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Trending Aspects of Green Synthesis of Silver Nanoparticles and Their Biomedical Applications: A Review

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Abstract

For the past few decades, researchers have been fascinated by nanotechnology and nanoparticles due to their unique physico-chemical characteristics, such as increased surface area, reduced size, and improved reactivity, making them useful for various industrial, scientific, and medicinal applications. Silver nanoparticles are widely used, particularly in the biomedical sciences, since they are less toxic than other metal nanoparticles, meaning that they do not harm healthy human or host cells. They are also non-reactive, incredibly stable, and biocompatible. Silver nanoparticles (Ag NPs) are promising tools for targeted drug therapy against a range of bacterial, fungal, and viral components. Ag NPs are also powerful anticancer agents. A contemporary research trend is focused on promoting approaches that are benign and reducing the use of chemical-based technologies. For nanoparticles that are often used in laboratories and industry, green synthesis is seen as a crucial tool to lessen the harmful consequences of existing methods, such as the use of hazardous chemicals, high energy consumption, time required, expense, etc. Scientific groups greatly value the use of natural materials that are environmentally benign and biodegradable. Ag NPs produced using green methods are more environmentally friendly, biocompatible, stable, and less toxic than those made using chemical or physical methods. The importance of living entities in reducing and stabilizing silver ions is highlighted in this paper, which examines recent developments in green synthesis techniques.
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Keywords: Biomedical applications, green synthesis, Nanotechnology, Nanoparticles, silver nanoparticle (Ag-NPs)

INTRODUCTION

Nanotechnology gives promising solutions in a variety of fields by making our routine work simple and easy. Excellent physical and chemical properties, size, shape, color, etc. of nanoparticles have fascinated many researchers nowadays. Small size (1–100 nm) of these particles has a large surface-to-volume ratio, diversity in shape, size, and structure, high reactivity, absorption, etc. [1]. These unique properties of nanoparticles have replaced many bulk particles in biomedical science, industry, pharmaceutical, agriculture, and environmental fields [2]. Silver, gold, copper, zinc, iron, magnesium, manganese, and calcium are among the metal nanoparticles that have popularly became topics of discussion over past two decades as these have high catalytic properties, high conductivity, optical properties, light scattering properties, etc. [3]. Silver nanoparticles (Ag NPs) alone have culminated into great medicinal properties in the field of biomedical sciences. Ag NPs have been

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reported to achieve targeted drug delivery, which makes them more efficient for antibiotics rather than conventional drugs. Along with drug delivery silver has good antimicrobial, anti-cancer, wound healing, and anti-diabetic properties [4]. The synthesis and characterization of metal nanoparticles in general can be done via chemical, physical biological, or green methods [5–6]. However green methods of synthesis are kept on the upper edge these days because they are single-step processes, eco-friendly, bear a low cost, and involve major living resources like bacteria, algae, plants, and fungi [5, 7]. In green methods, various phytochemicals present in bioactive materials help in reducing bulk particles into metal nanoparticles. Many reports are there to claim higher biocompatibility of green synthesized Ag NPs than those chemically and physically synthesized nanoparticles. Ag NPs are found widely useful in medical sciences as they are less toxic, easily available and potentially safe. They have wide range of spectrum against many species of microbes, which make their anti-microbial action more effective than conventional drugs. Ag NPs are found to be useful in cancer treatment as they can be oriented at specific location, without causing any harmful effect of healthy cells. Ag NPs were used in wound healing, dentistry, antidiabetic, and anti-inflammation [8–9].

This review paper aims to present current prospects of green synthesis and biomedical applications of Ag NPs. Systematic approaches in green synthesis will be presented with detailed outcomes and applications.

GENERAL SYNTHESIS OF NANOPARTICLES

Two approaches are used to synthesize nanoparticles, i.e., top-down and bottom-up approaches [5–6, 10]. In top-down approaches, bulk materials are reduced to smaller size to produce nanoparticles. However, bottom-up methods work from atoms to cluster to nanoparticles. The simple representation of these approaches is depicted in Figure 1.

