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Review Article

Silver Nanoparticles: Synthesis, Biomedical Applications, Antibacterial and Anticancer Activities, and their Hemato-biochemical Impacts: A Review

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Abstract

Nanobiotechnology has grown rapidly as an essential branch of modern research, which deals with synthesis, design, and manipulation of particles with at least one dimension <100nm. As well as they have an important role in diagnosis and treatment of modern diseases. AgNPs are mostly used NPs in a variety of applications because of their exceptional physicochemical characteristics with low toxicity and biocompatibility. Also, their great chemical stability, catalytic activity, conductivity, and antimicrobial potential leads to its high commercial use. AgNPs produced by the action of reducing reagents, such as, physical, chemical and biological techniques. Biosynthesized silver nanoparticles are most attractive nanomaterial of interest among several metallic nanoparticles, which characterized by its hazard free and eco-friendly cost-effective, biological, and therapeutic properties. The natural resources for biosynthesis of nanoparticles include plants, bacteria, yeast, algae, fungi and viruses. The AgNPs has great importance in several fields of the science and some technology as electronics, therapeutics, environmental protection, textile industry, cosmetics, biomedical, photonics and agriculture. Also they act as an effective antimicrobial, anticancer and diagnostic agents through the distinctive characteristics of Ag nanostructures, like its exceptional SERS/SPR, the properties and charge of its surface, variety of the shape, rate of dissolution, as well as its ability to organized Ag^+ release for mediating both antimicrobial toxicity and cytotoxicity toward cancer cells. This review provided an overview of synthesis of AgNPs along with their anti- microbial and anti- cancer activities. In addition to an overview on how AgNPs affect hemato-biochemical parameters.

KEYWORDS
Silver Nanoparticles, Synthesis, Characterization, Applications, Biochemical Parameters.

INTRODUCTION

In recent years, the need to find alternate methods to combat cancer and microorganisms which cause serious or even life-threatening illnesses has increased due to rising bacterial resistance to current antibiotics (Yuan *et al*., 2017; Zhang *et al*., 2020; Wypij *et al*., 2021).

Metallic nanoparticles are often used in nanomedicine as a drug carrier that they can easily penetrate the cell membrane by their tiny size. Silver nanoparticles (AgNPs), which are among metal-NPs, have drawn particular attention, mainly in biomedicine since they are less hazardous to human cells than others (Zhang *et al*., 2016; Xu *et al*., 2020; Abdellatif *et al*., 2022). AgNPs occupy an imperative role in nanomedicine by its aptitude to displayed angiogenesis, essential step in tumor growth, invasiveness, and metastasis (Gurunathan *et al*., 2009). The synthesis of nanoparticles occurred by using three different methods: physical, chemical, and biological methods. For optimal safety and effectiveness, AgNPs can be produced using biological techniques (Zhang *et al*., 2016; Xu *et al*., 2020; Abdellatif *et al*., 2022). Biological methods often maintain a chemical composition that is homogeneous and free of flaws. These environmentally friendly techniques offer AgNP synthesis alternatives to the conventional physical and chemical synthesizing for use in anti-cancer therapies (Deshmukh *et al*., 2019; Liu *et al*., 2021; Sofi *et al*., 2022). Biosynthesized AgNPs demonstrated less toxicity in relation to hepato-renal functions (Lee and Jun, 2019). The fundamental troubles for the wider utilize of AgNP incorporate challenges with their regularization and the associated insufficiency of biocompatibility certification (Zielińska-Górska *et al*., 2022).

With a concentrate on the biomedical aspects of AgNPs, their therapeutic applications, their mechanism of action and their impact on hemato-biochemical analysis, we offer a broad understanding of AgNPs properties, synthesis, characterization, and bio-applications in this review paper.

SYNTHESIS OF AgNPs

Different methods used in synthesis of AgNPs are presented in Fig. 1.

Physical methods used in synthesis of AgNPs

Nanoparticles in physical methods synthesized either by

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evaporation-condensation or laser ablation techniques. Both techniques are speed, no capping agent and high purity without chemicals hazardous or contamination of solvent included. On the other hand, the disadvantages are high power consumption, low yield, and long duration to achieve thermal stability which leads to high cost (Amendola and Meneghetti, 2009).

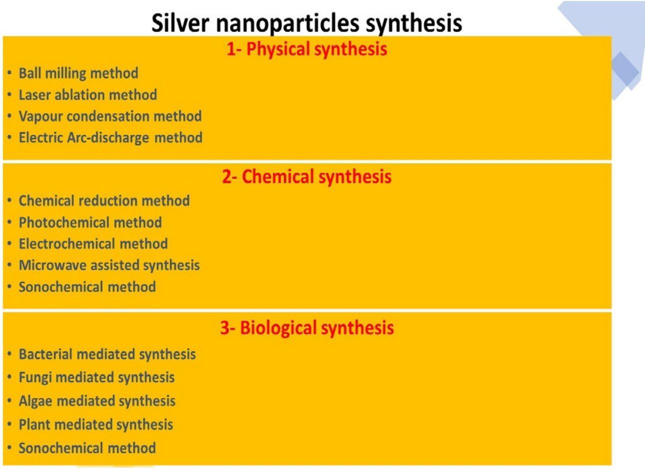

Fig. 1. Synthesis of silver nanoparticles.

