Chapter 4
Green Synthesized Metal Oxide Nanomaterials Photocatalysis in Combating Bacterial Infection

Prajita Paul, Yashmin Pattnaik, Pritam Kumar Panda, Ealisha Jha, Suresh K. Verma, and Mrutyunjay Suar

Contents

Abstract With the unprecedented progresses of nanotechnology, metallic nanoparticles (MNPs) synthesized by green approaches have received global attention due to their low toxicity for the mankind. The advent in nanomaterial studies and their applications provoked issue of their toxicity and biocompatibility with respect to ecosystem and human health. This chapter provides glimpse to green synthesis and functionalization of nanoparticles used for the environmental

P. Paul · Y. Pattnaik · M. Suar (✉)
School of Biotechnology, KIIT Deemed to be University, Bhubaneswar, India
e-mail: msuar@kiitbiotech.ac.in

P. K. Panda
Division of Pediatric Hematology and Oncology, University Medical Center, University of Freiburg, Freiburg, Germany

E. Jha
Department of Physics and Physical Oceanography, Memorial University of Newfoundland, Newfoundland and Labrador, NL, Canada

S. K. Verma (✉)
School of Biotechnology, KIIT Deemed to be University, Bhubaneswar, India

Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

M. Naushad et al. (eds.), *Green Methods for Wastewater Treatment*, Environmental Chemistry for a Sustainable World 35, https://doi.org/10.1007/978-3-030-16427-0_4

remediation as well as highlights the "state of the art" in exploring various environment-friendly synthesis approaches. However, the field of nanoscience has blossomed over the last two decades to unfold to unleash its power on our day-to-day lives of various nanotechnological production processes. Also new strategies have been applied for synthesis and industrial preparation. In particular, this chapter discusses green nanotechnology-based production of biocompatible Ag and Au nanoparticles and their biomedical applications and also enlightens the platform for innovative antibacterial efficacy and its cytotoxicity.

Keywords Nanotechnology · Metallic nanoparticles · Green synthesis · Antibacterial · Biocompatible · Cytotoxicity

4.1 Introduction

The amalgamation of science, engineering, and technology at nanoscale level gave birth to the field of nanotechnology. The term nano is obtained from the Greek word "nanos" which implies small and refers to particles above subatomic measurements nearly 1 billionth of a meter. It's a science which involves the study of extremely small things and further engineering them to have potential utility in various other scientific fields (Mazhar et al. 2017). Nanotechnology has been a developing area since a decade or two and finding extensive applications due to its enhanced properties of being lightweight as well as showing a greater chemical reactivity than their larger-scale counterparts (Naushad et al. 2017). Chemical synthesis of nanoparticles makes them toxic and renders them unsuitable for applications in medical fields (Prabu 2015). When nanoparticles are manufactured by synthetic routes using organic solvents and in harsh chemical conditions, it leads to accumulation of toxic residues which subsequently pose a threat to the environment (Molnár et al. 2018). To resolve the issues associated with chemical synthesis routes, green methods of synthesis came into role. Green nanobiotechnology refers to an eco-friendly route of synthesis of nanomaterials utilizing plants, microorganisms, and even their by-products like lipids and proteins (Patra and Baek 2014). The diagram below lists out the different methods of nanoparticles synthesis Fig. 4.1.

At present, due to the nontoxic effects, nonexpensive, and eco-friendly nature, researchers are more interested in introducing new approaches in the field of biology.

4.2 Scopes for Green Synthesis of Metal Nanoparticles

Various routes of biosynthesized green nanoparticles include algae, microbes (diatoms), plants, some biocompatible agents, and heterotrophic human cell lines which are known as green nanofactories and especially exploited for the production of inorganic nanoparticles (Narayanan and Sakthivel 2011; Prabu 2015; Shirsat et al. 2016). Thus the approach for biosynthesized nanoparticles follows the principles of

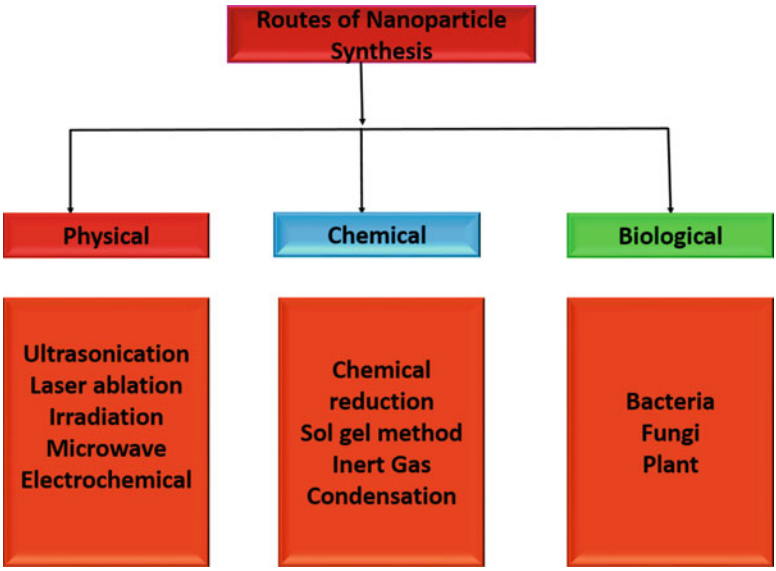

Fig. 4.1 Different routes for synthesis of nanoparticles

green chemistry. However, plants and plant resources are advantageous as sources of nanomaterials synthesis over prokaryotic microbes which further need downstream processing (Narayanan and Sakthivel 2011).

