



Green synthesis of silver nanoparticles using aqueous plant extracts and its application

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ABSTRACT

The development of eco-friendly and reliable techniques for synthesis of silver nanoparticles is a vital step in the area of nanotechnology. This review is importance the compensation and benefits of green synthesis of silver nanoparticles over the other nanoparticles, using various plant extracts and its application in a particular cancer disease treatment as well as in other diseases. Green synthesis of silver nanoparticles with controlled release, drug target, as well as significantly increases the bioavailability of drugs, which greatly overcome the weaknesses of traditional drug delivery

Keywords: Silver Nanoparticle, Green Synthesis, Plant Extract, Microbial enzyme.

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INTRODUCTION

These nanotechnology-based techniques can be applied widely in the management of different malignant diseases [1,2]. Silver nanoparticles (Ag-NPs) have been broadly studied for many decades due to their unique type and wide range of applications. Their uses include catalysis [3], bio-sensing [4], imaging [5] and antibacterial activity. Working with these extremely small structures is very much interesting due to its unique properties [6].

Nowadays, nanotechnology offers a novel move towards to natural source utilization in order to improve drug release and bioactivity. The optimization of nanotechnology products is a key step. The synthesis of nanoparticles is usually conducted using various physical and chemical methods, which often require high-energy inputs and/or the creation of toxic chemicals. In recent years, researchers in the field have strongly focused on the synthesis of metal nanoparticles because of their potential applications in the development of novel technologies. The increasing demand for nanomaterial's in the field of medicine, catalysis, water treatment, and solar energy conversion should be supported by eco-friendly synthesis routes in order to reduce energy inputs and hazardous waste [7]. Two main chemical and physical methods are used to synthesize nanoparticles, but they are often costly and potentially harmful to the social environment [8]. In this scenario, plant extracts have been used as novel and cheap bio reducing agents to produce nanoparticles for a wide number of applied purposes [9].

Silver nitrate is a chemical compound with the formula AgNO_3 . It consists of an ionic bond among the silver cation (Ag^+) and the nitrate anion (NO_3^-). Due to the ionic nature of this compound, it readily dissolves in water and dissociates into its constituent ions. Silver nitrate is a precursor to many compounds of silver, including the silver compounds used in photography. When compared to silver halides, which are used in photography due to their sensitivity to light, AgNO_3 is quite stable when exposed to light.

Structure of AgNO₃

An illustration describing the structure of the silver nitrate molecule is provided below. It can be observed that silver has an oxidation number of 1 in this compound represented in figure 1.

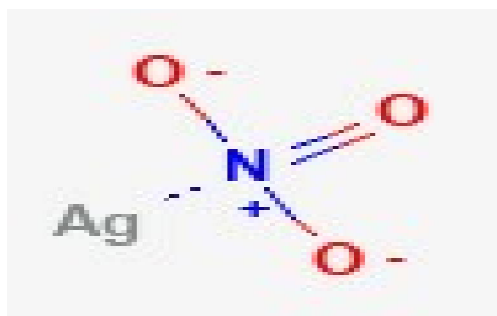


Figure 1. Structure of silver nitrate

Physical Properties of Silver Nitrate

- The molar mass of silver nitrate is 169.872 grams per mole.
- Silver nitrate is colorless and odorless.
- In its solid state, the density of silver nitrate is 4.35 grams per cubic centimeter. The density of silver nitrate in the liquid state temperature of 210oC is 3.97 g/cm₃.
- The melting and boiling points of silver nitrate are 482.8 K and 713 K respectively.
- Silver nitrate, like other ionic compounds, dissolves readily in water. The solubility of silver nitrate in water corresponds to 122g/100mL at 0oC and 256g/100mL at a temperature of 25oC.
- The crystal structure of the silver nitrate is orthorhombic [10, 11].

Chemical Properties of Silver Nitrate

- The hazards of silver nitrate include its toxic and corrosive nature.
- The reaction of silver nitrate and ethanol is more explosive.
- Silver present in silver nitrate is displaced by copper, which forms copper nitrate. The chemical equation for this reaction is $2\text{AgNO}_3 + \text{Cu} \rightarrow \text{Cu}(\text{NO}_3)_2 + 2\text{Ag}$
- When silver nitrate is heated to 440oC, it completely decomposes to give oxygen, nitrogen dioxide, and silver.

USES OF SILVER NITRATE

Silver nitrate has many applications in many fields like biology, chemical synthesis, and medicine. Some of these uses of silver nitrate are as follows:

- Silver nitrate is a versatile compound. The nitrate ion can easily be replaced by other ligands that bind to the silver ion.
- The ability of silver nitrate to form a precipitate of silver halides when treated with halide ions is in use while making photographic films.
- Many silver-based explosives are prepared with a precipitation reaction of silver nitrate.
- In the field of inorganic chemistry, halides are extracted with the help of silver nitrate.
- The branch of chemistry i.e., analytical chemistry uses this reaction to check for the presence of halide anions like iodide, bromide, or chloride ions.
- Mixtures of alkenes are separated with the help of silver nitrate as the silver cation binds with alkenes in a reversible fashion.
- Silver nitrate serves as an antiseptic in many setups of medical.
- Silver nitrate can be in use for the treatment and the removal of unwanted warts in human beings.
- When diluted with water to a concentration of 0.5%, silver nitrate can serve as an antiseptic in many medical setups.
- A diluted solution of AgNO₃ can be administered to the eyes of a baby which is born to a mother suffering from gonorrhoea, which combats the gonococcal bacteria and protects the baby from the onset of blindness.
- This compound is also known to be used for the treatment and the removal of unwanted warts in human beings [10, 11].

Green synthesis silver nanoparticle

Green synthesis of silver nanoparticles is evolving into an essential branch of nanotechnology as shown in Fig. 1. The Emerging significance of noble metal nanoparticles (gold and silver) in the area of

nanotechnology due to their size features and advantages over available chemical imaging drug agents and drugs, inorganic particles have been examined as potential tools not only for medical imaging also for treating diseases. Nanoparticles are structures ranging from approximately 1 - 100 nm [11]. Nano size results in specific physiochemical characteristics such as high surface area to volume ratio, which potentially results in high reactivity [12]. Physical method, Chemical method and Biological method (green synthesis) are the three major methods for synthesis of nanoparticles. Chemical approach is poisonous and expensive. Thus, there is a growing need to build up the environmentally and economically friendly process, which do not use toxic chemicals in the synthesis protocols. Thus the role of green synthetic method was emerged which utilizes bacteria, fungi, algae and plants for the synthesis of silver nanoparticles [13]. Nanoparticles can be served as a strong bridge between the bulk materials and atomic or molecular structures [14]. Synthesis of silver nanoparticles (Ag NPs) have gained considerable interest due to their unique properties such as excellent electrical and thermal conductivity, chemical stability, catalytic activity, nonlinear optical behaviour, anti-microbial and anti-bacterial effects [15,16]. Since the movement of "green chemistry" began in the late 1990s, the search for environmentally benign green solvents to replace petroleum-based organic solvents has been one of the major issues in the green chemistry community [17].