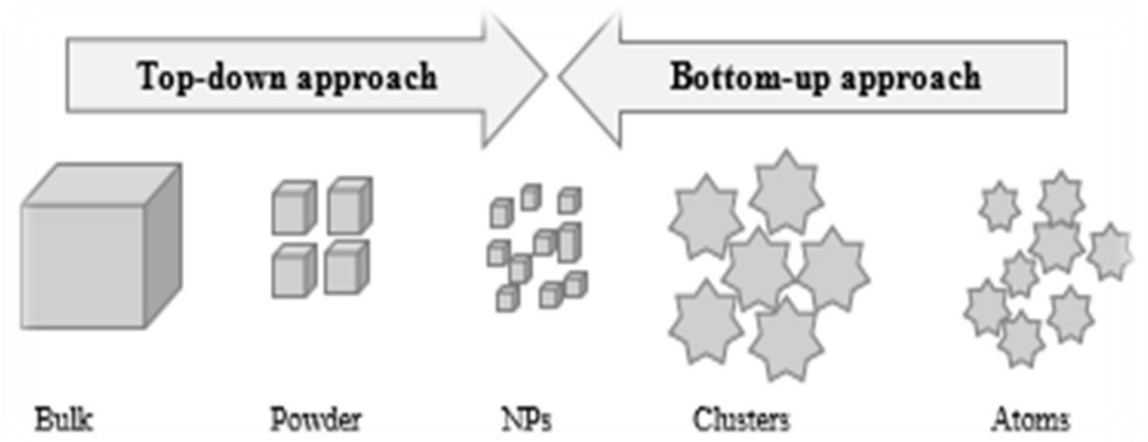

Figure 1. General Synthesis Approaches of Nanoparticles.

Top-Down Approach

In this approach, larger material or molecules are decomposed into smaller molecules or even transform into nanoparticles. Mechanical milling, lithography, laser ablation, sputtering, thermal decomposition etc. are included in top-down approach [5, 11–12]. The top-down approach has advantages, such as providing good control over shape and has drawbacks, such as using higher energy use, difficulty to achieve small particles, multiple stages used to get small particles due to that overall complexity increase and higher waste generation.

Bottom-Up Approach

A bottom-up approach is the buildup of materials from atoms to cluster to nanoparticles. Sol-gel, spinning, chemical vapor deposition, pyrolysis, biosynthesis or biological method etc. are included in

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bottom-up approach [5, 11–12]. A bottom-up approach has advantages like providing better control over structure, size and compositions, cost effectiveness, and low waste generation.

Methods of Synthesis of Nanoparticles

Chemical, physical and biological methods are used for formation of nanoparticles. In the physical method, materials are reduced in size by ultrasonication, microwave, electrochemical etc. In chemical methods, the major components are metal precursors, stabilizing, capping and reducing agents. Physical and chemical methods required toxic chemicals, time consumption, higher energy consumption, unfavorable conditions, etc., this is why biological or green methods are considered as superior [5, 13]. Major division can be detailed as follows:

Physical Methods

- Ball milling.
- Laser ablation.
- Physical vapour deposition.
- Arc Discharge method.
- Electronic beam lithography.

Chemical Methods

- Sol-Gel method.
- Chemical vapour deposition.
- Co-Precipitation.
- Pyrolysis.

Micro Emulsion Method

- Biological or green methods.
- Using plants and their extract.
- Using microorganisms.
- Using enzyme, algae.

BIOLOGICAL OR GREEN METHODS SYNTHESIS

In traditional chemical and physical methods, reducing agents involved in reduction of ions, and stabilizing agents used to prevent undesired agglomeration of produced nanoparticles, which results in risk of toxicity to environment. However, green synthesis or biosynthesis does not require expensive, harmful and use of toxic chemicals. These methods also provide alternative routes to chemical and physical methods [14]. Synthesis can be done in one step using bio sources, such as bacteria, yeast, algae, plants and their products. They have natural properties which are required, such as reducing, stabilizing and capping agents. The green synthesis process is summarized as follows obtaining an extract of bio resources, combining it with a metal precursor under conditions, reducing the metal particles, and separating the nanoparticles from the solution. Figure 2 provide detail procedure for green synthesis of Nanoparticles [15].

Green Synthesis of Silver Nanoparticles

Plants extract, bacteria, fungi, algae, yeast etc. are the various natural sources used for synthesis of nanoparticles. Phytochemicals present in plants, such as vitamin C, flavonoids, acids, volatile oils, Terpenoids, carbohydrates, lipids, oxalic acid, tannins, saponins etc. are act as stabilizing, reducing, or capping agents in green synthesis of nanoparticles [16].

