Review Article

Plant-Mediated Green Synthesis of Ag NPs and Their Possible Applications: A Critical Review

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The potential applications of Ag NPs are exciting and beneficial in a variety of fields; however, there is less awareness of the new risks posed by inappropriate disposal of Ag NPs. The Ag NPs have medicinal, plasmonic, and catalytic properties. The Ag NPs can be prepared via physical, chemical, or biological routes, and the selection of any specific route depends largely on the end-use. The downside of a physical and chemical approach is that it requires a wide space, high temperature, high temperature for a longer time to preserve the thermal stability of synthesized Ag NPs, and the use of toxic chemicals. Although these methods produce nanoparticles with high purity and well-defined morphology, it is critical to develop cost-effective, energy-efficient, and facile route, such as green synthesis; it suggests the desirable use of renewable resources by avoiding the use of additional solvents and toxic reagents in order to achieve the ultimate goal. However, each method has its pros and cons. The synthesized Ag NPs obtained using the green approach have larger biocompatibility and are less toxic towards the biotic systems. However, identifying the phytoconstituents that are responsible for nanoparticle synthesis is difficult and has been reported as a suitable candidate for biological application. The concentration of the effective bioreducing phytoconstituents plays a crucial role in deciding the morphology of the nanoparticle. Besides these reaction times, temperature, pH, and concentration of silver salt are some of the key factors that determine the morphology. Hence, careful optimization in the methodology is required as different morphologies have different properties and usage. It is due to which the development of methods to prepare nanoparticles effectively using various plant extracts is gaining rapid momentum in recent days. To make sense of what involves in the bioreduction of silver salt and to isolate the secondary metabolites from plants are yet challenging. This review focuses on the contribution of plant-mediated Ag NPs in different applications and their toxicity in the aquatic system.

1. Introduction

Nanomaterials are generally defined as structures that have at least one dimension below 100 nm. Recently, there has been an increased demand for nanomaterials because of their widespread application in multidisciplinary fields. The global market of nanoparticles is expected to reach USD 16.8 billion, and commercialized Ag NPs contribute to 17.86% by 2021 [1].

The green synthetic approach has been proposed as a cost-effective, energy-efficient, facile, and environmentally friendly method for the preparation of nanomaterials as the use of nontoxic bioreducing agents provides alternative solutions to various environmentally conscious products. Green synthesized nanoparticles have a high surface area to volume ratio, biocompatible surface properties, less toxicity, and chemical stability. Multifunctional applications such as antibacterial [2, 3], antiviral [4], antifungal [5], anti-inflammatory [6], antidiabetic [7], anticancer [8], metal sensing [9], catalysis [10], and dye degradation [11] are some of the reasons why Ag NPs are emerging as the most...
fascinating and studied nanomaterials among other metallic nanoparticles.

Despite these applications, some of their hazardous effects, especially in the aquatic biotic system when inappropriately disposed, cannot be underestimated [12]. Tons of Ag NPs have been reported to be disposed into the aquatic environment annually [13]. The toxicity of Ag NPs depends on the physicochemical properties of nanoparticles as they differ from bulk material due to the higher surface area to volume ratio which enhances their reactivity [14]. This increased reactivity also translates towards biological systems via the food chain, which raises concern regarding the Ag NPs toxicity that exhibits cytotoxic, genotoxic, and hepatotoxic properties in any tropical level due to generation of reactive oxygen species (ROS) [15] or dissolution induced release of silver ion [16]. The nanoparticles showed size- and dose-dependent cytotoxicity towards macrophages [17] and T cells [18]. Slightly lesser toxicity of Ag NPs in comparison to Ag+ ions was reported [19] in Escherichia coli. Ag NPs displayed cytotoxicity through apoptosis both in in vitro and in vivo in the human epithelial cells [20]. The toxicity of green synthesized Ag NPs has been observed to depend on capping agent and surface functionalization showing less toxicity, which increases their potential for various biomedical applications [21].

Several reviews have been published on the biogenesis/chemical/physical synthesis and characterization of Ag NPs. In this paper, we have attempted to provide comprehensive detail of plant-mediated Ag NPs applications and their toxicity in the aquatic system.

2. Properties of Ag NPs

Green synthesized Ag NPs display novel and size-related physicochemical properties. In addition to that they also exhibit optical properties such as loss of the optical frequency during the surface plasmon propagation, wide absorption of the visible and far infrared region of the light, and surface-enhanced Raman scattering (SERS). These particles also have high electrical and thermal conductivity, high reactivity, and excellent catalytic and biological activities. The biological activity of Ag NPs depends on various elements including surface chemistry, shape and size, size distribution, capping/stabilizing agents, and agglomeration to name a few [22]. Because of these properties, they can be utilized for a variety of applications.

3. Methods of Synthesis of Ag NPs

The synthetic procedure for Ag NPs can be broadly categorized as top-down and bottom-up strategies. In the top-down approach, bulk materials are disassembled to create the nanostructures needed, whereas in the bottom-up method, single atoms and molecules are integrated into larger nanostructures [23]. Moreover, the synthesis strategy can be categorized as physical, chemical, and biological approaches. Since this review is for biological methods, the other methods are only briefly discussed here.

3.1. Physical Methods. The physical process involves two methods: evaporation-condensation and laser ablation. Evaporation-condensation is an inert gas-phase route that uses a horizontal tube furnace at atmospheric pressure to create nanoparticles. Throughout the center of the tube, the furnace contains a boat with synthesizing metal source material that is vaporized into the carrier gas. This technique has been used to synthesize nanoparticles, such as Au [24] and PbS [25]. An inert gas condensation system was used to synthesize Ag NPs using liquid helium in the process chamber, and the particle size ranged from 9 to 32 nm [26]. Some disadvantages of this technique include the need for a large space, high temperature, and high temperature for a longer period of time in order to retain the thermal stability of produced Ag NPs.

In laser ablation, a portion of the firm target material in solution is irradiated by using a laser of suitable wavelength, resulting in the formation of nanoparticles. Ag NPs have been prepared by irradiating a target silver in pure water with a 532 nm laser beam [27]. Following laser irradiation, the liquid can only comprise the intended solid nanoparticles and no other ions, compounds, reducing agents, etc. [28]. Laser ablation synthesis of nanoparticles is clean and uncontaminated, as this process uses mild surfactants in the solvent without any other toxic or hazardous chemical reagents. Spherical, uniformly dispersed, and homogeneous sized Ag NPs are prepared by spark ablation processes [29]. Physical approaches, which are capable of producing nanoparticles with higher purity and well-defined morphologies, are costly.

3.2. Chemical Methods. Chemical reduction is one of the most widely employed techniques for the synthesis of Ag NPs that uses both inorganic and organic reducing agents. Silver nitrate is used as a precursor, and various reducing agents such as sodium citrate, ascorbate, sodium borohydride, elemental hydrogen, polyol cycle, Tollens’ reagent, N,N-dimethylformamide, poly(ethylene glycol)-block copolymers, hydrazine, and ammonium formate are used to reduce Ag+ ion [30]. Spherical Ag NPs are obtained by the use of reducing agents (trisodium citrate and sodium borohydride), and polyvinyl pyrrolidone act as a stabilizing agent [31]. The morphology of the product nanoparticles highly depends on the kind of reducing agent/stabilizing agents used and reaction conditions [32]. The disadvantage of chemical method is that toxic chemicals may be harmful to biotic components.

3.3. Biological Methods. Advancing biological synthesis over chemical and physical processes is environmentally sustainable, cost-effective, and quickly scaled up for the production of nanoparticles on a wide scale; however, each method has its pros and cons. The biological approach is a less expensive, biocompatible, cleaner, nontoxic, and often single-step process that uses secondary metabolites (phenolics, flavonoids, terpenes, carbohydrates, etc.) as well as biomolecules such as DNA, protein, and enzymes spread in fungi, microbes, algae, and plants as reducing,
capping, and stabilizing agents. Biomolecule-mediated synthesis (DNA, protein, and enzymes) provides specific nucleation site during nanoparticle synthesis, resulting in uniform sized nanoparticles that are selective and sensitive to biomolecular targets and have a wide range of biomedical applications. These techniques, however, are extremely susceptible to environmental conditions such as temperature and pH [33–36]. The size of synthesized nanoparticles is also affected by the molar ratio of silver salt and biomolecules. DNA-mediated nanoparticles showed good antibacterial activity [37–39], and protein-mediated nanoparticles showed sensing application on spike proteins [40].