Three mechanisms can generally explain the reduction of metal ions in glycerol: catalytic reduction, [18, and 19] reduction by aldehydes, or reduction by alkoxides [20, 21]. Under alkaline conditions, silver ions easily interact with hydroxide ions and form silver oxide (Ag₂O) particles. Silver ions could be catalytically reduced on the surface of silver oxide particles preformed in the alkaline solution at room temperature. found that silver nanoparticles could be synthesized in a glycerol solvent even at room temperature without adding any reducing agents when sodium hydroxide (NaOH) was added [22]. In this study, based on previous research papers, the authors examined a plausible mechanism for the reduction of silver ions and subsequent formation of silver nanoparticles at room temperature under highly alkaline conditions but did not discover any direct evidence.

Strong antibacterial activity is the main objective for the development of Nano silver products as it has been shown to affect more than 650 microbe types [23-25]. Increasing the surface area of silver nanoparticles makes one gram of silver.

Silver nanoparticles (AgNPs) represent a potential therapeutic tool for treatment of many diseases and parasites because of their anti-plasmodia, antibacterial, and antifungal activity [26-29]. Therefore, the green synthesis of nanoparticles is a hot research area nowadays, allowing the biosynthesis of safe, effective, low cost, and eco-friendly drugs, often mediated by the utilization of natural plant products. [26,29]. nanoparticles enough to kill bacteria on a surface area of one hundred square meters [30]. Synthesis of silver nanoparticles (Ag NPs) have gained considerable interest due to their unique properties such as excellent electrical and thermal conductivity, chemical stability, catalytic activity, nonlinear optical behaviour, anti-microbial and anti-bacterial effects.

Some work has been carried out for the production of Ag NPs using either the whole plant or plant parts extracts. [31, 32] Usage of plants or plant products give a distinctive edge over the microorganism routes since one need not undergo the cumbersome process of maintaining cultures. In this work we report an effective room temperature synthetic procedure for the reduction of Ag¹ to Ag⁰ using *Camellia sinensis* leaf extract, commonly known as tea [33-35].

The primary requirement of green synthesis of AgNPs is silver metal ion solution and a reducing biological agent. In most of the cases reducing agents or other constituents present in the cells acts as stabilizing and capping agents, so there is no need of adding capping and stabilizing agents from outside [36-38].

Biosynthesis of nanoparticles especially silver Nano materials from plant extracts or organic sources has been receiving huge interest because of their plentiful abilities and a wide range of bioactive reducing metabolites. Plants are known as highly preferable sources for synthesizing nanoparticles. Compared with bacteria and algae, plants are more renitent to metal toxicity, thereby offering a green alternative for synthesizing silver nanoparticles [39,40]. In this case, green leaves are used and selected for synthesizing silver nanoparticles more than other plants due to their origin for photosynthesis and availability of more H⁺ ions to reduce the creation of silver nitrate within the silver nanoparticles. Green synthesis of silver nanoparticles (Ag NPs) was successfully developed through Ephedra inter media stem extract. Hence, using chemical procedures for synthesizing Ag NPs have some disadvantages like being toxic to environment, human health and more seriously, they are harmful to different normal cells which may cause tremendous problems. Usage of plant extract for synthesis of nanoparticles is proved to have more advantages than microbial processes, because pathogenic bacteria may infect the nanoparticles that are used in medical fields [41-43]. Some plants and extracts such as *Artemisia vulgaris*, marine sediment fungi, *J. glaucoma*, *Morus alba*, *Nigel asativa*, *Corchorus capsular is*, *Coffee Arabica*, *Ficus benghalensis*,

Solanum tuberosum, and graph is echinoids, Alcee rose and *Chlorella vulgaris* are used for synthesis of silver nanoparticles due to their special ability for biologic applications. This section deals with the preparation of Ag NPs using green synthesis approaches, which has more advantages than conventional methods including chemical agents associated with environmental toxicity [44].

Separation of AgNPs

Centrifugation technique is mostly used by researchers to obtain the pellet or powder form of synthesized silver nanoparticles. The AgNPs suspensions were also oven dried to obtain the product in powder form [45]. Some common characterizations of AgNPs include UV-Vis Spectra, SEM, TEM, FTIR, XRD and EDAX or EDX/EDS. DLS study is mostly used for AgNPs synthesized from bio-polymers rather than plant extracts and microorganisms. Zeta potential values indicate the stability of synthesized AgNPs. Thermo-Gravimetric Analysis (TGA) is used to find the effect of AgNO₃ and L-cystine on the organic composition of AgNPs [46] to find out the amount of organic material in synthesized AgNPs [47] and predict the thermal stability of AgNPs [48,49]. Inductive. Coupled Plasma (ICP) analysis was performed to analyse the concentration and conversion of AgNPs [50].

Monitoring of AgNPs

The appearance of yellow to slight brownish-yellow colour in the colour less solution has been taken as indicative of AgNPs synthesis by almost all the researchers. The SPR peak of the synthesized AgNPs was witnessed in the range of 400 - 450 nm, the significant range for AgNPs [51]. The UV-Vis spectral analyses have been used to analyse the dependency of pH, metal ion concentration, extract content on the formation of AgNPs and reveal the size-stability of synthesized AgNPs by exhibiting red shift in the SPR peak with increase in size of nanoparticles and blue shift for decrease in size. The SEM morphological analysis in most of the studies revealed spherical AgNPs, whereas few authors reported irregular, triangular, hexagonal, isotropic, polyhedral, flake, flower, pentagonal, anisotropic, and rod like structures [52-61].

Benefits of Green Synthesis Silver Nanoparticles:

Green nanotechnology or green synthesis is nothing but an organic synthesis of nanoparticles using plant extracts and the synthesized nanoparticles are then known as biogenic nanoparticles. In numerous studies huge number of medicinal plants are used to synthesize the silver NPs [32- 34] like Mulberry leaves, [52] *Alternanthera dentate*, *Ocimum sanctum*, *Azadirachta indica*, *Brassica rapa*, *Cocciniabindica*, *Vitex Segundo*, *Meliadubia* are used have already been used to synthesize and stabilize metallic nanoparticles, very particularly biogenic silver (Ag) nanoparticles.

Advantages of Green Synthesis Silver Nanoparticle:

A lot of literature has been reported to till date on biological syntheses of silver nanoparticles using microorganisms including bacteria, fungi and plants; because of their antioxidant or reducing properties typically responsible for the reduction of metal compounds in their respective nanoparticles.

The advantages of Green Synthesis over Chemical and Physical Methods are:

Environment friendly, cost effective and Easily scaled up for large scale syntheses of nanoparticles, furthermore there is no need to use high temperature, pressure, energy and toxic chemicals represented in figure 3. [36].