Chemical methods used in synthesis of AgNPs.

Chemical methods included electrochemical techniques, chemical reduction, irradiation-assisted chemical methods, and pyrolysis (Wei *et al*., 2015). In chemical methods we used three main components metal precursors (silver), reducing agents (ascorbate, sodium citrate, sodium borohydride (NaBH4) ets.), and stabilizing/capping (thiols, amines, acids, and alcohols) agents. The previous components usually employ in two operations top-down and bottom-up for chemical synthesis of AgNPs (Iravani *et al*., 2014). The advantage of this method is high yield, opposing to physical methods. On the other hand, this method is expensive, toxic. Not give the expected purity, difficult to prepare with a well-defined AgNPs size and need further step to prevent the particle aggregation (Zhang *et al*., 2016). The top-down approach is used to shrink larger structures into the nanoscale range while maintaining their original properties without modifications at the atomic or subatomic scales (Tripathi and Goshisht, 2022), in this method, grinding, milling, sputtering, thermal/laser ablations, and other lithographic processes are used to size-reduce bulk materials into tiny particles (Ahmed *et al*., 2016; Vigneswari *et al*., 2021; Tariq *et al*., 2022). The bottom-up process allows for the chemical and biological AgNPs synthesis through the self-assembly of atoms into new nuclei, which then develop into nanoscale particles. The aerosol process, laser pyrolysis, plasma spraying synthesis, superficial fluid synthesis, and green synthesis are all used in the bottom-up strategy. The most popular method for creating AgNPs in the bottom-up method is chemical reduction.

Biological methods used in synthesis of AgNPs

To avoid sides effects of both physical and chemical methods, use of biological AgNPs synthesis is simple, cost effective, pollution-free, eco-friendly, has high density and stability. As well as it provides specific size particle and shape, this is an important factor for various biomedical applications (Thakkar *et al*., 2010; Khodashenas and Ghorbani, 2015). This method of AgNPs synthesis influenced by three factors: solvent, reducing agent and non-toxic material. The biological synthesis of AgNPs occurring by various biological systems such as fungi, bacteria, plant extracts (act as reducing and stabilizing agents), as well as vitamins and amino acids (Gurunathan *et al*., 2009; Sintubin *et al*., 2012; Gurunathan *et al*., 2014).

CHARACTERIZATION AND PROPERTIES OF SILVER NANOPARTICLE

Characterization of AgNPs is done to estimate functional aspects of the AgNPs. The behavior, bio-distribution, safety, and efficacy of nanoparticles are affected by their physicochemical properties. AgNPs have unique physicochemical properties. The physical properties include shape, size, size distribution, surface charge, crystallinity, particles morphology and composition. The chemical properties include surface coating/capping, elemental composition, agglomeration, solubility, dissolution rate, particle reactivity in solution, efficiency of ion release and cell type. These physicochemical properties give the AgNPs the ability of easy entrance into the cells and interact efficiently with biomolecules inside the cells producing chemical conditions, which induce a pro-oxidant environment in the cells (Ratan *et al*., 2020) leading to adverse biological consequences, begin with initiation of inflammatory pathways until the cell death (Kwon *et al*., 2012).

Physical properties (shape and size) play an important role in toxicity determination. Different types of nanostructures, such as nano- cubes, plates or rods, spherical and flower-like objects, have been employed in the biomedical sector (Zhang *et al*., 2016; Liao *et al*., 2019, Habeeb Rahuman *et al*., 2022). Nanoparticles' shapes rely on how they interact with stabilizes and inductors nearby, as well as how they were created.

Shape and size of AgNPs can be affected by several factors, changing the experimental conditions and the synthesis methods (chemical-physical and biological). According to the synthesis method, there are a range of particle sizes and shapes can be obtained such as cubes, prisms, spheres, rods, wires and plates (Sriram *et al*., 2012). For instance, the synthetized AgNPs from the culture supernatant of various Bacillus species as biological reducing agent are spherical, rod, octagonal, hexagonal, triangle and flower-like shaped particles (Folkman, 2002; Cobley *et al*., 2009).

There are different analytical techniques used for AgNPs characterization which include: Ultraviolet spectroscopy (UV–VIS spectroscopy) which reflects size, shape alterations and scattering color of AgNPs. X-ray diffractometry (XRD) which give us indication about the surface chemical composition of the AgNPs. Transmission electron microscopy (TEM) is another technique to determine the size and shape of AgNPs. Scanning electron microscopy (SEM) used in determination the surface morphology and atomic composition. Both of X-ray photoelectron spectroscopy (XPS), Fourier transform infrared spectroscopy (FTIR) and Energy dispersive spectroscopy (EDS) used for the analysis of surface properties. Dynamic light scattering (DLS) utilized to determine particle size and particle size distribution of small particles in a scale range from few nanometers to a few micrometers in solution or suspension and atomic force microscope (AFM) is an essential tool to study both surface morphology with nanometric resolution and for measurements of sensory forces (Gamboa *et al*., 2019).

