

Biogenic Silver Nanoparticles: Green Synthesis Approaches and Therapeutic Applications

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ABSTRACT

The green synthesis of metal nanoparticles by natural products has been recognized as a promising and sustainable technique in nanobiotechnology, especially for their applications in medicine. The conventional chemical and physical synthesis of nanoparticles has been associated with toxicity, high energy consumption, and environmental risks, whereas plant-mediated synthesis has been recognized as an eco-friendly, cost-effective, and biocompatible technique. The natural products used for synthesizing nanoparticles are leaves, roots, barks, fruits, seeds, latex, and other parts of plants, which contain bioactive molecules such as flavonoids, phenolic compounds, terpenoids, alkaloids, proteins, and polysaccharides that serve as reducing, capping, and stabilizing agents for nanoparticles. Among various metal nanoparticles, silver nanoparticles have been recognized for their excellent antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory, and anticancer activities. The excellent biological activities of nanoparticles synthesized by natural products may be attributed to their nanoscale dimensions, high surface area-to-volume ratio, generation of reactive oxygen species, and interaction with cell membranes, proteins, and DNA. Apart from their applications in medicine, plant-mediated metal nanoparticles have been recognized for their applications in diagnostics, biosensors, drug delivery systems, wound healing, catalytic degradation of pollutants, and tissue engineering. The present review article discusses the role of natural products in the synthesis of nanoparticles, reduction mechanisms, characterization, and their applications in medicine. The critical factors affecting nanoparticles, including size, shape, stability, and their biological activities, have also been discussed. The green nanotechnology technique has been recognized as a sustainable and innovative technique for the development of next-generation nanoparticles with excellent applications in medicine.

Keywords: Green synthesis, Medicinal analysis, Metals, Plant extract and silver nanoparticles.

1. INTRODUCTION

The word “nanotechnology” refers to the process of conceptualizing, constructing, and using functional structures that have at least one defining dimension that is measured in nanometers. This encompasses a broad range of activities. Due to the small size of the particles or molecules that make up such materials and systems, they can be engineered to exhibit novel and significantly improved physical, chemical, and biological properties, phenomena, and processes. This is possible thanks to the fact that these materials and systems can be designed. The reason for such an interesting and very useful behavior is that when characteristic structural features are intermediate in extent between isolated atoms and bulk microscopic materials, that is, in the range of 1–100 nm, the objects may display physical attributes that are substantially different from those displayed by either atoms or bulk materials. The reason for this interesting and very useful behavior is that when characteristic structural features are intermediate in extent between isolated atoms and bulk microscopic materials, the reason for this interesting and very useful behavior is that, in the end, this may result in the creation of new technical possibilities as well as new obstacles.

Over the course of the previous several centuries, medicinal plants have been an important component in the successful treatment of chronic and life-threatening illnesses. At the moment, natural

products are receiving a disproportionate amount of attention as a crucial instrument for drug development and medicinal chemistry in order to produce medications with fewer negative side effects [1,2]. Natural products such as these therapeutic plants and their chemical byproducts, including alkaloids, saponins, polyphenols, terpenoids, and tannins, have been demonstrated in trials to lower the likelihood of developing a tumor while also having few negative side effects [3,4]. Despite the absence of a specific site of action and mechanisms where green chemistry drugs are required for more active medicines [5], medicinal plants are primarily used for rapidly advancing prevention and treatment, particularly for tumors and related malicious diseases. This is the case even though medicinal plants are used. Both traditional and current treatments focus mostly on plants, and the products derived

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Graphical Abstract:

Green Synthesis of Silver Nanoparticles Using Natural Products



Eco-friendly phytosynthesis of silver nanoparticles using natural products for biomedical, agricultural, and technological applications.

from those plants are thought to be one of the potential sources of anticancer drugs that have fewer negative side effects. Other types of marine organisms, such as fungus, bacteria, algae, and seaweed, are also capable of producing a wide range of bioactive chemicals. Researchers have looked into the possibility that they could treat both short-term and long-term illnesses and make it less likely that people will get sick in the first place [6].

Plant metabolites that have been isolated and their synthetic equivalents, known as nanodrug molecules, have been tested in clinical trials and are sold on the market [7,8]. As a result, the current review focuses on the potential anticancer effects of plant-based substances, while data on the molecular behavior of cancerous cells is also being compiled. Silver nanoparticles (AgNPs) are being included in a wide variety of applications, ranging from photovoltaic cells to sensors used in biotic and biological processes due to their unique optical, electrical, and thermal capabilities. Only mercury is more poisonous than silver in its ionic state, which is known as Ag^+ . Silver is one of the most hazardous heavy metals. When Ag^+ is exposed to plant extract in the form of an aqueous silver nitrate solution, the phytochemicals in the plant extract convert it to its ionic form and reduce it to AgNPs. It is without a doubt the case that plant extracts play a significant part in the production of AgNPs, which are extremely resistant to the growth of microbes [9]. When it is in its ionic form, Ag^+ , the element displays poisonous behavior [10]. Ag^+ ion has a propensity to coordinate and form complexes with the byproducts of chemical substances that are found in the aqueous extract of medicinal plants, including alkaloids, saponins, polyphenols, terpenoids, and tannins [11,12].

In light of the fact that biological interactions are typically multivalent, the interaction between microbes and host cells frequently involves multiple copies of receptors and ligands that bind in a coordinated manner. This

binding results in enriched specificities, effectiveness, and strengths of such interfaces, which enables the microbial agent to take possession of the cell outbreak. The attachment and entrance of viruses into congregation cells is a prime example of such multivalent interactions between viral surface components and cell-covering receptors [13]. This interaction is responsible for the attachment and entry of viruses into congregation cells. Interfering with these gratitude events and blocking viral admittance into the cells is one of the most promising approaches being pursued in the development of new antiviral drugs and preventative topical microbicides [14-16]. One of the most promising ways to make new antiviral drugs is to try to stop these “thanksgiving” events from happening.

2. METALLIC SILVER

Silver's capacity to inhibit the growth of microorganisms is proportional to both the total quantity of silver present and the rate at which it is released. Ionization occurs when silver interacts with the moisture that is present in the skin as well as the fluid that is present in the wound [17]. Silver, in its metallic condition, is inert. Ionized silver is very reactive because it attaches to tissue proteins and causes structural changes in the cell wall and nuclear membrane of bacterial cells, which ultimately results in the cell being distorted and eventually dying [18]. Furthermore, silver sticks to the DNA and RNA of bacteria, which, when broken down, stops the bacteria from reproducing [19].

3. THE WORKINGS OF THE MECHANISM

However, based on the morphological and structural changes that have been discovered in bacterial cells, possible mechanisms of action of metallic silver, silver ions, and AgNPs have been suggested. No one knows exactly how silver kills microbes.

4. SILVER IONS AND AgNO_3 HAVE A SPECIFIC MODE OF ACTION

Silver ions have an antibacterial effect. However, the exact mechanism behind this effect is not well known. Alterations in the structure and morphology of bacteria are one way to study the impact that silver ions have on microorganisms [20,21]. It has been hypothesized that the replication of DNA may be carried out most successfully when the molecules that make up DNA are in a relaxed condition [22]. However, this capacity to replicate is lost when the DNA is compressed into a smaller space. When silver ions enter a bacterial cell, the DNA molecule undergoes a conformation change that causes it to lose its capacity for replication [23]. This ultimately results in the death of the bacterial cell. In addition, it has been found that when heavy metals interact with proteins, they inactivate the proteins by attaching themselves to the thiol groups that are present in the proteins [24].

