



Biogenic Metallic Nanoparticles: Synthesis and Applications Using Medicinal Plants

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Abstract

In the last decade, the synthesis of nanoparticles is one of the most concerned fields in research due to their high applicability in various segments of science and technology, ranging from material science to biotechnology. The environmentalists have grown interests in the preparation of nanoparticles from the point of view of biological and environmental safety. As the physicochemical production of nanoparticles requires an extreme environments and toxic chemicals in a

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large quantity, green methods of nanoparticle synthesis employing biological sources are in vogue. Green fabrications of metallic nanoparticles are growing rapidly due to their eco-friendly nature and low cost. In the past decade, the field of nanobiotechnology has been employed rigorously for biosynthesis of metallic nanoparticles. Due to their spectacular biophysical properties and enrichment in biocompatibility, the metallic nanoparticles have significant impact on the food processing, biomedical, environmental, agricultural, and industrial areas. Due to availability of various biologically active compounds such as phenolic acids, saponins, tannins, terpenoids, flavonoids, and alkaloids, plants have promising medicinal significance. Medicinal plant extracts were widely utilized for green synthesis of metallic nanoparticles as stabilizing agents. In order to synthesize biomolecule-encapsulated metallic nanoparticles, metallic ions are reduced by phytochemicals present in plant extracts. The growth of multiple drug-resistant bacteria may be inhibited by biogenic metallic nanoparticles. The present chapter provides information on highly stable, biocompatible, environment friendly, and cost-effective approach for metallic nanoparticles synthesis using diverse medicinal plants and their applications as a powerful nanomedicine against multidrug-resistant pathogens.

Keywords

Nanomaterials · Green synthesis · Plant extract · Biogenicnanoparticles · Nanomedicine

Introduction

Nanoscience and nanotechnology research and development have progressed at an unparalleled rate in recent years. Nanotechnology is a branch of study that has only been around for a 100 years. Since Nobel Laureate Richard P. Feynman represented “nanotechnology” during the famous 1959 lecture “There’s Plenty of Room at the Bottom,” there have been numerous current breakthroughs in the field of nanotechnology. There is increasing anticipation that nanotechnology, when used in medicine, will lead to significant improvements in the disease detection and treatment. At the nanoscale, nanotechnology created a variety of extensive materials which possess at least one dimension <100 nm. Based on their general form these materials may be zero, one, two, or three dimensional. The significance of these materials established when scientists discovered that size may impact the physiochemical properties of substance such as optical properties. The nanoparticles (NPs) may be of various structure, shape. and size like irregular, flat, spiral, hollow, conical, tubular, cylindrical, or spherical. The development of such advanced technologies for the restoration of the environment is required, but with least environmental hazard (Khan et al. 2021). In the last decade, various nanoparticles have been reported to be synthesized and applied for different applications (Gupta and Gupta 2015; Gupta 2016). In the recent era, one of the greatest challenges to

environmentalists is to ensure sustainable development for future generations through the use of green chemistry principles as well as green engineering to manufacture nanomaterials (NMs) without toxic by-products. The incorporation of green chemistry principles into nanotechnology has received considerable attention globally. Nanotechnology applications are explored due to their ability to produce solutions for air and water management and mitigation. Environmental cleanup technologies have also become improved by application of nanotechnology. Green nanotechnology considers sustainability using variety of applications. Compared to existing sanitation technologies, nanoremediation implies a global reduction of contamination. Due to a variety of applications, large-scale manufacturing of NPs is required. As a result, extensive variety of commercial techniques has evolved to prepare metal NPs. However, a lot of such techniques employ harmful solvents or excessive energy. Therefore, green synthesis is considered as most prominent approach for NPs preparation due to environment-friendly nature, low toxicity, and better biocompatibility. Various NPs, metallic as well as nonmetallic, have been synthesized using plants and microorganisms such as magnetite NPs by magnetotactic bacteria and siliceous material by diatoms and radiolarians.

Multiple species of microorganisms were reported for the development of NPs such as CdS quantum dots by fungi, gold NPs by *Verticillium* sp. etc. (Koul et al. 2021). Nanoparticles have been synthesized by varieties of agriculture-based waste products like fruit seeds, wheat bran, rice bran, palm oil mill effluent, corn cob, and *Cocos nucifera* coir. Such agricultural wastes were rich in secondary metabolites like proteins, phenolics, and flavonoids which work as bioreductants for green synthesis of various NPs.

Silver nanoparticles have come out with top benefaction in variety of uses like nanomedicine, chemical sensing, cell biology, drug delivery, agriculture, cosmetics, textiles, food industries, photodegradation of dyes, antioxidants, and antimicrobial agents. Silver nanoparticles act as most promising antimicrobial agent (Mani et al. 2021). Various investigations were reported on antimicrobial potential of silver nanoparticles. Silver NPs are majorly utilized for therapeutic applications due to their high bioavailability, long-lasting activity, and target specificity. Metal NPs may be prepared using diverse methods, including biological, chemical, and physical methods. Drug delivery methods based on nanotechnology are paving the way for a new era in the pharmaceutical sector. Plant metabolites combined with metal nanoparticles may be able to deliver medications. Nanoscale particles are currently being used extensively in the development of new antimicrobial agents to treat harmful microbes due to their reactivity and effectiveness (Patra et al. 2018). The biological method for the creation of NPs using leaves, roots, and fruits has several advantages. Metal NPs have also been prepared from plant leaf extracts, seed, fruit, stem, and bark.

