Pure Appl. Biol., 11(2): 421-438, June, 2022
http://dx.doi.org/10.19045/bspab.2022.110042

Review Article

Biological, physical and chemical synthesis of silver nanoparticles and their non-toxic bio-chemical application: A brief review

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Citation
Rabia Kanwar, Rida Fatima, Rashid Kanwar, Muhammad Tariq Javid, Uzma Wali Muhammad, Zahra Ashraf and Ayesha Khalid. Biological, physical and chemical synthesis of silver nanoparticles and their non-toxic bio-chemical application: A brief review. Pure and Applied Biology. Vol. 11, Issue 2, pp421-438.
http://dx.doi.org/10.19045/bspab.2022.110042

Received: 12/03/2021 Revised: 17/05/2021 Accepted: 29/05/2021 Online First: 26/08/2021

Abstract

Nanotechnology is gaining popularity, because of its wide use in every field. Nanotechnology is continuously improving medical advancements. Nanoparticles can be engineered for their biocompatibility, size, shape and selectivity. Silver Nanoparticles have been extensively used by researchers because of their unique and wide properties such as size, shape, electrical properties and antimicrobial. Due to these properties silver nanoparticles have been used almost in every field from engineering to chemical and biological. Just like their properties, silver nanoparticles can be synthesize by various method including physical (Gamma Irradiation, Laser ablation and electron irradiation, microwave processing), chemical (chemical reduction and photochemical method) and biological. Due to the less toxicity, the use of silver Nanoparticles in life sciences has been increasing. The aim of the following review is to discuss the various methods of silver nanoparticle synthesis and their non-toxic application in the field of life sciences for the treatment of various diseases including Antibiotic resistance challenge and a tool for cancer therapy. The life sciences field will benefit from a mechanistic understanding of SNP therapeutic activities, which will aid in the development of individualized treatment and healthcare techniques for the benefit of the human population.

Keywords: Antimicrobial; Biological synthesis; Nanotechnology; Silver Nanoparticles; Toxicity

Introduction

Nano technology which deals with the materials at nanoscale usually less than 100 nm in size. The nano-scaled particles have definitive properties, such as increased surface- to-volume ratio, and they present different types of chemical and the biological activity than general bulk particles. Nano represents 10^{-9} in unit; this means that nanometer is the one billionth of a meter on the scale [1]. Nanotechnology is gaining popularity now a day because of its most general application of undisputed consent. Its applications are advancing such as medicine,

food, best air quality, cleaning water, in electronics, in catalysis, in fuel cells, solar cells, batteries and manufacturing of fabrics [2]. It is generally accepted that nanoparticles are collections of atoms of approximately 1–100 nm of size. Cells of Living organisms are very small in size i.e. approximately 10 µm. Very small probes without interference of cellular machinery can be developed by using nanoparticles. It is strong driving force to develop nanotechnology for understanding biological processes. Some of the biological applications include drug and gene delivery [3] fluorescent biological labels [4], detection of proteins [5], probing of DNA structure [6], tissue engineering [7], tumor destruction via heating (hyperthermia) [8], purification of biological molecules and cells [9] and bio detection of pathogens [10]. Nanotechnology is continuously improving the medical advancements. Nanoparticles can be engineered for their biocompatibility, size, shape and selectivity.

Although the existence of nanoparticles in nature is ages old, but their true understanding took ample time to develop. It is more recently that these nanoparticles have been characterized and their application have widespread in a range of goods used in everyday life. The understanding of fundamental particles of matter and their optical properties have paralleled the understanding of nanoparticles and their related applications. Today, we not only have developed a reasonable understanding of nanoparticles but also we have been able to derive their applications in numerous ways. In this review, we summarized the synthesis and various Biological and Physical application of Silver nanoparticles.

Synthesis approaches of silver nanoparticles (AgNPs)

Nanostructures of different types can be prepared by various procedures, such as physical methods [11, 12], biological methods [13-15], photochemical methods [13] and chemical methods [16]. All these methods have their own merits and demerits. For example, physical method involves rapid processing which are time effective and do not use or contain toxic chemicals whereas a major disadvantage of this method is that it demands a big deal of energy consumption. Similarly, photo-induced synthetic method demands a big deal of expensive equipment [17].