5. MECHANISM OF ACTION OF AgNPs

The extraordinarily high surface area of the AgNPs, which allows for greater interaction with the bacteria, contributes to their effective antimicrobial activity as compared to the antimicrobial activity of other salts [25-27]. The nanoparticles not only enter the inside of the bacteria but also attach themselves to the cell membranes. The bacterial membrane is packed with proteins that contain sulfur, and the AgNPs interact not just with these proteins but also with phosphorus-containing substances like DNA. When AgNPs penetrate a bacterial cell, they generate a zone in the core of the bacterium with a low molecular weight into which the bacteria conglomerate, therefore shielding the DNA from the silver ions [28,29]. The nanoparticles tend to target the respiratory chain, the cell, and its division processes, which ultimately results in the death of the cell. The silver ions are released into the bacterial cells by the nanoparticles, which increases the bactericidal action of the nanoparticles. Figure 1, Schematic illustrating the green synthesis and antibacterial mechanism of AgNPs. Plant extract reduces AgNO_3 to form stabilized AgNPs via phytochemical capping. The nanoparticles attach to the bacterial membrane, disrupt membrane integrity, penetrate into the cytoplasm, interact with DNA and sulfur-containing proteins, inhibit the respiratory chain, and release Ag^+ ions,

collectively leading to bacterial cell death. The figure also highlights the influence of size and shape on antimicrobial activity, showing enhanced bactericidal efficiency for smaller (<10 nm) and triangular nanoparticles due to higher surface area and increased interaction with bacterial cells.

6. EFFECT OF SIZE AND SHAPE ON THE ANTIMICROBIAL ACTIVITY OF NANOPARTICLES

With an increase in particle size, the surface plasmon resonance absorption peak moves to a longer wavelength, which plays a significant role in the process of determining the optical absorption spectra of metal nanoparticles [30,31]. The fact that the nanoparticle is so small suggests that it has a substantial amount of exposed surface area that may interact with the bacterial cells. As a consequence of this, it will have a greater proportion of interaction in comparison to particles of a larger size. Nanoparticles of <10 nm have the ability to interact with bacteria, which results in the production of electrical effects that boost the nanoparticles' reactivity.

Therefore, it can be shown beyond a reasonable doubt that the bactericidal action of AgNPs is proportional to their size. The effectiveness of the nanoparticles as an antibacterial agent is also influenced by the forms the nanoparticles take. This may be shown via research on the prevention of bacterial growth by the use of a variety of nanoparticle shapes. Researchers like Pal *et al.* claim that truncated triangular nanoparticles with a silver concentration of 1 μg are able to prevent bacterial growth. A total silver concentration of 12.5 μg is required, however, in the case of spherical nanoparticles. A total of 50–100 μg of silver must be present in the rod-shaped particles. This shows that different shapes of AgNPs have different effects on the bacterial cells they come in contact with [32,33].

7. NANOPARTICLE SYNTHESIS USING SILVER

Producing AgNPs of varying sizes is the first thing that has to be done in order to acquire them. In addition to the more common chemical method, which is based on the chemical reduction of silver nitrate, AgNPs can also be made biologically. However, chemical synthesis is the more common method of production. The works written by Espenti

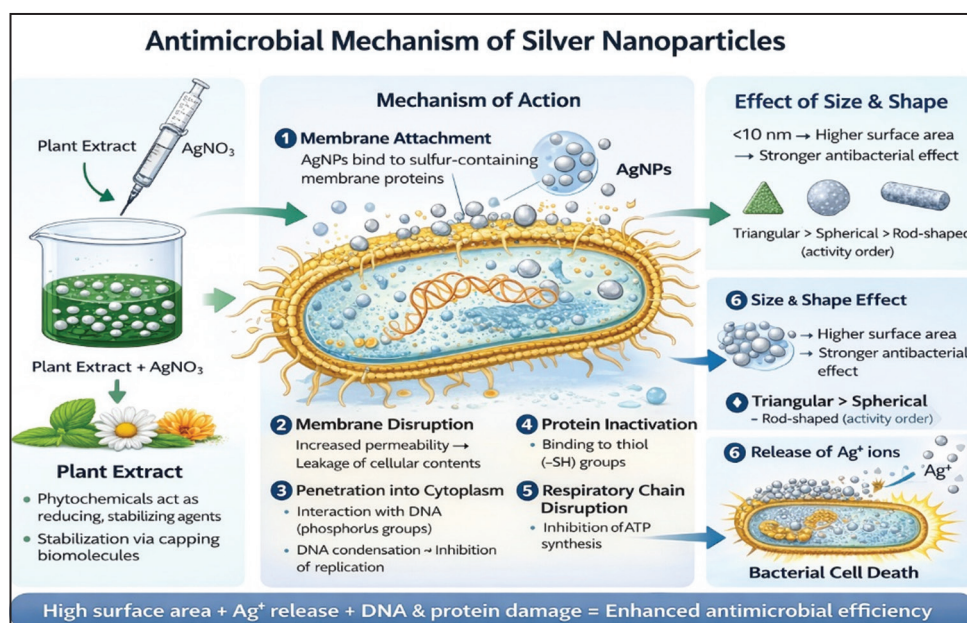


Figure 1: Schematic illustrating the green synthesis and antibacterial mechanism of AgNPs. Plant extract reduces AgNO_3 to form stabilized AgNPs via phytochemical capping.

et al. (2016) and (2018) [34,35] demonstrate that the production of AgNPs is possible by the reduction of aqueous Ag ion with the culture supernatants of bacteria such as *Bacillus subtilis* and *Escherichia coli*. Rama Krishna *et al.* (2020) also discussed about the synthesis and anti-bacterial applications towards the *B. subtilis* and *E. coli* [36]. Furthermore, numerous other researchers have described using fungus as a source of AgNPs. The takeaway from this study is that there are a variety of approaches to the synthesis of AgNPs, and that there are also a variety of approaches to their preparation, which can result in nanoparticles containing a variety of substrates on their surface, which are then exposed to the biological environment. No research has been done to compare how well the different kinds of AgNPs made by the different processes work.

In today's world, there has been a rise in the use of metallic nanoparticles (MNPs), the surfaces of which may or may not have been functionalized to maximize the effectiveness of the interactions between them. It is possible that the concept of using metals as a weapon against germs dates back to ancient times. In fact, the use of silver as a method for heating food and protecting water from contamination was a frequent practice in the past. However, the production of MNPs by chemical processes is not exactly kind to the surrounding ecosystem. Therefore, an alternative to the procedures that are harmful to the environment is offered, and that is the synthesis of MNPs through the biological approach (using plant extract) [37]. When it comes to the synthesis of MNPs for tissue engineering and other biomedical purposes [38], the noble metals (Ag, Au, Pb, Pt, Fe, and Cu) are by far the most popular choice. Silver is the metal of excellence among the noble metals due to the fact that it is utilized as a health supplement in its anti-microbial resistance as well as in traditional medicine [39] and demonstrates great toxicity termination to microorganisms. When compared to its Ag^+ form, the use of silver in the form of NPs seems to have reduced cellular toxicity but does not appear to have increased antibacterial activity [40]. In addition, silver and its compounds are often used in the treatment of a broad variety of bacterial infections as well as burns [41-44]. Ag^+ or salts of Ag, on the other hand, have a restricted applicability as antibacterial agents due to the limited release of their active ingredient. According to the findings of the research, utilizing AgNPs, which are highly reactive species due to their huge surface area, may be able to circumvent the limitation described in the previous sentence [45]. Plant extracts and microorganisms are both required for the bio-reduction of silver ions to silver nitrate [46,47]. It has been shown [48-51] that a wide range of plant extracts may be used in the production of AgNPs as green reactants. It has been proven by Panneerselvam and colleagues that the AgNPs that are generated by employing the leaf extract of *A. paniculata* have effective anti-plasmodia action [52].