APPLICATION AND MECHANISM OF ACTION OF AgNPs

Silver nanoparticles (AgNPs) used in many different fields (Fig. 2), among them medical sector, food, health care and industrial purposes (Mukherjee *et al*., 2001). Numerous antibacterial

(Yin *et al*., 2020) and antiviral (Wang *et al*., 2019) mechanisms have been reported.

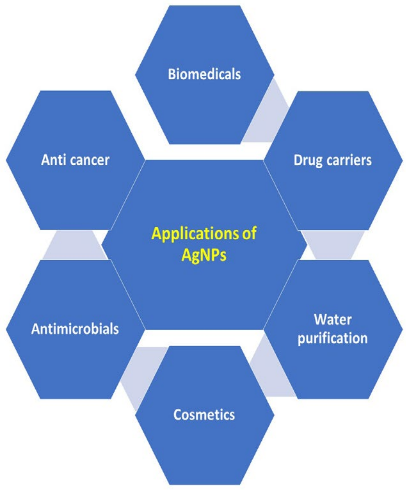

Fig. 2. Applications of silver nanoparticles

The Antibacterial Activity of Silver Nanoparticles

A comparative study of AgNPs, AgNO3 and AgCl revealed that AgNPs have stronger antibacterial activity than free silver ions (Choi *et al*., 2008). Most of the earlier research looked at the synergistic interaction between antibiotics and AgNPs (Deng *et al*., 2016; Patra and Baek 2017). AgNPs was discovered to be a more potent antibacterial agent and effective against a variety of antibiotics - resistant strains of Gram +ve and Gram -ve bacteria (Lok *et al*., 2007; Majnumeena *et al*., 2014), they performed their tasks by precipitating the cellular proteins and impeding the bacterial electron transport chain system (Barreiro *et al*., 2007). The thiol group of sulphur and hydrogen present in the bacterial proteins attaches to the silver ions released by the AgNPs and inhibits the growth of bacteria (Morones *et al*., 2005).

The antibacterial effectiveness of the AgNPs depends on their size, shape, and concentration. According to studies, increasing AgNPs' surface area can boost their antibacterial effectiveness (Ghodake *et al*., 2020). Researchers have confirmed that AgNPs have 50% inhibitory effect against multidrug resistant S. aureus and E. coli at a comparatively low level of 20 g/ml. It showed effective suppression of both bacteria at a higher dosage of around 40 g/mL. In a different investigation, pathogenic Gram +ve and Gram -ve bacteria including *Ps. aeruginosa, E. coli*, and *S. typhi* were successfully inhibited by biosynthesized AgNP made from the marine macroalgae Padina species. AgNPs with a concentration of 1mg/ml display a higher sensitivity against Ps. aeruginosa with inhibition diameter zone 13.33±0.76 mm and 15.17±0.58 mm for *S. aureus*, matched with the 0.00 mm of -ve control (Bhuyar *et al*., 2020). Another investigation showed a promising strategy with further testing in vivo, to develop novel antimicrobial agents and strategies to confront emerging antimicrobial resistance. AgNPs levels below 1mg/mL were non-cytotoxic, however the biocompatible concentration of AgNPs (1mg/mL) significantly inhibited the growth of numerous bacterial species that were resistant to both the antibiotics and AgNPs alone (Ipe *et al*., 2020).

The Antibacterial Mechanism of Silver Nanoparticles

The antibacterial efficacy of AgNPs against a wide range of pathogens, including bacteria, fungi, and viruses, has been studied by various reporters. Although AgNPs have been shown to be potent against more than 650 species, the exact mechanism of their antibacterial action is still not entirely known (Dakal *et al*., 2016). There have been many documented antibacterial mechanisms (Yin *et al*., 2020), including: Ag+ ions released by AgNPs stick to or pass through cell walls and cytoplasmic membranes, causing disruption of both structures; Ribosome denaturation: Silver ions denaturate ribosomes and stop protein synthesis; Adenosine triphosphate (ATP) generation is halted because silver ions render the respiratory enzyme on the cytoplasmic membrane inactive; Reactive oxygen species can rupture membranes. Reactive oxygen species are created when an electron transport chain breaks down; Replication of DNA is interfered with reactive oxygen species and silver, which attach to DNA and stop cell division; Denaturation of the membrane is brought on by the accumulation of silver nanoparticles in the cell wall pits; Membrane perforation: AgNPs directly pierce the cytoplasmic membrane, allowing the cell's organelles to be released.