Bacterial species are sources of bioreducing secondary metabolites for silver salts, and Bacillus amyloliquefaciens and Bacillus subtilis [41], Pseudomonas aeruginosa [42], Escherichia coli [43], and Acinetobacter calcoaceticus [44] have also been used in the synthesis of Ag NPs. However, microbe-controlled synthesis is not industrially feasible because of the high aseptic criteria and their management. Therefore, the usage of plant extracts for this purpose has proven as a facile route over microorganisms owing to the simplicity, least biohazardous, and the nonrequirement of cell culture maintenance. Plants are readily accessible and have a broad variety of active functional groups and contain varieties of secondary metabolites such as polysaccharides, tannins, saponins, phenolics, terpenoids, flavonoids, alkaloids, sugars, enzymes, carbohydrates, and amino acids that can be useful in reducing, capping, and stabilizing Ag NPs observed in FTIR analysis [30]. Plants such as Lippia citriodora [45], Terminalia arjuna [11], Cannabis sativa [46], Salvia officinalis [47], Jatropha curcas seed [48], Caesalpinia coriaria [49], Artemisia nilagirica [50], Parkia speciosa [51], Cinnamomum zeylanicum [52], Lysiloma acapulcensis [53], Euphorbia prostrata [54], Cocos nucifera coir [55], Camellia sinensis [56], Sideritis argyrea [57], and Ipomoea staphylinia [58] have been used for the synthesis of Ag NPs Figure 1.

Figure 1: Fourier transform infrared (FTIR) spectra of Ag NPs synthesized using AgNO₃ (1 mM, 40 mL) and Piper chaba extract (100 g/L, 2 mL) after the reaction for 1 h at 60°C and pH = 7, and Ag NPs synthesized without capping agent reduced by NaBH₄ [59] (open access and reprinted under CC BY 4.0).

4. Plant-Mediated Ag NPs and Factors Affecting the Formation of Ag NPs

Biocompatible and nontoxic synthesis of functional nanoparticles assumes a vital job in the field of nanotechnology. It has been portrayed as a facile synthetic method as it is environmentally friendly, safe, and of solvent-free nature and avoids toxins. Different secondary metabolites from plants serve as reducing, stabilizing, and capping agents. Different plants produce a different class of secondary metabolites from having a certain degree of bioreduction potential capability of donating electrons for the reduction of Ag⁺ ions to Ag⁰ that decides the morphology, size, and yield of Ag NPs [60]. For nanotransformation of silver salt, electrons are supposed to be derived from dehydrogenation of acids and alcohols/phenols in hydrophytes, keto to enol conversions in mesophytes, or both mechanisms in xerophyte plants. Upon the release of two electrons from bioreducing secondary metabolites, it leads to the reduction of two silver ions which cluster together resulting the formation of Ag NPs [61–63]. The size of the nanoparticle plays a crucial role in determining its properties. Almost all plant-mediated Ag NPs have a spherical shape [64, 65]. Along with the nature and concentration of the secondary metabolites, distinctive factors such as pH, temperature, reduction time, the ratio of the concentration of silver salts, and plant extract also influence the formation of nanoparticles [66, 67].

pH is a major parameter that determines the uniformity and size of Ag NPs. The change in the pH of the reaction mixture and the plant extract can alter the shape and size of the nanoparticles. There is an inverse correlation between the size of nanoparticles formed and the pH of the reaction mixture [68]. However, at acidic conditions, almost no Ag NPs were produced as confirmed by the absence of a strong surface plasmon resonance (SPR) peak in the ultraviolet-visible (UV-Vis) spectrum [69]. The reduction of silver salts to Ag NPs accelerated by increasing the pH of the reaction medium leads to the formation of nanoparticles. However, at a very high pH (pH > 11), there is the formation of agglomerated and unstable Ag NPs [70]. The optical band gap of Ag NPs in the basic condition is higher than in acidic and neutral conditions because of quantum size confinement [71].

Green approach synthesis of Ag NPs required a temperature lower than 100°C. The total reaction rate increased with the increasing temperature until optimum condition subsequently leading to nucleation resulting in smaller size nanoparticles. Beyond this temperature, synthesized nanoparticles have been shown to increase their size due to an increase in the fusion efficiency of metal ions that dematerialize supersaturation [72, 73].
The change in the color of plant extract during the reduction of silver salts over various times can demonstrate the formation of Ag NPs as monitored by UV-Vis spectroscopy. Similarly, Ag NPs show an SPR peak at around 450 nm. Both bathochromic and hypsochromic shifts in wavelength with reaction time have been related to different shape and size of nanoparticles formed. The shift in intensity and wavelength of the SPR peak decreased with the increase in the reaction time indicating the reduction of Ag⁺ ion to Ag⁰. The increase of the absorbance with the reaction time indicated an increase in the concentration of Ag NPs. Studies have shown that, after a certain time, there is no shift in the SPR peak [74, 75] indicating the stability of synthesized nanoparticles.

The concentration of silver salts determines the shape and size of product nanoparticles. Synthesis of nanoparticles can be done either by keeping salt concentration constant and adding various concentrations of extract or by preparing different concentrations of salt solution and mixed with fixed extract concentration [73]. The concentration of bio-reducing agents refers to the increase in the yield of Ag NPs production having smaller sizes [76]. Higher concentration of silver salts causes formation of agglomerated and unstable higher size Ag NPs [70] (Figures 2(a) and 2(b)).

5. Characterization of Ag NPs

Ag NPs can be characterized to evaluate the functional aspects of the synthesized particles. In situ confirmation of its formation in colloidal solution is a preliminary analysis, followed by subsequent centrifugation/ethanol precipitation, drying, and recharacterization to evaluate different parameters. A variety of analytical techniques are used for this purpose [77–79]. The most common characterization techniques are as follows.

5.1. Characterization during Nanoparticle Formation. Characterization of Ag NPs in a colloidal solution can be performed by exploiting their optical properties that depend on the size, shape, concentration, agglomeration state, and refractive index near the surface of the nanoparticles. These properties make UV-Vis spectroscopy an important preliminary method for recognizable proof and characterization in the colloidal state. Ag NPs exhibit a UV-Vis absorption maximum in the range of 400–500 nm depending upon the particle size, and a peak in this region indicates the formation of nanoparticles due to SPR electrons on the nanoparticle surface. The concentration of reducing agents results in smaller-sized nanoparticles, which give a shift towards a lower wavelength due to the surface plasmon resonance of Ag NPs in UV-Vis spectra [76]. SPR electron excitation is characteristic of size and shape, the dielectric properties of the synthesizing medium, and the inter-nanoparticle coupling interactions [79, 80]. Ag NPs of size 17.96 ± 0.16 nm revolved by TEM analysis were obtained when 4 : 5 ratio of 0.001 M AgNO₃ and aqueous extract of Citrullus lanatus fruit rind at the temperature of 80°C at pH 10 showed the SPR peak at 404 nm in UV-Vis spectroscopy [73].

Cyclic voltammetry utilizes the potentiodynamic electrochemical characterization of Ag NPs [81]. A significant change in the reduction potential of Ag⁺ from a higher oxidation state to Ag⁰ was observed during cyclic voltammetry. The cyclic voltammogram of standard 20 nm Ag NPs exhibited distinct oxidation and reduction peaks at +290 mV and +100 mV, whereas that of synthesized Ag NPs using aqueous extract of Citrullus lanatus fruit rind shows a distinct oxidation peak at +291 mV and no reduction peak with the size of 17.96 ± 0.16 nm [73, 82].

5.2. Characterization of Morphology and Particle Size. Transmission electron spectroscopy (TEM), scanning electron spectroscopy (SEM), atomic force microscopy (AFM), and dynamic light scattering (DLS) are characterization tools used to obtain quantitative measures of particle size, shape, and size distribution. TEM is a powerful, versatile, and high-resolution imaging technique to probe the local structure and chemistry of synthesized nanomaterials. For TEM analysis, the Ag NP sample must be ultrathin, loaded on carbon-coated copper grids by negative staining solution, and must withstand vacuum conditions. After loading, Ag NPs are allowed to dry under a mercury lamp and then exposed to a monochromatic beam of electrons to generate an image and the crystallographic structure of a sample [83, 84]. Synthesis of Ag NPs using the ethanolic root extract of Atropa belladonna and characterization by TEM showed the size of the nanoparticles ranged from 15 to 20 nm [6] (Figure 3).