8. IDENTIFICATION OF METAL NANOPARTICLES BY ANALYTICAL TECHNIQUES

In general, the various forms, sizes, surface areas, and polydispersity of metal nanoparticles are examined to determine their properties. Ultraviolet (UV)-visible absorbance spectroscopy: A double-beam UV-visible spectrophotometer was used in order to observe the bio-reduction of the nanoparticles that were produced by the metals. After that, the samples that were utilized for the analysis were examined in terms of the UV-visible spectrum at certain intervals of time. For the purpose of analysis, samples were put into a quartz cuvette that measured 1 cm in length. A sweep was performed throughout the spectrum, beginning at 200 nm and ending at 800 nm. Fourier transform infrared spectroscopy (FT-IR) analysis, also known as Fourier transform infrared analysis: Infrared spectroscopy is one of the few superior analytical instruments that allows for the potential of chemical identification. It is also one

of the most widely used techniques. It offers details on the makeup of a molecule's structure. The fundamental idea behind FT-IR is that a chemical substance exhibits selective absorption in the infrared region, which, across a broad wavelength range, results in a spectrum of absorption bands known as an IR absorption spectrum. The infrared spectrum of a chemical compound will have a variety of unique bands, each of which will correlate to a certain functional group or bond that is present in the material. DLS stands for "dynamic light scattering studies." Brownian motion is measured using dynamic light scattering (DLS), which is also known as PCS-photon correlation spectroscopy, and the results are related to the particle sizes. This is accomplished by providing instructions to the particles using a laser and monitoring the intensity variations in the light that is scattered. The DLS method was used to calculate the mean diameter as well as the size distribution of the metal nanoparticles.

A Zeta potential analyzer was used in order to get information on the surface charges of the AgNPs (Brookhaven Instruments Corporation, NY). Without using any dilution, we were able to calculate the average zeta potential of the dispersions. For the X-ray photoelectron spectroscopy examinations that were carried out, Mg $K\alpha$ X-radiation and a pass energy were both used. The peaks in the spectra that corresponded to binding energy demonstrated that metals had the capacity to form bonds with a variety of chemical compounds. Studies utilizing X-ray diffraction (XRD) were carried out with the intention of determining the development of the Ag crystal phase using Cu $K\alpha$ X-radiation with a wavelength of $\lambda = 0.154$ nm. The patterns were captured throughout a wide arc of the 2θ , from 10° to 90° . After the reaction was finished, the biomass was found to have settled at the bottom of the conical flasks. Samples of the suspended precipitate were collected and examined using transmission electron microscopy (TEM). The samples of green-synthesized metal nanoparticles were made by putting a drop of the suspension on carbon-coated copper grids, letting the films on the TEM grids sit for 2 min, removing the excess solution with blotting paper, and then letting the grid dry out before taking the measurement.

Figure 2 shows this green way to make AgNPs, using plant extract that acts as both a reducing agent and something to keep them stable. It's pretty eco-friendly since it avoids those nasty chemicals you might use in regular labs. Hence, in the setup, they take a beaker with plant extract and add in some silver nitrate solution, the aqueous kind. The

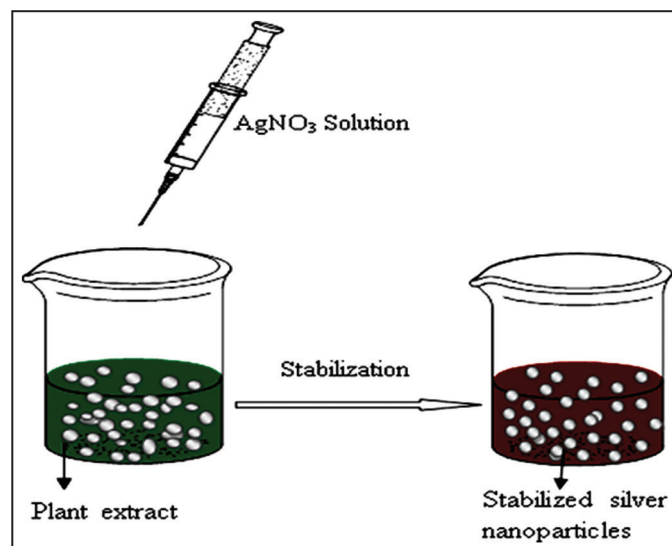


Figure 2: Schematic representation of formation and stabilization of silver nanoparticles from Plant extracts.

extract is full of these bioactive things from plants, like flavonoids, phenolics, terpenoids, alkaloids, plus proteins and sugars. I think those are what make the whole process work, doing double duty sort of. When the silver ions from AgNO_3 hit the extract, they get reduced by the functional groups in those phytochemicals, turning into actual silver atoms. That starts the nucleation, and then the particles grow in the solution. The color shifts, usually from yellow to brown, which I guess points to the nanoparticles forming due to that plasmon resonance effect on the surface. It seems the same plant compounds stick to the nanoparticles after that, coating them and stopping them from clumping up. They produce this repulsion, either electrostatic or steric, so the particles stay spread out and stable in the mix. This method feels sustainable and not too expensive, relying on plant extracts instead of external stabilizers or harmful reducers. The diagram captures that whole flow pretty well, though some parts might be a bit simplified.

AgNPs possess significant biomedical potential; however, their possible toxicity must be carefully considered in therapeutic applications. Reports of hypersensitivity reactions have been documented in a small proportion of burn patients treated with ionic silver formulations, indicating that silver-based treatments can induce adverse responses under certain clinical conditions [53]. *In vitro* studies have demonstrated that AgNPs may exert cytotoxic effects on various mammalian cell lines, primarily through mechanisms involving reactive oxygen species (ROS) generation, mitochondrial dysfunction, DNA damage, and membrane disruption [54,55]. Notably, toxicity appears to be size-dependent, with smaller nanoparticles generally exhibiting higher cellular uptake and increased biological reactivity [55].

Conversely, several investigations report that AgNPs exhibit relatively low toxicity at controlled concentrations, particularly when incorporated into wound dressings or surface-bound biomedical materials where systemic exposure is minimal [56,57]. *In vivo* studies suggest that toxicity depends on multiple factors, including particle size, surface chemistry, dosage, route of administration, and duration of exposure [53,55]. AgNPs-based wound dressings have been widely used in clinical practice for several years, and regulatory assessments indicate no widespread reports of systemic toxicity under approved usage conditions [58,59]. Nevertheless, comprehensive long-term human safety data remain limited, and continued investigation into biodistribution, chronic exposure effects, and standardized toxicity evaluation protocols is essential.

9. APPLICATIONS OF AgNPs

AgNPs are really getting a lot of attention in medicine these days. They are easy to get and not too expensive, plus they have this broad biological activity that makes them useful. I think their properties at the nanoscale, like the high surface area and that strong surface plasmon resonance thing, along with how reactive they are, help a bunch in biomedical stuff. It seems like over the last 10 years or so, they have become a bigger deal in medical research. When it comes to therapeutic uses, AgNPs stand out for being antimicrobial and antifungal, even antiviral and anti-inflammatory.