The Anticancer Activity of Silver Nanoparticles

Currently, tumor is viewed as a significant contributor to morbidity and mortality on a global scale (Xu *et al*., 2020; McDaniel *et al*., 2019). By 2035, there will be an estimated 14 million new instances of cancer, which will have a significant effect on the global economy and society (Pilleron *et al*., 2019). Surgery, chemo, and radiotherapy are frequently used to treat cancer. One of the most significant benefits of greenly manufactured AgNPs is that they may be more biocompatible than nanoparticles made from the same chemical element using a traditional chemical process (Rónavári *et al*., 2021). It is obvious that the development and use of NPs has increased community attentiveness of their toxicity and consequences on the environment (Brayner, 2008; Panda *et al*., 2011). AgNPs are thought to cause cytotoxicity by the production of ROS, which leads to a decrease in glutathione levels and an increase in ROS levels (Avalos*et al*., 2014). In vitro investigations on animal tissue and cultured cells revealed that exposure to AgNPs increased oxidative stress, apoptosis, and genotoxicity (Kim and Ryu, 2013). Multiple studies have shown that silver nanoparticles can get rid of human tumor cells while harming normal cells only very slightly (Al-Zahrani *et al*., 2022). In addition, AgNPs effectively cure hepato-cellular carcinoma, and cancers of lung, nasopharyngeal, colorectal, cervix, breast, and prostate in both in vitro and in vivo settings (Algotiml *et al*., 2022).

The Anticancer Mechanism of Silver Nanoparticles

A variety of mechanisms underlie AgNPs' broad-spectrum anticancer action (Fig. 3). AgNPs can reduce the viability and multiplication of cancer cells, according to numerous in vitro and in vivo tests. By damaging the ultra- structure of tumor cells, causing the generation of ROS, and causing DNA damage, AgNPs can trigger apoptosis and necrosis (Wang *et al*., 2019). Key genes like p53 and crucial signaling pathways like the hypoxia-inducible factor (HIF) pathway can both be up- or down-regulated by AgNPs to increase or decrease the amount of apoptosis (Yang, *et al*., 2016). Cell cycle arrest may also be seen in tumor cells treated with AgNPs (Zhang *et al*., 2017). A number of cancer cells are killed by apoptosis and sub-G1 arrest when exposed to AgNPs. Additionally, AgNPs can lessen distant metastasis by preventing the migration and angiogenesis of tumour cells (Homayouni-Tabrizi *et al*., 2019). AgNPs have been the subject of numerous studies aimed at improving their therapeutic utility as nanocarriers for targeted drug delivery, chemotherapeutic drugs, and as boosters for radiation and photodynamic treatment. A review of the accessible literature indicates that AgNPs can limit the development of cancer cells by a variety of mechanistic approaches (Xu *et al.*, 2020).

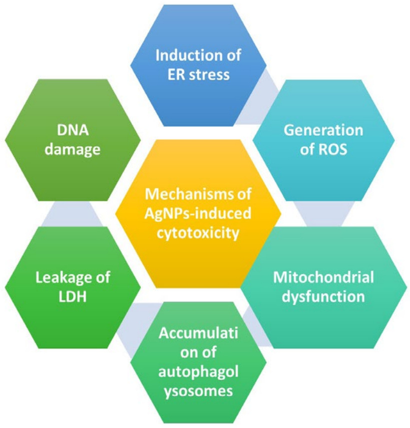

Fig. 3. The possible mechanisms of AgNP-induced cytotoxicity in cancer cell lines. Endoplasmic reticulum stress (ER), lactate dehydrogenase (LDH), reactive oxygen species (ROS).

THE HEMATO-BIOCHEMICAL CHANGES PRODUCED BY SILVER NANOPARTICLES

By examining the effects of administering AgNPs, it was revealed that there were some negative impacts on serum biochemistry. AgNPs have emerged as effective antibacterial agents and are currently being tested in a variety of medical applications, including silver-based dressings, and Ag -coated medical equipment. Hematological and histological abnormalities were not brought on by nano- silver wound dressing in the treatment group, although biochemical analyses revealed a significant increase in plasma alanine transaminase (ALT) at the study's endpoint, 21 days (Bidgoli *et al.*, 2013).

Earlier data revealed a significant increase in proteinogram levels in tissue homogenates of the mosquito larvae of Culex pipiens previously treated with the increasing of lethal concentrations (LC10, LC50, and LC90) of green synthesized silver nanoparticles (GSNPs), in addition to a significant increase of lipid peroxidation level in tissue homogenates of larvae (Ragheb *et al.*, 2020). For the goal of assessing the safety of intravenous injection of AgNP (10, 20, and 40 mg/kg), measurements of the rats' body weight, organ coefficient, whole blood count, biochemistry assays, comet assay, ROS, and histological parameter were made. The authors came to the conclusion that the hemato-biochemical parameters in the 40 and 20 mg/kg groups both had noteworthy alterations, whereas AgNPs at low levels (10 mg/kg) are secure for use in biomedicine and have no negative adverse outcomes, high doses are hazardous (Tiwari *et al.*, 2011). AgNPs administration to rats at varying concentrations did not result in a discernible reduction in feed consumption or body weight; however, significant increases in serum and tissue AST, ALT, and ALP levels were recorded (Adeyemi and Adewumi, 2014). Analysis of serum IL-1β and TNF-α established an augment in rats after administration of AgNPs 10 mg and 30 mg/kg/day (Mohamed *et al.*, 2020). Male albino rats were administered intraperitoneally with Ch-AgNPs at various doses resulted in the highest levels of MDA, ALT, AST, and the lowest levels of GSH, IgG, IgM, TPs (Hassanen *et al.*, 2019).