The principles of green chemistry have proved to be a promising alternate to produce biocompatible and steady nanoparticles having the added advantages of being nontoxic and environment-friendly (Parveen et al. 2016). With the advancement of green methods of nanoparticles synthesis, the scope of developments in other scientific fields like medicine has also increased multifold (Patra and Baek 2014). This chapter focusses on the strong cross-link between nanotechnology and its significant contribution to therapeutics especially in treating bacterial infections.

Recent years have shown immense increase in the production of gold nanoparticles, and their applications in biomedical spheres have also increased (Keighron and Keating 2010). Biogenic method of synthesis of silver and gold nanoparticles is seeking more attention owing to their intense antibacterial action as well as for their property of getting reduced to salts easily (Wang and Hu 2017). Biogenic Ag and Au nanoparticles act as good conduction centers and thereby facilitate transfer of electrons. The colloidal route of synthesis of silver and gold is predicted to create ion channels in between the prosthetic groups and to help the protein to acquire a favorable orientation.

The applications of nanoparticles in the area of medical science are known to be expanding due to their high stability both chemically and biologically and can be administered through almost all routes unlike other drugs which have certain limitations (Bao 2004). Introduction of nanoparticles into the cell generates a lot of structural modifications which often can lead to non-specific interactions between

the shell of the nanoparticles and proteins circulating in the bloodstream. Therefore an ideal nanoparticle used for therapeutics should be nontoxic, stable, non-immunogenic, biocompatible, noninflammatory, and biodegradable to ensure its potency and efficacy (Farkhani et al. 2014).

4.3 Biological Effect of Metal Nanoparticles

Following Table 4.1 listed below shows biosynthesis of nanoparticles from different bacteria. The extensive use of metallic oxide nanoparticles has shown remarkable applications in various areas such as antibacterial, antifungal, drug delivery, tissue engineering, wound healing, etc. (Martin-Ortigosa et al. 2014). In view of concern related to biocompatibility, green synthesized nanoparticles have been used (Vadlapudi et al. 2014). As far as beneficial effects are concerned, green synthesized metal nanoparticles have been studied for their antibacterial activities against pathogenic as well as nonpathogenic strains. The approach of green synthesis has been taken in prior to enhance the antibacterial activity of a metal nanoparticles like AgNPs, AuNPs, etc. However, their toxic effects can be ignored upon high usage and accumulation. Moreover, the toxic effect advances toward the environmental aspects and spread to other biotic factors of the ecosystem.

Table 4.1 Biosynthesis of nanoparticles from bacteria

Bacterial strains	Metal nanoparticles	Size	References
Pseudomonas stutzeri	AgNPs	100–200 nm	11
Lactobacillus sp.	AgNPs	15–30 nm	12
Morganella sp.	AgNPs	20–21 nm	13
Bacillus subtilis	AgNPs	5–50 nm	14
Bacillus indicus	AgNPs	2.5–13.3 nm	15
Pseudomonas antarctica	AgNPs	3–33 nm	15
Pseudomonas fluorescens	AgNPs	80–85 nm	16
Salmonella typhimurium	AgNPs	85–110 nm	17
Bacillus thuringiensis	AgNPs	20–30 nm	18
S. aureus	AgNPs	30–40 nm	18
S. typhimurium	AgNPs	40–50 nm	18
Bacillus subtilis	AuNPs	5–25 nm	19
Lactobacillus sp.	AuNPs	20–50 nm	20
Pseudomonas aeruginosa	AuNPs	15–30 nm	21
Escherichia coli	AuNPs	20–25 nm	22
Klebsiella pneumoniae	AuNPs	35–65 nm	23
Salmonella Typhimurium	AuNPs	20–40 nm	17

4.3.1 *Antibacterial Effects of Green Synthesized Metal Nanoparticles (AgNPs and AuNPs)*

Recently, successful biosynthesis of silver and gold nanoparticles was carried out by researchers via green route of methodology varying with morphology and desired size through natural reducing, capping, and stabilizing agents. These biosynthesized processes are widely favored due to their nontoxic, low-cost, naturally derived, eco-elegant features (Feng et al. 2000; Taylor et al. 2010) Fig. 4.2. The extracts such as amino acids, polysaccharides, enzymes/proteins, and vitamins from various organisms are found to be bioreduce with metallic ions in combinations with several biomolecules which are environmentally sustainable. However, several research groups reported green synthesis of Ag and Au metallic nanoparticles using bacteria, biological routes, and extraction of plant products. The biosynthesis of Au and Ag metallic nanoparticles is properly channelized through the organic compounds present in plant extracts for lower concentration of nanoparticles. The underlying molecular mechanism that permits inhibitory properties of biosynthesized Au and Ag nanoparticles cause reduction of ionic form of gold to its atomic state and ionic form of silver to its atomic state. This bioreduction occurs by absence of hydrogen due to OH groups present in the polyphenol molecules. The biosynthesis of such silver and gold nanoparticles can be achieved through different routes.