Various medicinal plants are utilized in the creation of nutritional and health care products as traditional medicine. During the conversion of silver ions to silver NPs, secondary metabolites from plants such as phenol and flavonoid act as capping, stabilizing, and reducing agents. Over the years, biologically generated AgNPs from medicinal plants have been extensively explored and analyzed. Nanoparticles

derived from medicinal plants are high in pharmacologically active chemicals and have been utilized in various industries, including health care, agriculture, food, textiles, cosmetics, and fashion (Zabin et al. 2022). As a result, a new era of nanomedicine is emerging, and medicinal plants are immensely employed in the production of metallic nanoparticles. The most beneficial method for metal NPs synthesis has been termed plant-mediated synthesis. Magnetic iron nanoparticles are particularly important among the nanoparticles synthesized because of their antioxidant, antibacterial, magnetic, and catalytic activity. The manufacture of iron NPs from various plant sources has been reported by a number of studies.

In light of growing concerns about toxicity and biosafety, scientists have synthesized a variety of medicinally important metal nanoparticles utilizing green chemistry strategy that is both environment friendly and economically effective compared to traditional chemical approaches (Barui et al. 2019). Different bioresource ingredients (e.g., plant, bacteria, fungus, etc.) have been discovered which are vitally important in creation and stabilization of green-synthesized metal nanoparticles. Despite the availability of several publications, the present chapter focuses on recent development of green-synthesized metal nanoparticles employing biogenic materials for a variety of applications.

Biogenic Synthesis of Nanoparticles

Green chemistry principles motivate researchers to create biologically based synthetic methodologies, with enzymes, microbes, and plant extracts playing a key role in nanoparticle creation. Nanoparticles are often made by various physical and chemical methods which are expensive as well as hazardous to the environment, as they entail the use of dangerous and poisonous compounds that can cause a variety of biological dangers. In general, the techniques for nanoparticle synthesis are “top to bottom” approach and a “bottom to up” approach. Chemical reduction is a prevalent strategy for NPs synthesis using specialized ablations such as sputtering, etching, mechanical milling, laser ablation, thermal decomposition, and lithography (Ahmed et al. 2016). Different organic and inorganic reducing agents are used for reduction of metal ions in aqueous or nonaqueous media. Capping agents are also utilized to keep NPs sizes stable. One of the most significant advantages of this technology is that it can produce a huge number of nanoparticles in a short amount of time. The chemicals utilized in these types of synthesis are hazardous, resulting in non-eco-friendly by-products. This could be the cause of green biosynthesis of NPs without the application of harmful chemicals, which is proving to be an increasing desire to develop environmentally friendly techniques. Green synthesis is becoming one of the most important disciplines of nanotechnology since it uses a green method to synthesize nanostructures and can replace chemical routes due to low toxicity. The basic goal of green or biosynthesis is environmental sustainability and waste minimization (Hosseinzadeh et al. 2020). Figure 1 provides the schematic representation for basic adopted procedure in green synthesis.



Fig. 1 Schematic representation for preparation of green NPs. (Reprinted from original article by Dutta and Das 2021 after permission through RightsLink)

Synthesis of Nanoparticles Using Algae

The green and valuable synthetic processes using algae provide a quick and inexpensive route to green nanoparticle production. Cyanobacterial technology has the advantages of environmentally benign approaches, such as the ability to produce huge quantities of products at room temperature (Jaggessar and Yarlagadda 2020). In comparison to plants, they develop significantly faster and may be readily handled. Algae were chosen for the synthesis of NPs as nucleation and developments of crystals were promoted by negative charge present on algal cells surface. Algal polysaccharides aid in the regulation of the size and shape of Ag NPs. The time span ranged from 30–360 h, while the size ranged from 38–88 nanometers. The cyanobacteria *Spirulina platensis* and *Nostoclinckia* were used to study AgNP synthesis strategies. Silver nitrate is reduced due to metabolites released by the *Chaetomorpha linum* algae's growing media. The production of gold nanoparticles was mediated by *Spirulina platensis*, and the biofunctionality was tested against *B. subtilis* and *S. aureus*. Few marine algae are capable of producing nanoparticles, and the NPs are also beneficial. The FTIR spectrum also verified the existence of particular functional groups such as proteins, which plays crucial role for biosynthesis of AgNPs as capping and stabilizing agent. As an ideal contender for nanoparticle biosynthesis, cyanobacteria could play a vital role in creation of AgNPs. The different metallic NPs synthesized using algae are given in Table 1.

Table 1 Metallic NPs synthesized using algae

Algae	Nanoparticles	Application	Reference
<i>Chlorella ellipsoidea</i>	Ag	Degradation of dye, Antibacterial	Borah et al. 2020
<i>Cladophora glomerata</i>	ZnO	Biomedical	Abdulwahid et al. 2019
<i>Botryococcus braunii</i>	Cu and Ag	Antimicrobial	Arya et al. 2018
<i>Neodesmus pupukensis</i>	Ag & Au	Antioxidant and antimicrobial	Omomowo et al. 2020
<i>Gelidiella acerosa</i>	Au	Antibacterial, antioxidant, and α -glucosidase enzyme inhibition	Senthilkumar et al. 2019
<i>Chlamydomonas reinhardtii</i>	CdS	Photodegradation of organic dyes	Rao and Pennathur 2017
<i>Anabaena cylindrica</i>	ZnO	Antimicrobial	Bhattacharya et al. 2020

Synthesis of Nanoparticles Using Fungus

Fungi have an advantage over other microorganisms as they produce enormous amounts of enzymes and proteins. The size of NPs is determined by factors such as capping agent, dispersion media, pH, temperature, and fungus species. The *Ashbya gossypii* fungus has the potential to produce vitamin riboflavin on a large scale. Fungi's ability to enzymatically change cellulose in plant cell walls makes their industrial cultivation cost-effective. The hydrated mucilaginous coating that frequently covers hyphae serves as a matrix for geochemical processes (Qianwei et al. [2021](#)). *T. reesei* fungi are meticulously grown, easy to handle, and fabricate. Reductive proteins secrete more extracellularly, which may be handled easily in downstream processes. For high-scale nanotechnology, biosynthesis of nanomaterials is the safest and most cost-effective technique; it is practical to employ fungi as most effective industrial biotechnology agents to satisfy competent industrial nanobiotechnology requirements (Zhang et al. [2020](#)). In this situation, having the ability to manipulate fungi will be excellent for maximizing the natural potential of fungi. Fungi have a wide range of capacities in terms of metal speciation, toxicity, motility, mineral production, dissolution, and deterioration, all of which are mediated by multiple interconnected biomechanical and biochemical pathways (Chi et al. [2021](#)).