Green Synthesis of Ag-NPs Using Plants Extract

Compared to microorganisms, plants have been exhaustively used because plants phytochemicals show grater reduction and stabilization in synthesis. Tulsi, orange, tea, sandalwood, apple, coriander etc. are reported bio sources for the synthesise of silver nanoparticles. Ag-NPs using fresh leaf of tulsi, produced Ag-NPs in range of 3–20 nm. In tulsi leaf, phytochemicals, such as alkaloids, glycosides, tannins, saponins, aromatic compounds etc. are naturally present for stabilizing, reducing or, capping agents [17]. *Citrus sinensis* extract act as reducing, stabilizing or, capping agents in the formation of Ag-NPs of 8–33 nm [18]. By using plants extract and silver salts solution, silver nanoparticles can be synthesised and synthesized particles are characterized by various characterization techniques, such as UV-Vi's spectrum, XRD, EDX, SEM, FTIR etc. Detailed literature survey has been summarized in Table 1.

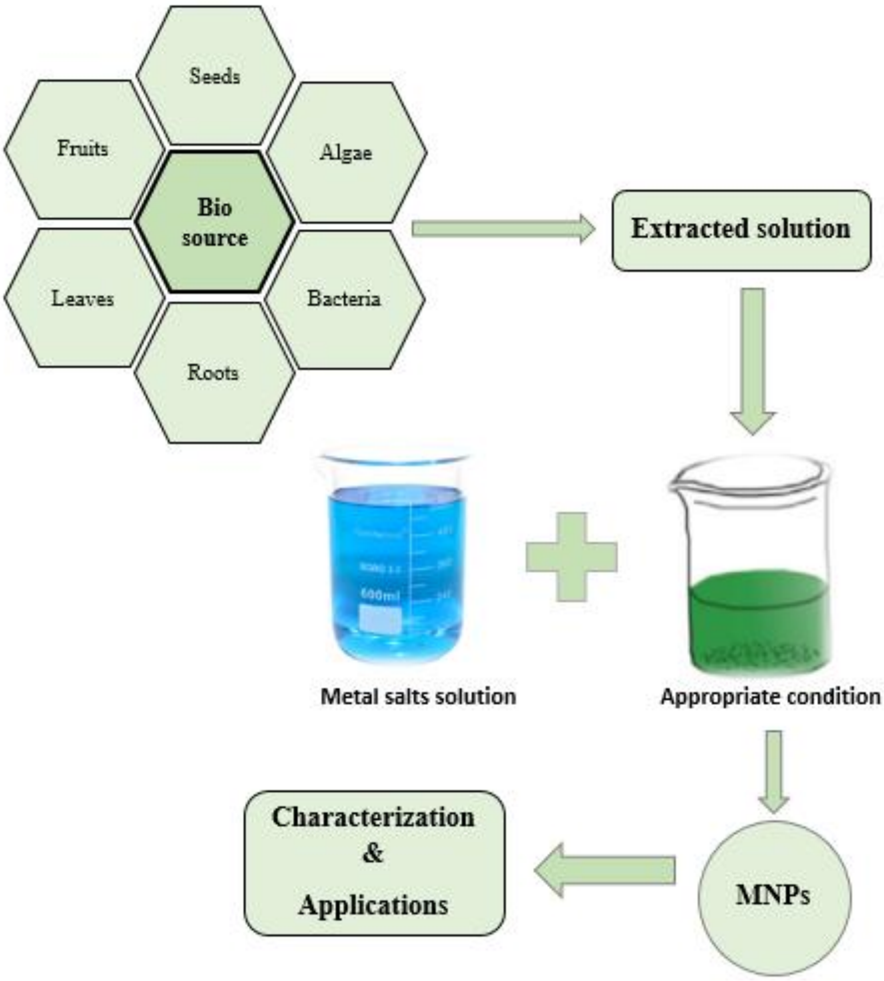

Figure 2. Representing the Green Synthesis of Nanoparticles.

Table 1. Various Plant Resources with Characterization Methods, Size and Shape.