Successful synthesis of biogenic silver nanoparticles (AgNPs) was carried out by a group of researchers in an eco-friendly manner. For example, the root extract of plant named *Zingiber officinale* were used in presence of metallic ion. The change in change indicated the formation of biosynthesized silver nanoparticles (AgNPs)

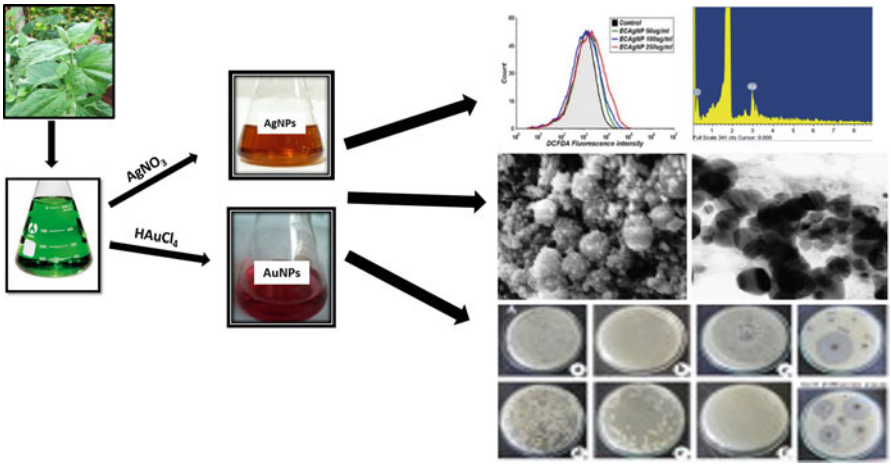

Fig. 4.2 Process outline for the synthesis of AgNPs and AuNPs along with its characterization techniques and antimicrobial activity

(Velmurugan et al. 2014). Another method of synthesis of AgNPs was done out by Ahmed group using plant extracts of *Azadirachta indica* (Ahmed et al. 2015). This plant extract functions as capping as well as reducing agent. For this method, leaves of plant extract were first cleaned by distilled water and air dried at room temperature. The leaves were boiled later in distilled water for 30 min, and the extract was stored in the refrigerator before use. This group also proposed a new, basic, one-step, easier, and quicker method for synthesizing of biogenic AgNPs by using plant extracts of *Crotalaria retusa* as well as *Terminalia arjuna* as reducing and stabilizing agents (Ahmed and Ikram 2015; Ahmed et al. 2016b). The biogenic silver nanoparticles (AgNPs) exhibited greater catalytic activity as well as excellent antibacterial premises against both Gram-negative and Gram-positive microorganisms.

Biosynthesis of gold nanoparticles (AuNPs) was also carried out by using environment-friendly material such as the plant extracts. For example, the plant extract of *Sphaeranthus indicus* was first washed, then transferred into conical of purified boiling water, and kept for 10 min. The plant extract was then filtered for further process. To it 1 mM of $HAuCl_4$ solution along with *S. indicus* plant extract was added and mixed well for 30 min; the change in color from light yellow to wine red indicated synthesis of Au NPs (pH 5.4) (Balalakshmi et al. 2017). Another set of synthesis of AuNPs were performed by different research group where they collected leaf, bark, stem, root, etc. These plant parts were properly cleaned with water, cut into small parts, and then allowed to boil in distilled water to obtain extract. Further, the purified extract is mixed with the metallic $HAuCl_4$ salt solution at room temperature to obtain Au NPs in a one-pot reaction (Ahmed et al. 2016a).

4.3.2 Cytotoxicity of Green Synthesized Metal Nanoparticles (AgNPs and AuNPs)

Cytotoxicity of a nanoparticle is defined as the alteration in cellular morphology leading to toxic effect of nanoparticle. Cytotoxicity has been considered as an important modality for proposing any nanomaterial for clinical applications. Nowadays both in vitro and in vivo biological models are being used to evaluate the cytotoxicity effect of engineered nanoparticles. In vitro evaluation has been described as the determination of cytotoxicity or in negative termed called as biocompatibility using mammalian cell lines as model, while in vivo evaluation describes the cytotoxicity determination in live models like mouse, rat, and zebrafish. Metallic nanoparticles such as silver and gold have been reported to exhibit cytotoxicity apart from their antibacterial efficacy. A number of studies have reported the cytotoxic effects of Ag NPs on neuronal cell, rat liver (Hussain 2005; Hussain et al. 2006), murine stem cells (Braydich-Stolle et al. 2005), and human lung epithelial cell (Lam et al. 2004; Asharani et al. 2009). The basic mechanism of AgNP toxicity has been understood since long time, yet detail

