

Chapter 3

Fungal Nanoparticles: A Novel Tool for a Green Biotechnology?



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Abstract Bio-nanotechnology is regarded as one of the key technologies of the twenty-first century. In bio-nanotechnology, green methods or green chemistry is employed with the biological systems to fabricate nanostructures. Microorganisms have a promising role in biosynthesis of nanoparticles, especially fungi that secrete enzymes and proteins as reducing agents which can be used for synthesis of metal nanoparticles from metal salts with great potential. In recent years, various approaches have been made to maximize the yield of nanoparticles of varying shape, size, and stability. Increased surface and shape of nanoparticles are responsible for their different chemical, optical, mechanical, and magnetic properties. Use of bio-nanotechnology for synthesis of nanoparticles is a rapidly developing and emerging field. However, nanoparticle biocompatibility must be tested to access their safety before use in different fields. Prior to the clinical use, in vivo evaluation of nanoparticles should demonstrate a high degree of biocompatibility, with minimal negative effects on cell viability, immune function, and blood components. Safety of using nanoparticles in food industry, medicine, pharmaceutical, and agriculture fields should be evaluated to assure human health. The extremely small size of nanomaterials makes them more readily taken up by living tissue and possibly dangerous to humans.

Keywords Nanocomposites · Food industry · Nano-emulsion · Cytotoxicity · Antimicrobial · Nano-coating

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3.1 Introduction

Nanotechnology is a rapidly growing field of science that has become an integral part of biotechnology and regarded as one of the key technologies of the twenty-first century. Nanotechnology has great potential in biological and medical applications such as gene and drug delivery, bio-sensing, diagnostics, and tissue engineering (Prasad 2014; Prasad et al. 2014, 2017). The field of nanotechnology has received much attention in many fields, and application of microorganisms in the green synthesis of inorganic nanoparticles has been extensively studied (Prasad et al. 2016; Shakeel et al. 2016; Khalid et al. 2017). Innovative biosynthesized nanoparticles are used in different areas such as medical applications (e.g., diagnostics and tissue engineering), pharmaceutical fields, feed (e.g., vitamins), packaging, agro-food production (i.e., processing of pesticides, fertilizers, food additives), cosmetics (Raj et al. 2012), textiles (Yetisen et al. 2016), and nano-bioremediation (Yadav et al. 2017). The vast majority of manufactured nanomaterials are available in different shapes and sizes. It is expected that their use will significantly increase in the next decade. Currently, nanoparticles are produced in the hundreds of thousands of tons and used in a variety of products, including electronics, automobiles, aerospace, sporting goods, household, and hygiene (Pulit-Prociak and Banach 2016). Production of nanoparticles and nanomaterials may be carried out by three types of methods: (1) chemical (e.g., chemical vapor deposition, chemical reduction), (2) physical (e.g., physical vapor deposition, production of thin films), and (3) biological (production of nanoparticles by microorganisms) (Pulit-Prociak and Banach 2016; Prasad et al. 2016). The physicochemical methods for production of metallic nanoparticles, in general, and of gold nanoparticles, in particular, rely either on a top-down or bottom-up approach (Rudramurthy et al. 2016).

Biosynthesis of nanoparticles is extensively produced from bacteria (Khandel and Kumar 2016; Chaudhari et al. 2016), fungi (Prasad et al. 2016; Karimi and Khabat 2016; Khwaja and Azamal 2016; Guilger et al. 2017; Mohana and Sumathi 2017; Ottoni et al. 2017), yeast (Pantidos and Louise 2014, Amin et al. 2015; Boroumand Moghaddam et al. 2015), algae (Derek et al. 2017), and plants as well (Prasad 2014; Pantidos and Louise 2014; Mohanta et al. 2017; Protima and Rauwel 2017). It is recognized that microorganisms grow fast, secrete extracellular reducing enzymes, and synthesize inorganic nanoparticles such as gold, silver, calcium, silicon, iron, and lead. Among the many possible bio-resources, fungi represent excellent nanoparticles and produce nanoparticles faster than some chemical synthesis methods. Downstream processing and handling of fungal biomass can be much simpler than the processes needed for chemical synthesis (Mandal et al. 2006). Exploration of fungi in nano-biotechnology has attracted more attention for production of metallic nanoparticles due to their toleration and metal uptake and accumulation capability (Volesky and Holan 1995; Sastry et al. 2003). Fungi have a number of advantages for nanoparticle synthesis compared with other microorganisms (Castro-Longoria et al. 2011). Particularly fungi (*a*) are relatively easy to be isolated and cultured, (*b*) secrete large amounts of extracellular enzymes, (*c*) tolerate higher