SEM is a direct surface imaging analytical technique capable of resolving different nanoparticle sizes, size distributions, nanomaterial shapes, and surface morphology. The dried Ag NPs are coated in conductive metal using a sputter coater under ultravacuum condition. SEM uses an energetic electron beam to produce the three-dimensional structure of the particle [86]. Synthesis of Ag NPs using aqueous extract of Musa balbisiana, Azadirachta indica, and Ocimum tenuiflorum formed approximately spherical, triangular, and cuboidal shape nanoparticles, respectively [87]. Similarly, the synthesis of Ag NPs using an aqueous extract of Rosa brunonii Lindl resulted in the formation of nanoparticles with spherical shapes [88] (Figure 4).

AFM is a very effective microscopic technique for the study of the morphology of nanoparticles and is capable of reaching ultrahigh resolution based on physical scanning in either liquid or gas medium. The instrument generates a topographical map of the Ag NPs based on the different forces (magnetic, electrostatic, and interatomic forces) between the probe and the surface of the nanoparticles [86]. Kumar et al. synthesized the Ag NPs using aqueous extract of Adansonia digitata fruit pulp with 25–57 nm size and spherical and polydispersed morphology confirmed by AFM [90].

DLS is utilized for deciding particle size and distribution by measuring the rotational and translational diffusion coefficients of the particle. It measures the size of Brownian particles in colloidal suspensions. At the point when a monochromatic light directs onto a solution of Ag NPs, a
Doppler shift occurs when the light hits the moving particles, along with changing the wavelength of the incoming beam of light by a value related to particle size and distribution using the Stokes–Einstein relationship \[91, 92\]. Synthesis of Ag NPs using aqueous extract of \textit{Chamaemelum nobile} and DLS analysis confirmed the 39–78.5 nm size at optimum condition \[93\].

5.3. Characterization of Surface Charge and Stability. The net effective electric charge at the double layer boundary is the zeta potential that gives an idea about the electropotential status of the Ag NPs in a dispersed medium. Laser Doppler electrophoresis is the most common and accepted method for surface charge characterization and stability of nanoparticles because of better resolution and more reliable results. The motion of nanoparticles depends on the surface charge, and the movement of nanoparticles is due to the Brownian motion and electrostatic forces under the impacts of applied electric fields. The high negative potential value of Ag NPs underpins long-term stability, high surface charge, good colloidal nature, and high dispersity of nanoparticles due to negative-negative repulsion \[94–96\]. Annona squamosa leaf was used to synthesize Ag NPs having a zeta potential of 37 mV \[97\]. Cynara scolymus leaf extract mediated Ag NPs with zeta potential values of $-32.3 \pm 0.8$ mV were reported indicating negatively charged and stable nanoparticles \[8\]; the zeta potential value higher than +30 mV or lower than $-30$ mV is considered to be very stable in the dispersion medium.

5.4. Characterization of Crystallinity. X-ray diffraction (XRD) is a nondestructive analytical technique to determine the crystallographic parameters of the nanoparticles. Examination of nanoparticles relies upon the formation of diffraction patterns which depends on the size and crystal structure. The 20, d-spacing values, lattice constant, and cell volume confirm the crystallinity of green synthesized nanoparticles and crystallite size. Average particle crystallite sizes are determined from the XRD spectra using the Debye–Scherrer equation \[98, 99\]. Broad XRD peaks indicate the presence of smaller size of Ag NPs and the crystallinity of Ag NPs. Ag NPs synthesized using ethanolic \textit{Santalum album} fruit extract and XRD analysis showed FCC crystal structure, and the average crystalline size is estimated to be 20 nm \[98\].

6. Challenges on the Plant-Mediated Synthesis of Ag NPs

High reproducibility is a demanding concern in the synthesis of nanoparticles. However, environmental factors (seasonal variation, geographic variation, water tension, lack of light access, attacks of herbivores and parasites, pH of the soil, etc.), unintentional and intentional factors (pollution and usage of herbicides and pesticides), and anthropogenic behavior may affect the formation of bioreducing secondary metabolites. In addition to this, powerful chemical reduction agents such as alkali metal borohydrides are favored compared to the weak reducing agents from plants’ secondary metabolites. It is because plant extracts serve as weak reducing agents, tend to nucleate particles far slower, and produce large nanoparticles and polydisperse products that may need postprocessing \[100, 101\], while stronger chemical reducing agents generate tiny nanoparticles \[102\]. Stronger secondary metabolites from the plant as reducing agents need to be identified, or new strategies need to be developed to increase the ability of existing green agents and to eliminate toxic reducing agents. Ligands are frequently used to passivate the surfaces of the nanoparticles, which serve to limit growth, stabilize against aggregation, and provide the
ability of functionalization. Secondary metabolites from natural products give a range of renewable options of stabilizing/capping agents that can be of low cost and manufactured locally; however, the polydispersity of the products is again a major issue with such alternative ligands. Usually, polydispersity involves postprocessing, which increases waste but can also restrict clinical applications if the physicochemical properties differ across lots. In this regard, the use of glutathione, a natural and ubiquitous tripeptide, is especially attractive in the synthesis of discrete molecular nanoparticles [103].

7. Application of Green Synthesized Ag NPs

7.1. Antibacterial Activity. Silver ions, Ag NPs, and synthesized nanoparticles doped with other compounds induce toxicity towards microorganisms [104, 105]. The synthesized Ag NPs demonstrate promising antimicrobial activities against both Gram-negative and Gram-positive bacteria [106]. Ag NPs show antibacterial properties by disabling the respiratory chain, or disrupting the cell membrane and causing rupture of cellular contents, or attaching to a functional group of proteins causing protein denaturation, or blocking genetic material replication [107].

Ag NPs synthesized using *Cestrum nocturnum* extracts have been shown to produce a spherical shape with 20 nm size. The MIC value of synthesized nanoparticles against *Citrobacter*, *E. faecalis*, *E. coli*, *P. vulgaris*, and *V. cholera* was found to be 16 μg/ml, 4 μg/ml, 16 μg/ml, 8 μg/ml, 8 μg/ml, and 16 μg/ml, respectively. The enhanced antibacterial activity was attributed to the presence of bioactive compounds on the surface of nanoparticles as stabilizing agents/capping agents [108].

In *Citrus limetta* peel extract mediated Ag NPs, 107 μg/ml concentration showed the highest zone of inhibition in *E. coli* among five test bacterial strains, while MIC, MBC, and IC₅₀ values of Ag NPs in *E. coli* are 4.75, 13.38, and 4.28 μg/ml, respectively [109]. *Moringa oleifera* flower extract used to synthesize Ag NPs was stable for six months and have more toxicity towards *S. aureus* with a zone of

![TEM micrograph of the synthesized Ag NPs. (a) SAED pattern of synthesized Ag NPs. (b) Analysis of the morphology of Ag NPs. (c) Histogram showing the size distribution of Ag NPs [85] (open access and reprinted under CC BY 4.0).](image_url)
inhibition of 29 mm as compared to *K. pneumoniae* with 17 mm [110]. Secondary metabolites present in *Mentha aquatica* leaf extracts act as a bioreducing agent for silver nitrate salt via ultrasound-assisted and hydrothermal methods. In *S. aureus*, the MIC values of synthesized Ag NPs via ultrasound-assisted route are significantly lower than the ones produced via hydrothermal route among four test bacterial strains [111]. Ag NPs synthesized using the extract of clove buds yielded particles with an average size of 9.42 nm, which was confirmed by TEM, and showed good marine antibacterial activity [112]. *Curcuma longa* L. was used to synthesize Ag NPs, and 35 μg concentration of the nanoparticles showed good antibacterial activity against *P. aeruginosa* and *S. aureus* with an MIC value of 1.25 μg/ml [113]. Ag NPs synthesized at neutral pH using *Ziziphus joazeiro* leaf extract showed good antibacterial activity against both Gram-positive and Gram-negative bacteria. In neutral pH, size control is more pronounced than in both acidic and basic pH. LQãhe Ag NPs synthesized under basic conditions have negligible antibacterial activity against *S. aureus* but superior activity against *E. coli*, while the ones synthesized in acidic conditions have oppositive activity.

**Figure 4:** SEM images at different magnifications: (a) 50,000x, (b) 100,000x, (c) 200,000x, and (d) 220,000x [89] (open access and reprinted under CC BY 4.0).