Physical method

Laser ablation and evaporation-condensation are the very important physical methods of nanoparticle (NP) synthesis. The size of NPs and their homogeneity are the best aspect of physical synthesis methodology as compared to chemical processes. This includes some demerits of tube furnace usage that requires a great amount of energy and occupies a large space during the operational procedures. As the environmental temperature increases it becomes tough job to achieve thermal stability; and also this is time consuming. The colloids of the metals can be synthesized by laser ablation technique without the use of hazardous chemical reagents in the solutions. This technique can easily be used for the preparation of pure metal colloids. During this technique, preheating time is always required for furnace to get a proper operating temperature for the procedures Silver nano-spheroids of 20-50 nm can be formed by laser ablation method in the water with the help of femto-second laser pulses recorded at 800 nm [18].

Biological method

Biological methods used for the synthesis of metallic NPs are usually highly productive, cost effective, harmless, and ecofriendly. Various natural sources, such as plants and plant products, algae, yeast, fungi, and bacteria may be used for synthesis of nanoparticles [18]. For example, algae can be used for the production of some noble metal nanoparticle; some algae have been tried to yield silver and gold NPs; some plants can be

used to make silver, zinc oxide, gold, platinum, magnetite, and palladium NPs; bacteria and yeasts have been in use for the production of metal NPs; and similarly, fungi is used for gold, silver and cadmium NPs synthesis [19].

Photochemical method

Silver nanoparticle (AgNP) synthesis can be executed by the use of photons. Various shapes of AgNPs can be synthesized by this method. The shape and the size of the AgNPs can easily be measured with the help of color of light used to initiate a photochemical growth process [20]. Usually, with the help of light, i.e., UV light alters colloidal solutions of the spherical AgNPs into more stable bigger nanoparticles with various sizes and shapes. In photochemical method, AgNPs can be prepared in the form of solutions of colloidal silver. It involves photo-reduction of the silver salts, such as silver perchlorate, silver nitrate and the availability of polymers as stabilizers which may include poly methacrylic acid (PMAA), Polyvinylpyrolidone (PVP), and Polymethyl methacrylate (PMMA). The Photochemical production of the AgNPs can be regulated by the concentrations of polymer stabilizer and selecting the light sources [21].

Chemical method

Chemical reduction method is commonly applied synthetic method. Synthesis of Ag-nanostructures in solution may have three main components: reducing agents, which is the metal precursor and may be the capping agents. Mostly used reducing agents may involve sodium citrate, sodium borohydride, ascorbic acid, different type of alcohols, and certain hydrazine compounds. Metal cations can be reduced easily to produce metal nanoparticles. Stable colloidal silver nanoparticles can be rapidly prepared in colloidal dispersions, organic solvents or water. Ascorbic acid, elemental hydrogen, trisodium citrate and sodium borohydride are commonly used reductants. AgNPs can be generally synthesized by reduction of silver ions (Ag^{2+}) in the colloidal form with a range of nanometer size. Primarily, Silver Ag^{2+} ions were reduced and silver atoms at zero valent state are formed which then aggregate into the oligomeric groups and clusters. These clusters finally form colloidal Ag nanoparticles [22-26]. Recent studies indicated that use of the powerful reductant, for example sodium borohydride, produced small sized nanoparticles that are almost mono-dispersed, but production of the larger nanoparticles was a challenge. Trisodium citrate is the weak reducing agent, which result in slow reduction process and polydispersity [27]. Chemical reduction method is the common method for synthesis of AgNPs by using organic and inorganic compounds as reducing agents. Usually, different reducing agents like sodium borohydride (NaBH4), trisodium citrate, polyol process, N, N- dimethylformamide (DMF), sodium borohydride (NaBH4), poly ethylene glycol-block polymers and Tollens reagent are basically utilized for the reduction of silver ions (Ag^{+}) as reducing agents in the aqueous solutions. Metallic Ag^{0} at zero valent stage are formed by reduction of Ag^{2+} to form oligomeric clusters in the form of colloids [28-31].