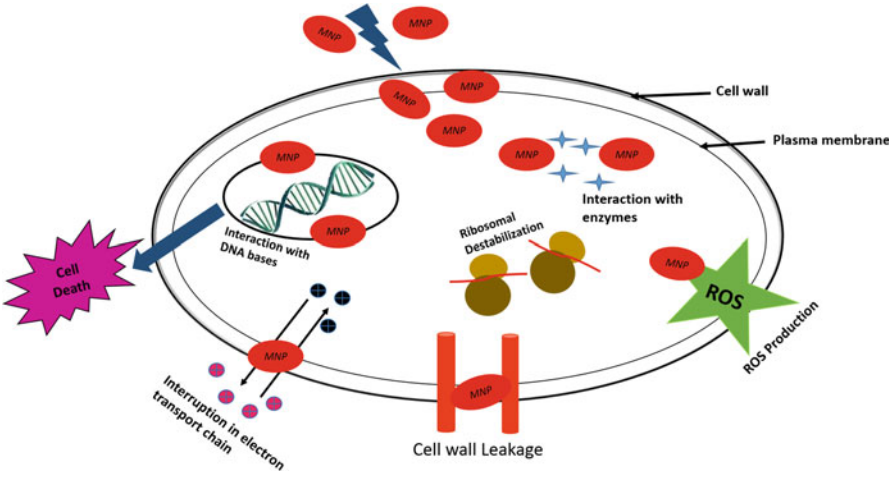

Fig. 4.3 Antibacterial mechanism of metal nanoparticles

explanation is still lacking. Ag NPs that get internalized inside cell through permeation of cell membrane create greater level of intracellular Ag+, leading toward genotoxic and cytotoxic effects carried out through the interruption of cell transport (Choi and Hu 2008). Smaller AgNP penetrates cell walls and membranes, while larger AgNP gets internalized through endosomal pathway (Xia et al. 2006). Through these basic mechanisms, the whole processes have been defined by many researchers. The mechanisms have been described in terms of three major cellular phenomena happening during their exposure: (1) generation of reactive oxygen species (ROS), (2) DNA damage, and (3) modulation of immunological factors like cytokine production. Uptake of AgNP can induce the generation of ROS at higher level which results toward oxidative stress and genotoxic effects. Induction of ROS proceeds toward disruption of flux of ions and electrons across the mitochondrial membrane leading to either apoptosis or necrosis (Asharani et al. 2009; Arora et al. 2008). The ROS induction, however, varies according to the physiochemical properties of the AgNPs Fig. 4.3.

As far as genotoxicity induced by AgNP is concerned, the toxic effects are induced by DNA damage as shown in case of human lung fibroblast, IMR90, and human glioblastoma cells, U251, by increasing ROS production or by diminishing energy production due to depleted ATP generation (Hsin et al. 2008). Apart from this, the mechanism of AgNP cytotoxicity has also been reported due to change in immunological responses. AgNP has been reported to elicit both stimulatory and suppressive effects on the production of cytokines associated with the inflammatory response and is found to be dependent on physiological parameters like size, dose, and cell types. Studies showed enhanced production of proinflammatory response mediators (TNF-α, MIP-2, and IL-1β) and an increase in IL-1β, IL-6, IL-8, and TNF-α in human epidermal cells (Carlson et al. 2008; Greulich et al. 2009).

Though the in vitro studies have provided detail information, in vivo studies have verified the toxicity of AgNP with regard to their exposure and organism basis. At gene level, the genes responsible for apoptosis and inflammation pathways have also been found to be in elicited regulation on AgNP exposure [24]. The toxicity of AgNP has also been reported in embryonic zebrafish model. Moreover, changes in morphology like abnormal organ formation, pericardial edema, and slow development have also been reported (Verma et al. 2017a, b). In brief, the mechanism of toxicity of AgNP has been defined with respect of both in vitro and in vivo model; however, the detailed understanding has come mostly from in vitro studies. In vivo studies have enlightened the detail but need to be excavated in more intensive and molecular way.

Similar to AgNP, the cytotoxic effects of AuNP have also been the matter of discussion with regard to their extensive studies. The toxicity of AuNPs has been discussed in frame of both in vitro and in vivo studies. Knowledge about toxicity in in vitro models have been done on a large scale on each and every types of cell lines. A group of researchers showed the in vitro biocompatibility of AuNPs obtained from tea flavonoids in PC-3 prostate cancer cells and MCF-7 breast cancer cells that marked up increase level of gold concentrations (Nune et al. 2009). Another group of researchers showed use of soybean phytochemical mediated AuNP biocompatibility toward fibroblast cell lines. For clinical purpose of AuNPs, it is necessary to unravel the mechanism of in vivo toxicity and biodistribution. Furthermore, this group also showed that mice injected with AuNPs synthesized from plant extract of *Lantana montevidensis* (LM) did not reveal in vivo toxicity as compared with untreated mice (Nune et al. 2009). Both serum histopathological evaluation and biochemical parameters were normal and without any symptoms of toxicity. All these in vivo results thus generated infer that AuNPs were nontoxic in animal models and can be recommended for biomedical applications. A group of researchers showed cinnamon phytochemical-derived AuNP biocompatibility toward animal models. They also demonstrated the in vivo biocompatibility of AuNPs after intraperitoneal injection (i.p.) in male Wistar rats (Ahmed et al. 2016a) where the major accumulation of these nanoparticles was observed in liver and spleen followed by kidneys and lungs. So far all the published articles gave evidence that AuNPs may serve as promising and secure to increase level of in vivo concentrations and potential in the field of pharmaceuticals and biomedical applications.