S. N.	Name of Plant	Parts of Plant	Characterization Methods	Phytochemicals Present in Plants	Size of Ag-NPs	Shape of Ag-NPs	Reference
1	*Ocimum tenuiflorum*	leaf	UV-Vis, TEM, XRD, FTIR	Alkaloids, glycosides, tannins, saponins, aromatic compounds	3–20 nm	Spherical	[17]
2	*Citrus sinensis*	Peels extract	UV-Vis, TEM, FTIR, XRD, FESEM, EDX	Vitamin C, flavonoids, terpenoids, acids, volatile oils	8–3 nm	Spherical	[18]

3	*Coriandrum sativum*	leaf	UV-Vis, TEM, FTIR, XRD	Carotene, thiamine, riboflavin, niacin, oxalic acid, sodium	8–75 nm	Spherical	[19]
4	*Mimusops elengi*	seed	UV-Vis, TEM, SEM, FTIR, XRD	Ascorbic acid, gallic acid, pyrogallol, resorcinol	12.8–30.48 nm	Spherical	[20]
5	*Syzygium cumini*	Seeds	UV-Vis, SEM, XRD, FTIR, DLS, HPLC	Gallic acid, p-coumaric acid, quercetin, 3,4-dihyroxybenzoic acid	40–100	Irregular Spherical	[21]
6	*Capsicum annuum*	leaf	UV-vis, TEM, FTIR, SAED, XRD, XPS, CV, DP	Proteins/enzymes, polysaccharides, amino acids, vitamins	10–12 nm	Spherical	[22]
7	*Annona squamosa*	Young leaf	UV-vis, XRD, TEM, FTIR, EDS	Glycoside, alkaloids, saponins, flavonoids, tannins phenolic compounds, phytosterols	20–100 nm	Spherical	[23]
8	*Hibiscus moscheutos*	Leaf	UV-vis, TEM, FTIR, XRD, SAED	Proteins, vitamin C, organic acids	13 nm	Spherical	[24]
9	*Origanum vulgare*	leaves	UV-vis, FESEM, FTIR, XRD, DLS	NA	FESEM (63–85 nm), DLS (136 nm)	Spherical	[25]
10	*Rhizophora mangle*	leaf	UV-vis, FTIR, XRD, AFM	Alkaloids, flavonoids, polyphenols, terpenoids	60–95 nm	Spherical	[26]

Green Synthesis of Ag-NPs Using Algae

Algae grow rapidly, they are easy to handle and a few times faster than plants. Algae are commonly used as bio sources in green synthesis as they have antioxidants, pigments, carbohydrates, fats, proteins, various phytochemicals, etc. These phytochemicals help in reducing metals. This reduction process is considered a multiple-phase process having an activation phase, formation of nanoparticles, and finally growth of nanoparticles. The Biosynthesis of NPs from algae could either be intra-cellular or extra-cellular depending on the place of nanoparticles formed. In the intra-cellular method, biosynthesis of NPs occurs inside the algae cell. For extra-cellular synthesis, metal ions are attached to the surface of algae cells. *Turbinaria ornate*, *Sargassum muticum*, *sargassum polycystin*, *Gracilaria edulis*, *Gelidium amansii*, *Oscillato riawillei*, *Spirulina platensis*, etc. are used for synthesizing Ag-NPs with different shapes and size range [27]. Ag-NPs have been synthesized by using fresh green algae, *chlorella vulgaris*. Synthesized Ag-NPscharcaterized by using FTIR, FESEM, XRD, etc. FESEM confirms the spherical shape of Ag-NPs with a size of around 55.06 nm. XRD showed a crystalline nature with an average particle size of 61.89 nm [28]. Further reports are summarized in Table 2 and biosynthesis of Ag NPs is demonstrated in Figure 3.

Table 2. Different Types of Algae, Characterization of Synthesized Ag-NP.

S. N.	Type of Algae	Intra/Extracellular	Characterization Methods	Size of Ag-NPs	Shape of Ag-NPs	Reference
1	*Sargassum polycystic*	Extracellular	UV-Vis, XRD, FTIR, SEM and TEM	7 nm	Spherical	[29]