Synthesis of anisotropic AgNPs

Different shapes of stable AgNPs can be prepared through chemical reduction method by the use of different reducing agents like hydrazine [32], ascorbic acid [33], dimethylformamide [34], ammonium formate [35], and sodium borohydride [36]. The reducing agent assigns the size, shape and distribution of AgNPs formed by reducing the metal salt. Different concentrations of hydrogen peroxide have also been reported for the formation of anisotropic AgNPs. Reducing agents like citrate and borohydride react slowly with hydrogen peroxide because it is a neutral reagent. Hydrogen peroxide (H_2O_2) is rapidly

decomposed to oxygen and water at the surface of metallic silver and bubbles evolve when AgNPs become large and the color will change to dark orange from pale yellow. Less stable morphologies of AgNPs like spherical, platelets and irregular will dissolve and result in oxidative etching. Generally, Ag nanoprisms are prepared with the help of chemical reduction methods or by other methods. Both methods depend on few variables, such as respective salt with metal precursor, and reducing agents which are present in solution medium. Chemical methods require stabilizing agents (form example, trisodium citrate, etc.) and certain oxidizing agents (H_2O_2) to produce oxidative etching in solution. When a molecule of O_2 and a ligand are present, both at a time in the solution, it results in aforementioned reaction. This may result in a strong oxidation for both seeds and nuclei [37]. Seeds present significant surface defects in colloidal solution. These clusters will change to triangular plates or hexagonal [32]. Ultraviolet or visible light is required to reduce silver ions (Ag^{2+}) in assisted methods and do not require oxidizing etching agents to grow anisotropic silver [38].

Surface plasmon resonance

Nano Particles show different behavior as compared to their bulk material as they are different in their electron density and their dimensions. This characteristic phenomenon is referred as quantum size effect. Certain examples of this effect include LSPR of the metallic NPs where geometric limits and delocalized electrons can be seen with the light. Different Plasmon resonance values are concerned with the shapes and sizes of the nanoparticles. Different ranges of absorbance of the UV wavelengths show difference in their absorbance and peaks with reference to the color of the NPs. Plasmon resonance of the AgNPs mainly depends upon many factors. For example shapes and sizes of the particles, distance between the particles and dielectric constants of the metal and surfaces [39]. AgNPs of the spherical shapes show peaks of the UV visible spectroscopy at the 400nm range and these peaks mainly depend upon the shape and size of the AgNPs [40].

General applications of silver nanoparticles

Photo-voltanic, biological and chemical sensors can be prepared from silver nanoparticles by exploiting the following properties like thermal, optical and electrical properties. Conductive inks, fillers and pastes are some examples which employ high stability to AgNPs with reference to the electrical conductivity and these also show low sintering temperatures. A progressively general application involve AgNPs for the antimicrobial coatings in titanium prosthetics, dental resins, and fabrics, biomedical instruments such as keyboards, wound dressings, now have AgNPs that constantly release a very low amount of silver ions and nanoparticles to defend and protect the wounded areas from the bacterial infections. Further applications include chemical sensing, photonic devices, biological sensing, and molecular diagnostics which improve the innovative optical, and some other concerned properties of nanomaterials. Colloidal silver nanoparticles are used for making nanoparticle inks that are dispersed in stable form. For obtaining high dispersion solubility, size of nanoparticle may be 50 nm or less for the use as silver inks [41]. Additionally, properties such as shape, size and monodispersity of the nanoparticles are the key components. Because the conductivity intensely depends on the density of nanoparticles filled into the superstructure that results after desiccating the ink vehicle from a printed trace.

Antibacterial applications

Antibacterial properties of the AgNPs mainly depend on the shape and size of the AgNPs [42]. Along with all these factors, stability of the AgNPs in the media, coating types and the

final charges, influence the activity of the AgNPs with the bacterial cells [43-46]. For the proper evaluations of the AgNPs proper stabilization and dispersions of the AgNPs are very essential. Interactions between bacteria and AgNPs are because of the shape and size of the silver NPs [47-50]. The change in wavelength of these plasmonic nanoparticles when they interact with molecules has also been studied for analytical measurements using silver nanoparticles [51]. However, stable nano-silver has a far lower minimal inhibitory concentration than its dissolved ionic equivalent, according to studies [52], silver ions in solution are strong antimicrobials, but chloride, phosphate, proteins, and other cellular components readily sequester them [53].