Metallic nanoparticles are currently receiving the greatest interest in the biomedical area for the treatment of a variety of acute infectious illnesses. Silver nanoparticles (AgNPs) are considered useful to solve various medical situations in comparison to other different metallic nanoparticles. Many biomolecules such as NADH and reductase enzymes can participate in the synthesis of silver NPs (Guilger-Casagrande and Lima [2019](#)). A variety of fungal species can produce

Table 2 Different metallic nanoparticles synthesized using fungi

Fungai	Nanoparticles	Application	Reference
<i>Penicillium chrysogenum</i>	MgO	Antimicrobial	El-Sayyad et al. 2018
<i>Trichoderma asperellum</i>	Fe ₂ O ₃	Treatment of waste water and biomedical applications	Mahanty et al. 2019
<i>Saccharomyces cerevisiae</i>	SeS	Antifungal	Asghari-Paskiabi et al. 2019
<i>Fusarium oxysporum</i>	Au, CdS	Therapeutic Antibacterial	Naimi-Shamel et al. 2019
<i>Trichoderma harzianum</i>	Ag, CuO, and ZnO	In biotechnological process	Consolo et al. 2020
<i>Phanerochaete chrysosporium</i>	Zno	Antimicrobial	Sharma et al. 2021
<i>Aspergillus sydowii</i>	Ag	Antifungal and antiproliferative activity to HeLa cells	Wang et al. 2021
<i>Rhizopus oryzae</i>	MgO	Tanning effluent treatment, mosquitocidal, and antimicrobial action	Hassan et al. 2021

nanoscale elemental particles of silver (reduction of Ag(I) to Ag(0)), gold (Au(III) to Au(0) reduction), palladium (Pd(II, IV) to Pd(0)reduction), and metalloids such as tellurium and selenium (Te/Se oxyanions reduction). Metal(loid)s may be found in nanominerals such as sulfides, tellurides, selenides, phosphates, carbonates, and oxides. Although various scientific studies have been reported on Ag NPs using fungi, but still the particular mechanisms are not exactly characterized. The ability of the fungus *Fusarium oxysporum* to synthesize silver NPs with diameters in the range 5–15 nm was confirmed, and fungal proteins were used to cap them in order to enhance stability. In contrast to previous studies using *Fusarium oxysporum* for intracellular production of Au and Ag NPs, PbS, CdS, ZnS, and MoS, it may also synthesize nanoparticles extracellularly. In order to reduce Ag⁺ ions, extracellular components of *Penicillium brevicompactum*, *Aspergillus clavatus*, *Aspergillus flavus*, and *Fusarium oxysporum* were used (Bahrulolum et al. 2021). Due to their high metal tolerance, wall binding capability, and internal metal uptake capacities, filamentous fungi have several specific advantages over bacteria.

The use of fungus for nanoparticle manufacturing has a number of advantages over bacteria, including easier scaling and downstream processing, lower cost, and a larger surface area supplied by the fungal mycelia.

Metal NPs of Ag, Au, Zr, SiO₂, Ti, Fe (magnetite), and Pt have been synthesized using fungal systems. Fungi are superior to other microbes in a variety of ways. The fungus *Fusarium oxysporum* and *Verticillium* species were used in the biosynthesis of magnetite. The fungus *Fusarium oxysporum* produces Au, Ag as well as bimetallic Au-Ag alloy nanoparticles outside of cells (Rai et al. 2021). The different metallic NPs synthesized using fungi are documented in Table 2.

Synthesis of Nanoparticles Using Bacteria

Nanoparticle biosynthesis using microorganisms is a green and environmentally beneficial process. Using various microbes, a range of inorganic nanoparticles have been manufactured, and their applicability in a variety of cutting-edge technical sectors has been investigated. Due to the availability of numerous reductase enzymes that can reduce metal salts to NPs, microorganisms are essential nanofactories that can accumulate and detoxify heavy metals (Singh et al. 2016). *Pyrobaculum islandicum*, an anaerobic hyperthermophilic microbe, has been shown to decrease a variety of heavy metals using hydrogen as an electron donor. *Desulfovibrio desulfuricans*, a sulfate-reducing bacterium, and *Sulfovibrio oneidensis*, metal-ion-reducing bacteria, could produce palladium nanoparticles. Silver nanoparticles, like their bulk counterparts, have antibacterial efficacy against gram-negative as well as gram-positive bacteria and highly multiresistant species like methicillin-resistant *Staphylococcus aureus*. Various bacteria have been shown to reduce Ag ions to generate AgNPs.

The creation of nanosized materials by microbial cells has proven to be useful method for metal nanoparticle synthesis. Microorganisms can produce nanomineral crystals and metallic nanoparticles with characteristics that are identical to chemically produced nanomaterials. Microorganisms can also be used to regulate shape, size, and content of NPs. Microbial cells are being investigated as possible biofactories to produce cadmium, silver, and gold sulfide NPs. Inorganic minerals can be synthesized by bacteria either intracellularly or extracellularly. The bioreduction process is used to create silver nanoparticles using microorganisms. The gold ion bioreduction was discovered to be activated by electron transfer from NADH through electron carrier NADH-dependent reductase. At the same time, the enzyme is oxidized by the reduction of silver ions to nanosilver. Silver ions are reduced to the nanoscale range by extracellular reductase enzymes generated by bacteria. The bioreduction of Ag ions to AgNPs is carried out by NADH-dependent reductase enzyme, according to a protein test of microorganisms. The nitrate-dependent reductase has been reported to cause bioreduction in some circumstances. The lowering occurs in a matter of minutes during the fast extracellular creation of nanoparticles. Gold NPs have been utilized to treat a variety of ailments for ages. Researchers have shown that by incubating bacterial cells with Au³⁺ ions, nanoscale gold particle size can be rapidly precipitated inside the cells.