Figure 2. Advantages of green synthesis of silver nitrate

The Advantages of use of Plant Extracts in Green Synthesis over Microorganisms are:

- Ease of improvement
- Less biohazard and
- Elaborate process of maintaining cell cultures
- Reduce the cost of production and product
- High scale production possibility.
- Long stability
- Freeze dried to form powder formulation, represented in figure 2 (Khalid Alaqad and TawfikA Saleh, 2016) [37]

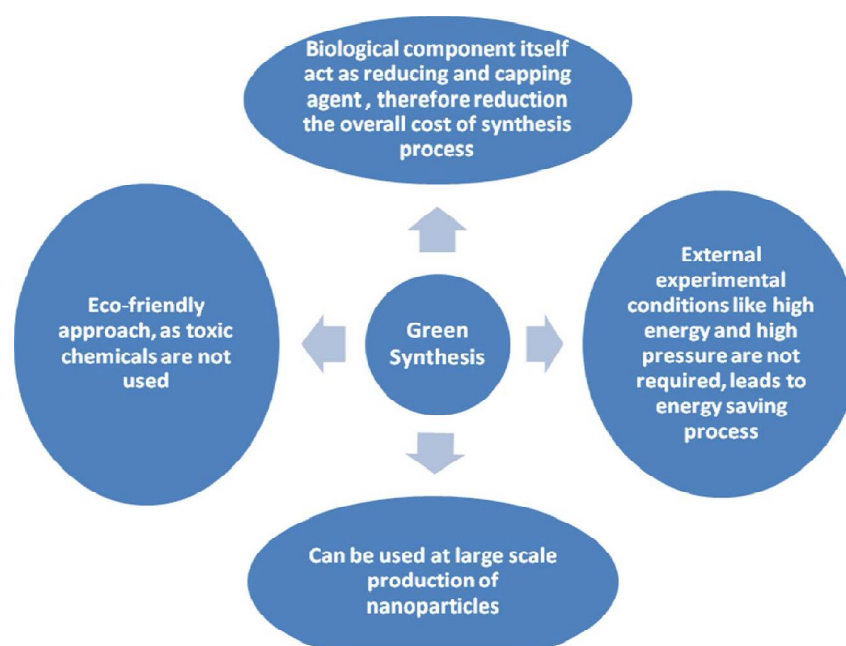


Figure 3: - Various process in green synthesis

Various methods involved in synthesis of AgNPs:

Recently, many techniques have been used for the synthesis of Ag-NPs by using chemical, physical, photochemical, and biological methods. Each method has its pros and cons with common problems of cost, scalability, uniform particle size, and the size distribution. Traditionally, metal nanoparticles are produced by physical methods like ion sputtering or pulsed laser ablation and chemical methods such as reduction, sol-gel, thermal synthesis, hydrothermal, sol-gel methods, and so on. Depending upon the selected path of synthesis and different experimental conditions, the silver NPs of different morphology, sizes, and shapes can be obtained. Nevertheless, the most important criteria are the size distribution that should be achieved as narrow as possible for the target specific applications [38]. Four important methods (chemical, physical, photochemical, and biological) for the synthesis of nanoparticles are discussed as follows.

Physical methods:

Nanoparticles are prepared by evaporation-condensation using a tube furnace at atmospheric pressure. Conventional physical methods including spark discharging and parolysis were used for the synthesis of AgNPs. The advantages of physical methods are speed, radiation used as reducing agents and no hazardous chemicals involved, but the downsides are low yield and high energy consumption, solvent contamination, and lack of uniform distribution [62].

Chemical methods:

Among the existing methods, the chemical methods have been most common used for the production of Ag-NPs. Generally, the chemical synthesis process of the Ag-NPs in solution usually employs the following three main components: (i) metal precursors (for formation of AgNPs: AgNO₃, AgClO₄, AgCl, (PPh₃)₃AgNO₃, CF₃COOAg), (ii) reducing agents, and (iii) stabilizing/ capping agents. This method uses water or organic solvents to prepare the silver nanoparticles. This process usually employs three main

components, such as metal precursors, reducing agents, and stabilizing/capping agents. Basically, the reduction of silver salts involves two stages

- (1) Nucleation
- (2) Subsequent growth

In general, “top-down” and “bottom-up” are the two methods by which Nano particles can be prepared [63].

Biological methods:

Biological methods have emerged to overcome all the problems related to physical and chemical methods. Silver nanoparticles are synthesised with definite size using different biological systems including bacteria, fungi, plant extracts, and small bio molecules like vitamins and amino acids as an alternative method to chemical methods not only for AgNPs, but also for the synthesis of several other nanoparticles. Biologically-mediated synthesis of nanoparticles has been shown to be simple, cost effective, dependable, and environmentally friendly approaches and much attention has been given to the high yield production of AgNPs [64].

Green synthesis silver nanoparticles in plant extract

The plant extract has been used in the production of silver nanoparticles had drawn attention due to its rapid, eco-friendly, non-pathogenic and providing a single step technique for the biosynthetic processes represented in figure 4.



Figure 4: -one-part green synthesis silver nanoparticles

Bio Nano factories for Green Synthesis of Silver Nanoparticles: Toward Antimicrobial application

The green chemistry perspective involves the three main steps generally involved in the preparation of nanoparticles. These include the selection of a solvent medium, focusing on the selection of a “green” alternative for the reducing agent and a harmless substance to stabilize the NPs, as a vast number of conventional methods depend on organic solvents, majorly contributing to the hydrophobic properties of the capping materials involved in the process [65].

Green Synthesis of Silver Nanoparticles

Plants have always been exploited by humans since the Stone Age for their metabolites, which have proven to be a pillar of human survival. Similarly, there have been numerous experiments for this emerging method of NP synthesis that can enhance the potential applications of the plants and their extracts in this field. Many studies have shown that phytoconstituents such as flavonoids, terpenoids, pectin, sugars, ascorbic acid, and carotenoids present in powders or extracts of roots, shoots, bark, leaves, peel, flowers, and fruits can function as reducing and capping agents to develop NPs [66]

Extracts of Roots

The synthesis of metallic nanoparticles using *Medicago sativa* [40] is perhaps one of the earliest records on the generation of AgNPs utilizing a plant part as a source. Alfalfa roots absorb the reduced silver (Ag⁺ to Ag⁰) from agar medium and transmit it to the shoots in the identical oxidation state (Ag⁰). Then, Ag atoms in the shoots organize themselves by joining together and forming larger arrangements to produce NPs. TEM/STEM analysis displayed the aggregation of Ag atoms in the interior of the plant tissue, whereby they underwent nucleation and NP formation. An aqueous root extract of *Parthenium*

hysterophorus has been employed to reduce silver ions and synthesize stable green NPs, which further showed piscicidal activity toward *Culex quinquefasciatus* in mosquito control [41].