2	*Turbinaria ornata*	extracellular	UV-Vis, EDS, FE-SEM, XRD and FTIR	22 nm	Spherical	[30\
3	*Sargassum muticum*	extracellular	UV-Vis, XRD, FTIR, SEM and TEM	43–79 nm	Spherical, crystalline	[31]
4	*Gracilaria edulis*	extracellular	UV-Vis, SEM, TEM, XRD, FTIR	12.5–100 nm	Spherical	[32]
5	*Oscillate riawillei*	extracellular	UV-Vis, EDS, FTIR, SEM	10–25 nm	Spherical	[33]
6	*Sargassum ilicifolium*	extracellular	UV-Vis, SEM, XRD and FTIR	33–40 nm	Spherical	[34]
7	*Padina pavonica*	extracellular	UV-Vis, SEM, XRD and FTIR	10–72 nm	Spherical	[35]
8	*Padina gymnospora*	extracellular	UV-Vis, TEM	25–40 nm	Spherical	[36]
9	*Gracilaria dura*	extracellular	EDX, XRD, SAED, TGA, TEM, and TGA	6 nm	Spherical	[37]
10	*Acanthophora specific*	extracellular	FTIR and XRD	81 nm	Cubic	[38]

Figure 3. Biosynthesis of Ag-NPs using Algae Extract.

Green Synthesis of Ag-NPs Using Fungi

Fungi has a higher potential for synthesizing many compounds that can be used in different applications. Fungi are widely used as reducing, capping, or stabilizing agents. Fungi can be used to produce nanoparticles with controlled size and morphology. They have an advantage over microorganisms as they produce large quantities of proteins and enzymes, some of these can be used for fast and sustainable synthesis of nanoparticles [39].

Like algae biosynthesis of nanoparticles using fungi may be intracellular or extracellular. Sometimes extraction of nanoparticles requires chemical treatments, centrifugation, and filtration or simple filtration, membrane, filtration, gel filtration, etc. In this context, Ag-NPs were synthesized using *Ganoderma applanatum* fungi and silver nitrate. The presence of Ag-NPs of 20-25 nm was observed by color change. Further confirmed by UV-Vis (420 nm), FTIR, PXRD (Crystal structure), SEM, etc. [40]. Other fungi can be used to synthesize NPs, such as *Fusarium oxysporum*, *Verticillium, Aspergillus fumigatus, Penicillium fellutanum,* etc. [16]. Table 3 details the fungus-mediated synthesis of Ag NPs.

Table 3. Fungus-Mediated Synthesis of Ag-NPs.

S. N.	Type of Fungi	Characterization Methods	Size of Ag-NPs	Shape of Ag-NPs	Reference
1	*Ganoderma applanatum*	UV-Vis, FTIR, PXRD, SEM	20–25 nm	Spherical	[40]
2	*Fusarium oxysporum*	UV-vis, TEM, FTIR	5–50 nm	Spherical and a few triangular	[41]
3	*Verticillium*	UV-vis, TEM, SEM, EDX	12–25 nm	Spherical	[42]
4	*Aspergillus fumigatus*	UV-vis, TEM, XRD	5–25 nm	Spherical and few triangular	[43]
5	*Penicillium fellutanum*	UV-vis, TEM	5–25 nm	Spherical	[44]
6	*Aspergillus flavus*	UV-vis, TEM, FTIR, XRD	Approx. 8.92 nm	NA	[45]
7	*Fusarium semitectum*	UV-vis, TEM, FTIR, XRD	10–60 nm	Spherical	[46]
8	*Alternaria alternata*	UV-vis, TEM, SEM, FTIR, EDX	20–60 nm	Spherical	[47]
9	*Rhizopus stolonifer*	UV-vis, TEM, SEM, FTIR, AFM	3 & 20 nm	Spherical	[48]
10	*Phanerochaete chrysosporium*	UV-vis, TEM, FTIR, AFM, TLC	34–90 nm	Spherical and oval	[49]

Note: *NA-Not Available.

Green Synthesis of Ag-NPs Using Bacteria

Synthesis of nanoparticles using bacteria is economic, rapid scale up, and environmental caring. The size and shape of Ag-NPs using microbes depend on the interaction of silver ions with bacteria. The present enzymes in microbes are responsible for the reduction of silver ions in the synthesis process. Silver nanoparticles were obtained using *bacteria T10 strain* isolated from an unusual environment. Synthesized Ag-NPs were characterized by UV-Vis, SEM, FTIR, and XRD. These NPs were spherical and size in the range of 46–52.7 nm [50]. Ag-NPs synthesized with cultural supernatant bacteria *Pseudomonas rhodesiae* showed a diameter of 20-100 nm and, nanocrystal shape [51]. Ag-NPs were synthesized using *Escherichia coli*, *Exiguobacterium aurantiacumm*, and *Brevundimonas diminuta* by Saeed et al. using different parameters i.e. pH, temperature, concentration, the findings of optimization study show that maximum production of Ag-NPs was carried out at 9 pH, 37°C, 1mM concentration of silver nitrate. And researchers also claim that all three bacteria have excellent antimicrobial properties [52].

