Green Synthesis of Metallic Nanoparticles and Various Biomedical Applications

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Fahima Dilnawaz and Amarendra Narayan Misra

Abstract

Nanobiotechnology has emerged as an advanced arena in conjunction with biology and nanotechnology. Biological entities involve living organisms of both prokaryotic and eukaryotic origins. Recently attention has been focused on the green synthesis of nanoparticles because of their natural availability and environmentally friendly synthesis approach. Every biological organism varies in its functional capabilities. However, only selective biological organisms can produce nanoparticles because of their enzymatic and intrinsic metabolic processes. These eligible biological entities or their extracts have been used for the green synthesis of metallic nanoparticles. These biosynthesized metallic nanoparticles have a range of unlimited biomedical applications, such as the delivery of drugs or genes, the detection of pathogens or proteins, and tissue engineering. This chapter will discuss various green synthesis routes of nanoparticles and their current use. The application of these metallic nanoparticles briefly discussed here includes antiviral, antibacterial, antioxidant, anticancer, anti-inflammatory, and antiparasitic wound-healing activities.

Sustainable Development Goals: Good health and well-being (SDG3), Responsible production and consumption (SDG12), Climate action (SDG13), Life on land (SDG15)

F. Dilnawaz (✉)
Department of Biotechnology, School of Engineering and Technology, Centurion University of Technology and Management, Bhubaneswar, India
e-mail: fahima.dilnawaz@cutm.ac.in

A. N. Misra
School of Applied Sciences, Centurion University of Technology and Management, Bhubaneswar, India
e-mail: amarendra.misra@cutm.ac.in

F. A. Sheikh et al. (eds.), *Interaction of Nanomaterials With Living Cells*,
https://doi.org/10.1007/978-981-99-2119-5_5

Keywords

Green synthesis · Metallic nanoparticles · Nanobiotechnology · Phytosynthesis · Reactive oxygen species · Antioxidant

5.1 Introduction

Nanotechnology-mediated formation of nanoparticles is currently being utilized in the various fields of human welfare (Dilnawaz et al. 2018). Nanoscale particles display unique physical and chemical properties, such as high surface-to-volume ratios, higher reactivity and strength, and colloidal stability. Mainly the metal (copper, iron, gold, silver, etc.) nanoparticles display better physical and optical characteristics (surface plasmon reverberation or surface plasmon resonance), which attracted significant attention for specific applications in medicine and science (Mauro et al. 2021). Moreover, the synthesis of nanoparticles (NPs) is being carried out through three different strategies (physical, chemical, and biological). Conventionally, in the chemical synthesis process, chemical reduction and microemulsion/colloidal, electrochemical, and thermal decomposition are used with the intervention of metal salt precursors and the addition of particular reducing agents. Although these chemical methods are economical for large-scale production, the use of toxic substances, in turn, produces harmful by-products that cause environmental damage, thereby limiting its clinical and biomedical applications (Hua et al. 2018). Recently, many research groups have utilized green synthetic routes to synthesize different nanomaterials to reduce the usage of harmful chemicals. Green synthetic methods are carried out under mild reaction condition, which consumes low energy, devoid of conditional requirement of high temperature and pressure, hazardous chemicals, and addition of external stabilizing or capping agent (Khan et al. 2020). Among various green synthetic routes, plant leaf extract-mediated approaches for the preparation of metal oxide nanomaterials have received enormous attention (Nguyen et al. 2021). Using the producer source of the biological kingdom, the green synthesis of metal oxide nanoparticles is being carried out. Scientists have given priority to plants that can execute this process due to their biomass abundance, response to stress factors (pathogens, herbivores, and climate changes), and survival modes (seasonal changes and reproductive stage variation) that contribute toward the development of plants' primary and secondary metabolites. Hence these naturally imbibed strategies of the plants serve as the main bioreactors and molecule suppliers for green synthesis (Iravani 2011). The plant leaves contain a lot of phytochemicals; the phenolic compounds (alkaloids, tannins, and flavonoids), along with the important constituents like proteins and carbohydrates, are taken into account for the synthesis of metal oxide nanoparticles (Biswal et al. 2020; Richardson et al. 2006). Further, the functional amino groups and proteins available in the plant extracts also contribute toward metal ion reduction (Li et al. 2007). In another study, Huang et al. discussed that the functional groups of alkaloids, flavones, and anthracenes, such as –C–O–C–, –C–O–, –C=C–, and –C=O–, assist the metal NP synthesis (Huang et al. 2007).