Extracts of Seeds

To illustrate AgNPs synthesis using plant seeds, Bar et al. described the fabrication of green silver NPs by utilizing the seed extract from *Jatropha curcas* [42], wherein it was noted that the major phytoconstituents including curcain (an enzyme), curcacycline A (a cyclic octapeptide), and curcacycline B (a cyclic nonapeptide) could be employed as reducing and capping agents. The subsequent reduction and stabilization of AgNPs happened in situ by the amide groups of the host peptide under suitable process conditions. Since the radius of most AgNPs obtained was comparable to the cavity of cyclic peptides, it was considered that the cyclic peptide cavity stabilized the smaller AgNPs, whereas the irregularly sized AgNPs were stabilized by the enzyme curcain, owing to its large, folded protein structure. Studies also concluded that the AgNPs synthesized by curcain latex were stable even after 1 month [43].

Extracts of Fruits

As per the literature, fruits have played a major role in eco-friendly AgNPs synthesis. Armin et al. employed fruit extract from the *Solanum xanthocarpum* plant for the reduction and capping of AgNPs. It is a thorny plant known as Indian nightshade or yellow-berried nightshade, which grows in various terrains of the Indo-Pakistan subcontinent. These fruits are a rich source of aliening glycosides, quercetin in, and flavonoids, and their extract displays antimicrobial, antioxidant, and anthelmintic properties [44]. This study concluded that pH, temperature, and the molar ratio of AgNO₃ to *S. xanthocarpum* extract (SXE) influence the reduction of Ag⁺ and size of AgNPs. These fabricated particles exhibited urease-inhibitory and anti-*H. pylori* activities; accordingly, the study hinted at the potential antibacterial and urease-inhibitory activities of the AgNPs. This synthesis route for the AgNPs utilized SXE extract with AgNO₃ at 45 °C for 25 min, resulting in a band centred at 406 nm with surface plasmon resonance (SPR). These synthesized particles were observed to be spherical and monodispersed in nature with a size of around 10 nm. These NPs displayed appreciable effectiveness against the antibiotic-susceptible and antibiotic-resistant strains of *H. pylori*.

Extracts of Leaves

Medicinal herbs such as Hibiscus Rosa sinuses are effectively utilized in the treatment of hypertension, pyrexia, liver disorder etc. Philip et al. successfully used the above for AgNPs synthesis, wherein a quick change of the solution colour to golden yellow indicated the formation of AgNPs. Its leaf extract contains antioxidant compounds and certain organic acids (essentially malic acid), proteins, flavonoids, anthocyanins, and vitamin C. Interestingly, in another examination, Singh et al. [45]

Studies suggested that the biosynthesized NPs are extremely toxic against various pathogenic fungi and bacteria at a concentration of 30 ppm for their growth control. The results from SEM and XRD studies displayed that the particle size range was 25–50 nm, and they were cubic in structure. The fact that the bio reduction of Ag⁺ ions to AgNPs was due to the capping action of the plant extract was further confirmed by FTIR analysis [46].

Another study designed a cost-effective, simple, and green synthesis method of AgNPs using an extract of mulberry leaves as a reducing and stabilizing agent. The generated NPs had a mean size of 20 nm and possessed a face-centered cubic (FCC) structure. It is quite evident that plants are “bio factories”, as the rate of synthesis of NPs with the application of plant products/extracts is faster than that when using microorganisms, while the resultant NPs are also more stable [47].

Microbial Synthesis of Silver NPs

Various types of microorganisms have been explored as bio factories for the synthesis of green NPs, and these strategies are extensively discussed in the literature [48,49]. Ahluwalia et al. demonstrated the utility of the fungus *Trichoderma reesei* for AgNPs synthesis, in addition to its extensive use as an agricultural fungicide [50]. The efficiency of the method was proven by the formation of NPs that are stable beyond 3 months of manufacturing. In addition, various types of broths such as lysogeny broth, peptone broth, nutrient broth, yeast extract, yeast mold broth, and tryptic soy broth have also been investigated for synthesis [51]. The formation of NPs is majorly impacted by two critical parameters, broth pH and light condition [52].

Bacteria-Mediated Green Synthesis of Silver NPs

Among the various classes of microbes [53], the use of bacteria is gaining importance and is prevalent because of its easy and extensively studied genetic modification protocols, simple handling, and rising accomplishments [54]. Bacteria are regarded as promising candidates for this ecofriendly route of synthesis, which is attributed to their intrinsic potential to reduce heavy metals. Several factors such as organic functional groups present in the bacterial cell wall work synergistically to carry out the reduction [55]. In one such study [56], *Enterococcus* species isolated from fermented foods and further extracts of

various strains ($n = 6$) were employed for the generation of nanoparticles. The prepared NPs displayed antimicrobial activity against multidrug-resistant species including *E. coli*, *K. pneumoniae*, and *P. vulgaris*. In addition, these NPs showed synergistic antimicrobial activity with ampicillin, ciprofloxacin, and cefuroxime. Thereafter, these NPs were used as Nano preservatives in white emulsion paint [57].

Enzyme-Based Synthesis of Silver NPs

The purity of available enzymes [58] and their structure make this synthetic route a prospective method to create silver nanoparticles of the desired form. The extracellular synthesis of AgNPs is attributed to the enzymes released by the cells [59]. The enzymes present in the extracts of plants could also act as a reducing agent in this green AgNPs synthesis. During the enzyme-based synthesis of AgNPs, a specific enzyme is obtained from the cultural supernatant of life forms such as bacteria. Kumar *et al.* (2007) first demonstrated the *in vitro* fabrication of AgNPs using the NADPH-dependent nitrate reductive enzyme obtained from the cultural supernatant of fungus *Fusarium oxysporum* and phytochelatin [60].

Yeast-Mediated Green Synthesis of Silver NPs

Yeasts represent another class of microorganisms explored for the green synthesis of AgNPs. Yeast is a eukaryotic, unicellular organism which has evolved from multicellular antecedents. Yeasts, being chemo organotrophs, utilize organic compounds such as carbon obtained from sugars as their primary source of energy. They are known to grow well in neutral or slightly acidic environments. Newer methods of cultivation of yeast are devoid of all the exasperating steps, thus resulting in a simpler and easier process [61].

Mechanism of AgNPs Synthesis

The synthesis of AgNPs by biological entities is due to the presence of large number of organic chemical like carbohydrate, fat, proteins, enzymes & coenzymes, phenols flavonoids, terpenoids, alkaloids, gum, etc capable of donating electron for the reduction of Ag^+ ions to Ag^0 . The active ingredient responsible for reduction of Ag^+ ions varies depending upon organism/extract used. For nano-transformation of AgNPs, electrons are supposed to be derived from dehydrogenation of acids (ascorbic acid) and alcohols (catechol) in hydrophytes, keto to in mesophytes or both mechanisms in xerophytes plants [62]. The microbial cellular and extracellular oxidoreductase enzymes can perform similar reduction processes.