Biomedical Applications of Ag-NPs

Since ancient times, silver has been utilized to heal illnesses and it has microbiological characteristics. Among the metals, silver has emerged as the top priority in the biomedical sciences because silver has its own antiviral, antibacterial, antifungal, anticancer, antidiabetic, and wound healing properties (Figure 4). Ag-NPs are utilized to treat cancer and other common and hazardous disorders, and they offer promising alternatives for reaching target drug delivery. Compared to bulk silver, Ag-NPs are more chemically reactive, have a greater surface-to-volume ratio, are highly biocompatible, and are less poisonous [53–54].

Figure 4. Biomedical Applications of Ag-NPs.

ANTIBACTERIAL APPLICATIONS OF SILVER NANOPARTICLES

Both gram-positive and gram-negative bacteria are susceptible to Ag-NPs. Ag-NPs exhibit antibacterial qualities against a range of organisms, *including pseudomonas, Staphylococcus, Bacillus cereus, Bacillus subtilis, and E.coli.* The size of the nanoparticles determines the antibacterial characteristics of Ag-NPs; when the size of the NPs decreases, the antibacterial properties rise because smaller NPs attack the bacterial cell wall or enter the bacterial cell directly [55]. Since plants have antibacterial qualities and act as a natural capping agent, the biocompatibility of plant-based produced Ag-NPs is higher, making the particles' antibacterial qualities even better [56]. *Spinacia oleracea* was used to create Ag-NPs by Miranda et al., who also found that triangular Ag possesses strong antibacterial qualities against *E. coli* bacteria [57]. The tentative mechanism for the same can be explained by Ag creating holes in the cell wall that allow cellular material to flow out, or Ag entering the cell and disrupting its functions via denatured ribosomes, inhibiting enzymes, damaged DNA, and ultimately causing cell death [58–59]. A detailed literature survey on the antibacterial activities of Ag NPs is presented in Table 4.

Table 4. Antibacterial Properties of Silver Nanoparticle.

S. N.	Biological Resources	Size (±0.5 nm) & Shape	Bacteria Species	Zone of Inhibition in mm (±0.05 mm)	Antibacterial action of Ag-NPs	Reference
1.	*E. camaldulensis*	43 nm, spherical shape	*E. coil*	8	Produced ROS, Penetration of NPs to cell, disturb cell function	[56]
2.	*E. camaldulensis*	43 nm, spherical shape	*Bacillus Subtilis*	13	Change in bacterial membrane permeability releases lipopolysaccharides, membrane proteins, and intracellular biomolecules, and dissipates proton motive force in the plasma membrane, producing ROS causes oxidative cell damage.	[56]
3.	*Lysiloma acapulcensis*	5 nm, spherical and quasi-spherical shape	*P. aeruginosa*	15	Interact with the bacterial cell membrane, disrupt the inter organelles, such as enzymes and DNA	[60]
4.	*Talaromyces purpureogenus*	49 nm, cubic crystal morphology	*Listeria monocytogenes*	13	Cell wall and membrane damage, generation ROS species, protein and DNA interface	[61]
5.	*Talaromyces purpureogenus*	49 nm, cubic crystal morphology	*Shigella dysenteriae*	18	Target cellular structure and disturb the cellular process	[61]
6.	*Moringa oleifera*	9 nm, spherical shape	*Escherichia coli*	17	Produced ROS, entered a cell, disturbed cellular process	[62]
7.	*Salvia officinalis*	17.16 nm, cubic shape	*A. baumannii*	19.47	Inhibit certain cytochrome in the membrane	[63]
8.	*Salvia officinalis*	17.16 nm, cubic shape	*Enterobacter cloacae*	22.09	Release of Ag^+ ions which penetrate bacteria cell walls, cause cellular damage	[63]
9.	*Cucumis prophetarum*	30 nm, irregular granular	*Staphylococcus aureus*	18	Produced ROS, entered a cell, disturbed cellular process	[64]
10.	*Cucumis prophetarum*	30 nm, irregular granular	*Salmonella typhi*	20	Ag-NPs are Attached to the membrane and inhibit cell wall synthesis but cannot maintain metabolic activity and cellular upkeep.	[64]