<table>
<thead>
<tr>
<th>Table 1: Morphology of Ag NPs and their antibacterial properties.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Size by TEM with morphology</strong></td>
</tr>
<tr>
<td>TEM 10–30 nm</td>
</tr>
<tr>
<td>Spherical in shape</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td>TEM 40–50 nm</td>
</tr>
<tr>
<td>SEM 50–60 nm</td>
</tr>
<tr>
<td>Spherical in shape</td>
</tr>
<tr>
<td>TEM 25 nm average</td>
</tr>
<tr>
<td>Spherical in shape</td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td>TEM 23.7 nm average</td>
</tr>
<tr>
<td>Spherical in shape</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>TEM 15–20 nm</td>
</tr>
<tr>
<td>Spherical in shape</td>
</tr>
<tr>
<td>TEM 15–20 nm</td>
</tr>
<tr>
<td>Spherical in shape</td>
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</tbody>
</table>

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### Table 2: Morphology of green synthesized Ag NPs and their anti-inflammatory activity on different viral strains.

<table>
<thead>
<tr>
<th>Phytoconstituents</th>
<th>Size by TEM/SEM with morphology</th>
<th>Viral strain</th>
<th>Antiviral activity (IC50/MNTD/TCID50/ml)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaloids, terpenoids, flavonoids, glycosides, phenols, and tannins</td>
<td>TEM 27.89 nm Spherical in shape</td>
<td>HSV-1, HAV-10, CoxB4</td>
<td>IC50: 36.36 μg/ml, 11.71 μg/ml, 12.24 μg/ml</td>
<td>[127]</td>
</tr>
<tr>
<td>Polyols, flavonoids, polyphenols, and terpenoids</td>
<td>SEM average size 70–95 nm</td>
<td>Chikungunya</td>
<td>MNTD: 31.25 μg/ml</td>
<td>[4]</td>
</tr>
<tr>
<td>Polyphenols</td>
<td>SEM average size 100 nm Spherical in shape</td>
<td>Dengue (DEN-2)</td>
<td>TCID50/ml Viral titer 3.2 log10 at 20 μl/ml Ag NPs</td>
<td>[128]</td>
</tr>
<tr>
<td>Lignocellulose</td>
<td>TEM 3–10 nm Narrow in shape</td>
<td>Chikungunya</td>
<td>IC50: 11.73 μg/ml</td>
<td>[129]</td>
</tr>
<tr>
<td>—</td>
<td>SEM average size 42 nm Spherical in shape</td>
<td>H7N3 influenza virus</td>
<td>IC50: 101 μg/ml (during viral infection) and 125 μg/ml (after viral infection)</td>
<td>[130]</td>
</tr>
</tbody>
</table>

### Table 3: Morphology of plant-mediated synthesized Ag NPs and their antifungal activity.

<table>
<thead>
<tr>
<th>Size by TEM with morphology</th>
<th>Operational condition</th>
<th>Fungal strains</th>
<th>ZOI</th>
<th>IC50/MIC50/MFC/MIC</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEM 18 nm average size with spherical shape</td>
<td>An aqueous solution of 0.001 N AgNO3 was mixed with Citrus limetta peel extract in a 5:1 ratio and continuously stirred</td>
<td>C. albicans, C. glabrata, C. parapsilosis, C. tropicalis</td>
<td>15 ± 0.75 mm, 14 ± 0.70 mm, 14 ± 0.70 mm, 14 ± 0.70 mm</td>
<td>4.75 μg/mL, 5.94 μg/mL, 4.75 μg/mL, 5.94 μg/mL</td>
<td>[109]</td>
</tr>
<tr>
<td>TEM 13 nm average size with spherical shape</td>
<td>1:4 ratio of Ligustrum lucidum leaf extract and 1 mM AgNO3 heated at 80°C</td>
<td>S. turcica</td>
<td>3.7 cm</td>
<td>170.20 μg/mL</td>
<td>[139]</td>
</tr>
<tr>
<td>TEM 10–32 nm with spherical shape</td>
<td>1:9 ratio of Amaranthus retroflexus leaf extract and 1 mM AgNO3 solution allowed to stand overnight</td>
<td>M. phaseolina, A. alternata, F. oxysporum</td>
<td>—</td>
<td>159.80 ± 14.49 μg/mL, 337.09 ± 19.72 μg/mL, 328.05 ± 13.29 μg/mL</td>
<td>[140]</td>
</tr>
<tr>
<td>TEM 20–40 nm size with spherical shape</td>
<td>1:9 ratio of Gelidium corneum extract and 1 mM AgNO3 exposed to a controlled temperature for 30 minutes</td>
<td>C. albicans</td>
<td>—</td>
<td>2.04 μg/mL (MFC), 0.51 μg/mL (MIC)</td>
<td>[141]</td>
</tr>
<tr>
<td>TEM 5–10 nm size with spherical shape</td>
<td>1:9 ratio of Selaginella bryopteris leaf extract and 1 mM AgNO3 with continuous stirring for 10 min followed by sonication at 80°C</td>
<td>A. niger</td>
<td>1 mm</td>
<td>10 mg/mL</td>
<td>[142]</td>
</tr>
</tbody>
</table>

### Table 4: Morphology of green synthesized Ag NPs and their anti-inflammatory activity on different inflammation models.

<table>
<thead>
<tr>
<th>Size by TEM/SEM with morphology</th>
<th>Inflammation model</th>
<th>%inhibition/IC50/binding constant</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEM 32–38 nm size with spherical shape</td>
<td>BSA protein</td>
<td>Binding constant (2.01 ± 0.06) × 10–4</td>
<td>[152]</td>
</tr>
<tr>
<td>TEM 15–20 nm size with spherical shape</td>
<td>BSA protein</td>
<td>IC50: 84 μM</td>
<td>[6]</td>
</tr>
<tr>
<td>—</td>
<td>Protein inhibitory activity</td>
<td>89.17 ± 1.4%</td>
<td>[153]</td>
</tr>
<tr>
<td>—</td>
<td>Albumin denaturation</td>
<td>84.64 ± 1.4%</td>
<td>[153]</td>
</tr>
<tr>
<td>—</td>
<td>Membrane stabilization</td>
<td>84.18 ± 1.4%</td>
<td>[153]</td>
</tr>
<tr>
<td>TEM 25 nm average size with spherical shape</td>
<td>HaCaT cells</td>
<td>IL-1α-55%, IL-1β-69%, IL-6-68%</td>
<td>[154]</td>
</tr>
<tr>
<td>TEM 20–80 nm size with spherical shape</td>
<td>HaCaT cells</td>
<td>IL-1α-49%, IL-1β-92%, IL-6-74%</td>
<td>[155]</td>
</tr>
</tbody>
</table>
[114]. Bioreduced Ag NPs showed higher antibacterial activity than the crude extract alone [115, 116]. Ag NPs synthesized using the extract of Ziziphus clinopodioides (pH of 8, 4 mM of AgNO\(_3\), and time of 2.5 hours) resulted in spherical nanoparticles with an average size of 25–50 nm. The synthesized Ag NPs showed excellent antibacterial properties in both Gram-positive (S. aureus) and Gram-negative E. coli [117]. Table 1 shows the morphology of Ag NPs and their antibacterial property against Gram-positive and Gram-negative bacteria.

### 7.2. Antiviral Activity

Various viruses are likely to erupt highly infectious diseases that increase day by day which threatens human health [121]. The surface chemistry of Ag NPs and their size determine the antiviral activity. The possible mode of action is to hamper the binding with the extracellular matrix inhibiting interaction towards outer cell receptors or with the genetic material [122]. The broad spectrum of Ag NPs is efficient and effective against viral strains and the risk of resistance by mutation [123]. Ag NPs with size ≤10 nm effectively bind to sulfur-bearing residues in gp120 glycoprotein knobs in the outer surface of the human immune deficiency virus (HIV-1) that hinders the binding with the host cell and thus inhibits its activity [124].

Quasi-Ag NPs synthesized from an aqueous extract of Panax ginseng roots are virucidal against the influenza A virus (strain A/PR/8). Slight anti-influenza effects have been observed with 0.005, 0.01, and 0.15 M concentrations of Ag NPs with inhibitory rates of 5.31%, 4.18%, and 5.97%, respectively. However, the virucidal inhibitory activity has been reported to have significantly increased to 7.10% and 15.12% at concentrations of 0.02 and 0.25 M, respectively [125]. Synthesis of Ag NPs from the aqueous leaf extracts of mangrove Rhizophora lamarkii resulting polydispersed spherical nanoparticles, with particle size ranging from 12 to 28 nm by TEM analysis, exhibited potent HIV-1 reverse transcriptase inhibitor activity with an IC\(_{50}\) value of 0.4 μg/mL [126]. Table 2 shows the morphology of green synthesized Ag NPs and their antiviral activity on various viral strains.