Life may continue to exist with a well-organized mineral deposit on this planet. The interaction of inorganic molecules with living organisms has recently piqued the curiosity of scientists. Many bacteria can create inorganic nanoparticles via an internal or extracellular pathway, according to research. However, more effort remains to be done to increase synthesis efficiency and particle size and morphology control. In comparison of physical and chemical techniques, synthesis of NPs employing microorganisms is known to be a very sluggish method (many hours to few days). This biosynthesis route will become considerably more appealing if the synthesis time is reduced. Table 3 provides information about different metallic nanoparticles synthesized using bacteria.

Table 3 Different metallic nanoparticles synthesized using bacteria

Bacteria	Nanoparticles	Application	Reference
<i>Bacillus megaterium</i>	ZnO	Therapeutic and antibacterial agents	Saravanan et al. 2018
<i>Nostoc linckia</i>	Ag	Antibacterial	Vanlalveni et al. 2018
<i>Enterobacter sp.</i>	ZrO	Antifungal	Ahmed et al. 2021
<i>Bacillus licheniformis</i>	Au	Antimicrobial	Scala et al. 2019
<i>Bacillus haynesii</i>	ZnO	Nonmedical and medical	Rehman et al. 2019
<i>Pseudoduganella eburnea</i>	Ag	Antimicrobial	Huq 2020
<i>Bacillus subtilis</i>	Ag	Antibacterial	Yu et al. 2021

Synthesis of Nanoparticles Using Plants

One of the alternate approaches to manufacture biocompatible nanoparticles is a novel green synthetic strategic approach. The synthesis protocols for an environmentally friendly nanoparticle production approach do not include any harmful compounds. Plants metabolites combined with metal NPs are used for a variety of therapeutic purposes. Drug delivery methods based on nanotechnology are paving the way for the new era in the pharmaceutical sector (Patra et al. [2018](#)).

The concept of green nanomaterials research has piqued the interest of the scientific community in recent years, as seen by the number of published studies. Furthermore, when compared to chemical and physical processes, biologically generated nanoparticles are more appropriate for medical usage, as harmful materials may adsorb on the surface of the nanoparticles, causing undesirable effects when utilized for therapeutic purposes. To meet the abovementioned goals of green nanoscience, the solvents, reductants, and stabilizing agents used in nanoparticle formation should be chosen from a green perspective (Jan et al. [2020](#)). Due to availability of stabilizing and capping agents in the form of amino acids, enzymes, proteins, as well as intracellular and extracellular metabolites, biological synthesis is a favored technique. Polysaccharides, tannins, phenolics, saponins, flavonoids, terpenoids, and alkaloids are plant-derived phytochemicals that aid in the decrease of nanoparticles (Shukla et al. [2021](#)). Because of the presence of tri-terpenoid phytochemicals called galthimines, the plant is used to treat asthma, malaria, diarrhea, allergies, and other ailments. Flavonoids, gallic acids, terpenoids, phenolics, and other phytochemicals abound in this plant. Anticarcinogenic, anti-inflammatory, antioxidant, and neuroprotective effects are all present in these phytochemicals (Chakraborty et al. [2021](#)). The plant materials of *Passiflora subpeltata*, which are rich in secondary metabolites, are commonly used to treat cancer and have antioxidant anti-inflammatory potential. The flavonoids and terpenoids of extract served as effective capping and stabilizing agents, as well as assisting in the creation of NPs that were valuable in medical sectors. Aside from bacteria, another

fascinating prospect for nanoparticle synthesis is the utilization of parts of plant-like roots, bark, stems leaves, fruits, seeds, and so on. Plants have an advantage over microorganisms in that they do not require the time-consuming process of cell cultivation. Plants have an advantage over microorganisms in that they do not require the time-consuming process of cell cultivation. Understanding the key ideas of plant extracts with AgNPs employed as therapeutic agents in traditional medicine can aid in the discovery of novel compounds for treating a variety of disorders (Loganathan et al. 2022). In plant stem extracts, due to the presence of aldehyde groups, Ag^+ ions are reduced to metallic AgNPs. It focuses on how numerous physicochemical variables affect AgNPs. *Catharanthus roseus*, *Piper nigrum*, *Tinospora cordifolia*, *Terminalia chebula*, *Cocos nucifera*, *Cinnamon zeylanicum*, *Ocimum tenuiflorum*, *Aloe vera*, and *Azadirachta indica* have all been used in plant-mediated AgNP synthesis investigations (Rajeshkumar and Bharath 2017). The antibacterial effect of the produced nanoparticles is also being investigated. Based on green synthesis advantages over other approaches, aqueous *Azadirachta indica* leaves extract was used to synthesize AgNPs. *Azadirachta indica* leaf extract was used to make various NPs, including gold, zinc oxide, and silver. Terpenoids and flavanones are phytochemicals found in neem that act as reducing and capping agent, assisting in NPs stabilization.

Silver NPs generated from plants are widely used in biological fields such as larvicidal, antibacterial, and anticancer effects. The Passifloraceae (Passion Flower Family) includes *Passiflora subpeltata* Ortega, which is also referred as “passion flower” and malaikovai (Tamil name). It was found on a few Pacific Islands. The exotic fast-growing vine *Passiflora subpeltata* has 2–3 beautiful flowers with yellow-green fruits. The plant has traditionally been used for antioxidant, analgesic, anti-inflammatory, antipyretic, and antiproliferative effects (Mani et al. 2021).