11.	*A. Wilhelmsen*	4.91 nm, spherical shape	*Staphylococcus aureus*	21	Absorption of Ag^+ which leads to reduced intracellular ATP levels and impaired DNA replication	[65]
12.	*A. Wilhelmsen*	4.91 nm, spherical shape	*Staphylococcus epidermidis*	20	The release of Ag^+ which is attached to the bacteria cell wall, disturbed cellular functions.	[65]

Anti-Cancer Applications of Silver Nanoparticles

On average, 15% of individuals die from cancer each year, making it one of the most lethal and hazardous diseases [66]. The condition known as cancer is typified by aberrant metabolism and signaling, which permits unchecked cell division and survival [67]. In the past, there were several cancer treatments and medications, such as chemotherapy and radiotherapy, but they had drawbacks, such as long-term side effects that damaged good tissues in addition to diseased cells, which may or may not be curable [68]. Ag-NPs' reduced size and better surface-to-volume ratio make them a viable way to transport drugs to the intended location [69]. Mousavi et al. synthesized silver nanoparticles (Ag-NPs) using plant extract from *Artemisia turcomanica*. They then used the MTT assay to compare the anticancer properties of commercial and biosynthesized Ag-NPs against gastric cancer cells (AGS) and normal fibroblast cells (L-929) to determine which had superior anticancer properties. Mousavi et al. investigate how dosage, duration, and concentration affect the increase in apoptosis observed in the instance of biosynthesized Ag-NPs [70]. The generation of ROS, which impairs mitochondrial functioning, damages DNA, activates caspases, damages cellular processes, and ultimately results in cell death, is the mechanism behind anticancer characteristics [69, 71]. Table 5 further demonstrates the reports published on the anticancer activity of silver nanoparticles.

Table 5. Anticancer Properties of Silver Nanoparticles.

S. N.	Biological Resources	Size (± 0.5 nm) & Shape	Cancer Cell Line	Mode of Action of Ag-NPs	Reference
1.	*Fusarium nygamai*	28 nm, cubic shape	HepG2	Inducing apoptosis, disrupting mitochondrial function	[72]
2.	*Fusarium nygamai*	28 nm, cubic shape	MCF7	Combine with DNA and proteins, change their physicochemical characteristics, causing unfavorable changes in their chromatin structure,	[72]
3.	*Cucumis prophetarum*	30 nm, irregular granular	MDA-MB-231	Combine with DNA and proteins, change their physicochemical characteristics, causing harmful changes in their chromatin structure.	[64]
4.	*C. parvula*	79 nm, cubic	A549	Interacted with the cell membrane, destroying the cell membrane and inhibition of the cell line	[72]
5.	*C. parvula*	79 nm, cubic	HT-2	Production of ROS, causing DNA damage, mitochondrial dysfunction, and apoptosis via caspase activation, disturbs cell cycle progress and modulates inflammatory and angiogenic pathways.	[73]

6.	*Photinia Glabra*	39.2 nm, spherical shape	Eca-109	Inducing oxidative stress and apoptosis by producing ROS, mitochondrial dysfunction	[74]
7.	Actinobacterial strain SF23	13.2 nm, spherical shape	MCF-7	Ag-NPs damage cell membranes, release intracellular molecular, and lead to LDH leakage, which leads to necrosis	[75]
8.	Actinobacterial strain SF23	13.2 nm, spherical shape	RAW 264.7	Ag-NPs damage cell membranes, release intracellular molecular and lead to LDH leakage, which leads to necrosis	[75]
9.	*Tridax procumbens*	20.2 nm spherical shape	A459	Interacted with the cell membrane, destroying the cell membrane and inhibition of the cell line	[76]
10.	*Allium cepa L*	155.2 nm, spherical shape	HT-29	Provoke DNA damage by ROS, causes apoptotic cell death	[77]
11.	*Allium cepa L*	155.2 nm, spherical shape	SW620	Produced Oxidative stress, cause oxidative damage	[77]