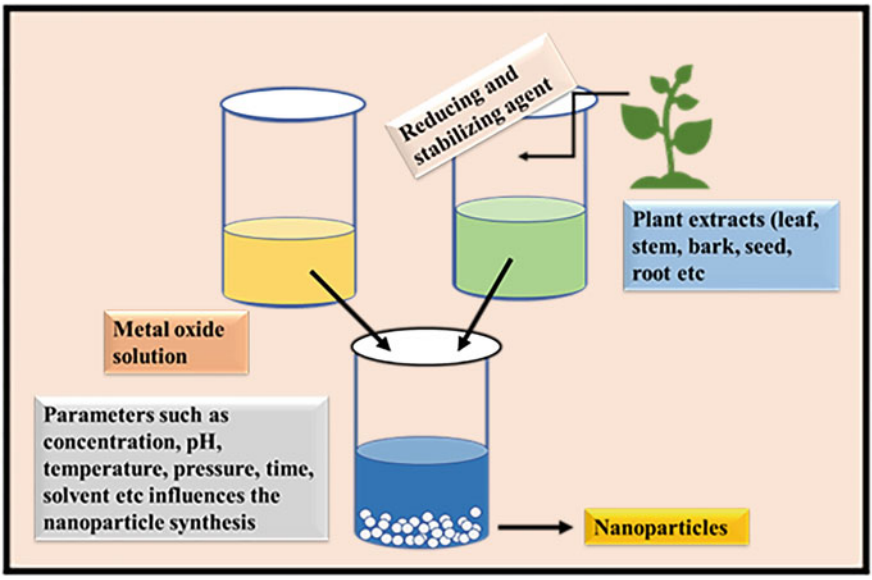

Fig. 5.1 Overview of green synthesis of nanoparticles

The metal ion reduction may also be carried out with the help of quinones and plastohydroquinone molecules present in the plant leaf extract (Kesharwani et al. 2009). All these studies indicated that extracellular metal oxide nanoparticle synthesis could be carried out by biomolecules and heterocyclic compounds present in plants. However, the vision and understanding of the metal oxide NP synthesis utilizing plant extracts are not well understood. It is comprehended that maybe the phytochemicals of the plants mediated the production of NPs through metal reduction. Thereafter, oxygen produced from either atmosphere or degrading phytochemicals links the reduced metal ions, and corresponding electrostatic attraction leads to NPs (Makarov et al. 2015). Plants, either the whole or tissues (Kumar and Yadav 2009; Marchiol 2012) or extracts of different parts (e.g., roots, barks, leaves, fruits, and seeds) (Kharissova et al. 2012; Rai et al. 2008), are taken into account for green synthesis (Fig. 5.1).

Particularly noble metals (gold and silver) are widely known for their use in medicine owing to their excellent intrinsic property, unique functional attributes, the scope for surface functionalization, etc. (Ahmad et al. 2019; Behzad et al. 2021). Therefore, the green synthesis method leading to the formation of biocompatible and environmentally friendly metal nanoparticles upsurge its applications in healthcare. The present book chapter will chronicle some of the critical biomedical applications of NPs toward better healthcare.

5.2 Biomedical Applications of Metallic Nanoparticles

Metal oxide nanoparticles are highly beneficial for biomedical applications owing to their limited toxicity. In the following sections, various applications of metallic nanoparticles are discussed (Fig. 5.2). Studies have shown that uptaken NPs can either disrupt the enzyme function, quench reactive oxygen species (ROS), or degrade DNA and protein, disrupting cellular mechanisms (Fig. 5.3).

5.2.1 Nanoparticles as Antiviral Agents

Viruses pose a severe challenge for biomedical applications, as life-threatening diseases caused by them are widespread. To combat viral infection, numerous efforts have been made for the development of antivirals and vaccines. Viruses have the innate capacity to quickly acclimatize to a host cell and bypass a defense mechanism by taking advantage of cellular metabolism. Although incredible improvements in the progress of antiviral chemotherapeutics for prevention and treatments are available, there is still scope for developing new potential antiviral using nanomaterials. Silver (Ag) nanoparticles (NPs) have been proven as potent antiviral agents against several virus families: *Retroviridae*, *Paramyxoviridae*, *Hepadnaviridae*, *Poxviridae*, *Herpesviridae*, *Arenaviridae*, and *Orthomyxoviridae* (Franci et al. 2015). With the implementation of Ag NPs, viruses are less likely to become resistant compared to conventional antiviral agents. Ag NPs have multivalent connections with surface components of virus and cell membrane receptors, by which they block their access