Applications of Green Silver Nanoparticles

Antibacterial Applications

It is well known that elemental silver and its various compounds [63] have been utilized for decades to preserve water in the form of silver coins/silver vessels. Since the Middle Ages, silver has been used as an inhibitory and antibacterial material, highlighting its activity as an antibacterial agent represented in figure 5. In one study, by employing black cohosh, geranium, aloe, etc. at a concentration of around 4 ppm exhibited an inhibitory effect on the proliferation of *E. coli*.

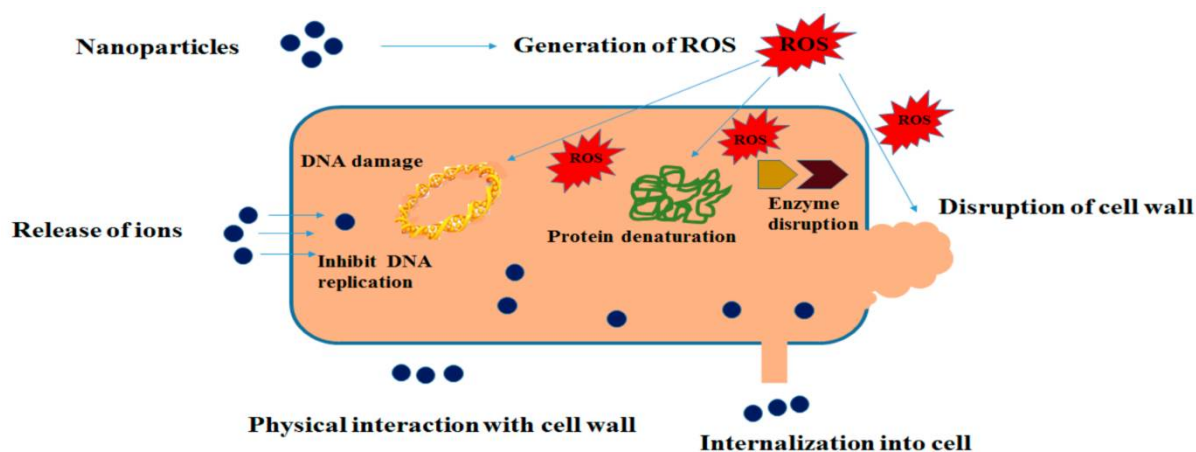


Figure 5. Various antibacterial activities of metal nanoparticles

Antifungal Applications

One study investigated the antifungal activity of AgNPs toward 10 fungal pathogens, including *Aspergillus* spp., *Candida* spp., and *Fusarium* spp., revealing significant antifungal activity in all cases. In addition, yeast is also one of the main causes of fungal diseases. In this study, the effect of AgNPs on the growth of yeast was investigated by adding AgNPs to YEPD. The growth curves of *Candida* (*C. albicans*, *C. parapsilosis*, *C. krusei*, and *C. tropicalis*) in the presence of AgNPs revealed that their growth can be

completely inhibited by AgNPs acting as fungi static agents. There is great scope for further research on a profitable alternative to treat various fungal diseases in the future [63].

Antimicrobial activity

Various studies have been carried out to ameliorate antimicrobial functions because of the growing microbial resistance towards common antiseptic and antibiotics. According to in vitro antimicrobial studies, the metallic nanoparticles effectively obstruct the several microbial species represented in figure 6. [64].

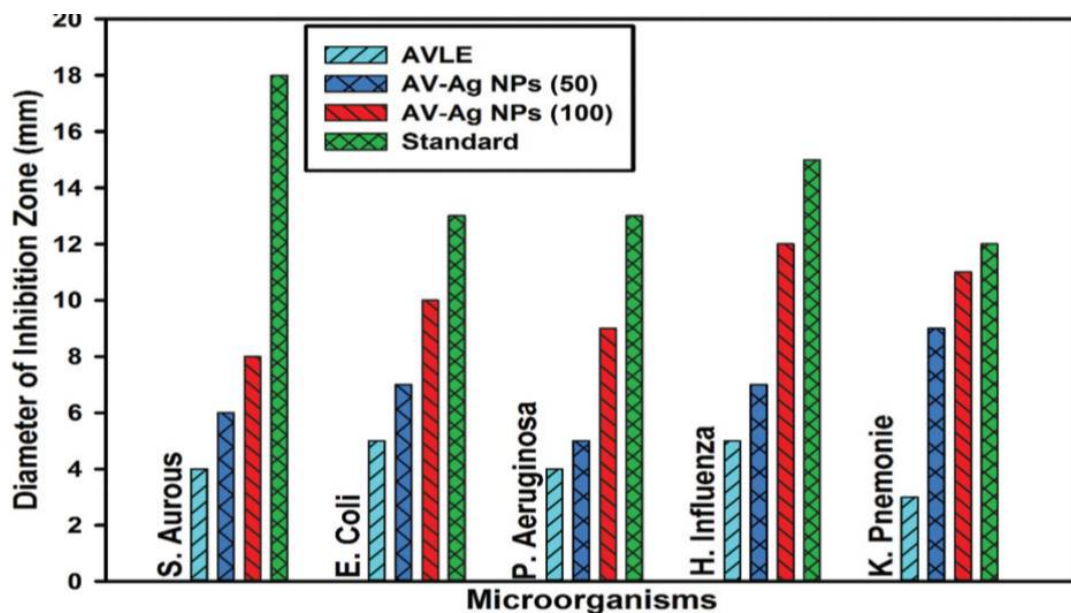


Figure 6. The antimicrobial activities of silver nanoparticles against different human pathogens

Polyol process

Monodispersed solution of silver nano cubes were synthesized in large quantities by reducing silver nitrate with ethylene glycol in the presence of the capping agent polyvinyl pyrrolidine(PVP) [65], which is an example of the so-called polyol process. In this case, ethylene glycol served as both reducing agent and solvent.

Precursor injection technique

In the precursor injection method, the injection rate and the reaction temperature were important factors for producing uniform-sized Ag-NPs with a reduced size. The injection of the dependent on these stages. Furthermore, for the synthesis of mono dispersed Ag-NPs with uniform size distribution, all nuclei [66] are required to form at the same time. In this case, all the nuclei are likely to have the same or similar size, and then they will have the same subsequent growth. But the nano dispersion of silver display red shift and the peak at 320 nm shifted to 416 nm that corresponds to the dipole resonance of silver nano spheres.

Physical method

In the physical synthesis process of Ag-NPs, usually, the physical energies (thermal, ac power, and arc discharge) are utilized to produce Ag-NPs with a narrow size particle distribution. This approach can permit us to produce large quantities of Ag-NPs samples in a single process. Under the physical methods, the metallic NPs can be generally fabricated by evaporation-condensation process that could be carried out in a tube furnace at atmospheric pressure.