Luffa acutangula, often known as ridge gourd, is a Cucurbitaceae plant that is used as a vegetable in Asia. The entire plant of *Luffa acutangula* L. has medicinal properties and frequently used in traditional Indian medicine (Anbumani et al. 2022). The fruits and seeds are widely utilized in the manufacture of herbal remedies to cure venereal illness, particularly gonorrhoea. In Mauritius, these seeds are also said to be used to get rid of intestinal worms. In addition, leaf juice can be applied to the skin to treat eczema. Insecticidal action is found in both the seed and the plant, indicating the possibility of antioxidant activity (Ramesh et al. 2022). The leaf juice is also used to treat jaundice, cancer, diabetes, eczema, and dysentery (Panimalar et al. 2022). *Luffa acutangula* fruit extract has greater antifungal and antibacterial action than seed oil used in dermatitis. The study was conducted to test the antibacterial activity of produced TiO_2 nanoparticles against infections using *L. acutangula* leaf extract. The TiO_2 NPs were generated using biological reduction (Panimalar et al. 2022; Rani and Shanker 2020). For creating TiO_2 NPs along with high surface area, monodispersity as well as porosity, the biological technique proved an appealing option. The leaves of *L. acutangula* were used as a good reducing agent to prepare TiO_2 NPs. Several studies have been published on green production of silver nanoparticles from plant sources. Furthermore, the most dependable and simple approach for biosynthesizing environmentally clean, economically stable, and

commercially viable silver nanoparticles by exploiting various natural sources, mostly plant-based materials, must be evaluated (Radhakrishnan et al. 2020). Various medicinal plants are utilized in the creation of nutritional and health care products as traditional medicine. The application of diverse biological agents, like plant extracts and waste from fruits and vegetables, in green NPs synthesis has received a lot of interest in current scenario. Bioactive chemicals in peas have antidiabetic, antioxidant, and antibacterial effects. A study was conducted to synthesize AgNPs from aqueous extract of pea pods and to assess their bioactive characteristics. Greenly produced AgNPs were reported to have significant antimicrobial action against pathogenic bacterial infections. Both gram-negative and gram-positive bacteria are susceptible to nanoparticles (Anju et al. 2019). As a result, the green NPs may be developed as antibacterial agent against gram-negative and gram-positive bacteria. These NPs were created utilizing an aqueous combination of *Ficus carica* leaf extract and irradiation in a recent study (Dutta and Das 2021).

The leaf extract was successfully utilized to synthesize silver and gold NPs with sizes ranging from 10–30 nm. As inferred from TEM imaging, the spherical nanoparticles were found at greater leaf extract concentrations (Zhang et al. 2020). The “passion flower,” *Passiflora subpeltata* Ortega, is a vine plant which is fast growing and exotic along with 2–3 beautiful blossoms yielding yellow-green fruits. The plant has traditionally been utilized for antioxidant, analgesic, anti-inflammatory, antipyretic, antibacterial, and other qualities (Kaur et al. 2021). *Passiflora subpeltata* Ortega leaf extract was utilized to synthesize ZnO-NPs using a very simple, low-cost, and nontoxic method. Although the specific method of NP synthesis from plant extracts is unknown, it is thought to be divided into three stages. By reacting zinc acetate salt with NaOH, zinc hydroxide is produced. Zinc hydroxide is then bioreduced and produces ZnO₂ nuclei during the activation phase. During the development phase, the nucleated ZnO expands to produce ZnONPs with specified morphology, which is then stabilized by phytochemicals that coat NP surfaces during final phase (Chunche Gowda et al. 2021). *Casuarina equisetifolia* is an evergreen tree with medicinal benefits, including relief from cough, diabetes, fever, toothache, dysentery, diarrhea, and headache (Khan et al. 2021). Phytochemicals have a critical role in ZnONPs green production. Drug delivery, antibacterial, anticancer, and antidiabetic properties are among the biological applications of ZnONPs. Due to the rise of multidrug-resistant bacterial infections, other therapeutic approaches are needed, and ZnONPs have gotten a lot of attention because of their exceptional therapeutic qualities. The enormous nanoparticle surface-area-to-volume ratio permits interaction with numerous ligands available on surface of NPs with bacterial receptors, resulting in their significant antibacterial activity (Agarwal et al. 2018). Drug-resistant bacterial strains pose serious health concerns around the world, and ZnO nanoparticles provide their safe and effective treatment.

In order to synthesize green NPs, the reaction mixture may be exposed with UV radiations to change the shape of NPs. Under UV light, *Polyscias scutellaria* extract has produced gold NPs (AuNPs). The plant extracts consist of active compounds which excite electrons by high-energy UV radiation, which aided in Au⁺³ ions reduction and produced stable 5–20 nm AuNPs. Another study looked at the effect

of UV light on form and size of AgNPs generated using *Aureobasidium pullulans* (Khan et al. 2019). The size of AgNPs reduced as the irradiation period increased due to production of smaller NPs by the breakdown of heated AgNPs. UV radiation thus played a role in influencing nanoparticle formation, size, and distribution.

Applications of Green Nanoparticles

Biocompatibility and the absence of harmful effects are essential requirements for biogenically produced nanomaterials. Green NPs are good substances for many applications in diverse sectors due to their structure, shape, size, and special chemical, physical, and biological capabilities (Huang et al. 2017). Green NPs are applied in animal health, nanodevices for plant genetic engineering, nanoformulations of agrochemicals, nanobiosensors for crop protection, nutrient availability, pesticides, food packaging, postharvest management, biomedical applications, antimicrobial action, cancer therapy, disease diagnosis, and drug delivery. Other fields in which biogenic nanotechnology plays a key role are water treatment, biodegradable polymers, pollution monitoring sensors, UV protection, and bioremediation (Fig. 2; Koul et al. 2021).