### 7.3. Antifungal Activity

Fungal infections, particularly nosocomial fungal infections, are a major health risk [131] against which biomediated Ag NPs can be employed. Antibacterial activities of Ag NPs are well established, while antifungal activities have still not been thoroughly examined. Ag NPs are commonly known for strong antimicrobial activity even at very low concentrations [132]. Ag NPs showing antifungal properties lead to the destruction of either cell wall or cell membrane and deposition around the cell leading to damage or degeneration of organelles (chromatin, ribosomes, and mitochondria) [133]. Several experiments have demonstrated that Ag NPs exhibit strong antifungal properties against Colletotrichum coccoide, Monilinia species [134], and Candida species [135]. Ag NPs synthesized using the methanolic leaf extract of Atalantia monophylla (2 mM of AgNO\(_3\) and time of 15 minutes) result in spherical Ag NPs (average size of 35 nm) that exhibit better antifungal activity against Candida albicans [136].

**Table 5**: Morphology of green synthesized Ag NPs and their antidiabetic activity.

<table>
<thead>
<tr>
<th>Size by TEM/SEM with morphology</th>
<th>Operational condition</th>
<th>Antidiabetic activity</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SEM 10–25 nm with spherical shape</td>
<td>1:10 ratio of <em>Pisum sativum</em> L. outer peel extract and 1 mM AgNO(_3) stirred continuously for 24 hours</td>
<td>α-Glucosidase</td>
<td>2.10 μg/mL [94]</td>
</tr>
<tr>
<td>TEM 5–50 nm with rod, spherical, and triangular shape</td>
<td>1:2 ratio of different concentrations of AgNO(_3) and <em>Cleome viscosa</em> whole plant at room temperature</td>
<td>α-Amylase, α-Glucosidase</td>
<td>21.92 ± 1.74 μg/mL, 21.76 ± 1.91 μg/mL [167]</td>
</tr>
<tr>
<td>TEM mean diameter of 3.45 ± 0.16 nm with monodispersed and spherical shape</td>
<td>40:1 ratio of 1 mM AgNO(_3) and aqueous flower extract of <em>Dregea volubilis</em> at 121°C and 15°psi pressure for 20 minutes</td>
<td>α-Amylase, α-Glucosidase</td>
<td>10.62 ± 0.22 μg/mL, 6.49 ± 0.03 μg/mL [168]</td>
</tr>
<tr>
<td>TEM 5–15 nm with polydispersed and spherical shape</td>
<td>1:99 ratio of 1 mM AgNO(_3) and flower aqueous extract of <em>Bauhinia variegate</em> incubated in dark at room temperature for 1 hour</td>
<td>α-Amylase</td>
<td>38 μg/mL [169]</td>
</tr>
<tr>
<td>SEM 50 nm with polydispersed shape</td>
<td>1:19 ratio of <em>Xylocarpus granatum</em> bark aqueous extract and 10 mM AgNO(_3) at room temperature for 6 hours</td>
<td>α-Amylase, α-Glucosidase</td>
<td>0.19 mg/mL, 0.13 mg/mL [170]</td>
</tr>
</tbody>
</table>
bioactive compounds as stabilizing agents/capping agents on the surface of Ag NPs enhanced its antifungal activity [138]. Table 3 shows the morphology of plant-mediated synthesized Ag NPs and their antifungal activity on different fungal strains.

7.4. Anti-Inflammatory Properties. Researchers have already demonstrated that nanoparticles tend to have anti-inflammatory properties, where Ag NPs have been involved in decreasing inflammation in peritoneal adhesions with no noticeable toxic effects [143]. Inflammation although is a...
significant form of defense in the human body [144], excessive inflammation, may cause multiple diseases including cancer, arthritis, and neurological disorders [145] distinguished by the development of proinflammatory cytokines and by the stimulation of immune system cells. The pathways of the nuclear factor-kappa B (NF-κB) play a crucial role in the inflammation cycle, raising the rates of cytokines and inflammatory mediators such as nitric oxide, prostaglandin E2, inducible nitric oxide synthase, and lipopolysaccharides-2 [146]. The intracellular blocking of inflammatory pathways and downregulating proinflammatory cytokines could be the potential mechanism of Ag NPs anti-inflammatory properties [147]. Green synthesized Ag NPs suppressed LPS-mediated induction of protein levels through NF-κB signaling via the p38 MAPK pathway and can be used as an effective agent in anti-inflammation [148].

Avicennia marina ethanol extract synthesized Ag NPs exhibit an effective inhibition of heat-induced albumin denaturation of 68.92% and 72.1%, respectively [149]. Belle Ebanda Kedi et al. studied the ability of the Selaginella moysurus extract mediated Ag NPs to inhibit thermally induced egg albumin denaturation by arthritic reactions and development of tissue damage during the inflammation process indicating their ability to control protein denaturation [150]. The anti-inflammatory potential of synthesized Ag NPs using Atropa acuminata aqueous leaf extract was shown by albumin denaturation and antiproteinase activity with IC$_{50}$ values 12.98 and 18.401 μg/mL, respectively, which is lesser than the standard anti-inflammatory drug, diclofenac sodium salt. This is because inhibiting the production of autoantigens that reduce the denaturation of albumin and retard the production of neutrophils leads to prevent tissue damage. It is evident that green synthesized Ag NPs exhibited strong anti-inflammatory activities and could be used as potential anti-inflammatory drugs [151]. Table 4 shows the morphology of green synthesized Ag NPs and their anti-inflammatory activity on different inflammation models.

7.5. Antidiabetic Activity. Diabetes mellitus (DM) is a group of metabolic chronic disorders characterized by postprandial hyperglycemia resulting from anomalous insulin secretion, insulin action, or both and disturbances of carbohydrate, lipid, and protein metabolism, creating a high risk of premature mortality, bringing immense financial pressure on public health systems and national economies. It is estimated that 463 million people have diabetes, and this figure is expected to hit 578 million by 2030 and 700 million by 2045 [156]. Diabetes may lead to long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, blood vessels, and so on [157–159]. α-Amylase and α-glucosidase are major hydrolytic enzymes involved in diabetes and responsible for the hydrolysis of carbohydrates in the luminal digestive tract. These two enzymes act at the same time, and the α-glucosidase activity is the rate-determining step in carbohydrate hydrolysis [160]. Inhibition of α-amylase and α-glucosidase enzymes leads to a decrease in blood glucose level in the body [161]. Acarbose, voglibose, and miglitol are commercially available drugs to inhibit these digestive enzymes in diabetic patients, but adverse effects such as meteorism, flatulence, and diarrhea are frequently observed [162]. This warrants the search for safe and effective treatment modalities that have lesser side effects than the currently available drugs; the green synthesized Ag NPs modality is one of them. Ag NPs synthesized from aqueous leaf extract of Lonicera japonica showed potent inhibition against carbohydrate digestive enzymes such as α-glucosidase and α-amylase with IC$_{50}$ values of 37.86 and 54.56 μg/mL, respectively. Besides, kinetic studies have revealed Ag NPs to be reversible noncompetitive inhibitors with Ki values of 25.9 and 24.6 μg for α-amylase and α-glucosidase, respectively [163].

Punica granatum leaf extract used to synthesize Ag NPs with an average size of 20–45 nm with spherical shape showed effective inhibition against α-amylase and α-glucosidase with IC$_{50}$ values of 65.2 and 53.8 μg/mL, respectively. Synthesized nanoparticles have higher hydrolytic enzyme inhibition potential than plant extract and slightly lower than standard drug acarbose [164]. Ag NPs synthesized from the flower aqueous extract of Momordica charantia are spherical with 22.5 nm by SEM analysis. The nanoparticles showed a decrease in blood glucose at a dose of 200 mg/kg in STZ-induced diabetic rats, and similarly, the regeneration of necrotic beta cells was especially pronounced at that dose [165]. Outer peel extract of the fruit Ananas comosus was used to synthesize Ag NPs exhibiting promising α-glucosidase inhibition potential in a dose-dependent manner. 100% inhibition of α-glucosidase was