Photochemical synthesis

The photo-induced synthesis of Ag-NPs has two main approaches: that is the photo physical (top down) and photochemical (bottom up) ones. In former way, NPs could be prepared by the fragmentation of the bulk metals and followed by generation of the NPs from ionic precursors. The NPs are formed by the direct photo reduction of a metal ion using photochemical generated intermediates, such as excited molecules and radicals, which are often known as photosensitization of NPs [67,68]. The main advantages of the photo-induced process are: clean process, high spatial resolution, convenience of use, the controllable in-situ reducing agent's generation; the formation of NPs can be triggered by the photo irradiation, (iii) enables one to fabricate the NPs in various mediums including emulsion, surfactant micelles, polymer films, glasses, cells, etc. The direct photo-reduction process of AgNO₃ takes place in the

presence of sodium citrate using different light thermal sources (UV, white, blue, cyan, green, and orange) at room temperature [69].

Biological synthesis

Usually, wet-chemical or physical method is used to prepare the metal nanoparticles. However, the chemicals used in physical and chemical methods are generally expensive, harmful and inflammable but the Biogenic methods are a cost effective, energy saver and having environmentally benign protocols technique for green synthesis of silver nanoparticles from different microorganisms (yeast, fungi and bacteria, etc.) and plant tissues (leaves, fruit, latex, peel, flower, root, stem, etc.) [69,70]

CONCLUSION

Owing to the drawbacks associated with synthetic approaches such as the employment of the reactive and toxic reducing and stabilizing agents that lead to adverse effects, a similar scenario has evolved in nanoparticles synthesis, especially silver nanoparticles fabrication methods. Responding to this challenge, the current review covered various ecofriendly AgNPs synthesis methods including photosynthesis, microbial-mediated synthesis, and enzyme-based synthesis, revealing the potential of various organisms and bio molecules to be employed as biomanufactories for green synthesis. It has appeared as a novel concept for development and implementation of chemical processes in order to decrease or remove the use of hazardous substances. Compared with the use of plant extracts, biosynthesis of AgNPs using microorganisms requires a precise process of cultivating and maintaining microbial cells, which in some cases can be pathogenic to humans. The ease of handling, the availability and a broad viability of metabolites are among the advantages of using plant extracts. Due to the broad availability of plant extracts as well as a wide range of biodegradable biologically active metabolites, biosynthesis of nanoparticles from plant extracts is receiving great interest. The results, however, are conflicting and there is a need for more work to resolve this issue. The potential of AgNPs for their use as drug carriers in cancer therapy as biosensors for metabolites and pollutants as catalyst etc. is quite high and requires intensive and integrated research activity for harnessing it.

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ETHICAL APPROVAL

The study did not require ethics committee approval or patient informed consent because it did not focus on any clinical parameters and did not utilize any humans or animals for the processing of work.

CONFLICTS OF INTEREST

No conflict of interest was declared by the authors. The authors alone are responsible for the content and writing of the paper.

REFERENCES

1. Ravindra B. Chintamani, Kishor S. Salunkhe and Machindra J. Chavan. (2018). Emerging Use Of Green Synthesis Silver Nanoparticle: *IJPSR*,; Vol. 9(10): 4029-4055
2. Yezhelyev MV, Gao X, Xing Y and Al-Hajj A: (2006). Emerging use of nanoparticles in diagnosis and treatment of breast cancer. *Lancet Oncol*; 7: 657-67.
3. Pradhan N, Pal A and Pal T: (2002). Silver nanoparticle catalyzed reduction of aromatic nitro compounds. *Colloids and Surfaces A: Physicochemical and Engineering Aspects*; 196: 247-257. doi 10.1016/s0927-7757(01)01040-8.
4. Anker JN, Hall WP, Lyandres O, Shah NC, Zhao J and Duyne VRP: (2008). Bio sensing with plasmonic nanosensors. *Nature Materials*; 7: 442-453. doi 10.1038/nmat2162.
5. Lee KS and El-Sayed MA: (2006). Gold and silver nanoparticles in sensing and imaging: sensitivity of plasmon response to size, shape, and metal composition. *The Journal of Physical Chemistry B*; 110: 19220-19225. doi 10.1021/jp062536y
6. Ajithadasaruna et al, (2014), 'Synthesis and Characterization of Silver Nanoparticles of Insulin Plant (*costuspictus*D. Don) Leaves', *Asian Journal of Biomedical and Pharmaceutical Sciences*, volume: 4 (34), page number: 1-6
7. Dahl JA, Maddux BL, Hutchison JE. (2007). Toward greener nanosynthesis. *Chem Rev*. 107(6):2228-2269.
8. Raveendran P, Jie F, Scott LW. (2003). Completely "green" synthesis and stabilization of metal nanoparticles. *J Am Chem Soc*.125(46):13940-13941.
9. Benelli G. (2016). Plant-mediated biosynthesis of nanoparticles as an emerging tool against mosquitoes of medical and veterinary: a review. *Parasitol Res*. 115(1):23-34.