AgNPs have emerged as highly versatile nanomaterials in biomedical applications due to their potent antimicrobial, anticancer, drug delivery, and diagnostic capabilities (Figure 3). In wound dressings and as coatings on medical devices, AgNPs exhibit strong antibacterial activity, including effectiveness against multidrug-resistant strains. Their antimicrobial mechanism primarily involves disruption of bacterial cell membranes, increased membrane permeability, and the generation of ROS, which induce oxidative stress, protein denaturation, and DNA damage, ultimately leading to cell death. In anticancer therapy, AgNPs interfere with cellular metabolism, mitochondrial

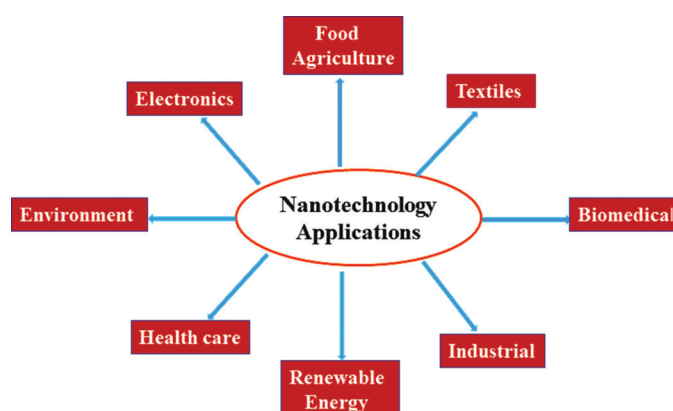


Figure 3: Applications of nanotechnology in various fields.

function, and intracellular signaling pathways, promoting apoptosis through ROS-mediated mechanisms and selective cytotoxicity toward cancer cells.

In therapeutic applications, AgNPs have been extensively investigated for wound management. Their broad-spectrum antimicrobial activity, including effectiveness against multidrug-resistant bacteria, supports their integration into advanced wound dressings and hydrogel systems [56-58,60]. AgNPs promote faster wound closure, reduce microbial load, and enhance tissue remodeling. Recent reports indicate improved collagen alignment and strengthened regenerated tissue in AgNP-treated wounds, contributing to superior mechanical integrity and esthetic healing outcomes [58,60]. In addition, AgNP-incorporated biomedical interfaces and coatings have shown enhanced antibacterial performance and reduced biofilm formation, which is crucial for preventing device-associated infections [61].

Early and accurate diagnosis is essential for effective disease management, particularly in oncology, where timely intervention significantly improves survival outcomes. AgNP-based surface-enhanced Raman spectroscopy (SERS) has emerged as a highly sensitive diagnostic tool for non-invasive cancer detection and biomarker identification [62-65]. The strong localized surface plasmon resonance properties of AgNPs enhance Raman signal intensity, enabling the detection of trace-level disease markers. Recent studies integrating AgNP-based SERS platforms with machine learning algorithms have further improved diagnostic accuracy and clinical applicability [62,63]. These advances demonstrate the growing importance of AgNPs in precision oncology diagnostics.

In oncology treatment strategies, AgNPs demonstrate promising anticancer properties through mechanisms such as ROS generation, mitochondrial dysfunction, and apoptosis induction [57,66]. Their plasmonic characteristics also enable photothermal and photodynamic therapeutic applications, improving cancer cell targeting efficiency [66,67]. Furthermore, AgNP-based nanoplatforms have been explored for controlled drug delivery, improving drug stability, bioavailability, and therapeutic index [68].

Table 1 presents a compilation of studies reporting the green synthesis of AgNPs using various plant-derived extracts. Different plant parts, including leaves, roots, bark, fruits, seeds, peels, latex, flowers, and gums, have been successfully employed as natural reducing and stabilizing agents for the conversion of silver ions (Ag^+) into metallic AgNPs (Ag^0). The phytochemicals present in these extracts, such as flavonoids, phenolic compounds, terpenoids, alkaloids, proteins, and polysaccharides play a crucial role in the bioreduction process and nanoparticle stabilization. The reported particle sizes of biosynthesized AgNPs vary widely, typically ranging from 1 nm to over 120 nm,

Table 1: Biosynthesis of AgNPs using different plant extracts

S. No.	Plant	Part	Metals	Size (nm)	Activity	References
1.	<i>Trianthema decandra</i>	Roots	Ag and Au	36, 47, 60 and 94	All microorganisms	[69]
2.	<i>Rhinacanthus nasutus</i>	Leaf	Ag	34 and 99	All microorganisms	[70]
3.	<i>Tanacetum vulgare</i>	Fruit	Ag and Au	22 and 11	Anti-microbial activity	[71]
4.	<i>Potamogeton pectinatus</i> L.	Sago Ponds	Ag and Au	10–40	-----	[72]
5.	<i>Carob</i>	Leaf	Ag	40	-----	[73]
6.	<i>Eclipta prostrata</i>	Leaf	Ag	45	<i>Escherichia coli</i>	[74]
7.	<i>Aegle marmelos</i>	Leaf	Ag	60	Larvicidal activity	[75]
8.	<i>Jatropha curcas</i>	Seed	Ag	30–35	-----	[76]
9.	<i>Jatwapha curcas</i>	Latex	Ag	20–30	-----	[77]
10.	<i>Piper betel</i> L.	Leaf	Ag	28	-----	[78]
11.	<i>Banana</i>	Peel	Ag	-----	Anti-microbial	[79]
12.	<i>Coscinium fenestratum</i>	Leaf	Ag	28–68	Cytotoxicity	[80]
13.	<i>Ocimum sanctum</i>	Leaf	Ag	42	-----	[81]
14.	<i>Phytolacca decandra</i>	Leaf	Ag	90	Cytotoxicity	[82]
15.	<i>Gelsemium sempervirens</i>	Leaf	Ag	112	Cytotoxicity	[82]
16.	<i>Hydrastic canadensis</i>	Leaf	Ag	110	Cytotoxicity	[82]
17.	<i>Thuja occidentalis</i>	Leaf	Ag	122	Cytotoxicity	[82]
18.	<i>Cochlo sperum gossypium</i>	Gum	Ag, Au and Pt	5.5 7.8 2.4	Cytotoxicity	[83]
19.	<i>Mentha piperita</i>	Leaf	Ag and Au	90 150	Anti-bacterial assay	[84]
20.	<i>Achyranthues aspera</i>	Leaf	Ag	-----	-----	[85]
21.	<i>Piper pedicellatum</i>	Leaf	Ag Au Ag-Au	2–30 2–40 3–45	-----	[86]
22.	<i>Volvariella volvacea</i>	-----	Ag Au Ag-Au	15 40 35	-----	[87]
23.	<i>Swietenia mahoguin JACQ</i>	Leaf	Ag Au Ag-Au	Different shapes	-----	[88]
24.	<i>Chenopodium album</i>	Leaf	Ag and Au	10–30	-----	[89]
25.	<i>Anacardium occidehtate</i>	Leaf	Ag Au Ag-Au	15 8 10	-----	[90]
26.	<i>Olive</i>	Leaf	Ag	51	-----	[91]
27.	<i>Terminalia bellirica</i>	Fruit	Ag	20	Anti-microbial and Anti-oxidant activity	[92]
28.	<i>Black tea</i>	Leaf	Ag and Au	20	-----	[93]
29.	<i>Taxus baccata</i>	Flower	Ag	75	Anti-cancer	[94]
30.	<i>Lantana camara</i>	Leaf	Ag	40	Anti-bacterial	[95]
31.	<i>Euphorbia condylocarpa M. bieb</i>	Root	Au and Pd	80	-----	[96]
32.	<i>Zizyphus xylopyrus</i>	Bark	Ag	60-70	-----	[97]
33.	<i>Desmostachya bipinnata</i>	Leaf	Ag	8 and 60	catalytic activity	[98]
34.	<i>Limonia acidissima</i>	Leaf and bark	Ag	25 and 12	Anti-bacterial	[99]
35.	<i>Terminalia chebula</i>	Leaf	Ag	10–30	Anti-bacterial	[34]
36.	<i>Potamogeton pectinatus</i>	-----	Ag	1–40	Anti-bacterial	[101]

AgNPs: Silver nanoparticles

depending on factors such as plant species, extract concentration, reaction time, pH, temperature, and silver precursor concentration. Leaf extracts are the most frequently used source due to their high phytochemical content and ease of availability. The synthesized AgNPs exhibit diverse biological activities, including antibacterial, antimicrobial, antioxidant, larvicidal, cytotoxic, anticancer, and catalytic properties.

