nanoparticles by wrapping around the surface of Ag + ions and then reducing silver ions enzymatically by the enzymes of Naphthoquinones, Anthraquinones and nitrate reducing enzymes (Jha et al., 2009; (Klaus et al., 2009; Karna et al., 2016; Krishnan et al., 2020). But what differentiates the use of microorganisms (bacteria and fungi) in the synthesis of nanoparticles is that it is a slow process and it represents the main disadvantages when compared to the use of plant extracts. Thus, apart from the advantages of using plant extracts in the synthesis of silver nanoparticles, it is very fast compared to bacteria and fungi. It has been reported that plant chemicals that have an active role in the synthesis of nanoparticles directly reduce silver ions (Sakamoto et al., 2009). These chemicals found in plant extracts are flavonoids, terpenoids, aldehydes, carboxylic acids, ketones and terpenoids (Franco-Molina et al., 2010; de Martel et al., 2020; Ferlay et al., 2021; El Hanandeh et al., 2021).

More than 225 species of fungi have been detected in indoor habitats, which is a small number when compared to the estimated and proposed 1.5 million species of fungi (McGinnis, 2007). The most prevalent allergenic fungal genera include Aspergillus, Cladosporium, Fusarium, and Alternaria, while more than 80 fungi genera have been linked to respiratory allergies and symptoms (Horner et al., 1995). Excessive exposure to the four conidia genera is thought to be a primary cause of various disorders, including Aspergillosis ( Latgé JP.,1999) , lung infections and asthma (Cuijpers et al., 1995; Hu et al., 1997), sepsis, and allergic alveolitis (Flannigan, 1997).

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