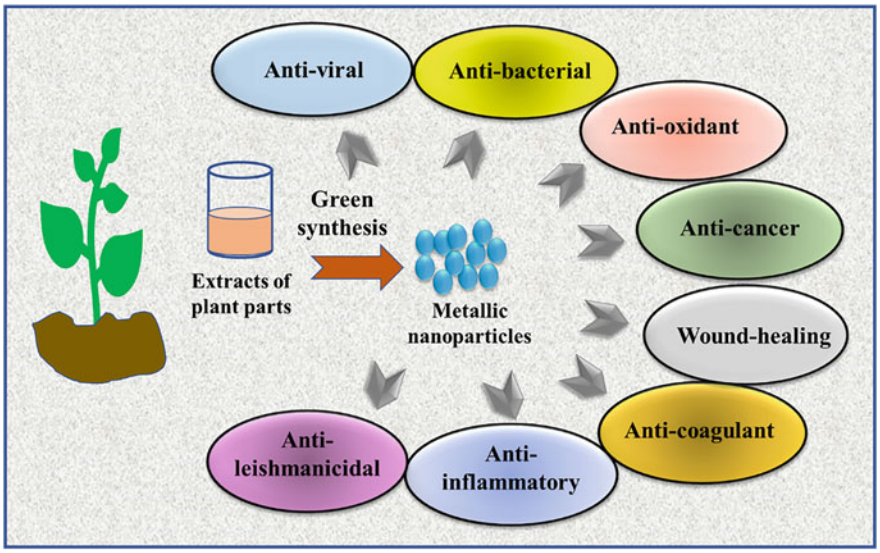

Fig. 5.2 Various modes of applications of metallic nanoparticles obtained through the green synthesis process

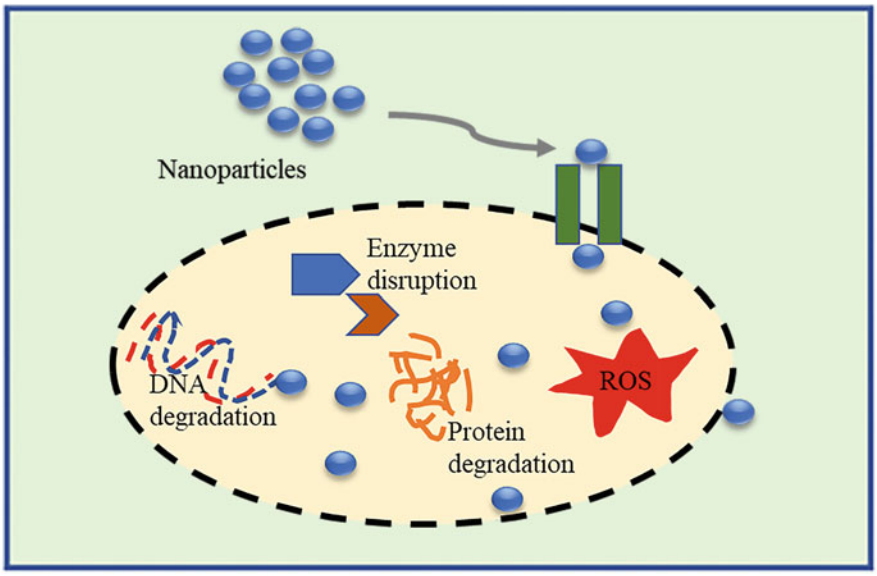

Fig. 5.3 Possible mechanism of interaction of nanoparticles with the cellular components and their effects

into the cells. The antiviral agents act directly on viral particles by binding to their viral coat proteins by disrupting their function or structure (Sharma et al. 2019). Ag NPs were synthesized by engaging the extracts of *Phyllanthus niruri*, *Andrographis paniculata*, and *Tinospora cordifolia*, and its antiviral efficacy was evaluated against the chikungunya virus. The in vitro antiviral assay of Ag NPs was evaluated based on the degree of inhibition of cytopathic effect (CPE), which showed *A. paniculata* Ag NPs to be most effective, followed by *T. cordifolia* Ag NPs and *P. niruri* Ag NPs. The cytotoxicity assay illustrated that *A. paniculata* Ag NPs inhibited the virus to a great extent. This study could indicate alternative treatment options against viral disease (Sharma et al. 2019). Orłowski et al. used tannic acid (TA) for the synthesis of Ag NPs, which served as an effective microbicide in the mucosal tissues. TA Ag NPs, when treated intravaginally in a virally infected mouse model, demonstrated better anti-herpes simplex virus-2 immune response by showing improved clinical scores with lower viral titer in the vaginal tissues (Orłowski et al. 2018). Ag NPs were synthesized utilizing the leaf extracts of *Carica papaya*, which hold antiviral activity and good binding affinity against nonstructural protein 1 of the dengue type 2 virus (Renganathan et al. 2018). In another study, Ag NPs were synthesized using the leaf extract of *Eucalyptus procera*, and its adjuvant effect on veterinary rabies vaccine was evaluated. Ag NP-loaded vaccine concentrations at 15 and 20 mg/kg showed the highest percentage of viability after injecting into the mice. At the same time, the alum-containing vaccine at the concentration of 10 mg/mL was toxic, whereas Ag NPs were nontoxic, elucidating the safety effect of the Ag NP-based vaccine (Asgary et al. 2016).