Plant-mediated synthesis of silver and gold nanoparticles has attracted considerable attention due to its eco-friendly, cost-effective, and sustainable approach. Various medicinal plants have been successfully employed for the green synthesis of Ag and Au nanoparticles with notable antimicrobial properties. For instance, *Tinospora cordifolia* leaf extract has been used to synthesize both silver and gold nanoparticles with particle sizes ranging from 36 to 94 nm, demonstrating broad-spectrum antimicrobial activity against multiple microorganisms [69]. Similarly, leaf extract of *Rhinacanthus nasutus* has been utilized for the synthesis of AgNPs of sizes 34 and 99 nm, exhibiting effective antimicrobial action against diverse microbial strains [70]. In another study, fruit extract of *Tanacetum vulgare* facilitated the formation of both Ag and Au nanoparticles with sizes around 22 nm and 11 nm, respectively, showing significant antimicrobial activity [71].

Aquatic plant sources have also been explored; *Potamogeton pectinatus* L., collected from sago ponds, enabled the synthesis of silver and gold nanoparticles within the size range of 10–40 nm, highlighting the versatility of plant-based nanomaterial fabrication [72]. In addition, leaf extract of carob has been reported to produce AgNPs of approximately 40 nm in size [73]. The leaf extract of *Eclipta prostrata* has been employed to synthesize AgNPs of about 45 nm, demonstrating specific antibacterial activity against *E. coli* [74]. These studies collectively indicate that plant-derived biomolecules act as reducing and stabilizing agents during nanoparticle synthesis, yielding bio-functional nanomaterials with promising antimicrobial potential.

Green synthesis of AgNPs using diverse plant materials continues to demonstrate significant biological potential across antimicrobial, larvicidal, and cytotoxic applications. Leaf extract of *Aegle marmelos* has been reported to produce AgNPs with an average particle size of approximately 60 nm, exhibiting notable larvicidal activity, thereby highlighting its potential in vector control strategies [75]. Similarly, seed extract of *Jatropha curcas* has been utilized for the biosynthesis of AgNPs within the size range of 30–35 nm [76], while latex derived from *J. curcas* enabled the formation of comparatively smaller nanoparticles ranging from 20 to 30 nm, indicating that different plant parts can influence particle size distribution and physicochemical characteristics [77].

In another study, leaf extract of *Piper betel* L. facilitated the synthesis of AgNPs with an average size of 28 nm [78]. Banana peel extract has also been employed as an effective bioreducing agent for AgNP synthesis, with the resulting nanoparticles demonstrating significant antimicrobial activity [79]. Furthermore, leaf extract of *Coscinium fenestratum* has been used to generate AgNPs in the size range of 28–68 nm, exhibiting measurable cytotoxic effects, which suggests potential applications in anticancer research [80]. Collectively, these findings underscore the versatility of plant-mediated nanoparticle synthesis, where phytochemicals such as flavonoids, alkaloids, terpenoids, and phenolic compounds function as natural reducing and stabilizing agents, yielding bioactive nanomaterials with diverse biomedical and environmental applications.

Additional plant species have also been explored for the green synthesis of silver and other noble metal nanoparticles with notable biological activities. Leaf extract of *Ocimum sanctum* has been reported to produce AgNPs with an average size of approximately

42 nm, demonstrating the feasibility of phytochemical-mediated nanoparticle formation [81]. Similarly, leaf extracts of *Phytolacca decandra*, *Gelsemium sempervirens*, *Hydrastis canadensis*, and *Thuja occidentalis* have been utilized for the synthesis of AgNPs with particle sizes around 90 nm, 112 nm, 110 nm, and 122 nm, respectively. These nanoparticles exhibited measurable cytotoxic activity, indicating their potential relevance in anticancer applications [82].

In another study, gum extract of *Cochlospermum gossypium* enabled the synthesis of multi-metal nanoparticles, including silver, gold, and platinum, with remarkably small particle sizes of approximately 5.5 nm (Ag), 7.8 nm (Au), and 2.4 nm (Pt). These nanoparticles demonstrated significant cytotoxic properties, highlighting the influence of plant-derived stabilizing agents on particle size control and biological performance [83]. Leaf extract of *Mentha piperita* facilitated the synthesis of both silver and gold nanoparticles with sizes around 90 nm and 150 nm, respectively, and the resulting nanomaterials showed antibacterial activity in standard bioassays [84]. Furthermore, *Achyranthes aspera* leaf extract has also been reported for the biosynthesis of AgNPs, although detailed characterization data and biological evaluation were not extensively reported in that study [85]. Collectively, these findings reinforce the versatility of plant-mediated nanoparticle synthesis, where diverse phytochemicals serve as reducing and capping agents, producing bioactive nanomaterials suitable for antimicrobial and cytotoxic applications.

Further studies have expanded the diversity of biological sources employed in the green synthesis of silver, gold, and bimetallic nanoparticles with tunable physicochemical properties. Leaf extract of *Piper pedicellatum* has been utilized for the synthesis of silver, gold, and Ag–Au bimetallic nanoparticles with size ranges of 2–30 nm, 2–40 nm, and 3–45 nm, respectively, demonstrating efficient size control through phytochemical mediation [86]. Similarly, the mushroom *Volvariella volvacea* has been reported as a biological source for synthesizing Ag, Au, and Ag–Au nanoparticles with particle sizes of approximately 15 nm, 40 nm, and 35 nm, respectively, highlighting the role of fungal biomolecules in nanoparticle formation [87]. Leaf extract of *Swietenia mahogani* Jacq. Enabled the synthesis of Ag, Au, and Ag–Au nanoparticles with varied morphologies, suggesting that plant metabolites influence not only size but also nanoparticle shape and structural characteristics [88].

Leaf extract of *Chenopodium album* facilitated the formation of silver and gold nanoparticles within the size range of 10–30 nm [89], while *Anacardium occidentale* leaf extract produced Ag, Au, and Ag–Au nanoparticles with sizes around 15 nm, 8 nm, and 10 nm, respectively, reflecting efficient bioreduction and stabilization [90]. Olive (*Olea europaea*) leaf extract has also been reported to generate AgNPs of approximately 51 nm in size [91]. Fruit extract of *Terminalia bellirica* yielded AgNPs of about 20 nm, exhibiting both antimicrobial and antioxidant activities, thereby indicating multifunctional bioactivity [92]. In addition, black tea leaf extract has been employed for synthesizing both silver and gold nanoparticles of roughly 20 nm [93]. Flower extract of *Taxus baccata* enabled the production of AgNPs around 75 nm, demonstrating notable anticancer activity [94], whereas *Lantana camara* leaf-mediated AgNPs of approximately 40 nm showed significant antibacterial properties [95]. Collectively, these reports underscore the broad applicability of plant- and fungus-mediated nanoparticle synthesis in generating mono- and bimetallic nanomaterials with diverse biomedical functionalities.