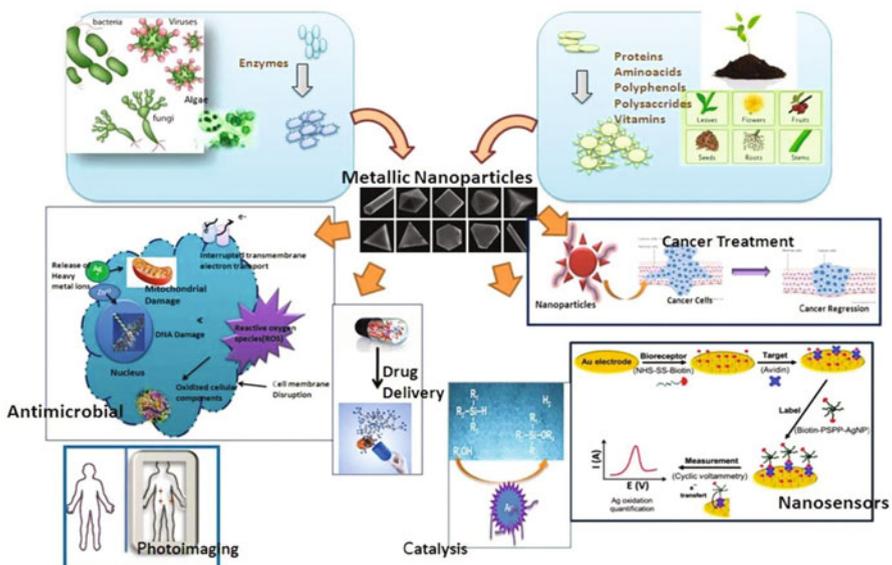


Fig. 2 Applications of biogenic metallic nanoparticles. (Reprinted from original open access article by Zhang et al. 2020)

Biomedical Applications of Nanoparticles

The toxicity of metals is unknown in many domains, but their uses and relevance are well understood. The quantity of nanoparticles produced is increasing day by day, particularly for biological features. Antibiotic resistance develops when pathogenic bacteria alter their metabolic pathways and target locations (Thangavelu et al. 2020). Furthermore, as a result of their constant exposure, these microorganisms become more pathogenic and resistant to antibiotics. As a result, it is critical to discover alternative, unconventional, potent antimicrobial drugs that are both less expensive and safe. Biofabricated NPs are smaller and possess bigger surface area. Nanomedicine encompasses the application of nanotechnology to treat fictitious diseases, as well as the analysis, nursing, and control of biological systems.

The monostructured nanoparticles that were created can be designed to self-assemble and build structure for tissue engineering, effectively mimicking mineralization procedures. Given the abundance of studies, this chapter focuses on the most recent developments in medicinally significant biosynthesized metal nanoparticles made from various natural resources. Because of their properties, NPs can interact efficiently with microbial cell membranes and infiltrate cells, interfering with metabolic pathways and DNA replication. Many studies have looked into the antibacterial properties of various NPs. Furthermore, if NPs are utilized in conjunction with standard medicines, the antibacterial efficacy of NPs can be increased. Banu and colleagues, for example, investigated the combined action of AgNPs and antibiotics (carbenicillin, nitrofurantoin, and ciprofloxacin) against Enterobacteriaceae (ESBL strains) and discovered substantial antibacterial potential.

In comparison to traditional antibiotics, AgNPs were found to induce bigger zones of inhibition (amoxicillin, streptomycin, and ofloxacin). Similarly, Roychoudhury and colleagues generated silver NPs by bacterium *Lyngbya majuscula* and discovered that these AgNPs were efficient against *P. aeruginosa* and also have antiproliferative properties in REH cell lines and leukemic cells (Roychoudhury et al. 2016). Al-dhabi studied antibacterial action against *B. subtilis*, *S. aureus*, *E. faecalis*, and *S. epidermidis* strain. There are various reports available on AgNPs' use as antibacterial agents (Al-Dhabi et al. 2018). ZnONPs also have anticancer properties involving preferential killing of cancer cells via an apoptotic mechanism involving the production of reactive oxygen species (ROS). Because standard cancer treatments, like chemotherapy and radiation therapy, have a significant level of rapidly damaging dividing cells, they are not recommended (Ogunyemi et al. 2019). Alternative anticancer drugs that are toxic to tumor cells but not to normal cells are required. All of these uses necessitate NPs administration in people in order to demonstrate therapeutic benefits and for this reason safety is paramount. As a result, green-synthesized NPs should be preferred for biomedical applications since they are safe and more biocompatible. MCF-7 cells demonstrate morphological alterations, control of cell proliferation, and finally clattering and death due to AuNPs after optical microscopy inspection (Khan et al. 2016). The feasibility of cells reduces when nanoparticle concentrations rise. The highest cytotoxic effect (75%) was reported in MCF-7 cells at a dose of 100 g/mL, with

MCF-7 cells showing 25% viability at this concentration. At various doses, no hemolytic capabilities of AuNPs have been reported against red blood cells. Moreover, as gold nanoparticles are nontoxic, inert, stable, and consist of high binding capacity, they are frequently used as anticancer medication carriers. The influence of AuNPs on cancer cell MCF-7 was studied at various doses. While employing the lower concentration of AuNPs, it is obvious that the AuNPs demonstrated significant action and that cell growth was reduced. Anti-leishmanial action was also demonstrated by the nanomaterials. Different scientists tested several plant extracts and discovered that they were active. They exhibit substantial activity even at very low doses. Noble metal NPs are capable of generating reactive oxygen species (ROS) that kill microorganisms via a simple mechanism known as the respiratory burst mechanism. Macrophages are a type of resistant cell found in humans that can produce significant levels of reactive oxygen species (ROS) to kill infections. Leishmanial organisms can inhibit some ROS-producing enzymes from forming a route in macrophages, allowing them to thrive in resistant cells. The AuNPs allow for nanoenzymatic ROS foundation and extinguishment of infected organism (Khan et al. 2017).