Nanoparticles are often coated with non-toxic and non-inflammatory capping agents such as collagen, peptides, and biopolymers to enhance their effectiveness and stability in biomedical and other applications, ideally without substantially altering their scale, shape, or antimicrobial properties [54-56]. Some findings regarding the action of AgNPs indicate that particle stability can influence the bactericidal mode [54], AgNPs conjugated with poly-lysine, for example, were less successful than collagen-capped AgNPs due to aggregation. Multidrug-resistant bacteria are a major source of concern for health professionals since they exhibit high resistance to a variety of antibiotics. As a result, new antibacterial methods are urgently needed [57]. AgNPs' antimicrobial activity can be enhanced with further studies and new advances in the field. Antibacterial effect of AgNPs can be enhanced by influence of different factors as shown in (Fig. 1).

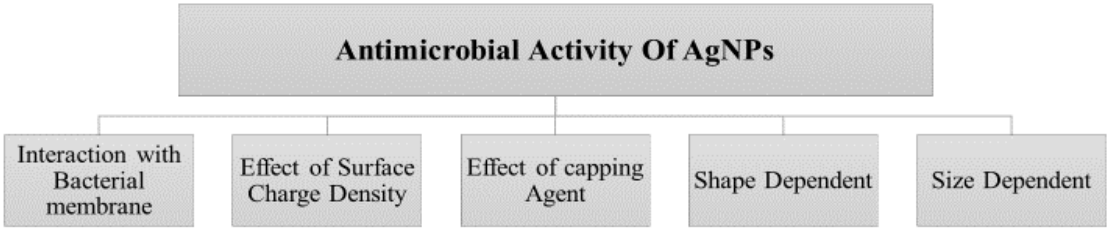

Figure 1. Factors effecting antimicrobial activity of silver nanoparticles

Size dependent application of silver nanoparticles

Larger surface areas of the AgNPs facilitate the smooth entry of the AgNPs inside the cell and hence their interaction percentage is increased with comparison to the other large size particles of different nature [58-60]. Because of decrease in size of particle the contact surface area of the particles increased bactericidal activity increased as for example surface contact increased by 10^9 as decreasing particle size from 10 µm to 10 nm.Smaller the size, efficient the particles for entry and reaction inside the cell. Hence one can easily say that the size of the NPs effect bactericidal activity [61-63].

Shape dependent application of silver NP

AgNPs react differently with different biosystems and demand is going to be increased as microbicide. Nanoparticles with same size but different shapes have different surface area with regard to shape to interact with microorganism. Antibacterial properties of AgNPs depend upon the various shapes of

the NPs [50]. Shape of the NPs play a great role toward the efficacy of the nanoparticles in the antibacterial studies. Different shaped NPs show differential growth inhibition in the bacteria [64-66]. Triangular NPs with truncation, performed bacterial inhibitory function with Ag value nearly of 1 µg. While in case of spherical nanoparticles this value increased to12.5 µg. The nanoparticles with the rod shaped require a value ranging from 50 to 100 µg of silver content values. In this manner, the AgNPs of various shapes differently behave with bacterial cell [67].

Effect of capping agent

As the stability of NPs is ligand-specific, so it is possible that the non-capped NPs may not carry on similarly. It is subsequently critical to examine the colloidal stability for particular conditions. AgNPs are frequently synthesized within the availability of capping agents, for example, surfactants or polymers, which act as capping and stabilizing agent for AgNPs formation [68] to avoid molecule aggregation and acquire stable AgNPs. Colloidal stability of such NPs varied with different ionic values, charges, acidity, and availability of organic species [69, 70].