Intraperitoneally AgNPs administration (5 mg/kg/day) persuade hepatic injure as specified by reduction in levels of glutathione, total antioxidant capacity, SOD, CAT, and GSH-peroxidase, and increase in level of CRP. These findings advocate that AgNPs treatment causes hepato- toxicity in rats; however, selenium supplements mitigate these effects (Ansar *et al.*, 2017). Incorporating AgNPs into *C. tiglium* extract caused an improvement in the erythrogram (RBCs, HB, HCT, MCV, MCH and MCHC), RDW, MPV, PLT and WBCs with its differential count levels, liver enzymes (ALT, AST and ALP), total proteins, albumin, as well as renal parameters (urea and creatinine) when compared to azoxymethane (AOM) induced colon cancer in rats (Aboulthana *et al.*, 2020). Oral administration of silver NPs at different doses had no impact on the function of the rat liver but likely caused early apoptotic phases with elevated caspase-3 (Pourhamzeh *et al.*, 2016).

CONCLUSION

The silver nanoparticles demonstrate exceptional anticancer effectiveness against many cancers cell types and antibacterial effect against both Gram+ve and Gram-ve bacteria. The AgNPs' cytotoxic properties are considerably influenced by the various synthesis techniques. There are some negative impacts of AgNPs usage on the serum biochemistry. Finally, notwithstanding AgNPs' high medicinal promise, it is important to emphasize that more study with toxicity proof is urgently needed because AgNPs' potential health and environmental risks are still unknown.

CONFLICT OF INTEREST

There are no conflicts of interest that the authors need to disclose

REFERENCES

Abdellatif, A.A.H., Alhathloul, S.S., Aljohani, A.S.M., Maswadeh, H., Abdallah, E.M., Hamid Musa, K., El Hamd, M.A., 2022. Green Synthesis of Silver Nanoparticles Incorporated Aromatherapies Utilized for Their Antioxidant and Antimicrobial Activities against Some Clinical Bacterial Isolates. Bioinorg. Chem. Appl. 11, 2432758.

Aboulthana, W.M., Ibrahim, N.E., Osman, N.M., Seif, M.M., Hassan, A.K., Youssef, A.M., El-Feky, A.M., Madboli, A.A., 2020. Evaluation of the Biological Efficiency of Silver Nanoparticles Biosynthesized Using Croton tiglium L. Seeds Extract against Azoxymethane Induced Colon Cancer in Rats. Asian. Pac. J. Cancer. Prev. 21, 1369-1389.

Adeyemi, O.S., Adewumi, I., 2014. Biochemical Evaluation of Silver Nanoparticles in Wistar Rats. Int. Sch. Res. 2014, 196091.

Ahmed, S., Ahmad, M., Swami, B.L., Ikram, S., 2016. A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: A green expertise. J. Adv. Res. 7, 17-28.

Algotiml, R., Gab-Alla, A., Seoudi, R., Abulreesh, H.H., El-Readi, M.Z., Elbanna K., 2022. Anticancer and antimicrobial activity of biosynthesized Red Sea marine algal silver nanoparticles. Sci Rep. 12, 2421.

Al-Zahrani, S.A., Bhat, R.S., Al-Onazi, M.A., Alwhibi, M.S., Soliman, D.A., Aljebrin, N.A., 2022. Anticancer potential of biogenic silver nanoparticles using the stem extract of Commiphora gileadensis against human colon cancer cells" Green Processing and Synthesis, 11, 435-444.

Amendola V, Meneghetti M., 2009. Laser ablation synthesis in solution and size manipulation of noble metal nanoparticles. Phys Chem Chem Phys. 11, 3805-21

Ansar, S., Alshehri, S.M., Abudawood , M., Hamed, S.S., Ahamad, T., 2017. Antioxidant and hepatoprotective role of selenium against silver nanoparticles. Int. J. Nanomedicine. 12, 7789-7797.

Avalos, A., Haza A.I., Mateo D., Morales P., 2014. Cytotoxicity and ROS production of manufactured silver nanoparticles of different sizes in hepatoma and leukemia cells. J. Appl. Toxicol. 34, 413-23.

Barreiro, E., Casas, J.S., Couce, M.D., Sánchez, A., Seoane, R., Sord, O. J., 2007. Synthesis and antimicrobial activities of silver (i) sulfanylcarboxylates. Structural isomers with identically or unequally coordinated Ag centers in an Ag 4 S 4 ring. Dalton. Transactions. 28, 3074-3085.