5.2.2 Nanoparticles as an Antibacterial Agent

Drug resistance or antibiotic resistance is gradually increasing due to the rampant use of antibiotics. Multidrug resistance (MDR) emerges, as the bacteria move toward horizontal gene transfer of antibiotic resistance genes. There is an adjustment in the antibiotic target and mutational changes in the biofilm formation and efflux pumps (Qayyum and Khan 2016; Singh and Nalwa 2011). Therefore, in this regard, application of metal nanoparticles as an antimicrobial agent and for drug delivery purposes is widely considered. In a study, Prasannaraj et al. used ten medicinal plants (leaf, root, bark, etc.) for the phytosynthesis of Ag NPs and evaluated their antibacterial property against clinically isolated microbial pathogens. The active cellular metabolic activity is an indicator of cell viability, proliferation, and cytotoxicity, which is affected by the application of bioengineered NPs. Ag NPs illustrated maximal growth inhibition in liquid culture and potential anti-biofilm activity (Prasannaraj and Venkatachalam 2017). The Ag NPs at lower doses illustrated better multidrug-resistant bacterial infections with an increased level of reactive oxygen species (ROS). Ramkumar et al. synthesized Ag NPs from the aqueous extract of seaweed (*Enteromorpha compressa*), which displayed potent antibacterial properties toward *E. coli*, *K. pneumoniae*, *P. aeruginosa*, *S. aureus*, and *S. paratyphi*. *Panax ginseng*, the herbal medicinal plant having an active ingredient of ginsenosides, has been explored for the synthesis of Ag NPs using its root extract. The produced Ag NPs at 3 μg/mL exhibited potent antibacterial action against *S. enterica*, *B. anthracis*, *V. parahaemolyticus*, *S. aureus*, *E. coli*, and *B. cereus* and completely inhibited the biofilm of *S. aureus* and *P. aeruginosa* at 4 μg/mL (Ramkumar et al. 2017). Phytosynthesis of Ag NPs using extracts of ten plants (*Pongamia glabra*, *Hamelia patens*, *Tectona grandis*, *Thevetia peruviana*, *Ficus petiolaris*, *Ficus busking*, *Caryota urens*, *Juniper communis*, *Calendula officinalis*, and *Bauhinia purpurea*) illustrated minimum inhibitory concentration (MIC) of 16–26 μg/mL for *E. coli*, *K. pneumoniae*, *E. cloacae*, *S. mutans*, and *S. aureus* (Qayyum and Khan 2016). A lot of studies have been carried out, and corresponding pieces of literature are available exclusively for the antibacterial effects of Ag NPs that were compiled in a review article (Lateef et al. 2019). Application of Ag NPs induces better permeability of cell membranes and produces ROS by interrupting replication of deoxyribonucleic acid (DNA) by releasing silver ions to the bacterial cell, thereby prompting cell death (Dwyer et al. 2012).

5.2.3 Nanoparticles as Antioxidant Agents

In biological systems, antioxidants play a dynamic role in scavenging toxic free radicals. The oxidative stress injuries to the cellular components such as DNA, proteins, and lipids generated by free radicals are quenched by antioxidants. Nitric oxide (NO) plays a major role in a diversity of biological functions, including neurotransmission, blood pressure regulation, smooth muscle relaxation, and antimicrobial and antitumor activities. The NO can react with the generated superoxide