Additional biological sources have further demonstrated the versatility of green nanotechnology in synthesizing noble metal nanoparticles with diverse functional properties. Root extract of *Euphorbia*

condylocarpa M. bieb. has been reported to facilitate the synthesis of gold (Au) and palladium (Pd) nanoparticles with an average particle size of approximately 80 nm, highlighting the potential of plant roots as reducing and stabilizing agents for multi-metal nanoparticle systems [96]. Bark extract of *Zizyphus xylopyrus* has been employed for the biosynthesis of AgNPs with sizes ranging from 60 to 70 nm, indicating effective phytochemical-mediated reduction processes [97].

Leaf extract of *Desmostachya bipinnata* has enabled the synthesis of AgNPs of approximately 8 nm and 60 nm, which exhibited notable catalytic activity, suggesting applications beyond biomedicine, including environmental remediation and green catalysis [98]. Similarly, leaf and bark extracts of *Limonia acidissima* have been used to generate AgNPs of about 25 nm and 12 nm, respectively, demonstrating significant antibacterial activity [99]. Leaf-mediated synthesis using *Terminalia chebula* and *Bryophyllum pinnatum* produced AgNPs within the size range of 10–30 nm, which showed effective antibacterial properties against pathogenic strains [34,100]. Furthermore, *P. pectinatus* has been reported to synthesize AgNPs with sizes ranging from 1 to 40 nm, exhibiting strong antibacterial activity [101]. Collectively, these findings emphasize that plant-derived biomolecules not only enable controlled nanoparticle synthesis but also impart functional bioactivity, including antimicrobial and catalytic performance, thereby broadening the scope of green nanomaterials in biomedical and environmental applications.

10. CURRENT APPLICATIONS

A communication device that is able to capture biological signals and transform them into electrical signals will be required in order to establish a link between the human body and the internet. Sensors that are based on NPs have the potential to become adaptors in the process of transcribing biological information. Researchers have developed nanomechanical sensors that are suitable for medical diagnostics and may be compatible with smart gadgets. These sensors might be used in conjunction with such devices.

These AgNPs are effective bactericidal agents against a wide range of bacteria, and when combined with antibiotic-resistant bacteria, AgNPs

with a diameter of up to 20 nm can inhibit HIV-1 virus replication. These are just two examples of the significant biological activities that can be attributed to AgNPs. These not only have the ability to change the production of proteinases, which are mostly involved in the inflammatory and renovation cell cycle, but they can also eliminate tumor necrosis factor and interleukin and cause apoptosis to occur in inflammatory cells that are found in DNA. The possible applications of nanofibers include medical devices, solar cells, and implants. However, due to the high cost of the material and the difficulties associated with producing it on a wide scale, it has mostly been studied in laboratories up to this point. Will we be able to use nanofibers to their fullest extent now that engineers have come up with a new way to make them cheaper and easier to make?

Figure 4 presents a comprehensive schematic representation of plant- and fungus-mediated green synthesis of noble metal nanoparticles. On the left side, various biological sources such as leaf, root, bark, fruit, peel, latex, and mushroom extracts are depicted, emphasizing their role as natural reducing and stabilizing agents. These biological extracts contain phytochemicals, including flavonoids, phenolics, alkaloids, terpenoids, proteins, and polysaccharides, which facilitate the reduction of metal ions into nanoscale particles. The central section illustrates nanoparticle synthesis pathways, including the formation of AgNPs, AuNPs, and bimetallic nanoparticles such as Ag–Au and Au–Pd. The bioreduction and stabilization process is shown schematically, indicating the transformation of metal ions into stabilized nanostructures through phytochemical interactions. Morphological variations and size control are implied through graphical representations of spherical and clustered nanoparticles. The right panel summarizes key applications of the synthesized nanoparticles. These include antimicrobial activity, anticancer potential, catalytic activity, larvicidal effects, antioxidant properties, and cytotoxicity toward targeted cells. The diagram highlights how green-synthesized nanoparticles integrate environmentally sustainable production methods with multifunctional biomedical and environmental applications.

11. ANTIMICROBIAL PHARMACODYNAMICS OF AGNPS

Antimicrobial treatment using antibiotic substances may be effective,

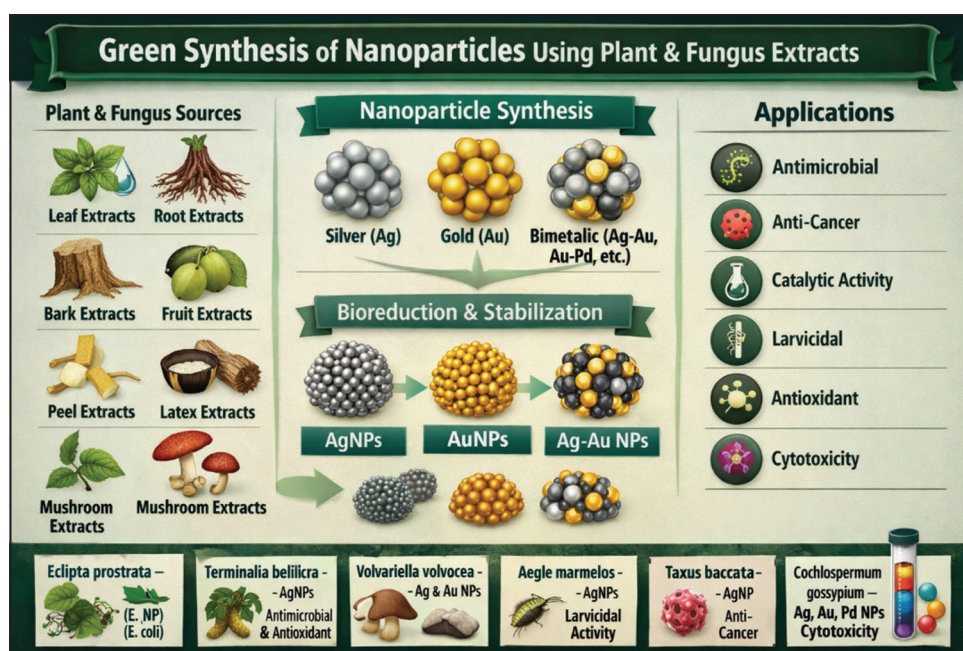


Figure 4: Schematic illustration of green synthesis of silver, gold, and bimetallic nanoparticles using plant and fungal extracts, highlighting biological sources, bioreduction mechanisms, nanoparticle formation, and major biomedical applications.

but this result is contingent on a number of different conditions. A few examples of these include the defensive systems of the host, the location of the infection, and the pharmacokinetic and pharmacodynamics features of the antibiotics. An antibiotic's ability to kill bacteria can depend on when the bacteria are at a certain stage of growth. Often, it also needs the bacteria to keep making new cells and keep their metabolism going.