Bhuyar, P., Rahim, M. H. A., Sundararaju, S., Ramaraj, R., Maniam, G.P., Govindan, N., 2020. Synthesis of silver nanoparticles using marine macroalgae Padina sp. and its antibacterial activity towards pathogenic bacteria. Beni-Suef Uni. J. Basic and App. Sci. 9, 1-15.

Bidgoli, S.A., Mahdavi, M., Rezayat, S.M., Korani, M., Amani, A., Ziarati, P., 2013. Toxicity assessment of nanosilver wound dressing in Wistar rat. Acta. Med. Iran. 51, 203-208.

Brayner, R., 2008. The toxicological impact of nanoparticles. Nanotoday. 3, 48-55.

Choi, O., Deng, K.K., Kim, N.J., Ross, L., Surampalli, R.Y., Hu, Z., 2008. Theinhibitory effects of silver nanoparticles, silver ions, and silver chloride colloids on microbial growth. Water Res. 42, 3066-3074.

Cobley, C.M., Skrabalak, S.E., Campbell, D.J., Xia, Y., 2009. Shape-controlled synthesis of silver nanoparticles for plasmonic and sensing applications. Plasmonics 4, 171–179.

Dakal, T.C., Kumar, A., Majumdar, R.S., Yadav, V., 2016. Mechanistic Basis of Antimicrobial Actions of Silver Nanoparticles. Front. Microbiol. 7, 1831.

Deng, H., McShan, D., Zhang, Y., Sinha, S. S., Arslan, Z., Ray, P. C., 2016. Mechanistic study of the synergistic antibacterial activity of combined silver nanoparticles and common antibiotics. Environ. Sci. Technol. 50, 8840-8848.

Deshmukh, S.P., Patil, S.M., Mullani, S.B., Delekar, S.D., 2019. Silver nanoparticles as an effective disinfectant: A review. Mater Sci. Eng. C 97, 954-965.

Folkman, J., 2002. Role of angiogenesis in tumor growth and metastasis. In Seminars in Oncology; Elsevier: Amsterdam, the Netherlands, pp. 15–18.

Gamboa, S.M., Rojas E.R., Martínez V.V., Baudrit J.V., 2019. Synthesis and characterization of silver nanoparticles and their application as an antibacterial agent. Int. J. Biosen Bioelectron. 5, 166-173.

Ghodake, G., Kim, M., Sung, J. S., Shinde, S., Yang, J., Hwang, K., Kim, D.Y., 2020. Extracellular synthesis and characterization of silver nanoparticles: Antibacterial activity against multidrug-resistant bacterial strains. Nanomat. 10, 360.

Gurunathan, S., Kalishwaralal, K., Vaidyanathan, R., Venkataraman, D., Pandian, S.R., Muniyandi, J., Hariharan, N., Eom, S.H., 2009. Biosynthesis, purification and characterization of silver nanoparticles using Escherichia coli. Colloids Surf. B Biointerfaces 74, 328–335.

Gurunathan, S.; Han, J.W.; Kwon, D.N.; Kim, J.H., 2014. Enhanced antibacterial and anti-biofilm activities of silvernanoparticles against Gram-negative and Gram-positive bacteria. Nanoscale Res. Lett., 9, 373.

Habeeb Rahuman, H.B., Dhandapani, R., Narayanan, S., Palanivel, V., Paramasivam R., Subbarayalu, R., *et al.*, 2022. Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications. IET Nanobiotechnol. 16(4), 115-144.

Hassanen, E.I., Khalaf, A.A., Tohamy, A.F., Mohammed, E.R., Farroh, K.Y., 2019. Toxicopathological and immunological studies on different concentrations of chitosan-coated silver nanoparticles in rats. Int. J. Nanomed. 14, 4723-4739.

Homayouni-Tabrizi, M., Soltani, M., Karimi, E., Namvar, F., Pouresmaeil, V., Es-haghi, A., 2019. Putative mechanism for anticancer properties of Ag-PP (NPs) extract. IET nanobiotechnol. 13, 617-620.

Ipe, D.S., Kumar, P.T.S., Love, R.M., Hamlet, S.M., 2020. Silver Nanoparticles at Biocompatible Dosage Synergistically Increases Bacterial Susceptibility to Antibiotics. Front Microbiol. 11, 1074.

Iravani, S., Korbekandi, H., Mirmohammadi, S.V., Zolfaghari, B., 2014. Synthesis of silver nanoparticles: chemical, physical and biological methods. Res Pharm Sci. 9, 385-406.

Khodashenas, B., Ghorbani, H.R., 2015. Synthesis of silver nanoparticles with different shapes. Arab. J. Chem. 12, 1823-1838.

Kim, S., Ryu, D.Y., 2013. Silver nanoparticle-induced oxidative stress, genotoxicity and apoptosis in cultured cells and animal tissues. J. Appl. Toxicol. 33, 78-89.