Effect of surface charge density of AgNP

A positive value of zeta potential supports the interaction between the particles and bacteria (gram-negative and gram-positive) [71]. The productivity of the ionic silver against microbes with contrarily charged layers is identified with the electrostatic forces brought on by the positive potentials of the nanoparticles [72]. In the present review, the positive zeta potential of AgNP is one of the perspectives that may clarify the ideal results of its action as an antimicrobial agent. The surface charge of nanoparticles affects cellular uptake. [73, 74] owing to electrostatic interactions with the negatively charged cell surface, those with cations on their surface bind and are internalized more easily. Negatively charged silver nanoparticles, on the other hand, have been reported to be effective antibacterial agents. The linking of calix arenes to Ag nanoparticles, for example, can reduce the strongly negative charge of the calix-arene tail groups, enabling Ag nanoparticles to penetrate membranes more easily [75]. The redox potential of Ag0 atoms on the NP surface, which is supposed to cause the generation of free radicals and reactive oxygen species, could also explain the efficacy of negatively charged AgNPs [76-78]. The interactions between bacterial cell membranes and AgNPs have been documented to be aided by opposite surface charges [79]. When the content of NaBH4 is increased for AgNPs formation, it leads to the reduction in the zeta potential of the resultant silver nanoparticles. The reason between the increments of the proportion of NaBH4 in connection to the particles size enlargement of the nanoparticles is because of the release of electrons brought about by NaBH4. Since when the concentration of NaBH4 is increased, it provides good quantity of free electrons, which further cause the reductions in the zeta potential, which influence the aggregation and agglomeration of the silver nanoparticles [80].

The action against bacterium is encouraged by the electrostatic communications and interactive relations between the positively charged AgNPs and negative charge bearing microbial cell membranes. Besides, these electrostatic forces appeared to be another important concept as to the antibacterial activity of Ag nanoparticles (AgNPs). Presumably the shape, size, cationic properties and positive zeta potential of AgNP encourages the antimicrobial activity against gram positive bacterium. It is known that the zeta potential estimations of synthetic AgNPs typified by the formed cationic surfactants act more noteworthy than +30 mV which be sign and account for the high stability of AgNPs, which block the process of agglomeration. The high estimation of the

zeta potential show that the surface charge on silver nanoparticles is high enough so that the electrostatic forces of repulsion between nanoparticles remain always high up to the extent, which prevent particles agglomeration and keep them stable. The positive values of zeta potential is mostly because of the utilized capping agent with their cationic surfactant, which along with them carry positive charges [80].

Interaction of bacterial membrane with AgNP

A few scientists argued that silver species discharge Ag^{2+} ion and further they interact with thiol functional group in microbial proteins, influencing the DNA replication [81]. It is additionally reported that Ag^{2+} ions leads to uncoupling of the respiratory chain from the oxidative phosphorylation or block the proton-motive process and forces over the cytoplasmic channels [82]. Bacterial contaminations remain a noteworthy reason for death, sickness and financial losses for a huge number of individuals around the world, and quick development of antibiotic resistant microbes have made the circumstances more confused. Advancement of drug resistance bacteria against normal antimicrobials preferences to new medication or material to battle against pathogenic microorganisms. At this time, the nanoparticle based sterilization and other therapeutic techniques has been considered as a promising option for enhancing the diagnostic and preventive framework because of their exceptional chemical and physical properties [83]. To comprehend these issues, green synthesis method of metallic nanoparticles utilizing proteins or different biomolecules has achieved huge significance [84]. To upgrade the biomedical uses of biosynthesized AgNPs, it is fundamental to comprehend the interaction of AgNPs with the microorganisms and their consequent cell reactions. Despite that, the crucial molecular mechanism of antibacterial action of AgNPs did not seem to be exceptionally well; there is still discussion on the activity of the AgNPs. Different procedures have been proposed for AgNPs intervened cell death including interruption of the cell envelope, oxidation of the cell components and its organelles, inactivation of the respiratory chain compounds, creation of the Reactive oxygen species (ROS), decay of the cell segments, and so on [85]. It is reported for AgNPs that they execute the bacterial cells through cell inhibition mode [86]. As the AgNPs come in contact with the cell membrane of bacteria, the porosity of membrane increases which generate penetrable pits. This prompts an osmotic fall in the cells and discharges the intracellular materials. The other conceivable system incorporates binding of AgNPs with the cell surface proteins or carbohydrates moieties harms the cell membrane, which causes denaturation of the compounds and disturbance of the electron transport pathway prompting the cell death [87]. Antibacterial activity of the AgNPs is mainly concerned with the oxidative stress and under this stress, reactive oxygen species are produced, which induce further stress [88-90]. Formation of ROS species such as hydroxyl radicals $OH^{\bullet}$, superoxide ions $O2 \rightarrow H2O2$ are the resultant of the inhibition of respiratory enzymes by AgNPs, these ROS further react to form hydroperoxyl radicals, which induce cell and cellular component's damage by synthesis oxidative decomposition. During all the antibacterial activities and pathways, the interaction of AgNPs with the bacterial cells disintegrates the cell membrane and harm the bacteria in certain way. However, particle size have role in the entry of AgNPs in the bacterial cells, certain structural contents of the bacterial cell wall may effect these interaction. Gram-negative bacteria have a minute peptidoglycan layer ranges 2–3 nm between outer and the cytoplasmic membrane [74]. In comparison, Gram-positive bacteria deficient of the outermost