to form the peroxynitrite anion, which causes DNA fragmentation and initiates lipid peroxidation (Lone et al. 2013). The active oxygen species, present in the body, can cause several disorders such as carcinogenesis, aging, atherosclerosis, cataracts, inflammation, mutation, and cell death (Ragu et al. 2007). The most reactive and poisonous free radicals are hydroxyl radicals which demonstrate great oxidative power, as they can combine rapidly with almost all molecules in their immediate vicinity (Sousa et al. 2009). Gold (Au) NPs were synthesized using an aqueous extract of *Elettaria cardamomum* seeds which displayed good antioxidant activities. 2,2-Diphenylpicrylhydrazyl (DPPH) free radical scavenging is used for screening the antioxidant activity. The antioxidant activity scavenged by DPPH, NO, and OH radical methods has increased with the application of AuNPs. Au and Ag nanoparticles synthesized from seed extracts of *Embelia ribes* elucidated excellent antioxidant activity as displayed by DPPH free radical scavenging and the phosphomolybdenum assay. In another study, Ag NPs synthesized from leaf extracts of *Aristolochia indica* displayed better antioxidant activity at 100 μg/mL (Shanmugam et al. 2016). Ag NPs synthesized from pod extracts of *C. nitida* exhibited strong antioxidant activity by scavenging DPPH and ferric ions at a concentration between 20 and 100 μg/mL, similarly Bhakya et al. reported the better DPPH scavenging activity of Ag NPs formed through the root extracts of *Helicteres isora* (Bhakya et al. 2016). The fruit extract of *Couroupita guianensis* was used for the synthesis of AuNPs, which illustrated antioxidant potentials at IC50 of 36 g/mL and DPPH effects through hydroxyl radical scavenging at 37 g/mL. However, with increasing concentration, the scavenging activity upsurges for inhibition to around 90% (Sathishkumar et al. 2016a). Abbai et al. synthesized AuNPs from Siberian ginseng (*Eleutherococcus senticosus*) using its stem extract, which displayed good antioxidant potentiality (Abbai et al. 2016). Similarly in another study, *Cassia tora* leaf powder was used for the production of AuNPs. Its antioxidant potentiality was evaluated via catalase activity, and an increase in catalase activity correspondingly increased the antioxidant activity and also suppressed the release of hydrogen peroxide (Abel et al. 2016).

5.2.4 Nanoparticles as an Anticancer Agent

Cancer is a devastating disease and the leading cause of death globally. The metallic nanoparticles induce autophagy and promote cell death. Castro-Aceituno et al. synthesized Ag NPs from *Panax ginseng* fresh leaves, and its anticancer effect was evaluated on different human cancer cell lines. In human cancer cell lines (A549, MCF7, and HepG2), treatment of Ag NPs inhibited cell viability and induced oxidative stress. In A549 cells, the Ag NPs inhibited the epidermal growth factor (EGF)-enhanced migration, decreased the mRNA levels and phosphorylation of EGF receptors, and increased the apoptotic effect that was linked to the stimulation of the p38 MAPK/p53 pathway. In MCF-7 and HepG2 cells, Ag NPs induced cytotoxicity and ROS generation (Castro-Aceituno et al. 2016). In another study, Castro-Aceituno et al. synthesized Ag NPs from *Dendropanax morbifera* Léveille,

which exhibited antimicrobial activity and reduced the viability of cancer cells without affecting the viability of RAW 264.7 macrophage-like cells, where it demonstrated the cytotoxic effect by generating ROS against A549 and HepG2 cell lines at different concentrations (Castro Aceituno et al. 2016). In another study, longan peel, powder-mediated Ag NPs were synthesized, and their anticancer ability was evaluated in H1299 cells as well as in the mouse model. Dose-dependent cytotoxicity and stimulation of apoptosis were observed in H1299 cells, by inhibiting the NF-κB activity, a decrease in Bcl-2, and an increase in caspase-3 and survivin expression. In a xenograft combined immunodeficient (SCID) mouse model, the tumor growth was significantly suppressed demonstrating the potential anticancer activity (He et al. 2016). Sankar et al. synthesized copper oxide NPs from *Ficus religiosa* leaf extract, which imposed an apoptotic effect by the generating ROS, in which there was disruption of mitochondrial membrane potential activity in A549 cells (Sankar et al. 2014). Wang et al., synthesized AuNPs and evaluated their anticancer activity against pancreatic cancer cell line (PANC-1), where it illustrated dose-dependent cytotoxic activity in a time- and dose-dependent manner. Further, the expression of Bcl-2 protein was decreased with an increased dose of Ag NPs, promoting the cancer cell apoptosis by increasing the apoptosis-related protein expressions in time- and dose-dependent mode (Wang et al. 2019). Cheng et al. synthesized zinc oxide (ZnO) NPs from *Rehmanniae Radix*, a Chinese herb. It exerts anticancer activity against osteosarcoma cell line MG-63, by generating more ROS, and decreased mitochondrial membrane potential (MMP) activity. The decreased MMPs tempt toward increased levels of apoptotic proteins Bax, caspase-3, and caspase-9 leading to the induction of apoptosis (Cheng et al. 2020). Dsouza et al. synthesized bimetallic (silver/zinc oxide) nanostructures from the fruit extracts of *Vateria indica*. The in vitro anticancer study performed on triple-negative breast cancer cells MDA-MB468 revealed the enhancement of antiproliferative activity compared to only Ag NPs (D'Souza et al. 2022). Satpathy et al. synthesized Ag NPs using *Pueraria tuberosa*, which demonstrated good anticancer activity in different cancer cell lines (SKOV-3, NCI/ADR, U-87, MCF-7, MDA-MB-231) ~ 29.3, 25.4, 6.05, 3.8, and 1.1 μg/mL respectively. The comparative anticancer activity showed in terms of IC_{50} lowest for MDA-MB-231 and highest for SKOV-3 (Satpathy et al. 2018). Satishkumar et al. synthesized Ag NPs using *Coriandrum sativum* leaf extract, which has shown remarkable anticancer activity in MCF-7 (Sathishkumar et al. 2016b).