10. Devi LS and Joshi SR: (2014). Ultra structures of silver nanoparticles biosynthesized using entophytic fungi. *Journal of Microscopy and Ultrastructure*; 3: 29-37.
11. Scientific Committee on Emerging and Newly Identified Health Risk (SCENHIR) (2008) Opinion on: The Scientific Aspects of the Existing and Proposed Definitions Relating to Products of Nano science and Nanotechnologies, European Commission Health & Consumer Protection Directorate– General Directorate C-Public Health and Risk Assessment C7-RiskAssessment.
12. Peijnenburg: (2009). Nano silver: A Review of Available Data and Knowledge Gaps in Human and Environmental Risk Assessment. *JNanotoxicology*; 3(2): 10
13. Irvani S, Korbekandi H, Mirmohammadi SV and Zolfaghari B: Synthesis of silver nanoparticles: chemical, Available form: <https://www.sciencelearn.org.nz/resources/1676-novel-properties-emergeat-the-nanoscale>
14. M. Brust, C. Kiely, (2002). *Colloid. Surf. A*, 202, 175–186.
15. P. V. Kamat, (2002). *J. Phys. Chem. B*, 106, 7729–7744. (21)
16. Sarkar, A.; Kapoor, S.; Mukherjee, T. (2010). Synthesis and characterization of silver nanoparticles in viscous solvents and its transfer into non-polar solvents. *Res. Chem. Intermed.* 36, 411–421
17. Clark, J. H.; Tavener, S. J. (2007). Alternative solvents: shades of green. *Org. Process Res. Dev.* 11, 149–155.
18. Sarkar, A.; Kapoor, S.; Mukherjee, T. (2010). Synthesis and characterization of silver nanoparticles in viscous solvents and its transfer into non-polar solvents. *Res. Chem. Intermed.* 36, 411–421.
19. Chou, K.-S.; Ren, C.-Y. (2000). Synthesis of Nanosized silver particles by chemical reduction method. *Mater. Chem. Phys.* 64, 241–246.
20. Gomes, J. F.; Garcia, A. C.; Ferreira, E. B.; Pires, C.; Oliveira, V.L.; Tremiliosi-Filho, G.; Gasparotto, L. H. S. (2015). New insights into the formation mechanism of Ag, Au and Ag nanoparticles in aqueous alkaline media: alkoxides from alcohols, aldehydes and ketones as universal reducing agents. *Phys. Chem. Chem. Phys.* 17, 21683–21693.
21. Huang, Z. Y.; Mills, G.; Hajek, B. (1993). Spontaneous formation of silver particles in basic 2-propanol. *J. Phys. Chem. A* 97, 11542–11550.
22. Jo, J.; Cho, S.-P.; Lim, J. K. Template synthesis of hollow silver hexapods using hexapod-shaped silver oxide mesoparticles. *J. Colloid Interface Sci.* 2015, 448, 208–214.
23. M. Khaksar, S. Vasileiadis, R. Sekine et al, “Chemical characterisation, antibacterial activity, and (nano) silver transformation of commercial personal care products exposed to household greywater,” *Environmental Science: Nano*, vol.6, no. 10, pp. 3027-3028, 2019.
24. A. Lateef, S. A. Ojo, and J. A. Elegbede, “The emerging roles of arthropods and their metabolites in the green synthesis of metallic nanoparticles,” *Nanotechnology Reviews*, vol. 5, no. 6, pp. 601–622, 2016.
25. M. Singh, S. Singh, S. Prasad, and I. Gambhir, “Nanotechnology in medicine and antibacterial effect of silver nanoparticles,” *Digest Journal of Nanomaterials and Biostructures*, vol. 3, no. 3, pp. 115–122, 2008.
26. Benelli G. Plant-mediated biosynthesis of nanoparticles as an emerging tool against mosquitoes of medical and veterinary importance: a review. *Parasitol Res.* 2016;115(1):23–34.
27. Asmaa AA, Dina R, El-Gowell HM, Amal HK. Green synthesis of silver nanoparticles using cranberry powder aqueous extract: characterization and antimicrobial properties. *Int J Nanomed.* 2015; 10:7207–7221.
28. Rajeshkumar S, Malarkodi C. In-vitro antibacterial activity and mechanism of silver nanoparticles against foodborne pathogens. *Bioinorg Chem Appl.* 2014;2014(581890):1–10.
29. Narahari Narayan Palei, S. Ramu, V. Vijaya, K. Thamizhvanan, Anna Balaji. Green synthesis of silver nanoparticles using leaf extract of *Lantana camara* and its antimicrobial activity. *International Journal of Green Pharmacy.* 2022;14(1): 1-7.
30. Roy N, Gaur A, Jain A, Bhattacharya S, Rani V. Green synthesis of silver nanoparticles: an approach to overcome toxicity. *Environ Toxicol Pharmacol.* 2013;36(3):807–812.
31. J. Huang, Q. Li, D. Sun, Y. Lu, Y. Su, X. Yang, H. Wang, Y. Wang, W. Shao, N. He, J. Hong, C. Chen, *Nanotechnology*, 2007,
32. J. Y. Song, B. S. Kim, (2009). *Bioprocess Biosyst. Eng.* 32, 79–84.
33. Singh J, Bajaj R, Harpreet K, Harjot K and Navneet K: (2016). Chemo-bio Synthesis of Silver Nanoparticles. *J Nanomed Res*; 4(3): 00092.
34. Singh J, Singh N, Rathi A, Kukkar D and Rawat M: (2017). Facile approach to synthesize and characterization of silver nanoparticles by using mulberry leaves extract in aqueous medium and its application in antimicrobial activity. *J Nanostructures* 7(2): 134-140.
35. Sathish kumar P, Vennila K, Jayakumar R, Yusoff ARM and Hadibarata T: (2016). Phyto-synthesis of silver nanoparticles using *Alternanthera tenella* leaf extract: An effective inhibitor for the migration of human breast adeno-carcinoma (MCF-7) cells. *Bioprocess Biosyst Eng*; 39(4): 651-659.
36. Singhal G, Bhavesh R, Kasariya K, Sharma AR and Singh RP: (2011). Singh R.P. Biosynthesis of silver nanoparticles using *Ocimum sanctum* (Tulsi) leaf extract and screening its antimicrobial activity. *J. Nanoparticle Res.* 13(7):2981–2988.
37. Dhuper S, Panda D and Nayak PL: Green synthesis and characterization of zero valent iron nanoparticles from the leaf extract of *Mangifera indica*. *Nano Trends: J Nanotech App* 2012; 13(2): 16-22.
38. Kalishwaralal K, Deepak V, Pandian RK, Kottaisamy Barathmani SM, Kartikeyan KS and Gurunathan BS: Biosynthesis of silver nitrate
39. Christy AJ, Uma Devi M. (2012). Synthesis and characterization of monodispersed silver nanoparticles. *Advances in Natural Sciences: Nanoscience and Nanotechnology.* 3(3):035013. DOI: 10.1088/2043-6262/3/3/035013/meta