membrane, but they have a thick peptidoglycan layer of about 30 nm around its outer region [91]. The Gram-positive bacterial thick cell wall plays an important role as a protective barrier against the entry of AgNPs or Ag^{+} ions into cell cytoplasm. Because of this thick barrier, Gram-positive bacteria are more resistant to the entry of AgNPs. The cell wall also have some other content as well, i.e. lipids and other protein components, surrounding a lipid membrane which aid in more protection against invasions. Gram-negative bacteria on the contrast have a much thinner peptidoglycan layer present in between two cell membranes. The outer membrane may have proteins, such as porins, and lipopolysaccharides (LPS), sometimes also referred as endotoxin. Both types of bacteria may contain flagella on their cells. Biosensing can be performed by using intracellular cell contents such as, proteins, DNA, and RNA. The microbial strains may regulate the biological availability of Ag^{2+} ions produced from the AgNPs by changing: The extracellular disintegration of the AgNPs by means of bacterial exudates (peptides, bio surfactants, and organic acids).

The cell take-up of Ag^{+} ions through cell-NP interactions, structure and charge mediated interactions of the cell wall [92]. The cell content of Gram-positive microbes is very rich in teichoic acids, where its basic role is to give rigidity by pulling in cations, for example, Mg^{2+} [93]. Antimicrobial Peptides are viewed as fabulous antimicrobial agents [94] on the grounds that their macrocyclicamido functional group can take part in the metal–ligand p-bonding, delivering the complex with Ca^{2+} and Mg^{2+} cations.polymyxin E (PE) and Bacitracin A (BA)are polypeptides which have cationic macrocyclicamido as a functional group, which are known as antimicrobial peptides (AMPs). The Peptides were used by for the formation of AgNPs for the treatment of gram-negative bacteria (*E. coli* and *P. aeruginosa*) and gram-positive bacteria (*Staphylococcus aureus* and *Bacillus amyloliquefaciens*) [95]. The immobilization of peptides on the AgNP surface expanded their antimicrobial movement upto the 10 times without causing any side effects of the bacterial resistance. In this way, it has been proposed that Bacitracin A and polymyxin E on the AgNP surface can chelate Mg^{2+} and Ca^{2+} and concentrate them from the first restricting site in teichoic acids, in this way harming the bacterial cell wall [96] In addition, a similar review demonstrated the availability of BA/PE- nanoparticles inside the nucleoid of the bacteria. Recent discoveries proposed that AgNPs can attach to ribosomes, chromosomes, and bringing about an inhibition of action of ribosomes and concealment of replication of the DNA, eventually causing cell damage [97].

It is trusted that significant antimicrobial impact of AgNPs is intervened by incomplete oxidation and the final release of Ag^{+} ions. Peptidoglycan present in the bacterial cell wall and membrane associate with the AgNPs, thus disturbing protein formation, preventing DNA replication and finally causing cell lysis. Antimicrobial action of AgNPs lower the bacterial resistance rates. Likewise AgNPs can specifically harm and enter the cell membrane and cell wall. Latest reports describe the significance of interactions in the antimicrobial action of AgNPs, as they can translocate over, and progress towards inside the cell, through the vesicles or the cytoplasm, whose consequent breakdown caused by an oxidizing and acidic pH of plasma membrane might prompt high concentrations of Ag^{2+} ions [95]. One reason which makes AgNPs interesting as antibacterial agents in the way that microscopic organisms are not prone to resistance to antibiotics, because of the extensive variety of understandable interactions of Ag^{2+} ions within the biological molecules [98]. Though the effect of AgNPs

on physicochemical properties, such as surface charge, roughness, chemical composition, cell wall rigidity, and adhesion property, of the bacterial cell are yet need further researches and few are under considerations in the recent ages.