5.2.5 Nanoparticles as a Wound-Healing Agent

The wound takes place due to the sharp injuries that occur to the skin where the dermal layers are cut, punctured, or torn due to trauma (Nethi et al. 2019). The wounds can be acute or chronic depending upon the healing period as well as other complications (Eming et al. 2014). Healing of the wound takes place with the interaction of various types of cells, coagulation factors, connective tissue, growth factor, and cytokines (Katas et al. 2018). Healing of the wound is dependent on four

phases (hemostasis phase, inflammatory phase, proliferative phase, and maturation phase). These phases are quite complex and function in a coordinated manner. Failure or lack of functionality in any stage leads to chronic wounds (Katas et al. 2018; Martin and Nunan 2015). Nano-based approaches for wound-healing involving herbal extracts can effectively address the specificity associated with the wound. Ahn et al. generated Ag NPs from seven plant extracts (*Cratoxylum formosum*, *Ceratostigma minus*, *Phoebe lanceolate*, *Scurrula parasitica*, *Mucuna birdwoodiana*, *Myrsine africana*, and *Lindera strychnifolia*). Out of these studied plant extracts, Ag NPs generated from *Lindera strychnifolia* illustrated wound-healing properties. The cell scratch method utilized for wound-healing activity on mouse fibroblast cells (NIH3T3) illustrated better healing activity (Ahn et al. 2019). Ag NP hydrogel using root extract of *Arnebia nobilis* exhibits splendid antibacterial and wound-healing activity in excision albino Wistar animals. Naraginti et al. synthesized Ag NPs and AuNPs from the root extracts of *Coleus forskohlii*. These nanoparticles displayed noticeable wound-healing activity in excision wounds in albino Wistar male rats. However, topical application of formulated AuNPs is more effective in suppressing inflammation and stimulating reepithelialization compared to Ag NPs during the healing process (Naraginti and Sivakumar 2014). Titanium oxide NPs synthesized from *Origanum vulgare* efficacy were examined in the excision wound model illustrating significant wound-healing activity in albino rats (Sankar et al. 2014). Magnetic nanoparticles were biosynthesized by using *Aloe vera* extract in newly isolated bacterial nanocellulose (BNC) RM1, which was evaluated for wound-healing activity in human dermal fibroblast cells. The genes that are responsible for wound healing were TGF-B1, MMP2, MMP9, Wnt4, CTNNB1, hsa-miR-29b, and hsa-miR-29c. These genes responded in a time-dependent manner for the therapy of cutaneous wound healing (Moniri et al. 2018). ZnONPs were synthesized using an aqueous leaf extract plant of *Barleria gibsoni*. These developed ZnO-NP gels worked effectively for the healing of burn infections in rats. Copper oxide NPs were synthesized from *Ficus religious* leaf extract, and its wound-healing efficacy was evaluated. The copper oxide NPs demonstrated superior wound-healing activity by upregulation of major wound-healing proteins in the different phases of wound repair, wound contraction, and reepithelialization process (Sankar et al. 2014).