4.3.3 Biomedical Application of AgNP and AuNP

In the field of biology, metallic nanoparticles (MNPs) have drawn several promising applications owing to their catalytic properties, biocompatibility, optical nature, conductivity, surface volume, and density (Li and Li 2014; Boote et al. 2014). As compared to route of colloidal metallic nanoparticles (MNPs), biosynthesized NPs are superior to colloidal stability and their proficiency to conjugate with organic molecules. Metallic nanoparticles (MNPs) have been used in various applications

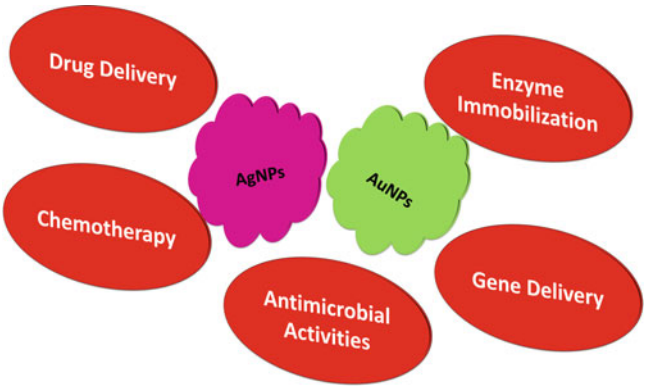

Fig. 4.4 Biomedical applications of AgNPs and AuNPs

such as drug delivery, enzyme immobilization, gene delivery, chemotherapy, and antimicrobial activity (Fig. 4.4).

Drug Delivery

This method includes targeted drug delivery and traditional mechanisms. Targeted drug delivery are preferred more than traditional drug delivery mechanisms since the drugs are chosen at a distinct affected area and doses are administrated locally without any undesirable effects. Several groups of work have been carried forward by scientists following these traditional drug delivery mechanisms (Li and Li 2014; Anandhakumar et al. 2012). The importance of metallic nanoparticles (MNPs) for efficient drug delivery mechanisms implies because of their distinct biophysical and biochemical properties with strong binding attraction for carboxylic acid aptamers, proteins, thiols, and disulfides. Therefore, they have been recommended for anticancer therapy. The toxicity of MNP depends on the surface coating, route of synthesis, size, shape, charge, and functionalized molecules, but its cytotoxicity relies at a minimal acceptable level of nanoparticles. The flexibility of MNPs involves their monolayers to provide an efficient system (Ajnai et al. 2014).

Enzyme Immobilization

The process of enzyme immobilization has been applied on solvent media for intensifying enzyme activity and stability (Iyer and Ananthanarayan 2008). In the field of biotechnology, the immobilization of enzyme seeks attention for their minimal expenses in industrial-based operational stability and ease of separation of products for long period (Mateo et al. 2007). Enormous scale of immobilization techniques can be used for covalent and adsorption on solid supports (Alonso et al. 2005). This method can be achieved by selecting matrix support and designing the

carrier. To be utilized as host matrices, MNPs such as gold and silver are used due to their surface stability and good electronic properties. Both these MNPs serve as good conduction centers to facilitate transfer of electrons (Chi et al. 2008). The enzyme immobilization of biogenic nanoparticle depends on solid supports either as isolated cells or whole cell enzymes, such as lysozyme (Vertegel et al. 2004), aminopeptidase, as well as alcohol dehydrogenase (Keighron and Keating 2010) and glucose oxidase (Li and Xu 2014).

Gene Delivery

The mechanism of gene delivery technique implies on gene of interest to specify its encoded protein into an appropriate host cell (Li and Xu 2014). Several types of gene delivery techniques are transfection, electroporation, and use of vectors such as retroviruses and adenoviruses (Farkhani et al. 2014). The gene delivery machinery in viral vectors occurs by introduction of nucleic acid sequences into the desired host genome of interest excluding any side effects. Therefore, these methods are secure in biomedical applications based on improvements in their efficiency (Martin-Ortigosa et al. 2014). In basic science, several nanoparticles have been applied, particularly to in vitro cells for stimulating the transfection efficiency. As a consequence, composite nanoparticles and nucleic acid are first supplied into in vitro cell medium and toward the surface of the cell followed by the magnetic force. Conditions due to the presence of higher toxicity of these nanoparticle biomedical applications are limited toward in vivo and in vitro conditions (Syu et al. 2014). Therefore, nanoparticles are encrusted with molecules, such as proteins and carbohydrates, synthetic organic polyethylene glycol, polyvinyl alcohol, poly-L-lactic acid, and silica to minimize toxic effect (Bao 2004). The process of developing new nonviral methods facilitates rate of transfection efficiency. At present, biosynthesized NPs hold an alternative approach for gene transfection (Seisenbaeva et al. 2017; Cai et al. 2008).