Anticancerous effect on HeLa cell line

In 2012, 8.2 million cancer-related deaths and almost 14 million new cancer cases were estimated. Lung cancer is causing greatest mortality (1.5 million deaths), as compare to the other types of the Cancer(s). Other data are recorded further include by liver (745,000 deaths), stomach (72,000 deaths), colorectal (694,000 deaths), breast (521000 deaths) and esophageal cancer (400,000 deaths) [99]. In the next two decades new cancers cases are increasing by 70% or more than that [100]. Almost 70 % of the cancer deaths occur in the populations of Africa, Asia, Central and South America, and other 60% of the total new annual cancer cases are reported worldwide [101]. Various types of cancer are treated by several available therapies. Most common and feasible treatment include chemotherapy in combination with cytotoxic agents to control many types of cancer [102]. However, these treatment approaches sometime cause serious side effects, particularly multidrug resistance (MDR) [103]. Various undesirable side effects of chemotherapy alone or in combination with cytotoxic drug therapy or radiation therapy are common during these therapies [104]. On the basis of these unwanted side effects, the National Cancer Institute (USA) has encouraged the researches and investigation of the potential antitumor activities by using plant extracts [105]. Nanoparticles cast a pivotal role in treatment of several chronic diseases by using natural ingredients, including cancer. Metallic nanoparticles, silver nanoparticles (AgNPs) are a good choice in disease management due to their particular interaction and communications with and disintegration of the mitochondrial respiratory chain. DNA of the cell is damaged by AgNPs as it disrupt mitochondrial function which result by the generation of ROS and which further suppress ATP synthesis. The characterizations of the nanoparticles are important for estimating the potential toxicity of nanoparticles, yet main parameters which affect the biological activity of AgNPs have not been fully tested and need further findings in this regard. A full characterization of AgNPs may be required according to the following points. i.e. measurements of size, shape, material's basic chemistry, solubility, surface area, dispersion state, surface chemistry, and many other physico-chemical properties [106, 107]. Many researchers in the field of nanotechnology have reported that AgNPs significantly cause cell necrosis or apoptosis in numerous cell types e.g. AgNP less than 3 nm in size may induce cytotoxicity in macrophages [108]. The Reduction in the cell viability was additionally seen in liver and neuron cells which were exposed to AgNPs [109-111]. Gender related tissue distribution of AgNPs, genotoxicity and 28-days oral toxicity in rodent was examined [112]. Subchronic inward breath lethality of AgNPs was additionally examined [113]. In those reports, histopathological examinations showed dose dependent response in lesions identified with AgNP administration, including chronic alveolar aggravation, and little granulomatous sores. In any case, coordinate proof on toxic impacts of non-modified AgNPs was not completely recorded in the cell and at the molecular level. This is not completely studied in light of the fact that unmodified AgNPs are unstable in cell culture media of cell lines.

Silver nanoparticles based biological sensor

Biosensor based surface plasmon resonance (SPR) is a kind of optical sensor that uses surface plasmon polariton (SPP) waves. Use of SPR as biosensors to screen and give data about organic procedures indicates

exceptionally encouraging outcomes particularly in contemplating biomolecular associations. SPR-based biosensor is exceptionally delicate and receptive to changes in the refractive record of the analyte, so biosensors of this kind can be utilized to identify the presence of biomolecules with biocompatible component which is utilized as the material of the analyte as DNA, protein, catalysts, antibodies and peptides [114]. In such manner, amongnoble metal nonmaterial, silver nanoparticles (AgNPs) have gotten extensive consideration because of their appealing physicochemical properties. AgNPs display a more extraordinary SPR band than AuNPs. Additionally, the (AgNP) SPR band is more sensitive to natural and ecological adjustments. These two properties permit the identification of a lower concentrations of target species when functionalized AgNPs are utilized rather than gold ones ([115]. It is outstanding that nanostructures with sharp edges or gaps can improve SERS values.The geometry of particles significantly affects the optical properties, nanoparticles with sharp edges for the most part display high detection sensitivity, nanorods, nanostars , nanoholes , and bipyramids have all been used for the development of nanoparticle plasmonic sensors [116].