5.2.6 Nanoparticles as an Anti-inflammatory Agent

During inflammation, our body is protected from invaders through chemicals produced by the body's white blood cells that enter the blood or tissues. Inflammation is a phenomenon that occurs as a result of injury, infection, and stress, where chemicals are released through multiple mechanisms and, in turn, recruit macrophages and killer cells such as cytokines like IL-1, IL-1β, and TNF-α to the desired site (Ong et al. 2007). Metallic nanoparticles synthesized through the green route have demonstrated anti-inflammatory properties. Utilizing the aqueous extract of *Selaginella myosurus*, Ag NPs were developed, and under in vivo and in vitro conditions, it

demonstrated anti-inflammatory potential. Application of Ag-NPs inhibits protein denaturation and prevents the release of acute inflammatory mediators [histamines, serotonin, kinins, prostaglandins, and cyclooxygenase products] in the Carrageenan-induced rat hind paw edema model (Kedi et al. 2018). In another study from *Prunus serrulata*, AuNPs were synthesized and evaluated against lipopolysaccharide (LPS)-induced RAW264.7 macrophage. These NPs in LPS-induced RAW264.7 cells suppressed the production of inflammatory mediators and pro-inflammatory cytokines by inhibiting NF-κB activation (Singh et al. 2018). Zinc oxide NPs developed from *Polygala tenuifolia* root extract exhibited promising anti-inflammatory activity by inhibiting the expressions of proteins iNOS, COX-2, IL-1b, IL-6, and TNF-α (Nagajyothi et al. 2017). Kup et al. used aqueous extracts of *Aesculus hippocastanum* (horse chestnut) as a reducing agent for the synthesized Ag NPs (Küp et al. 2020). With the application of Ag NPs, the superoxide radical scavenging activity is increased with increasing concentrations, and inhibition was about 62.9% as compared to the activity of plant extract (Küp et al. 2020). Green synthesized NPs act by blocking pro-inflammatory cytokines and ROS scavenging mechanisms and inhibiting the NF-κB and COX-2 pathways to minimize the inflammation with greater efficiency.

5.2.7 Nanoparticles as Antileishmanial Agent

Leishmaniasis is caused by infection with Leishmania parasites, which are spread by the bite of phlebotomine sand flies. It is another essential life-threatening disease. It is classified based on severity and intensity as visceral, cutaneous, and post kala-azar dermal leishmaniasis and mucocutaneous leishmaniasis (Arenas et al. 2017). The disease is treated with antileishmanial drugs, but in the long run, it develops resistance due to the increased efflux mechanism, inhibition of drug activation, and inactivation of active drug, which hampers the drug activity as well as decreased drug concentration inside the parasite (Mohapatra 2014). Ullah et al. synthesized from the aqueous extract of *Teucrium stocksianum* and displayed a strong antagonistic assay against *Leishmania infantum* promastigotes compared to chemically synthesized Ag NPs (Ullah et al. 2018). The cytotoxic assay based on MTT reagent (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide) revealed toxic effects of chemical Ag NPs, compared to green synthesized Ag NPs. Synthesis of AuNPs from an extract of *Maytenus royleanus* demonstrated significant antileishmaniasis against *Leishmania tropica* promastigotes (Ahmad et al. 2016). Sumbal et al. developed monometallic ZnO NPs and Ag NPs and bimetallic (ZnO/Ag) NPs using *Mirabilis jalapa* leaf extract. Bimetallic NPs displayed greater potentiality for antileishmanial activity compared to monometallic NPs (Sumbal et al. 2019). Awad et al. synthesized Ag NPs using *Commiphora molmol* (myrrh). Different concentrations (10, 50, 80, 100, and 150 μL/100 μL) of Ag NPs were applied and studied for antileishmanial activity. At higher concentrations such as 100 and 150 μL/100 μL, significantly greater inhibitory effect was observed compared to the chemical nanoparticles and pentostam at the same concentrations. After

21 days of post-administration of green synthesized Ag NPs, the lesion was healed completely, whereas the commercial NPs illustrated a moderate healing effect in vivo (Awad et al. 2021).