<table>
<thead>
<tr>
<th>Size by TEM/SEM with morphology</th>
<th>Substrate</th>
<th>Catalytic activity</th>
<th>Type of reaction</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEM 10–50 nm with spherical shape</td>
<td>4-Nitrophenol</td>
<td>Reduction</td>
<td>20</td>
<td>88.80</td>
<td>[11]</td>
<td></td>
</tr>
<tr>
<td>TEM 20–60 nm with spherical shape</td>
<td>1-Phenylenol</td>
<td>Oxidation</td>
<td>480</td>
<td>62</td>
<td>[200]</td>
<td></td>
</tr>
<tr>
<td>Spherical in shape with narrow size</td>
<td>4-Methyl phenyl cyanide</td>
<td>Hydration</td>
<td>60</td>
<td>95</td>
<td>[201]</td>
<td></td>
</tr>
<tr>
<td>TEM 2.76 nm with spherical shape</td>
<td>Benzaldehyde, morpholine, phenylacetylene</td>
<td>A$^1$ coupling</td>
<td>480</td>
<td>95</td>
<td>[202]</td>
<td></td>
</tr>
<tr>
<td>TEM 10–35 nm with spherical and oval shape</td>
<td>3-Amino indazoles, 2-methoxy benzaldehyde, and ethynyl benzene</td>
<td>A$^1$ coupling</td>
<td>60</td>
<td>96</td>
<td>[203]</td>
<td></td>
</tr>
</tbody>
</table>
aqueous extract behave as anticancer agents. In vitro average size of 43.5 nm synthesized using with biomolecules inside the cells. Spherical Ag NPs with an sized Ag NPs and their entrance into the cells can interact their safety, low toxicity, and cheaper cost [172–174].

reduced Ag NPs are used for the treatment of cancer due to role in the angiogenesis within cancer. Phytochemically function of the vascular permeability factor and play a major apoptosis, or mitochondrial damage. Ag NPs alter the and lead to DNA damage, oxidative stress, induction of triphosphate synthesis. Ag NPs are toxic to cancerous cells and their LC50 value of 24 to 80 nm synthesized using Delonix regia leaf aqueous extract behave as anticancer agents. In vitro examination on A549 and SiHa cell line by MTT assay and Ag NPs have shown to have potent antiproliferative activity. Half-maximal inhibitory concentration (IC50) gives the 50% inhibition of biological or biochemical function. The green synthesized nanoparticles exhibited an IC50 value of 14.96 and 15.96 μg/mL after 48 hours for A549 and SiHa, respectively [175].

Spherical and triangular Ag NPs with sizes varying from 24 to 80 nm synthesized using Commelina nudiflora L. have shown potent cytotoxicity against HCT-116 colon cancer cells. The cytotoxicity increased by the increase in concentrations with an IC50 value of 100 μg/mL in 24 hours of exposure. The use of Ag NPs has shown 90% cell death at 250 μg/mL concentration, the treated cell line underwent membrane blebbing, and morphological change led to induced apoptosis [176]. Cornus officinalis used to synthesize Ag NPs having well-dispersed and quasispherical shape with an average size of 11.7 nm showed cytotoxicity against PC-3 and HepG2 cell lines with LC50 values of 25.54 and 21.46 μg/mL in 48 hours [177]. Caesalpinia pulcherrima used to synthesize Ag NPs showed in vitro cytotoxicity against HCT-116 cells having an IC50 value of 3.8 μg/mL [178]. Table 6 shows operational conditions during the synthesis of Ag NPs and their anticancer activity on different cell lines.

Table 9: Morphology of green synthesized Ag NPs and their dye degradation activity.

<table>
<thead>
<tr>
<th>Phytocomponent present</th>
<th>TEM with morphology</th>
<th>Dye used</th>
<th>Reaction time (min)</th>
<th>Rate constant (min⁻¹)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenols and flavonoids</td>
<td>TEM 19.06 nm average size with spherical shape</td>
<td>Methyl orange</td>
<td>9</td>
<td>0.9906</td>
<td>[216]</td>
</tr>
<tr>
<td>Phenols and flavonoids</td>
<td>TEM 10–25 nm with spherical shape</td>
<td>Congo red</td>
<td>9</td>
<td>0.6</td>
<td>[217]</td>
</tr>
<tr>
<td>Polyphenol and flavonoids</td>
<td>TEM 16 nm average size with spherical shape</td>
<td>Brilliant blue</td>
<td>20</td>
<td>0.2097</td>
<td>[210]</td>
</tr>
<tr>
<td>Phenol</td>
<td>TEM 62.51 nm with spherical shape</td>
<td>Methylene blue</td>
<td>18</td>
<td>0.1448</td>
<td>[218]</td>
</tr>
<tr>
<td>Polyphenol</td>
<td>TEM 7 nm with spherical size</td>
<td>Methylene blue</td>
<td>0.83</td>
<td>5.18</td>
<td>[202]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rhodamine B</td>
<td>1</td>
<td>3.44</td>
<td></td>
</tr>
</tbody>
</table>

observed at 0.063 μg/mL concentration of synthesized nanoparticles [166]. Table 5 shows the morphology of Ag NPs, operational condition, and antidiabetic activity by inhibitory activity on two major enzymes, α-glucosidase and α-amylase.

7.6. Anticancer Activity. Cancer is a life-threatening disease that emerges from the deterioration of normal cells into tumor cells in a multistage process due to genetic factors and physical, chemical, and biological carcinogens [171]. Distinctive types of cancers are known; among them, lung, colorectal, stomach, liver, and breast cancers are more common according to WHO. Green synthesized Ag NPs have proven to have antiproliferative and apoptosis-inducing properties and are thus used as anticancer agents. Ag NPs enter the mitochondria by endocytosis, which leads to the generation of ROS, and alteration of the adenosine triphosphate synthesis. Ag NPs are toxic to cancerous cells and lead to DNA damage, oxidative stress, induction of apoptosis, or mitochondrial damage. Ag NPs alter the function of the vascular permeability factor and play a major role in the angiogenesis within cancer. Physicochemically reduced Ag NPs are used for the treatment of cancer due to their safety, low toxicity, and cheaper cost [172–174].

The unique physicochemical property of green synthesized Ag NPs and their entrance into the cells can interact with biomolecules inside the cells. Spherical Ag NPs with an average size of 43.5 nm synthesized using Delonix regia leaf aqueous extract behave as anticancer agents. In vitro examination on A549 and SiHa cell line by MTT assay and Ag NPs have shown to have potent antiproliferative activity. Half-maximal inhibitory concentration (IC50) gives the 50% inhibition of biological or biochemical function. The green synthesized nanoparticles exhibited an IC50 value of 14.96 and 15.96 μg/mL after 48 hours for A549 and SiHa, respectively [175].

Spherical and triangular Ag NPs with sizes varying from 24 to 80 nm synthesized using Commelina nudiflora L. have shown potent cytotoxicity against HCT-116 colon cancer cells. The cytotoxicity increased by the increase in concentrations with an IC50 value of 100 μg/mL in 24 hours of exposure. The use of Ag NPs has shown 90% cell death at 250 μg/mL concentration, the treated cell line underwent membrane blebbing, and morphological change led to induced apoptosis [176]. Cornus officinalis used to synthesize Ag NPs having well-dispersed and quasispherical shape with an average size of 11.7 nm showed cytotoxicity against PC-3 and HepG2 cell lines with LC50 values of 25.54 and 21.46 μg/mL in 48 hours [177]. Caesalpinia pulcherrima used to synthesize Ag NPs showed in vitro cytotoxicity against HCT-116 cells having an IC50 value of 3.8 μg/mL [178]. Table 6 shows operational conditions during the synthesis of Ag NPs and their anticancer activity on different cell lines.

7.7. Nanopesticide Activity. Pesticides have been deeming as one of the world’s main leading factors to environmental pollution. The intended applications of these chemicals have proven to be toxic to pests and disease vectors, with over 1000 active ingredients sold as insecticides, herbicides, and fungicides [183]. Although pesticides have primarily improved the quality of human life and the prevention of infectious diseases, however, pesticide toxicity is believed to be related to a variety of health problems such as Parkinson’s disease [184], endocrine destruction [185], cardiovascular diseases, cancer, reproductive disorders [186], and so on. Therefore, this review is based on nanopesticides due to their nature of being less toxic and ecofriendly. Ag NPs act as an effective pest management product and are nontoxic, stable, and innovative pest control tool. Researchers have reported the potential application of UV-irradiated Ag NPs in pest biocontrollers, such as mosquito larvae. Delphinium denudatum aqueous root extract is used in the synthesis of polydispersed and spherical shape Ag NPs. These nanoparticles showed potent larvicidal activity against the dengue vector Aedes aegypti second-instar larva with an LC50 value of 9.6 ppm in 48 hours of exposure. Aedes aegypti second-instar larvae can no longer survive at higher concentrations, and no significant difference was found between the time of exposure [187]. Similarly, the green synthesized nanoparticles showed lower LC50 value as compared to AgNO3 on
the third larva stage of *Culex pipiens* and *Musca domestica* [188]. The green synthesized Ag NPs from the aqueous aerial extract of *Ammannia baccifera* showed significant toxic effects against the larvae of *Anopheles subpictus* and *Culex quinquefasciatus* with LC$_{50}$ values of 29.54 ppm and 22.32 ppm, respectively [189]. Table 7 shows the morphology

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**Table 10:** Morphology of Ag NPs, their metal sensing activity, and their detection limit.