metal concentrations than bacteria and secrete abundant extracellular redox proteins that reduce soluble metal ions to their insoluble form, and (d) harbor untapped biological diversity and may provide novel metal reductases for metal detoxification and bioreduction (Mandal et al. 2006; Kitching et al. 2015; Prasad 2016, 2017; Prasad et al. 2016). Production of nanomaterials, biologically, is inexpensive, undemanding, effective, energy-saving, and environment-friendly. Shape and size of biologically synthesized nanoparticles by various fungal species, including *Aspergillus*, *Fusarium*, *Penicillium*, *Rhizopus*, *Mucor*, *Trichoderma*, and *Pleurotus*, are studied (Rai et al. 2014; Xue et al. 2016; Aziz et al. 2016; Prasad 2016, 2017; Khalid et al. 2017; Ottoni et al. 2017). This chapter is an up-to-date review that deals with fungal nanotechnology as a new science for green synthesis of nanoparticles. Benefits and health risks of nanoparticles in different areas are highlighted, with a special attention to the nano-toxicology and regulatory recommendations related to the use of nanoparticles.

3.2 Nanoparticles and Nanotechnology

Nanoparticles can be defined as natural substances or manufactured materials containing particles in a free state or as aggregates. Nanoparticles are also called nanomaterials, nanocrystals, or nano-powders. Nanoparticles are intentionally produced or engineered to have specific properties, wherein one or more dimensions are typically between 1 and 100 nm (Pulit-Prociak and Banach 2016). Nano-biotechnology, bio-nanotechnology, and nano-biology are terms that refer to employ biological systems to produce bio-nanoparticles, which exhibit benefits for improving biocompatibility. Nanoparticles can be synthesized in numerous shapes (e.g., spherical, triangular, rods) from various metal ions (Rai et al. 2009). Nanoparticles have high surface area-to-volume ratio, nanometer regime, and unique properties, which makes them highly applicable. Myco-nanotechnology (myco = fungi, nanotechnology = creation and exploitation of materials in the size range of 1–100 nm) is defined as the fabrication of nanoparticles by fungi and their subsequent application, particularly in medicine (Rai et al. 2009). Myco-nanotechnology is the interface between mycology and nanotechnology and is an exciting new applied science that may have considerable potential, partly due to the wide range and diversity of fungi (Gupta et al. 2012). According to the definition, nanoparticles occur naturally or can be prepared intentionally. The latter group is divided into the following categories (The global market 2015).

1. Nonmetallic inorganic nanoparticles (TiO_2 , SiO_2 , ZnO , $\text{Al}(\text{OH})_3$, Fe_2O_3 , Fe_3O_4 , CeO_2 , ZrO_2 , CaO , ITO, ATO)
2. Metals and metal alloys (Au, Ag, Pt, Pd, Cu, Fe, Ni, Co, Al, Mn, Mo)
3. Nanomaterials based on carbon (fullerenes, carbon nanotubes, carbon nanofibers, graphene)

4. Nanopolymers and dendrimers (polymeric nanoparticles, polymer nanotubes, nanowires and nanorods, nanocellulose, nanostructured polymer films)
5. Quantum dots (cadmium telluride, cadmium selenide, quantum dots free of cadmium)

3.2.1 History

Although, in general, nanoparticles are considered a discovery of modern science, they actually have a very long history. Nanoparticles were used by artisans as far back as the ninth century in Mesopotamia for generating a glittering effect on the surface of pots (Reiss and Hutten 2010). The first scientific description regarding the properties of nanoparticles was provided by Michael Faraday in his famous paper “Experimental relations of gold to light.” In 1959, Richard Feynman gave a talk on nanotechnology describing molecular machines built with atomic precision, entitled “There’s plenty of space at the bottom” (Feynman 1991).

The word “nano” is derived from the Greek word for dwarf and means “a billionth.” A nanometer is a billionth of a meter, which is 250 millionth of an inch. The term “nanotechnology” was coined by Prof. Norio Taniguchi, Tokyo Science University, in 1974, to describe the precision manufacture of materials with nanometer tolerances and was unknowingly appropriated by Eric Drexler in his 1986 book *Engines of Creation: The Coming Era of Nanotechnology* (Drexler 1981). By the mid-1970s, Asilomar guidelines were developed by biotechnologists seeking to conduct their early work in ways both safe and publicly acceptable. It was not until 1990 that the first journal and funding of nanotech projects in Japan were begun. The first textbook about nanoparticles was published in 1992 (Markus and James 1995).

The first Feynman Prize in Nanotechnology was awarded in 1993 for modeling a hydrogen abstraction tool useful in nanotechnology (Peterson 2004). The first nano-bio-conference was in 1996, and the [first nanomedicine book](#) was published in 1999 (Peterson 2004). First report on nanotech industry, first [nanotech industry conference](#), and first [policy conference on advanced nanotech](#) were accomplished from 2001 to 2004 (Markus and James 1995). Foresight in 1999 published draft guidelines for safe development of molecular nanotechnology, including specific recommendations for environmental protection such as requiring artificial rather than natural fuel sources (Foresight Guidelines, Freitas 1999).