5.2.8 Nanoparticles as an Anticoagulant Agent

Loss of blood in the human body is protected through the clotting mechanism. The clotting mechanism is contributed by the numerous components such as platelets, coagulation factors, prostaglandins, enzymes, and proteins which act together to form clots and stop the bleeding. Clots also include stroke, pulmonary embolism, deep venous thrombosis (DVT), acute coronary syndrome (ACS), and acute myocardial infarction (AMI). A blood clot formed from infection or contamination damages the tissues leading to organ failure linked to cardiovascular disorders, autoimmune reactions, allergic responses, injuries, and the emergence of cancer (Levi et al. 2010; Davalos and Akassoglou 2012; Prandoni et al. 2007). Anticoagulants are used for the prevention of blood clots to avert the disorders associated with thrombosis. Commonly used anticoagulants are warfarin, rivaroxaban, dabigatran, and heparin products, which are closely linked with adverse drug events (Alquwaizani et al. 2013). Researchers have demonstrated the anticoagulant efficacy of green synthesized metallic NPs. Abbasi et al. synthesized Ag NPs using an aqueous extract of dried Juglans regia green husk, which has blood clot prevention efficacy within 72 h in a dose-dependent manner (Abbasi et al. 2017). Ag NPs were synthesized from *Bridelia retusa* fruit extract, which prevented blood clots in human blood samples and is used in nanomedicine (Vinayagam et al. 2017). *Peltophorum pterocarpum*-synthesized Ag NPs also showed anticoagulant activity (Raja et al. 2015). Ag NPs synthesized from cocoa beans demonstrated antiplatelet activity, and it prevented blood coagulation without disturbing the morphological features of red blood cells (Azeez et al. 2017). Lateef et al. used the seed and leaf of *Synsepalum dulcificum* for the synthesis of Ag NPs (Lateef et al. 2016), and the pods, seeds, and shell of *Cola nitida* were used for the synthesis of Ag NPs (Lateef et al. 2017), which showed anticoagulant activity and prevent clot formation for a longer period. Leaf extract of *Petiveria alliacea* was used for the synthesis of Ag NPs, which inhibited aggregation of platelets, thus preventing clot formation for a longer period, likewise the activity similar to EDTA (Lateef et al. 2018).

5.3 Conclusion

The biological synthesis of nanoparticles has received unrivaled focus to upsurge their applications in biomedicine. The green synthesis process provides a clean, nontoxic, and eco-friendly approach to the synthesis of metal NPs compared to other conventional techniques. Studies have illustrated better biomedical applications compared to their chemically synthesized counterparts. This will open up the ways for exploring the development of improved healthcare for the clinical application of mankind.

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Fahima Dilnawaz is an Associate Professor at Centurion University of Technology and Management, Bhubaneswar. She has earned her doctorate, postgraduate, and M.Phil. in Plant Biology. She won her ITC Fellowship from the Hungarian Academy of Sciences and National Postdoctoral Fellowship from the Department of Biotechnology. She worked in the convergence of science, particularly in the nanomedicinal approach in biomedical science as Women Scientist (WOS-A) at the Institute of Life Sciences (an autonomous institute of the Department of Biotechnology, GOI) Bhubaneswar, Odisha, India, for more than 10 years. To her credit, she has published more than 30 scientific papers and review articles and more than 20 book chapters in reputed journals and publishing houses. Apart from that, she has coauthored one book (*Remedial Biology*) for pharmaceutical students and coauthored two patents, one of which has been acclaimed in the USA, Europe, and Australia and the other has an Indian patent. Her research interest is basically focused on polymeric nanoparticles, magnetic nanoparticles, and mesoporous silica nanoparticle-based drug delivery systems for cancer therapy. She has been invited to various scientific organizations to deliver talks in India and abroad. She is serving as a reviewer for multiple journals as well as an associated editorial board member.

Amarendra Narayan Misra is a distinguished professor at the Centurion University of Technology and Management, Bhubaneswar. He has teaching experience of more than 40 years and research experience of more than 45 years. He served as a Full Professor (20 years), out of which 16 years serving as Head, Dean (Academic), Dean of School, Chairman-PG Council, Director-IQAC, Member of the Academic Council, Senate, Syndicate, Executive Council, and Vice-Chancellor. His research collaborations with US, European, and Japanese universities availed funds from the Commission of European Communities (CEC), Japanese Societies for Promotion of Science (JSPS), Tokyo University, Geneva University, DBT, INSA, FICCI, DST, etc. He worked at the best international universities like Imperial College, London, University of Wales, Tokyo University, Osaka University, Geneva University etc. As a Fulbright Scholar, he interacted with the Presidents, Vice-Chancellors, and Senior Administrative Personnel of more than 25 American universities and colleges under Fulbright Academic Administrator's Seminar 2013. Many scholars from Europe, America, Canada, Africa, and Asia have visited and worked in his laboratory as Guest Professors, Exchange Scientists, and Researchers since 1998. As a Vice-Chancellor of Khallikote University (state), he signed MOUs with ten foreign universities for faculty and student exchange.

He has earned his doctorate in the field of plant biology and biochemistry. His research field is bioenergetics, bio-signals and biosensors, molecular biology, and bioinstrumentation. He used luminescence techniques like fast fluorescence kinetics, thermoluminescence, positron-annihilation spectroscopy, flash photolysis of water and oxy-graphs, proteomics, and radioisotopes in plant biology, collaborating with electronics, physics, chemistry, and instrumentation professionals.