<table>
<thead>
<tr>
<th>Phytoconstituents</th>
<th>TEM with morphology</th>
<th>Metal ions</th>
<th>Operational condition</th>
<th>Concentration range</th>
<th>Detection limit</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavonoids, phenols, sugars, and P-substituted aryl compounds</td>
<td>TEM 15 nm with spherical shape</td>
<td>Fe$^{3+}$</td>
<td>Ag NPs addition of various metal ions (Al$^{3+}$, Fe$^{3+}$, Co$^{2+}$, Pb$^{2+}$, Cu$^{2+}$, Ni$^{2+}$, Zn$^{2+}$, Cr$^{3+}$, Mn$^{2+}$, and Cd$^{2+}$) showed selective detection towards Fe$^{3+}$ only</td>
<td>30–150 μm</td>
<td>4.5 μm</td>
<td>[227]</td>
</tr>
<tr>
<td>—</td>
<td>TEM 15–20 nm with spherical shape</td>
<td>Cu$^{2+}$</td>
<td>Rhodamine 6G dye fixed on the surface of Ag NPs to which 1 mL of test solution of various metal ions (Cu$^{2+}$, Mg$^{2+}$, K$^+$, Mn$^{2+}$, Fe$^{3+}$, Zn$^{2+}$, Co$^{2+}$, and Ba$^{2+}$) was added</td>
<td>10$^{-6}$–10$^{-13}$ mol/L</td>
<td>10$^{-13}$ mol/L</td>
<td>[228]</td>
</tr>
<tr>
<td>Flavonoids, tannins, phenol, saponins, and glycosides</td>
<td>TEM 25 ± 5 nm average size with spherical shape</td>
<td>Hg$^{2+}$</td>
<td>10$^{-3}$ M solution of Li$^+$, Al$^{3+}$, Cr$^{3+}$, Mn$^{2+}$, Fe$^{3+}$, Co$^{2+}$, Ni$^{2+}$, Cu$^{2+}$, Zn$^{2+}$, Cd$^{2+}$, and Pb$^{2+}$ added to equal amount of Ag NPs</td>
<td>10$^{-4}$–10$^{-6}$ M</td>
<td>10$^{-3}$ M</td>
<td>[229]</td>
</tr>
<tr>
<td>Polyphenols and flavonoids</td>
<td>TEM 19.7 nm with spherical shape</td>
<td>Cd$^{2+}$</td>
<td>Cd$^{2+}$, Ni$^{2+}$, Cu$^{2+}$, Zn$^{2+}$, Cr$^{3+}$, Fe$^{2+}$, Pb$^{2+}$, Co$^{2+}$, and Hg$^{2+}$ solution added to Ag NPs which showed a selective detection towards Cd$^{2+}$ only with the highest response at a pH of 6</td>
<td>10–90 μM</td>
<td>70 μM</td>
<td>[230]</td>
</tr>
<tr>
<td>Citric acid</td>
<td>TEM 10.82 nm with spherical shape</td>
<td>Cr$^{3+}$</td>
<td>Ag NPs tested by adding different metal ions (Cu$^{2+}$, Zn$^{2+}$, Cd$^{2+}$, Hg$^{2+}$, Pb$^{2+}$, Co$^{2+}$, and Cr$^{3+}$) and color change observed only for Cr$^{3+}$ at an optimum pH of 8</td>
<td>10–90 μM</td>
<td>0.804 μM</td>
<td>[231]</td>
</tr>
</tbody>
</table>

---

**Table 11:** Morphology of Ag NPs and their aquatic toxicity in different species.

<table>
<thead>
<tr>
<th>Size by TEM with morphology</th>
<th>Species</th>
<th>LC$_{50}$/LC</th>
<th>Toxicity in aquatic species</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>—</td>
<td><em>Poecilia reticulata</em></td>
<td>3 μg/mL</td>
<td>Gill stimulation and increased mucus secretion</td>
<td>[236]</td>
</tr>
<tr>
<td>—</td>
<td><em>Ceriodaphnia cornuta</em></td>
<td>35 μg/mL</td>
<td>Aggregates in gastrointestinal tract damage in the organs</td>
<td></td>
</tr>
<tr>
<td>TEM 10–50 nm with spherical and polydispersed shape</td>
<td><em>Ceriodaphnia cornuta</em></td>
<td>23.5 μg/ml</td>
<td>Bioaccumulation of nanoparticles in the internal gut region and blackening of the intestine lead to rupture of the abdomen</td>
<td>[237]</td>
</tr>
<tr>
<td>—</td>
<td><em>Paramecium sp.</em></td>
<td>15.5 μg/mL</td>
<td>Morphological deformities</td>
<td></td>
</tr>
<tr>
<td>—</td>
<td><em>Poecilia reticulata</em></td>
<td>38.3 μg/mL</td>
<td>Congestion in the hepatic parenchyma</td>
<td></td>
</tr>
<tr>
<td>TEM 10 nm average size with spherical shape</td>
<td><em>Danio rerio</em></td>
<td>3 × 10$^{-4}$ mL$^{-1}$</td>
<td>Damage in the gill cells</td>
<td>[238]</td>
</tr>
<tr>
<td>—</td>
<td><em>Danio rerio</em></td>
<td>80 μg/ml</td>
<td>Disorders in organogenesis throughout the development</td>
<td>[239]</td>
</tr>
<tr>
<td>TEM 76.94 ± 36.82 nm with spherical and quasispherical shape</td>
<td><em>Daphnia magna</em></td>
<td>1.86 ± 0.12 μg/L</td>
<td>Generation of ROS and oxidative stress and cause negative effects</td>
<td>[240]</td>
</tr>
<tr>
<td>TEM 5–50 nm with spherical shape</td>
<td><em>Danio rerio</em></td>
<td>142.2 μg/L</td>
<td>Oxidative stress and immunotoxicity</td>
<td>[241]</td>
</tr>
<tr>
<td>TEM 50 nm average size with spherical shape</td>
<td><em>Labeo rohita</em></td>
<td>25 μg/L</td>
<td>Oxidative stress and histopathological alterations in the gills, liver, and kidney</td>
<td>[242]</td>
</tr>
</tbody>
</table>
of green synthesized Ag NPs and their pesticide activity on different species.

7.8. Catalytic Activity. Catalysis has become an ambitious field in nanoscience and emerging applications because of its unique properties such as high surface-to-volume ratio, compositional tenability, and ease of recovery [195]. Ag NPs can oxidize and then reduce metal back to zero under mild conditions, allowing Ag NPs to behave as strong catalysts in both reductive and oxidative processes due to the particular location of Ag+/Ag0 couple redox potential [196]. Ag NPs also have a fascinating optical feature, the localized surface plasmon resonance (LSPR), which has been at the forefront of recent catalytic growth for oxidation, reduction, and coupling reaction.

The synthesized Ag NPs from Botryococcus braunii have 40–90 nm size revolved by SEM analysis and catalytic reduction of 2-nitroaniline to 2-(4-nitrophenyl)-1H-benzimidazole with a yield of 80% within 12 hours [197]. Moreover, Aristolochia indica was used to synthesize spherical Ag NPs implicated as a catalyst for the oxidation of benzyl alcohol to benzaldehyde; however, no oxidation reaction occurs at room temperature because secondary metabolites on the surface of nanoparticles retard the reaction. After heating the synthesized nanoparticles above 900°C, the stabilizing/capping agents are removed from the surface of nanoparticles and oxidation reaction occurs with a rate constant of 0.82 × 10^3 M min^-1 followed by zero-order kinetics [198]. Similarly, Ag NPs synthesized using the stem extract of Piper chaba were found to be in almost spherical shape with a mean size of 19 nm by TEM analysis and reduction of 4-nitrophenol within 9 minutes [59].