Kwon, T., Woo, H.J., Kim, Y.H., Lee, H.J., Park, K.H., Park, S., Youn, B., 2012. Optimizing hemo compatibility of surfactant-coated silver nanoparticles in human erythrocytes.J. Nanosci. Nanotechnol., 12, 6168–6175.

Lee, S.H., Jun, B.H., 2019. Silver Nanoparticles: Synthesis and Application for Nanomedicine. Int. J. Mol. Sci. 20, 865.

Liao, C., Li, Y., Tjong, S.C., 2019. Bactericidal and Cytotoxic Properties of Silver Nanoparticles. Int J Mol Sci. 20, 449.

Liu, X., Chen, JL., Yang, WY., Qian, Y.C., Pan, J.Y., Zhu, C.N., Liu, L., Ou, W.B., Zhao, H.X., Zhang, D.P., 2021. Biosynthesis of silver nanoparticles with antimicrobial and anticancer properties using two novel yeasts. Sci. Rep. 11, 15795.

Lok, C. N., Ho, C. M., Chen, R., He, Q. Y., Yu, W. Y., Sun, H., Tam, P.K., Chiu, J.F., Che, C.M., 2007. Silver nanoparticles: partial oxidation and antibacterial activities. J. Biol. Inorganic Chem. 12, 527-534.

Majnumeena, R., Duraibabu, D., Sudha, J., Kalaichelvan, P., 2014. Biogenic nanosilver incorporated reverse osmosis membrane for antibacterial and antifungal activities against selected pathogenic strains: an enhanced eco-friendly water disinfection approach. J. Environ. Sci. Health. 49, 1125-1133.

McDaniel, J.T., Nuhu, K., Ruiz, J., Alorbi, G., 2019. Social determinants of cancer incidence and mortality around the world: an ecological study. Glob. Health. Promot. 26, 41-49.

Mohamed, E.M., Kattaia, A.A.A., Abdul-Maksoud, R.S., Abd El-Baset, S.A., 2020. Cellular, Molecular and Biochemical Impacts of Silver Nanoparticles on Rat Cerebellar Cortex. Cells. 10, 7.

Morones, J.R., Elechiguerra, J.L., Camacho, A., Holt, K., Kouri, J.B., Ramírez, J.T., 2005. The bactericidal effect of silver nanoparticles. Nanotech. 16, 2346.

Mukherjee, P., Ahmad, A., Mandal, D., Senapati, S., Sainkar, S.R., Khan, M.I., Renu, P., Ajaykumar, P.V., Alam, M., Kumar, R., Sastry, M., 2001. Fungus-mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: A novel biological approach to nanoparticle synthesis. Nano Lett. 1, 515–519.

Panda, K.K., Achary, V.M.M., Krishnaveni, R., Padhi, B.K., Sarangi, S.N., Sahu, S.N., Panda, B.B., 2011. In vitro biosynthesis and genotoxicity bioassay of silver nanoparticles using plants. Toxicol. Vitro. 25:1097-1105.

Patra, J. K., Baek, K. H., 2017. Antibacterial Activity and Synergistic Antibacterial Potential of Biosynthesized Silver Nanoparticles against Foodborne Pathogenic Bacteria along with its Anticandidal and Antioxidant Effects. Front Microbiol. 8,167.

Pilleron, S., Sarfati, D., Janssen-Heijnen, M., Vignat, J., Ferlay, J., Bray, F. Soerjomataram, I., 2019. Global cancer incidence in older adults, 2012 and 2035: A population-based study. Int. J. Cancer. 144, 49-58.

Pourhamzeh, M., Gholami Mahmoudian, Z., Saidijam, M., Asari, M.G., Alizadeh, Z., 2016. The Effect of Silver Nanoparticles on the Biochemical Parameters of Liver Function in Serum, and the Expression of Caspase-3 in the Liver Tissues of Male Rats. Avicenna. J. Med. Biochem. 4, e35557.

Ragheb, M., Mikhael, M.W., Allam, K.A., Mohame, E.H., 2020. Silver Nanoparticles Affect Biochemical Parameters in Tissues of Mosquitoes Larva. Egy. J. Chem. 63, 3995- 4003.

Ratan, Z.A., Haidere, M.F., Nurunnabi, M., Shahriar, S.M., Ahammad, A.J.S., Shim, Y.Y., Reaney, M.J.T., Cho, J.Y., 2020. Green Chemistry Synthesis of Silver Nanoparticles and Their Potential Anticancer Effects. Cancers (Basel) 12,855.

Rónavári, A., Igaz, N., Adamecz, D.I., Szerencsés, B, Molnar, C., Kónya, Z., Pfeiffer, I., Kiricsi, M., 2021. Green Silver and Gold Nanoparticles: Biological Synthesis Approaches and Potentials for Biomedical Applications. Molecules 26, 844.

Sintubin, L.,Verstraete, W., Boon, N., 2012. Biologically produced nanosilver: Current state and future perspectives. Biotechnol. Bioeng, 109, 2422–2436.