40. Amin, M.; Anwar, F.; Janjua, M.R.S.A.; Iqbal, M.A.; Rashid, U. Green Synthesis of Silver Nanoparticles through Reduction with *Solanum xanthocarpum* L. Berry Extract: Characterization, Antimicrobial and Urease Inhibitory Activities against *Helicobacter pylori*. *Int. J. Mol. Sci.* 2012, 13, 9923–9941.
41. Gardea-Torresdey, J.L.; Gomez, E.; Peralta-Videa, J.R.; Parsons, J.G.; Troiani, H.; Jose-Yacaman, M. Alfalfa sprouts: A natural source for the synthesis of silver nanoparticles. *Langmuir* 2003, 19, 1357–1361.
42. Mondal, N.K.; Chowdhury, A.; Dey, U.; Mukhopadhyaya, P.; Chatterjee, S.; DAS, K.; Datta, J.K. Green synthesis of silver nanoparticles and its application for mosquito control. *Asian Pac. J. Trop. Dis.* 2014, 4, S204–S210.
43. Gardea-Torresdey, J.L.; Gomez, E.; Peralta-Videa, J.R.; Parsons, J.G.; Troiani, H.; Jose-Yacaman, M. Alfalfa sprouts: A natural source for the synthesis of silver nanoparticles. *Langmuir* 2003, 19, 1357–1361.
44. Bar, H.; Bhui, D.K.; Sahoo, G.P.; Sarkar, P.; De, S.P.; Misra, A. Green synthesis of silver nanoparticles using latex of *Jatropha curcas*. *Colloids Surf. A Physicochem. Eng. Asp.* 2009, 339, 134–139.
45. Singh, A.; Jain, D.; Upadhyay, M.K.; Khandelwal, N.; Verma, H.N. Green synthesis of silver nanoparticles using *Argemone mexicana* leaf extract and evaluation of their antimicrobial activities. *Dig. J. Nanomater. Biostruct.* 2010, 5, 483–489.
46. Awwad, A.M.; Salem, N.M. Green Synthesis of Silver Nanoparticles by Mulberry Leaves Extract. *Nanosci. Nanotechnol.* 2012, 2, 125–128.
47. Hulkoti, N.I.; Taranath, T. Biosynthesis of nanoparticles using microbes—A review. *Colloids Surf. B Biointerfaces.* 2014, 121, 474–483.
48. Das, S.K.; Liang, J.; Schmidt, M.; Laffir, F.; Marsili, E. Biomineralization Mechanism of Gold by Zygomycete Fungi *Rhizopusoryzae*. *ACS Nano* 2012, 6, 6165–6173.
49. Ahluwalia, V.; Kumar, J.; Sisodia, R.; Shakil, N.A.; Walia, S. Green synthesis of silver nanoparticles by *Trichoderma reesei* and their bio-efficacy evaluation against *Staphylococcus aureus* and *Klebsiella pneumoniae*. *Ind. Crop. Prod.* 2014, 55, 202–206.
50. Vigneswaran, N., Ashtaputre, N.M., Varadarajan, P.V., Nachane, R.P., Paralikar, K.M. and Balasubramanya, R.H.(2007) Biological Synthesis of Silver Nanoparticles Using the Fungus *Aspergillus flavus*. *Materials Letters*, 61, 1413-1418.
51. Liu, L.; Liu, T.; Tade, M.; Wang, S.; Li, X.; Liu, S. Less is more, greener microbial synthesis of silver nanoparticles. *Enzym. Microb. Technol.* 2014, 67, 53–58.
52. Velusamy, P.; Kumar, G.V.; Jeyanthi, V.; Das, J.; Pachaiappan, R. Bio-Inspired Green Nanoparticles: Synthesis, Mechanism, and Antibacterial Application. *Toxicol. Res.* 2016, 32, 95–102.
53. Mondal, A.H.; Yadav, D.; Mitra, S.; Mukhopadhyay, K. Biosynthesis of silver nanoparticles using culture supernatant of *Shewanella sp. ARY1* and their antibacterial activity. *Int. J. Nanomed.* 2020, 15, 8295–8310.
54. Chandra, H.; Kumari, P.; Bontempi, E.; Yadav, S. Medicinal plants: Treasure trove for green synthesis of metallic nanoparticles and their biomedical applications. *Biocatal. Agric. Biotechnol.* 2020, 24, 101518
55. Gour, A.; Jain, N.K. Advances in green synthesis of nanoparticles. *Artif. Cells Nanomed. Biotechnol.* 2019, 47, 844–851
56. Rauwel, P.; Küüna, S.; Ferdov, S.; Rauwel, E. A Review on the Green Synthesis of Silver Nanoparticles and Their Morphologies Studied via TEM. *Adv. Mater. Sci. Eng.* 2015, 2015, 682749.
57. Kumar, S.A.; Abyaneh, M.K.; Gosavi, S.W.; Kulkarni, S.K.; Pasricha, R.; Ahmad, A.; Khan, M.I. Nitrate reductase-mediated synthesis of silver nanoparticles from $AgNO_3$. *Biotechnol. Lett.* 2007, 29, 439–445.
58. Balaji, D.; Basavaraja, S.; Deshpande, R.; Mahesh, D.B.; Prabhakar, B.; Venkataraman, A. Extracellular biosynthesis of functionalized silver nanoparticles by strains of *Cladosporium cladosporioides* fungus. *Colloids Surf. B Biointerfaces.* 2009, 68, 88–92.
59. Ahmed, S.; Saifullah; Ahmad, M.; Swami, B.L.; Ikram, S. Green synthesis of silver nanoparticles using *Azadirachta indica* aqueous leaf extract. *J. Radiat. Res. Appl. Sci.* 2016, 9, 1–7.
60. Okafor, F.; Janen, A.; Kukhtareva, T.; Edwards, V.; Curley, M. Green synthesis of silver nanoparticles, their characterization/application and antibacterial activity. *Int. J. Environ. Res. Public Health* 2013, 10, 5221–5238
61. Xue, B.; He, D.; Gao, S.; Wang, D.; Yokoyama, K.; Wang, L. Biosynthesis of silver nanoparticles by the fungus *Arthroderma fulvum* and its antifungal activity against genera of *Candida*, *Aspergillus* and *Fusarium*. *Int. J. Nanomed.* 2016, 11, 1899–1906.
62. Blagojević N, Radulović N, Palić R, et al. Chemical composition of the essential oils of Serbian wild-growing *Artemisia absinthium* and *Artemisia vulgaris*. *J Agric Food Chem.* 2006; 54:4780–4789
63. Dizaj SM, Lotfipour F, Barzegar-Jalali M, et al. Antimicrobial activity of the metals and metal oxide nanoparticles. *Mater Sci Eng C.* 2014; 44:278–84
64. Rauwel P, Rauwel E, Ferdov S, Singh MP. Chapter 1: Silver Nanoparticles: Synthesis, Properties, and Applications in the book *Advances in Materials Science and Engineering*. 2015. pp. 624394 (2 pages). DOI: 10.1155/2015/624394
65. Fievet F, Lagier JP, Figlarz M. (1989). Preparing monodisperse metal powders in micrometer and submicrometer sizes by the polyol process. *MRS Bulletin.* 12:29-34. DOI: 10.1557/S0883769400060930
66. Sato-Berrú R, Redón R, Vázquez-Olmos A, Saniger JM. (2009). Silver nanoparticles synthesized by direct photoreduction of metal salts. Application in surface-enhanced Raman spectroscopy. *Journal of Raman Spectroscopy.* 40(4):376-380. DOI: 10.1002/jrs.2135.
67. Eman Mohamed Halawani ,(2017). Rapid Biosynthesis Method and Characterization of Silver Nanoparticles Using *Zizyphus spinachristi* Leaf Extract and their Journal of Biomaterials and Antibacterial Efficacy in therapeutic application nano biotechnology, volume number: 8, page number: 22-35

68. Pandey S, Mewada A, Thakur M, et al. (2013). Biogenic gold nanoparticles as photostable and efficient photocatalysts for the degradation of berberine hydrochloride using folic acid as a molecular road map. *Mater Sci Eng C*. 33:3716–3722.
69. Singh A, Dar MY, Joshi B, et al. (2018). Phytofabrication of silver nanoparticles: novel drug to overcome hepatocellular ailments. *Toxicol Rep*. 5:333–342
70. Sadeghi, B. and Gholamhoseinpoor, F. (2015) A Study on Stability and Green Synthesis of Silver Nanoparticles Using *Ziziphora tenuior* (Zt) Extract at Room Temperature. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 134, 310-315.
71. Ramu Samineni, Jithendra Chimakurthy, K Udayaratna, K Devatulasi, B Varshitha Reddy, G Keerthi Sri, (2022). Ager Deng Goc. A Quick Overview of Nanomedicine Applications in Breast Cancer Detection, Imaging, and Therapy. *Asian Journal of Advances in Medical Science*. 44-56.

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