Antifungal Applications of Silver Nanoparticles

Because fungi grow so quickly, fungal illnesses are the most prevalent issue in the biomedical sciences. Creating effective fungicides using traditional fungicides seems to be challenging. Against most species, Cu NPs exhibit strong antifungal activity [78]. Even at low concentrations, Ag-NPs exhibit outstanding antifungal activity against practically all fungal species. *Penicillium italicum, Rhizoctonia solani, Fusarium oxysporum, Alternaria alternata, Curvularia lunata, Aspergillus, yeast,* and *Candida albicans* are all susceptible to the fungicidal effects of Ag-NPs [79]. To evaluate the antifungal characteristics of Ag-NPs made from neem leaves against *Alternaria solani*, which causes disease in tomato plants, Ansari et al. observed that a 50-ppm concentration caused 70–100% inhibition, which disrupts the cell membrane and stops the budding process [80]. Although the precise mechanism of Ag-NPs' antifungal capabilities is yet unknown, they likely produce ROS species, disrupt cell membranes and cell walls, damage DNA and protein chains, and prevent the formation of biofilms and spore germinations [81–82]. A few more research reports are discussed in Table 6.

Table 6. Antifungal Properties of Silver Nanoparticles.

S. N.	Biological Resources	Size (±0.5 nm) & Shape	Fungal Species	Zone of Inhibition in mm (±0.05 mm)	Antifungal Action of Ag-NPs	Reference
1.	*Avena fatua Extract*	25 nm, cubic structure	*Fusarium oxysporum*	15.5	Ag-NPs Disrupt DNA replication and inactivate the functions of cellular proteins and enzymes, preventing the normal functioning of Fungi.	[83]
2.	*Coriander sativum*	29.24 nm, cubic structure	*Fusarium solani*	90	Ag-NPs tend to agglomerate around the cell membrane,	[84]

					generating ROS, that deactivate the cellular enzymes causing cell dehydration and the loss of nutrients	
3.	*Coriander sativum*	29.24 nm, cubic structure	*Rhizopus stolonifer*	35.08	Release Ag^{+} causing malfunctions and leading to cell apoptosis	[84]
4.	*Jasminum nudiflorum*	13 nm, cubic structure	*A. longipes*	60	Mycelial cell membrane leakage, lipid peroxidation, inhibition of respiratory chain dehydrogenase activity, and disruption of the mycelium nucleus, resulting in the death of the fungi	[85]
5.	*Cedrela odorata*	19.80 nm, spherical structure	*Fusarium circinatum*	11.38	Disrupting cell wall integrity, by formation of ROS generation, impairing mitochondrial function, and inhibiting spore germination and hyphal growth.	[86]
6.	*A. graecorum*	22 nm, spherical shape	*Candida albicans*	14	Penetrate ion in fungal cell walls and disrupt their membranes, leading to increased permeability and cell lysis	[87]
7.	*A. graecorum*	22 nm, spherical shape	*Candida glabrata*	18	Disturbed cellular process by entering in cell wall, increase permeability and cell lysis	[88]
8.	*Ganoderma applanatum*	20 nm, spherical shape	*Botrytis cinerea*	12	Change's structure and function of fungi cell, interact with DNA, its replication and protein synthesis	[88]
9.	*Ganoderma applanatum*	20 nm, spherical shape	*Colletotrichum gloeosporioides*	10.2	Disturbing cell membranes and inhibit fungal growth	[88]
10.	*Aspergillus sydowii*	12.2 nm, spherical	*Fusarium oxysporum*	4	Disturbing cell membranes and inhibit fungal growth by entering into cell wall	[89]
11.	*Melia azedarach leaf*	23 nm, cubic crystal	*Verticillium dahlia*	18	Reduced mycelial growth and spore germination	[90]

Other Biomedical Applications of Silver Nanoparticles

Ag-NPs exhibit outstanding antidiabetic qualities, including improving insulin sensitivity, reducing reactive oxygen species (ROS), increasing glucose uptake by controlling glucose transporter (GLUT) proteins, and influencing the activity of important enzymes involved in glucose metabolism, such as α-amylase and α-glucosidase, to control postprandial hyperglycemia [91–92]. Ag-NPs deliver drugs precisely and have a greater therapeutic index than traditional drugs because of their smaller size and higher surface to volume ratio [47]. By improving antibacterial qualities, decreasing inflammation, promoting angiogenesis and cell proliferation, boosting collagen production, and encouraging tissue renewal, Ag-NPs exhibit wound healing qualities more quickly [93].

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