Chemotherapy

Chemotherapy is drug therapy for anticancer treatment of varied types. The main obstacles in cancer treatment are its toxic effect on healthy proliferating cells acquired by multidrug resistance (Gottesman et al. 2002). Therefore it is required for appropriate concentrations of anticancer drugs to be administered for reducing the toxic side effects (Maeda 2001). In these days, nanotechnology field has achieved the only alternative approach to overcome such problems by the application of nanotherapeutics, particularly for delivering drug to gene, siRNA, and antitumor therapy, biosensing, and bioimaging. Apart from MNPs, AuNPs also play an important role in drug delivery applications because of their size, shapes, surface-dependent properties, and minimal cytotoxic effects (Ghosh et al. 2008; Han et al. 2007). Therefore, nanoparticles can be recommended for efficient therapy toward drug delivery of targeted cancer cells.

Antimicrobial Activities

Due to the presence of high antimicrobial properties, metallic nanoparticles (MNPs) are used against various microorganisms. At present in the field of medical and pharmaceutical industries, inert nanomaterials serve as antimicrobial drugs. Compared to several metallic nanoparticles (MNPs), AgNPs showed effective bactericidal activity toward Gram-ve and Gram+ve bacteria including those antimicrobial-resistant strains (Li and Li 2014). AgNPs and its corresponding ions have drawn attention owing to their antibacterial nature either bacteriocidal or bacteriostatic and are also considered "oligo dynamic." Based on observation ionic form of Ag (silver) inactivates the interaction with thiol groups of essential proteins/enzymes. It is therefore known that ionic form of silver interaction with bacteria permits depolarization in the cell membrane, thereby inhibiting DNA replication machinery (Elechiguerra et al. 2005).

4.4 Conclusion and Future Outlook

This chapter primely focusses on eco-friendly biosynthesis of silver and gold nanoparticles as an alternative approach with relevant biomedical implications. These biogenic NPs have been used in the photocatalytic degradation of dyes. Therefore, metal/metal oxide hybrid nanocomposites might be use as a photocatalyst with enhanced antimicrobial activity. These nanoparticles have explored the therapy of nanomedicine which can be perceived from advancements of several AgNP- and AuNP-based nanomedicines. Green synthesized nanoparticles have been proved as beneficial in respect of high antibacterial efficacy with a biocompatibility at same platform. Furthermore, for the stability of in vitro and in vivo biodistribution, both AgNPs and AuNPs were used. This chapter highlights a novel opportunity with scope in advancement of designing convenient techniques to fabricate silver and gold nanoparticles with appropriate features to ensemble antibacterial activities, anticancer treatment, and therapeutic applications. Therefore, the potent role of these NPs should deliberate as cost worthy for therapeutic applications in the field of bioscience and biomedicine in the near future.

References

Ahmed S, Ikram S (2015) Silver nanoparticles: one pot green synthesis using terminalia arjuna extract for biological application. J Nanomed Nanotechnol 6:309. https://doi.org/10.4172/2157-7439.1000309

Ahmed S, Ullah S, Ahmad M, Swami BL (2015) Green synthesis of silver nanoparticles using *Azadirachta indica* aqueous leaf extract. J Radiat Res Appl Sci 9:1–7. https://doi.org/10.1016/j.jrras.2015.06.006

Ahmed S, Annu, Ikram S, Yudha S (2016a) Biosynthesis of gold nanoparticles: a green approach. J Photochem Photobiol B Biol 161:141–153. https://doi.org/10.1016/j.jphotobiol.2016.04.034

Ahmed S, Manzoor K, Ikram S (2016b) Synthesis of silver nanoparticles using leaf extract of Crotalaria retusa as antimicrobial green catalyst. J Bionanosci 10:282–287. https://doi.org/10.1166/jbns.2016.1376

Ajnai G, Chiu A, Kan T et al (2014) Trends of gold nanoparticle-based drug delivery system in cancer therapy. J Exp Clin Med 6:172–178. https://doi.org/10.1016/j.jecm.2014.10.015

Alonso N, Fernando L, Betancor L et al (2005) Immobilization and stabilization of glutaryl acylase on aminated sepabeads supports by the glutaraldehyde crosslinking method. J Mol Catal B Enzym 35:57–61. https://doi.org/10.1016/j.molcatb.2005.05.007

Anandhakumar S, Mahalakshmi V, Raichur AM (2012) Silver nanoparticles modified nanocapsules for ultrasonically activated drug delivery. Mater Sci Eng C 32:2349–2355. https://doi.org/10.1016/j.msec.2012.07.006

Arora S, Jain J, Rajwade JM, Paknikar KM (2008) Cellular responses induced by silver nanoparticles: in vitro studies. Toxicol Lett 179:93–100. https://doi.org/10.1016/j.toxlet.2008.04.009

Asharani PV, Low G, Mun K et al (2009) Cytotoxicity and genotoxicity of Silver. ACS Nano 3:279–290

Balalakshmi C, Gopinath K, Lokesh R et al (2017) Green synthesis of gold nanoparticles using a cheap Sphaeranthus indicus extract: impact on plant cells and the aquatic crustacean Artemia nauplii. J Photochem Photobiol B Biol 173:598–605. https://doi.org/10.1016/j.jphotobiol.2017.06.040