Applying well-diffusion method, the antibacterial activity of synthesized iron NPs was investigated and it was discovered that iron nanoparticles synthesized had better activity against *Staphylococcus aureus*. Researchers believe that iron nanoparticles can be used in medical and pharmaceutical industries as a result of the antibacterial experiment. Groiss and colleagues investigated the preparation of iron oxide NPs employing *Cynometra ramiflora* leaf extract. Iron oxide NPs were tested for antibacterial and catalytic activity against *Staphylococcus epidermidis*, *Escherichia coli*, and the rhodamine B dye (Groiss et al. 2017).

Role of NPs in Diagnostics and Drug Delivery

A major component in developing an efficient drug delivery system is drug transportation (DDS). Drug delivery is one of the most cutting-edge ways in modern health care research for treating diseases such as cancer. Traditional therapeutic medications have a number of drawbacks, including inadequate absorption, non-specificity, quick clearance, unpleasant side effects, and so on. Nanomaterials have a number of advantages over standard medication delivery systems. Metal nanoparticle-based DDSs may be able to circumvent these constraints by delivering drugs to a specific spot in the body system over time without harming healthy cells (Barui et al. 2019). To specifically release medications to the intended areas, DDSs are connected with either passive or active targeting. The traditional techniques of disease diagnosis are time consuming, costly, and inefficient. Pathogens and chronic diseases can be detected with NPs in a cost-effective, quick, specific, and precise manner. Cancer, which is defined by uncontrolled cell development, is currently a dangerous disease. Traditional cancer treatment approaches (chemotherapy, radiation, and surgery) have certain side effects. Furthermore, tailored treatment administrations to the damaged organ as well as early detection of this deadly disease are still in their infancy. As a

result, developing alternate means of detection and therapy for this disease is critical. It has been stated that nanomedicines can be used to successfully diagnose tumors and treat them with targeted drug delivery (Sutradhar and Amin 2014). Due to the purposeful plasticity of their monolayers, gold nanoparticles provide an ideal approach for DDS technique. Various kinds of cancer cell lines have been treated with nanomedicines. Women with breast cancer have a high recurrence rate. Biosynthesized SeNPs had anticancer properties as well. SeNPs extracellularly synthesized from bacteria *Streptomyces minutiscleroticus* M10A62 demonstrated significant antiproliferative activity against HeLa and HepG2 cell lines, according to Afzal and coworkers (Afzal et al. 2021). As a result, NPs have been used in a variety of studies for their anticancer properties under controlled conditions. However, issues including toxicity, dosages, and the host immunological response during treatment must all be addressed before they can be commercialized. Khan et al. investigated the effectiveness of ZnONPs biofabricated from *Rhodococcus pyridinivorans* as anthraquinone nanovehicles (Khan et al. 2021). ZnONPs loaded with anthraquinone showed concentration-dependent cytotoxicity against HT-29 colon cancer cells, leading to the conclusion that anthraquinone-loaded ZnONPs may be used for targeted drug administration. Through improved diffusion, nanomaterials with hydrophilic characteristics can boost drug absorption and enhance drug cytotoxicity (Zhang et al. 2020). Fluorescent NPs can be utilized to image chronic diseases, like cancer in their early stages. Magnetic nanoparticles may be employed to detect advanced methods like MRI. Biofabricated *Candida albicans* AuNPs were employed as probe for cancer cells of liver, where cancer cells bounded by AuNPs made it easier to distinguish cancer cells from normal cells. As a result, microbe-based NPs play an important role to diagnosis the disease; nevertheless, the applications of NPs in diagnosis as well as detection of diseases are still in primary stages and require more research in this area (Chauhan et al. 2011).

Application of NPs in Food Industry

In the food sector, NPs may be applied in two key segments: food processing and food packaging. ZnO NPs are employed in the manufacture of packaging materials in polymeric materials. Antibacterial properties of the newly manufactured packing tissue were improved. Other research has proposed that ZnO nanoparticles may be used to create containers and nutritious coverings for packing. The application of nanoparticles in material of packaging keeps food fresh and prevents infection (Karima et al. 2016). AgNPs have unique capability to puncture bacterial cellbiofilm, providing them the stress resistance. As a result, AgNPs may be used in cleaning and decontamination of packaged food (Saleem et al. 2019).

Applications of Nanoparticles in Agriculture

NPs are currently widely applied in a wide range of fields, such as health, cosmetics, agriculture, and food science (Rani and Shanker 2018). The manufacture of metal nanoparticles (MtNPs) using microbes and plants has recently been recognized as an eco-friendly and cost-effective way for utilizing microorganisms as nanofactories (Baharulolum et al. 2021). MtNPs have proven to promote germination in agricultural seedlings, hence nanotechnology could be a viable alternative for producing fertilizer. Other uses include the delivery of fertilizers, insecticides, plant growth regulators, and other related substances using nanoscale carriers (Bartolucci et al. 2020). In the case of *D. dadantii*, TiO₂NPs made from lemon fruit demonstrated antibacterial efficacy comparable to ZnONPs (Hano and Abbasi 2022). AgNPs produced from a wheat extract dramatically reduced the deleterious effects of salinity stress in wheat by changing abscisic acid content, ion homeostasis, and defense mechanisms that included both enzymatic and nonenzymatic antioxidants. ZnONPs were found to have low toxicity and the ability to trigger the antioxidant response in flax seedlings. In agriculture, NPs are used as nanofertilizers, nanopesticides, and nanoinsecticides (Saleem et al. 2019).

Nanoparticles as Fungicides

Metal nanoparticles as well as metal oxide nanoparticles show good antifungal activities. One of the most dangerous categories of plant pathogenesis fungi, causing a variety of diseases, *Streptomyces spp.*-biofabricated NPs of copper and its oxide have been found to have good antifungal properties against a variety of pathogenic fungi, including *Aspergillus niger*, *Fusarium oxysporum*, *Alternaria alternata*, and *Pythium ultimum* (Arya et al. 2018). It was discovered that AgNPs had a very high antifungal effect. As a result, fungal diseases in plants can be treated by employing NPs as fungicides. However, dosage and toxicity of NPs are still important concerns for their commercialization as fungicides (Kaur et al. 2018).