AgNP as chemosensor with special emphasis on detection of heavy metal

This term “heavy metal” refers to any metallic component that is moderately high in density and is harmful or noxious at lower values e.g. chromium (Cr), cadmium (Cd), thallium (Tl), arsenic (As), mercury (Hg), and lead (Pb). Although heavy metals are components that are present through all the worlds outside layer, pollution and human activities resulted from different exercises, for example, refining and mining operations, mechanical creation and utilization of non-metals and metallic compounds [117]. Natural pollution can likewise happen through metal decompositions at natural level, climatic changes, soil disintegration of metal, draining of substantial materials, sediments re-suspension and the metal vanishing from the water assets to the soil and the ground water. Normal marvels, for example, volcanic emissions and weathering have been said for addition of heavy metal contamination to the soil systems [118, 119]. Modern sources incorporate metal coal consuming in power plants, preparing in refineries, oil burning and high strain lines, plastics, materials, microelectronics, wood protection and paper handling [120]. Harmful impacts may be the brain damage, along with the damages of the kidneys and lungs [121]. Mercury may cause about a few ailments, including Hunter-Russell syndrome acrodynia [122] and Minamata disease [123]. Methylmercury is a known neurotoxin that represents a critical wellbeing danger to people. Various anaerobic bacterial species methylate oxidized mercury to methylmercury on the earth [124].

Hg^{2+} is a standout amongst the most poisonous heavy metal particles and represents a noteworthy hazard to human wellbeing even following a minute exposure of it. Hg^{2+} can bring about long term harm to natural living systems by upsetting organic and cellular events at the cellular level, which results in disease productions, and trigger the onset of many diseases, for example, cancer and cancer like diseases [125]. Mercury explicitly accumulates in the food chains of life, however its poisonous quality is not clear [126]. As indicated by the Environment Protection Agency (EPA) rules, Hg^{2+} must be below than 2 ppb (10 nM) in drinking water. The World Health Organization (WHO) suggests a greatest admission of methylmercury of 1.6 $\mu g\, kg^{-1}$ per week [127]. United States Environmental Protection Agency (EPA) and the National Research Council (NRC) [128] built up a reference measurements of 0.1 µg/kg of the body

weight every day for the average adult organism. Organo-mercury was restricted from rural use in the 1970s in Europe and somewhere else [129]. These days it is notable that any mercury discharged into the earth experiences biogeochemical change forms and can be changed over into the most harmful methylmercury, which may cause serious threats to human health in certain ways. Along these lines, industrial nations and countries have attempted extraordinary actions to displace any mercury in items (e.g. amalgam fillings, thermometers, switches) and modern procedures (impetus in e.g. acetaldehyde generation, amalgam in chlorine-antacid electrolysis) by different substances or procedures in late decades. Despite the fact that various methodologies for Hg^{2+} recognition have been created techniques with a high level of precision and truthfulness are as yet expected to meet the functional prerequisite. Moreover, an assay that could be utilized to recognize distinctive parts of analytes would be an awesome favorable position.

Old methodologies are operational for the investigation of heavy metals in the earth, yet have certain confinements, for example, tedious specimen preparation, and the prerequisite of costly apparatus and trained people to work on them. In spite of the fact that the conventional instrumental systems, for example cold vapor nuclear fluorescence spectrometry, adsorption spectroscopy, and gas chromatography give the immediate and quantitative recognition of Hg^{2+}concentration [130, 131]. To date, a few strategies giving the optical input to the recognition of Hg^{2+} in light of fluorophores [132] chromogenic redox based fluorescent strategy [133], chromophores [134], polymer [135], and noble metal-based tests have been created. In such manner, amongst the metallic nonmaterial of the noble metals, AgNPs have gotten extensive consideration because of their appealing physic-chemical types of properties. Surface plasmon resonance and vast viable diffusing cross segment of AgNPs make them perfect possibility for using in sub-atomic and molecular labeling [135].

Conclusion

Flexibility in synthesis and due to the unique properties, silver Nanoparticles have been used almost in every field. Various experiment proved their nontoxic use in biological application. Antimicrobial application of AgNPs have been used widely. Different methods have been adopted for synthesis of AgNPs including Physical, chemical and Biological.

Authors' contributions

All authors Participate equally in the preparation of manuscript.

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