Sofi M.A., Sunitha S., Sofi, M.A., Khadheer Pasha S.K., Choi D., 2022. An overview of antimicrobial and anticancer potential of silver Nanoparticles. J. King Saud Uni. Sci. 34, 101791.

Sriram, M.I., Kalishwaralal, K., Barathmanikanth, S., Gurunathani, S., 2012. Size-based cytotoxicity of silver nanoparticles in bovine retinal endothelial cells. Nanosci. Methods, 1, 56–77.

Tariq, M., Mohammad, K.N., Ahmed, B., Siddiqui, M.A., Lee, J., 2022. Biological Synthesis of Silver Nanoparticles and Prospects in Plant Disease Management. Mol. 27, 4754.

Thakkar, K.N.; Mhatre, S.S.; Parikh, R.Y., 2010. Biological synthesis of metallic nanoparticles.Nanomedicine 6, 257–262.

Tiwari, D.K., Jin, T., Behari, J., 2011. Dose-dependent in-vivo toxicity assessment of silver nanoparticle in Wistar rats. Toxicol. Mech. Methods. 21, 13-24.

Tripathi, N., Goshisht, M.K., 2022. Recent Advances and Mechanistic Insights into Antibacterial Activity, Antibiofilm Activity, and Cytotoxicity of Silver Nanoparticles. ACS Appl. Bio. Mater. 5, 1391-1463.

Vigneswari, S., Amelia, T.S.M., Hazwan, M.H., Mouriya, G.K., Bhubalan, K., Amirul, A.A., Ramakrishna, S., 2021. Transformation of Biowaste for Medical Applications: Incorporation of Biologically Derived Silver Nanoparticles as Antimicrobial Coating. Antibiotics (Basel). 10, 229.

Wang, Z.X., Chen, C.Y., Wang, Y., Li, F.X.Z., Huang, J., Luo, Z.W., 2019. Ångstrom scale silver particles as a promising agent for low toxicity broad spectrum potent anticancer therapy. Adv. Funct. Mater. 29, 1808556.

Wei, L., Lu, J., Xu, H., Pate, A., Chen, Zhe-Sh, Chen, G., 2015. Silver nanoparticles: synthesis, properties and therapeutic applications, Drug Discov Today. 20, 595–601

Wypij, M., Je drzejewski, T., Trzcin ´ska-Wencel, J., Ostrowski, M., Rai, M., Golin ´ska, P., 2021. Green Synthesized Silver Nanoparticles: Antibacterial and Anticancer Activities, Biocompatibility, and Analyses of Surface-Attached Proteins. Front. Microbiol. 12, 632505.

Xu, L., Wang, Y.Y., Huang, J., Chen, C.Y., Wang, Z.X., Xie, H., 2020. Silver nanoparticles: Synthesis, medical applications and biosafety. Theranostics. 10, 8996-9031.

Yang, T., Yao, Q., Cao, F., Liu, Q., Liu, B., Wang, X.H., 2016. Silver nanoparticles inhibit the function of hypoxia-inducible factor-1 and target genes: insight into the cytotoxicity and antiangiogenesis. Int. J. Nanomed. 11, 6679-6692.

Yin, I.X., Zhang, J., Zhao, I.S., Mei, M.L., Li, Q., Chu, C.H., 2020. The Antibacterial Mechanism of Silver Nanoparticles and Its Application in Dentistry. Int. J. Nanomed. 15, 2555-2562.

Yuan, Y. G., Peng, Q. L., Gurunathan, S., 2017. Effects of silver nanoparticles on multiple drug-resistant strains of Staphylococcus aureus and Pseudomonas aeruginosa from mastitis-infected goats: An alternative approach for antimicrobial therapy. Int. J. Mol. Sci. 18, 569.

Zhang, D., Ma, X.L., Gu, Y., Huang, H., Zhang, G.W., 2020 Green Synthesis of Metallic Nanoparticles and Their Potential Applications to Treat Cancer. Front Chem. 8, 799.

Zhang, X.F., Liu, Z.G., Shen, W., Gurunathan, S., 2016. Silver Nanoparticles: Synthesis, Characterization, Properties, Applications, and Therapeutic Approaches. Int. J. Mol. Sci. 17, 1534.

Zhang, Y., Lu, H., Yu, D., Zhao, D., 2017. AgNPs and Ag/C225 Exert Anticancerous Effects via Cell Cycle Regulation and Cytotoxicity Enhancement. J. Nanomater. 2017 | Article ID 7920368.

Zielińska-Górska, M., Sawosz, E., Sosnowska, M., Hotowy, A., Grodzik, M., Górski, K.; Strojny-Cie´slak, B., Wierzbicki, M., Chwalibog, A., 2022. Molecular Biocompatibility of a Silver Nanoparticle Complex with Graphene Oxide to Human Skin in a 3D Epidermis In Vitro Model. Pharmaceutics 14, 1398.