Bao G (2004) Functionalization and peptide-based delivery of magnetic nanoparticles as an intracellular MRI contrast agent. J Biol Inorg Chem 9:706–712. https://doi.org/10.1007/s00775-004-0560-1

Boote BW, Byun H, Kim J, Lib C (2014) Silver – gold bimetallic nanoparticles and their applications as optical materials. J Nanosci Nanotechnol 14:1563–1577. https://doi.org/10.1166/jnn.2014.9077

Braydich-Stolle L, Hussain S, Schlager JJ, Hofmann MC (2005) In vitro cytotoxicity of nanoparticles in mammalian germline stem cells. Toxicol Sci 88:412–419. https://doi.org/10.1093/toxsci/kfi256

Cai X, Conley S, Naash M (2008) Nanoparticle applications in ocular gene therapy. Vis Res 48:319–324. https://doi.org/10.1016/j.visres.2007.07.012

Carlson C, Hussain SM, Schrand AM et al (2008) Unique cellular interaction of silver nanoparticles: size-dependent generation of reactive oxygen species. J Phys Chem B 112:13608–13619

Chi M, Lyu R, Lin L, Huang H (2008) Characterization of Bacillus kaustophilus leucine aminopeptidase immobilized in Ca-alginate/k-carrageenan beads. Biochem Eng J 39:376–382. https://doi.org/10.1016/j.bej.2007.10.008

Choi O, Hu Z (2008) Size dependent and reactive oxygen species related nanosilver toxicity to nitrifying bacteria. Environ Sci Technol 42:4583–4588

Elechiguerra JL, Burt JL, Morones JR et al (2005) Interaction of silver nanoparticles with HIV-1. J Nanobiotechnol 10:1–10. https://doi.org/10.1186/1477-3155-3-6

Farkhani SM, Valizadeh A, Karami H et al (2014) Nanoparticles, nanocarriers, therapeutic and diagnostic molecules. Peptides 57:1–17. https://doi.org/10.1016/j.peptides.2014.04.015

Feng QL, Wu J, Chen GQ et al (2000) A mechanistic study of the antibacterial effect of silver ions on Escherichia coli and *Staphylococcus aureus*. J Biomed Mater Res 52(4):662–668

Ghosh P, Han G, De M et al (2008) Gold nanoparticles in delivery applications ☆. Adv Drug Deliv Rev 60:1307–1315. https://doi.org/10.1016/j.addr.2008.03.016

Gottesman MM, Fojo T, Bates SE (2002) Multidrug resistance in cancer: role of ATP-dependent transporters. Nat Rev Cancer 2:48–58. https://doi.org/10.1038/nrc706

Greulich C, Kittler S, Epple M et al (2009) Studies on the biocompatibility and the interaction of silver nanoparticles with human mesenchymal stem cells (hMSCs). Langenbeck's Arch Surg 394:495–502. https://doi.org/10.1007/s00423-009-0472-1

Han G, Ghosh P, Rotello VM (2007) Functionalized gold nanoparticles for drug delivery. Nanomedicine 2:113–123

Hsin Y, Chen C, Huang S et al (2008) The apoptotic effect of nanosilver is mediated by a ROS- and JNK-dependent mechanism involving the mitochondrial pathway in NIH3T3 cells. Toxicol Lett 179:130–139. https://doi.org/10.1016/j.toxlet.2008.04.015

Hussain SM (2005) In vitro toxicity of nanoparticles in BRL 3A rat liver cells. Toxicol In Vitro 19:975–983. https://doi.org/10.1016/j.tiv.2005.06.034

Hussain SM, Javorina AK, Schrand AM et al (2006) The interaction of manganese nanoparticles with PC-12 cells induces dopamine depletion. Toxicol Sci 92:456–463. https://doi.org/10.1093/toxsci/kfl020

Iyer PV, Ananthanarayan L (2008) Enzyme stability and stabilization — aqueous and non-aqueous environment. Process Biochem 43:1019–1032. https://doi.org/10.1016/j.procbio.2008.06.004

Keighron JD, Keating CD (2010) Enzyme: nanoparticle bioconjugates with two sequential enzymes: stoichiometry and activity of malate dehydrogenase and citrate synthase on Au nanoparticles. Langmuir 26:18992–19000. https://doi.org/10.1021/la1040882

Lam C, James JT, Mccluskey R, Hunter RL (2004) Pulmonary toxicity of single-wall carbon nanotubes in mice 7 and 90 days after intratracheal instillation. Toxicol Sci 134:126–134. https://doi.org/10.1093/toxsci/kfg243

Li Q, Li X (2014) Nanosilver particles in medical applications: synthesis, performance, and toxicity. Int J Nanomedicine 9:2399–2407

Li H, Xu D (2014) Trends in analytical chemistry silver nanoparticles as labels for applications in bioassays. Trends Anal Chem 61:67–73. https://doi.org/10.1016/j.trac.2014.05.003

Maeda H (2001) SMANCS and polymer-conjugated macromolecular drugs: advantages in cancer chemotherapy. Adv Drug Deliv Rev 46:169–185