7.9. Dye Degradation Activity. The presence of colored dyes in the discharged effluent reduces the penetration of light in the water bodies disturbing the photosynthesis and development of aqua communities [204]. Such dyes and their derivatives are particularly toxic, carcinogenic, and non-degradable, causing various complications such as skin infections and hepatic and kidney dysfunction and even damaging the living organism’s nervous system [205]. Over the past few decades, various physical and chemical processes such as ultraviolet radiation [206], adsorption [207], electrochemical reduction [208], and advanced oxidation processes [209] have been developed to remove or degrade dyes in water. Most of these processes suffer from problems such as high prices and complex procedures, so it is critically necessary to create an environmentally sustainable and cost-effective solution for the deterioration of dyes in wastewater. The catalytic degradation of organic dyes using biologically synthesized nanoparticles can be employed [210]. The migration of electrons between Ag NPs and dye molecules plays a vital role in the degradation of dyes [211, 212].

The green synthesized nanoparticles using Ekebergia capensis showed good degradation activity against Allura red in less than 45 min and may involve electron relay mechanism [213]. The green synthesis of Ag NPs from Terminalia arjuna leaf exhibited strong degradation of the methyl orange (86.68%), methylene blue (93.60%), and Congo red (92.20%) by completing the reduction reaction within 20 minutes [11]. Ag NPs synthesized using Vaccinium macrocarpon fruit extract had spherical shape with size ranging from 15 to 30 nm as a catalyst for complete degradation of methyl orange, methylene blue, Rhodamine B, and Congo red within less than 300 seconds in the presence of sodium borohydride [214]. The biosynthesis of Ag NPs using Polygonum hydropiper extract and dye degradation effectiveness monitored for reduction of methylene blue in the presence of sodium borohydride showed a very fast reaction that changes the methylene blue into leucocyanide blue (colorless) within 13 minutes. However, sodium borohydride alone is unable to degrade the methylene blue as it is a strong reducing agent [215]. Table 9 shows the morphology of green synthesized Ag NPs and their dye degradation activity on different dyes.

7.10. Metal Sensing Activity. Heavy metals are naturally occurring materials present on the earth’s surface, with much chemical degradation and human consumption arising from anthropogenic practices. Within plants and animals, the basic heavy metals perform oxidative and physiological roles [204, 219]. However, heavy metals have been reported to deteriorate the cellular organelles and components [220] within biological systems. Metal ion was observed to interfere with DNA, and nuclear proteins disrupt DNA and shifts in conformation [221]. There are several conventional methods to examine heavy metal concentration such as neutron activation analysis (NAA), atomic absorption spectroscopy (AAS), inductively coupled plasma mass spectroscopy (ICP-MS), and X-ray fluorescence spectrometry (XRF) [222], but such approaches must be supplemented with additional chromatographic techniques that are costly and time-consuming. Colorimetric metal sensing can be achieved in situ without any additional instruments using plasmonic Ag NPs. Ag NPs utilized in visual identification have characteristic SPR that is sensitive to the shape, size of the nanoparticle, and their local environment. This makes them a very suitable candidate for various optical sensing and detection applications such as heavy toxic metal sensing. The sensitivity of the nanoparticle towards the local environment depends on the morphology of the nanoparticles with rod shape (especially longer rods) and core shell (especially with thin metal shell) structure yielding a better SPR response monitored by using a UV-Vis spectrometer [223].

Apart from this, Ag NPs synthesized from various plant extracts have been used for optical sensing of various heavy metal ions. Camellia sinensis leaves were used to synthesize Ag NPs for the detection of Cu2+ and Pb2+ ions [224]. Ag
NPs were synthesized using leaves of *Amomum subulatum* for detection of Zn$^{2+}$ in solution in the concentration range from $1 \times 10^{-5}$ to $8 \times 10^{-5}$ [225]. Ag NPs were synthesized using the aqueous extract from leaves of *Anancadium occidentale* for optical sensing of Cr$^{3+}$ ions [226]. Ginkgo biloba leaf extract was used to synthesize Ag NPs as a fluorescence sensor for Cr$^{3+}$ [139]. Table 10 shows the morphology of plant-mediated synthesis of Ag NPs, their metal sensing activity, and their detection limit.

### 7.11. The Hazardous Effect of Ag NPs in the Aquatic Biotic System

The use of Ag NPs in various potential applications is radically increasing day by day; however, numerous hazardous effects are only slowly recognized and evaluated in the aquatic biotic system [232, 233]. A huge amount of Ag NPs is synthesized every year by green and chemical as well as physical approaches. The green synthesized Ag NPs have lower toxicity than chemically synthesized nanoparticles. However, inappropriate disposal of nanoparticles in the environment resulting from either release during production and use or release after disposal of nanoparticle-containing products causes environmental fate due to aggregation, transformation, persistence, and sequestration leading to accumulation in the food chain and their consequences on human health [232, 234]. Different aquatic organisms directly face the toxicity of Ag NPs. Toxicity of Ag NPs in the aquatic system includes some test guidance such as acute immobilization test, acute toxicity test, and growth inhibition test estimated on median lethal concentrations/lethal concentration of Ag NPs [13]. Ag NPs induce toxicity, which largely depends on the particle surface properties, size, and exposure time which can be explained by the number of silver ions released from nanoparticles [235]. Table 11 shows the morphology of Ag NPs and their toxicity in different aquatic species.

### 8. Conclusion

Over the past decade, because of the diverse utility, Ag NPs have been more researched and synthesized. Green synthesis provides an ecofriendly one-pot strategy to synthesize biocompatible Ag NPs with a wide range of practical applications easily and cost effectively. The challenging parts of green synthetic strategy are method optimization to get the desirable size and stability of synthesized nanoparticles besides these identification of bioreducing secondary metabolites for silver salt that acts as either reducing agents or stabilizing and capping agents or both. Stronger secondary metabolites from plant sources play an important role in determining the morphology and stability of synthesized Ag NPs. Plant-mediated synthesis of Ag NPs has good biocompatibility and provides multifunctional applications in biological systems as well as catalysis and heavy metal sensing. In this study, we discussed the synthetic routes, characterization techniques, applications of plant-mediated Ag NPs, and their aquatic toxicity. Besides several advantages, there are some harmful effects of Ag NPs too, which are not covered extensively in this review.

### Abbreviations

- Ag NPs: Silver nanoparticles
- UV-Vis: Ultraviolet visible
- SPR: Surface plasmon resonance
- SERS: Surface-enhanced Raman scattering
- TEM: Transmission electron microscopy
- SEM: Scanning electron microscopy
- AFM: Atomic force microscopy
- DLS: Dynamic light scattering
- XRD: X-ray diffraction
- VSM: Vibrating sample magnetometer
- DNA: Deoxyribonucleic acid
- RNA: Ribonucleic acid
- ROS: Reactive oxygen species
- MIC: Minimum inhibitory concentration
- ZOI: Zone of inhibition
- MBC: Minimum bactericidal concentration
- SARS: Severe acute respiratory syndrome coronavirus
- CoV:
- HIV: Human immunodeficiency virus
- HBV: Hepatitis B virus
- IC$_{50}$: Half maximal inhibitory concentration
- MNTD: Maximum nontoxic dose
- TCID$_{50}$: Median tissue culture infectious dose
- DMSO: Dimethyl sulfoxide
- FCC: Face-centered cubic
- MBC$_{50}$: Half minimum inhibitory concentration
- MFC: Minimum fungicidal concentration
- BSA: Bovine serum albumin
- WHO: World Health Organization
- MTI: 3-[4,5-Dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide
- LC: Lethal concentration
- LC$_{50}$: Median lethal concentration
- NAA: Neutron activation analysis
- AAS: Atomic absorption spectroscopy
- ICP-MS: Inductively coupled plasma mass spectroscopy
- XRF: X-ray fluorescence spectrometry

### Data Availability

No data were used to support this study.

### Conflicts of Interest

The authors declare that they have no conflicts of interest.
Authors’ Contributions
All authors contributed equally to this study.

References


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W. R. Rolim, M. T. Pelegrino, B. de Araújo Lima et al., "Green tea extract mediated biogenic synthesis of silver nanoparticles: characterization, cytotoxicity evaluation and..."


[195] X. Zuo, K. Chang, J. Zhao et al., “Bubble-template-assisted synthesis of hollow fullerene-like MoS 2 nanocages as a...


[233] J. N. Smith, D. G. Thomas, H. Jolley et al., ”All that is silver is not toxic: silver ion and particle kinetics reveals the role of silver ion aging and dosimetry on the toxicity of silver nanoparticles,” *Particle and Fibre Toxicology*, vol. 15, no. 1, p. 47, 2018.