Nanoparticles as Fertilizers

Overutilization of chemical fertilizers has resulted in ever-decreasing soil fertility, which is a serious issue in the agriculture industry. Alternative nanofertilizers made from NPs are harmless, efficient, and environmentally beneficial (Gudkov et al. 2020). In a recent study, researchers employed carbon-based nanomaterials as soil fertilizers and found that they might reduce use of chemical fertilizers. Another study discovered that nanoclay minerals and zeolites may be employed as fertilizers in other investigations (Guo et al. 2018). It has been established that putting a nanomaterial on potash fertilizer causes it to release slowly, reducing fertilizer loss and the need for chemical fertilizers.

Nanoparticles as Pesticides

Nanoparticles can also be employed to make nanopesticides. NPs can be found as organic constituents like nanopolymers, particles, micelles, and inorganic constituents like metal oxides in nanopesticides (Rani et al. 2017). Many new formulations incorporating NPs were developed and utilized as insecticides in recent years. Many studies have shown that MtNPs may be employed as efficient insecticides against a variety of insects and pests that cause crop losses in agriculture around the world (Rawtani et al. 2018). It has been established that a unique nanoemulsion based on oil–water (O/W) can be employed to transport the insecticide β -pypermethrin (β -PP). The study reported that β -PP coated to O/W nanoemulsion distributed to a greater extent compared to regular beta-PP, reducing overall pesticide application. As a result, NPs can be utilized as insecticides. However, NP dosage and plant toxicity remain important concerns for the commercialization of NPs as insecticides (Koul et al. 2021).

Applications of Nanoparticles in Bioremediation

Water pollution that is xenobiotic and highly persistent occurs due to azo dyes, acid dyes, cationic dyes, etc. that must be remedied by wastewater treatment. The pollutants increase water contamination and have a negative impact on aquatic life. Due to their larger surface area and smaller size, NPs may catalyze or adsorb pollutants. Various studies have looked at catalytic characteristics of various NPs combined to biological components in order to decrease hazardous contaminants (Koul et al. 2021). Both Ag and AuNPs have been shown to have significant catalytic activity to eliminate organic dyes. Nanoparticles reduce the amount of time it takes to remove dye and increase the rate of response. Gold nanoparticles may be employed as adsorbents of organic dyes. The *Cladosporium oxysporum* AJP03-induced AuNPs with surface proteins were found to increase adsorption of organic dye, rhodamine B. The involvements of nanosponges, nanotubes, nanoclays, magnetic NPs, bimetallic NPs, FeNPs, and TiO₂ NPs in soil bioremediation were recently reported by Koul and Taak. Green NP synthesis could be a viable solution to soil and water pollution (Koul and Taak 2018).

Future Perspectives and Conclusions

NMs have become increasingly important in commercial development during the last 20 years. Advances in nanotechnology are likely to bring a slew of new discoveries and opportunities for the global economy. With the potential for widespread usage of NMs in the future, they could be used extensively in a variety of sectors, including tumor therapy. Researchers are concentrating on ecologically friendly and green NP synthesis. Various studies have been reported on plant extract–mediated synthesis of NPs as well as its potential applications. The use of

NMs in tumor therapy is projected to vastly improve present methods of tumor therapy, tumor imaging, and tumor-cell detection. Moreover, it also lowers toxicity in comparison to traditional tumor treatments. However, there are a number of obstacles along the way, and there are still questions regarding the potential risks of anticancer therapy. Potential acute and chronic toxic effects are most serious issues; the potential toxicity chronic in anticancer therapy must be overlooked. NMs have been linked to toxicity in the past. CNTs' blood incompatibility limits their application in clinical settings. Although several researchers have demonstrated that functionalizing carbon nanotubes can improve their water solubility, there is currently little evidence of their safety and biocompatibility. Because QDs may contain heavy metals, their toxicity cannot be overlooked when they are used in the body. To ensure the safety of future applications in people, comprehensive toxicity research is required. Unless the toxicity issue is resolved, more studies may not be beneficial in clinical use of nanomaterials or industrial manufacturing. Furthermore, only a few types of materials are approved, and only a few NMs are approved as anticancer medicines to enter into Phase III clinical trials or market, indicating that a better understanding of nanomaterials is required before their use in tumor therapy. In living systems, long-term NMs toxicity must be thoroughly investigated. Before NMs may be used in tumor treatments, scientists believe that more research into the mechanisms of cell harm caused by NMs is required. Tumor therapy development is a diverse area, where rigorous studies are required on NMs, molecular biology, tumor immunology, and tumor biology, to develop a perfect therapy or NM for the treatment of tumors. Nanotechnology's transition to mainstream clinical practice will necessitate multidisciplinary research based on social, ethical as well as clinical considerations.

Based on the above review of various relevant studies, it is likely that mankind will be highly benefited from NMs in near future, particularly in tumor therapy. The green NPs could be used for a range of applications, such as water disinfection for environmental remediation and phytopathogen therapy in agriculture. The presently discussed environmentally friendly method of NP synthesis is gaining popularity and is projected to grow exponentially in near future. This chapter brought together cutting-edge research on plant-based green synthesis of NPs, as well as their applications, in order to provide the most comprehensive overview of all of these aspects and future challenges. However, techniques for large-scale nanoparticle synthesis must be improved to make these technologies cost-effective and comparable to older methods. Furthermore, the majority of these techniques are still in primary stages, and obstacles must be addressed. These include nanoparticle stability and aggregation, as well as crystal development, shape, and size management. Another crucial characteristic that needs to be investigated further is nanoparticle separation and purification. Genetically modified organisms have a wonderful potential to optimize the production and stability of nanoparticles. Based on the studies, it can be suggested that genetic changes to improve accumulation capacity and metal tolerance will be the future strategy for improving metal nanoparticle production using the "green synthesis" method.

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