12. ANTIBIOTIC RESISTANCE OF AGNPS

Kajani *et al.* (2014) reported the controlled synthesis of anisotropic, hexagonal, and truncated triangular AgNPs using *T. baccata* extract [94]. The nanoparticles, with an average size of 75.1 nm, exhibited significant anticancer activity against MCF-7 breast cancer cells as confirmed by MTT assay. Similarly, Pradeep *et al.* (2015) synthesized stable AgNPs (~42 nm) using *L. camara* leaf extract, which demonstrated strong antibacterial activity against ATCC strains [95]. Green synthesis using *Capsicum cerasiforme* leaf extract revealed that proteins containing amine functional groups function as reducing and stabilizing agents during nanoparticle formation Li *et al.*, (2008). Over time, nanoparticles transitioned from polycrystalline to single-crystalline structures as particle growth occurred. In addition to silver, Nasrollahzadeh *et al.* (2014) synthesized environmentally friendly Au/Pd bimetallic nanoparticles using *E. condylocarpa* root extract [96]. These nanoparticles catalyzed Suzuki and Heck coupling reactions in aqueous media. Liang *et al.* (2012) reported the synthesis of Ag/TiO₂ and Au/TiO₂ nanocomposites using *Citrus limon* extract, demonstrating efficient catalytic degradation of organic dyes and pH-controlled particle morphology.

The emergence of antibiotic resistance is a well-recognized consequence of microbial evolution under selective pressure imposed by antibiotic therapy. During treatment, bacterial populations may acquire resistance either through spontaneous genetic mutations or via horizontal gene transfer mechanisms. Such inheritable resistance traits can persist in microbial communities and reduce the clinical effectiveness of widely used antibiotics such as penicillin and erythromycin. Although resistance may impose a biological fitness cost, compensatory mutations can restore bacterial viability while maintaining resistance. This phenomenon has been extensively discussed in antimicrobial resistance literature [102]. AgNPs have gained attention as alternative antimicrobial agents due to their broad-spectrum activity and multi-target mode of action [20,103,104]. Unlike conventional antibiotics that act on specific molecular targets, AgNPs disrupt microbial cells through multiple mechanisms, including membrane damage, interaction with thiol groups of proteins, generation of ROS, and interference with DNA replication [23,24,103]. This multi-mechanistic activity significantly reduces the probability of rapid resistance development.

Kim *et al.* (2008) demonstrated that spherical AgNPs exhibited stronger antifungal activity against *Trichophyton mentagrophytes*, *Trichosporon beigelii*, and *Candida albicans* compared with conventional antifungal agents such as amphotericin B and fluconazole [105]. Stable colloidal AgNP solutions (up to 35 ppm) were also reported to show effective antifungal activity against *Aspergillus*, *Penicillium*, and *Trichoderma* species [27]. Green synthesis approaches further improve the biomedical applicability of AgNPs. Rapid reduction of Ag⁺ ions using plant extracts, such as geranium leaves, has been shown to produce stable crystalline nanoparticles more efficiently than microbial routes like *Fusarium oxysporum* [37]. Plant-mediated synthesis is advantageous because phytochemicals act as both reducing and stabilizing agents.

Espenti *et al.* (2020) reported the green synthesis of AgNPs using *Salacia mulbarica* leaf extract as a natural reducing and stabilizing

agent [106]. The phytochemicals present in the extract facilitated the rapid conversion of Ag⁺ ions into metallic silver (Ag⁰), resulting in predominantly spherical nanoparticles with an average diameter of approximately 13.95 nm. Detailed physicochemical characterization confirmed the formation, crystallinity, and stability of the synthesized nanoparticles. The biosynthesized AgNPs exhibited significant antibacterial activity against both *E. coli* and *B. subtilis*. Mechanistic analysis indicated that the antimicrobial effect was primarily associated with the generation of ROS, which induced oxidative stress and cellular damage. Furthermore, the study demonstrated interactions between AgNPs and calf thymus DNA, suggesting possible interference with bacterial genetic material. These findings emphasize the potential of *S. mulbarica*-mediated AgNPs as promising antimicrobial nanomaterials for biomedical applications.

Birusanti *et al.* (2018) described a sustainable green synthesis method for AgNPs using aqueous leaf extract of *Rangoon creeper* as both reducing and capping agents, highlighting the role of plant phytochemicals in nanoparticle assembly and stabilization [107]. The biosynthesis was carried out in a simple one-pot reaction in which silver nitrate was mixed with the leaf extract, leading to rapid reduction of Ag⁺ ions and formation of stable AgNPs, as evidenced by a characteristic surface plasmon resonance peak in the UV-visible spectrum.

The synthesized AgNPs displayed controlled size distribution and good colloidal stability, attributed to the organic biomolecules in the plant extract that act simultaneously as reducing and capping agents. Antibacterial evaluation of the AgNPs demonstrated significant activity against a range of microbial strains, supporting their potential applications as eco-friendly antimicrobial agents in biomedical and environmental contexts. Schematic illustration showing the role of the catechol group present in rutin during the reduction of silver ions (Ag⁺) to AgNPs in Figure 5. The ortho-dihydroxyl (catechol) moiety of rutin undergoes oxidation, releasing two protons (-2H⁺) while coordinating with Ag⁺ ions. This redox process facilitates the conversion of Ag⁺ into metallic silver (Ag⁰), leading to the nucleation and formation of AgNPs. The oxidized rutin molecules subsequently act as stabilizing agents by binding to the nanoparticle surface, preventing aggregation and enhancing colloidal stability. The study exemplifies how plant-based biomolecules can be harnessed effectively for the green fabrication of nanomaterials without hazardous chemicals and complex procedures, offering a scalable and environmentally compatible alternative to traditional chemical synthesis routes.

Sekhar *et al.* (2018) reported a simple and eco-friendly green synthesis of AgNPs using aqueous stem bark extract of *Syzygium cumini* [35]. The formation of nanoparticles was confirmed through UV-Visible spectroscopy, showing a characteristic surface plasmon resonance peak at approximately 420 nm. FTIR analysis revealed that hydroxyl, carbonyl, and amine functional groups present in the bark extract were involved in the reduction and stabilization of silver ions. DLS and TEM confirmed that the nanoparticles were spherical, monodispersed, and had an average size of ~14 nm [108]. The synthesized AgNPs demonstrated significant antibacterial activity against *E. coli* and *B. subtilis*, showing larger zones of inhibition compared to pure extract and AgNO₃ solution. The study concluded that *Syzygium cumini* bark extract serves as an effective reducing and capping agent for the rapid, cost-effective, and environmentally benign synthesis of bioactive AgNPs.

Espenti *et al.* (2024) reported a green and eco-friendly approach to fabricate durably antimicrobial cellulose cotton fabric by coating it with AgNPs synthesized through a phytochemical-mediated route [100]. In this study, leaf extract was employed as a natural