Martin-Ortigosa S, Peterson DJ, Valenstein JS, Victor S, Lin Y, Brian G, Trewyn L, Lyznik A, Wang K (2014) Mesoporous silica nanopa intracellular Cre protein delivery for maize genome editing via loxP site excision. Plant Physiol. https://doi.org/10.1104/pp.113.233650

Mateo C, Palomo JM, Fernandez-lorente G et al (2007) Improvement of enzyme activity, stability and selectivity via immobilization techniques. Enzym Microb Technol 40:1451–1463. https://doi.org/10.1016/j.enzmictec.2007.01.018

Mazhar T, Shrivastava V, Tomar RS (2017) Green synthesis of bimetallic nanoparticles and its applications: a review. J Pharm Sci Res 9:102–110

Molnár Z, Bódai V, Szakacs G et al (2018) Green synthesis of gold nanoparticles by thermophilic filamentous fungi. Sci Rep 8:1–12. https://doi.org/10.1038/s41598-018-22112-3

Narayanan KB, Sakthivel N (2011) Green synthesis of biogenic metal nanoparticles by terrestrial and aquatic phototrophic and heterotrophic eukaryotes and biocompatible agents. Adv Colloid Interf Sci 169:59–79. https://doi.org/10.1016/j.cis.2011.08.004

Naushad M, Ahamad T, Al-Maswari BM et al (2017) Nickel ferrite bearing nitrogen-doped mesoporous carbon as efficient adsorbent for the removal of highly toxic metal ion from aqueous medium. Chem Eng J 330:1351–1360. https://doi.org/10.1016/j.cej.2017.08.079

Nune SK, Chanda N, Shukla R et al (2009) Green nanotechnology from tea: phytochemicals in tea as building blocks for production of biocompatible gold nanoparticles †. J Mater Chem 19:2912–2920. https://doi.org/10.1039/b822015h

Parveen K, Banse V, Ledwani L (2016) Green synthesis of nanoparticles: their advantages and disadvantages. AIP Conf Proc 1724:020048. https://doi.org/10.1063/1.4945168

Patra JK, Baek K (2014) Green nanobiotechnology: factors affecting synthesis and characterization techniques. J Nanomater 2014:417305

Prabu IJHJ (2015) Green synthesis and characterization of silver nanoparticles by leaf extracts of *Cycas circinalis*, Ficus amplissima, *Commelina benghalensis* and *Lippia nodiflora*. Int Nano Lett 5:43–51. https://doi.org/10.1007/s40089-014-0136-1

Seisenbaeva GA, Fromell K, Vinogradov VV et al (2017) Dispersion of TiO_2 nanoparticles improves burn wound healing and tissue regeneration through specific interaction with blood serum proteins. Sci Rep 7:1–11. https://doi.org/10.1038/s41598-017-15792-w

Shirsat S, Kadam A, Jadhav VV et al (2016) An eco-friendly physicocultural-based rapid synthesis of selenium nanoparticles. RSC Adv 6:48420–48426. https://doi.org/10.1039/C6RA08275K

Syu Y, Hung J, Chen J, Chuang H (2014) Plant physiology and biochemistry impacts of size and shape of silver nanoparticles on Arabidopsis plant growth and gene expression. Plant Physiol Biochem 83:57–64. https://doi.org/10.1016/j.plaphy.2014.07.010

Taylor P, Jha AK, Prasad K (2010) Green synthesis of silver nanoparticles using Cycas leaf. Int J Green Nanotechnol: Phys Chem 1:37–41. https://doi.org/10.1080/19430871003684572

Vadlapudi V, Behara M, Devamma MN (2014) Green synthesis and biocompatibility of nanoparticles. Rasayan J Chem 7:219–223

Velmurugan P, Anbalagan K, Manosathyadevan M (2014) Green synthesis of silver and gold nanoparticles using *Zingiber officinale* root extract and antibacterial activity of silver nanoparticles against food pathogens. Bioprocess Biosyst Eng 37:1935–1943. https://doi.org/10.1007/s00449-014-1169-6

Verma SK, Jha E, Sahoo B et al (2017a) RSC advances mechanistic insight into the rapid one-step facile biofabrication of antibacterial silver nanoparticles from bacterial release and their biogenicity and. RSC Adv 7:40034–40045. https://doi.org/10.1039/C7RA05943D

Verma SK, Panda PK, Jha E, Suar M (2017b) Altered physiochemical properties in industrially synthesized ZnO nanoparticles regulate oxidative stress; induce in vivo cytotoxicity in embryonic zebrafish by apoptosis. Sci Rep 7:1–16. https://doi.org/10.1038/s41598-017-14039-y

Vertegel AA, Siegel RW, Dordick JS (2004) Silica nanoparticle size influences the structure and enzymatic activity of adsorbed lysozyme. Langmuir 20(16):6800–6807

Wang L, Hu C (2017) The antimicrobial activity of nanoparticles: present situation and prospects for the future. Int J Nanomedicine 12:1227–1249

Xia T, Kovochich M, Brant J et al (2006) Comparison of the abilities of ambient and manufactured nanoparticles to induce cellular toxicity according to an oxidative stress paradigm. Nano Lett 6 (8):1794–1807