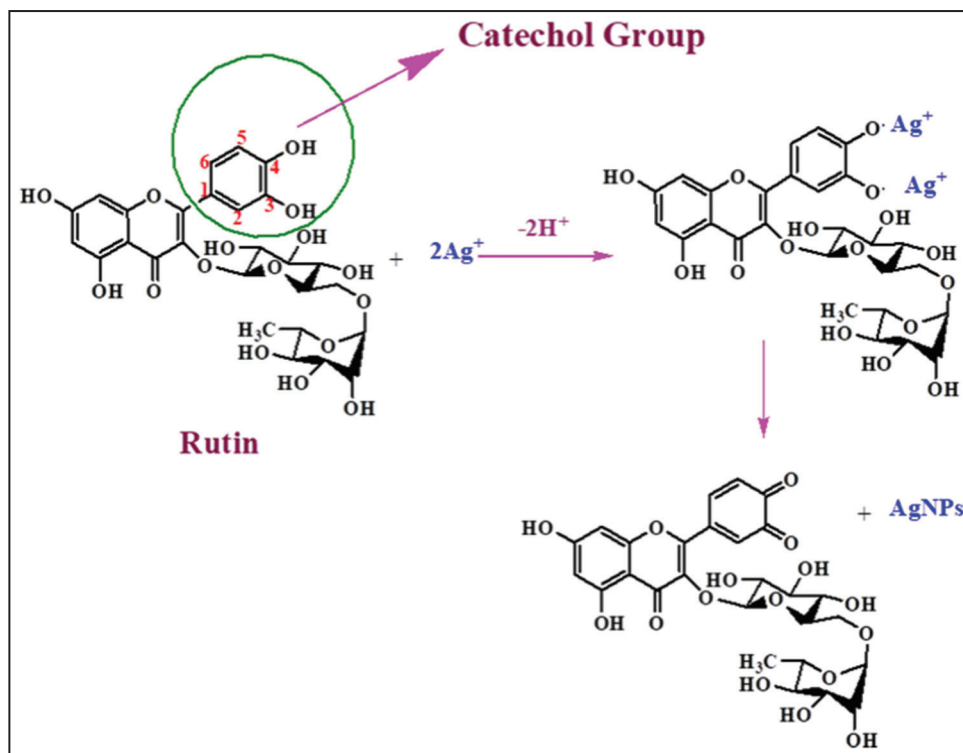


Figure 5: Proposed mechanism for the green synthesis of silver nanoparticles mediated by rutin. The figure was reprinted with permission from John Wiley and Sons (Birusanti *et al.*, 2018).

reducing and stabilizing agent to produce AgNPs under ambient conditions, leveraging the abundant bioactive compounds in the extract to facilitate rapid reduction of silver ions and formation of uniformly dispersed nanoparticles.

The synthesized AgNPs were characterized using techniques such as UV-visible spectroscopy, FTIR, scanning electron microscope with energy dispersive X-ray spectrometry, and XRD to confirm their size, morphology, and crystalline structure. These nanoparticles were subsequently deposited onto biocompatible cotton fabric using a green coating method. The resulting AgNP-coated textile exhibited significant and durable antimicrobial efficacy, demonstrating that plant-mediated AgNPs synthesis can be effectively integrated with textile treatment to yield functional materials with long-lasting antimicrobial properties. Representative agar plates showing zone of inhibition (ZOI) formed by varying concentrations of biosynthesized AgNPs against *Staphylococcus aureus* (top left), *E. coli* (top right), and *B. subtilis* (bottom) in Figure 6. The wells were loaded with varying concentrations of AgNPs (0, 0.01, 0.02, 0.03, 0.04, and 0.05 mg/mL), and antimicrobial efficacy was determined based on the ZOI formed around each well. Increase in ZOI formed with increase in concentration of AgNPs indicates concentration-dependent antimicrobial activity against Gram-positive and Gram-negative bacterial strains [109,110].

13. FUTURE DIRECTIONS

The continuations of green synthesis of metal nanoparticles, mainly AgNPs, may be geared to standardized, scalable, and clinically translatable methods. Even though various plant extracts have been used successfully to fabricate nanoparticles, clear molecular mechanisms mediating phytochemical reduction, nucleation, growth, and stabilization processes need to be unraveled through systematic studies. Besides, correlating the specific phytochemical substances responsible for nanoparticle formation will increase the reproducibility and allow the synthesis of nanoparticles with a predictable size,

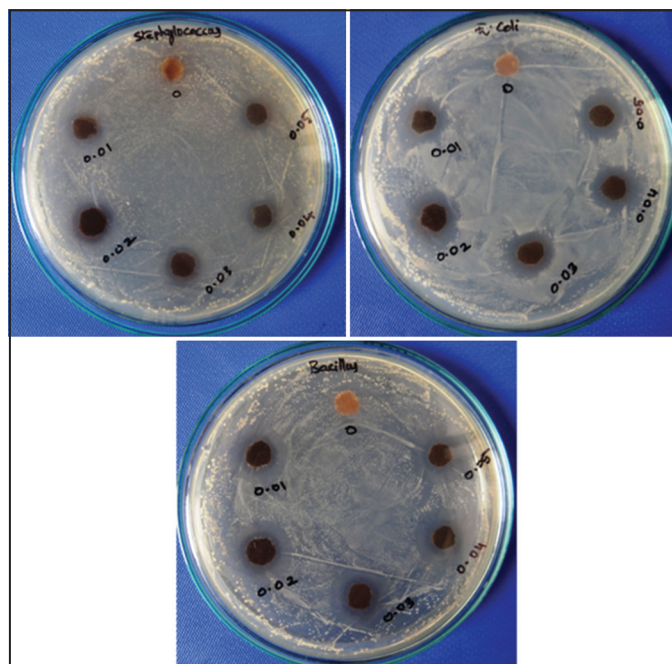


Figure 6: Antibacterial activity of green-synthesized silver nanoparticles evaluated by agar well diffusion method. The figure was reprinted with permission from Elsevier (Espenti *et al.*, 2024).

morphology, and surface functionality. Besides that, future research should be directed towards the development of large-scale production methods that can keep the uniformity and stability of the nanoparticles while satisfying the industrial and pharmaceutical standards. The optimization of reaction parameters such as pH, temperature, extract concentration, and precursor dosage should be standardized to

guarantee batch, to, batch consistency. Moreover, the combination of green synthesis and advanced nanofabrication techniques may give rise to multifunctional and hybrid nanomaterials for targeted biomedical applications. Thorough *in vivo* studies have to be carried out to assess the long, term toxicity, biodistribution, metabolism, and clearance of green-synthesised nanoparticles. It will be critical to have detailed pharmacokinetic and pharmacodynamic studies for clinical translation. Besides, in-depth research is needed on the interplay of nanoparticles and the immune system, microbiome, and cellular signaling pathways to ensure safety. Some novel areas like nanotheranostics, targeted drug delivery, and precision oncology.

14. CONCLUSION

The present review article clearly proves that natural products, especially plant extracts, have a pivotal role to play in the green synthesis of AgNPs and other metal nanoparticles for advanced biomedical applications. The plant-mediated synthesis is a sustainable, cost-effective, and eco-friendly method that replaces conventional chemical and physical synthesis techniques by eliminating the requirement for toxic reducing and capping agents. The bioactive compounds present in plant extracts, including flavonoids, phenolic compounds, terpenoids, alkaloids, proteins, and polysaccharides, function as reducing and capping agents that allow for precise control over nanoparticle size, shape, dispersion, and stability. Green-synthesised AgNPs possess excellent and broad-spectrum biological activities, including antimicrobial, antifungal, antiviral, anti-inflammatory, and anticancer activities. The enhanced efficacy of green-synthesised nanoparticles is attributed to their nanoscale size, larger surface area to volume ratio, generation of ROS, membrane-disruptive activity, interaction with intracellular biomolecules, including DNA and sulfur-containing proteins, and slow release of Ag⁺ ions. Moreover, the size, shape, and surface chemistry of nanoparticles also play a crucial role in determining their efficacy, with smaller nanoparticles showing enhanced antimicrobial activities. The variety of plants used for synthesizing nanoparticles proves that phytosynthesis is an extremely versatile technique. Apart from their antimicrobial activities, green synthesized nanoparticles possess strong potential for applications in drug delivery systems, biosensors, diagnostic imaging, tissue engineering, catalytic degradation, and therapeutic nanomedicine. However, despite their excellent efficacy, a comprehensive evaluation of their toxicity, pharmacokinetics, dosage, biocompatibility, and impact on the environment is essential.

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