3.2.2 Properties

Properties and behavior of materials at the nanoscale differ significantly when compared to microscale, i.e., there are two basic factors which cause nanomaterials to behave differently than macromaterials (Gatti and Rivasi 2002). These are surface

effects (properties of surface atoms fraction) and quantum effects (Pulit-Prociak and Banach 2016). These factors affect the chemical reactivity of materials and determine their mechanical, optical, electrical, and magnetic properties (The global market 2015). Nanoparticles show enhanced electrical, optical, and magnetic properties. Compared to microparticles, the fraction of surface atoms in nanoparticle is increased, i.e., in relation to microparticles, nanoparticles are characterized by increased mass of surface particles. The ratio of surface area to mass in nanometric particles is 1000-fold greater than in micrometric particles. The nanometric particles are, thus, characterized by increased chemical reactivity, which is approximately 1000-fold higher compared to micrometric particles (The global market 2015, Khatoon and Ahmad 2012). Favorable modification of the properties of materials by changing their size is possible, enhancing their profitability to be used in a broad spectrum of scientific fields.

3.3 Green Syntheses of Nanoparticles

Nanoparticles can be produced by chemical methods in large quantities with a defined size and shape in a relatively short time. Synthetic techniques being employed for assembly of metallic nanoparticles are, however, quite costly with hazardous effect on the environment. Such process is not only expensive but also produces a toxic chemical that poses health threats. Therefore, biosynthetic approach is adopted to design nanoparticles with unique properties for potential scientific applications (Khan et al. 2017). Biosynthetic methods are clean and cost-effective compared to chemical methods which may lead to presence of some toxic chemicals absorbed on the surface. Green synthesis through microorganisms might overcome these toxicity issues. Biological methods for synthesis of nanoparticles using microorganisms have been suggested as a possible eco-friendly alternative to chemical methods and to be suitable for large-scale synthesis of nanoparticles (Karimi and Khabat 2016). Nanomaterials synthesized by bacteria, yeast, fungi, and algae are characterized by their mechanical strength and chemical properties. Frequently used strains of fungi and yeasts for metal nanoparticle synthesis are shown in Fig. 3.1.

Green synthesis provides advancement over chemical and physical methods as it is cost-effective, environment-friendly, and easily scaled up for large-scale synthesis and in such method there is no need to use high pressure, energy, and temperature and toxic chemicals (Chaudhari et al. 2016). Nanoparticles are biosynthesized when microorganisms grab target ions from their environment and then turn the metal ions into the element metal through enzymes generated by the cell activities (Sunkar and Valli 2013). Putative mechanisms during intracellular synthesis include heavy metal binding to fungal cell wall by proteins or enzymes present on via electrostatic interactions. The metal ions are reduced by enzymes present in cell wall. This leads to aggregation of metal ions and formation of nanoparticles.

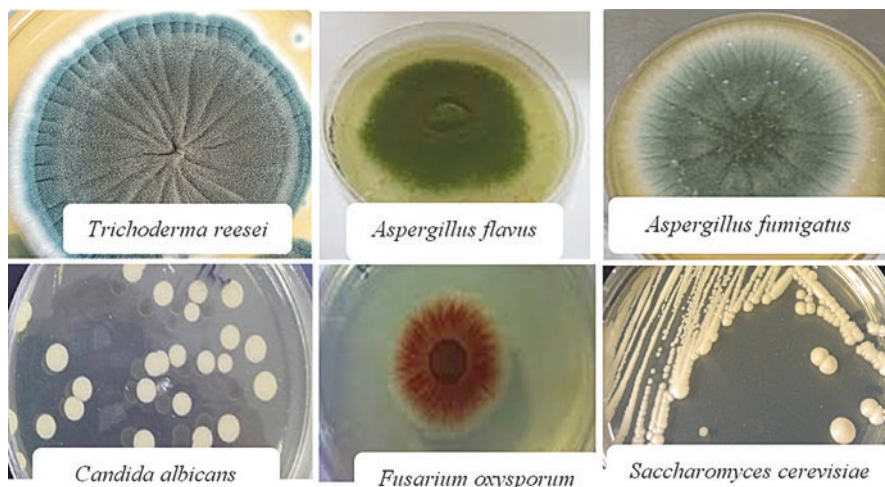


Fig. 3.1 Fungi and yeasts frequently used for metal nanoparticle synthesis

Development of green processes for biosynthesis of nanoparticles by fungi evolves an important branch of nanotechnology (Gupta et al. 2012; Chaudhari et al. 2016; Velusamy et al. 2016). Fungal species can readily synthesize metal nanoparticles both intra- or extracellularly using high levels of secreted proteins and/or enzymes (Rai et al. 2009; Ingale and Chaudhari 2013; Chaudhari et al. 2016). However, extracellular synthesis has advantages over an intracellular one: (a) fungal nanoparticles are mostly precipitated outside the cells and do not require lysis of fungal cells; (b) fungal biomass can withstand flow pressure and agitation conditions in bioreactors and other chambers; (c) it can be easily handled in downstream processing and, therefore, has advantages through processing for recovery and purification of nanoparticles and does not require equipment or long processing techniques; and (d) it is extremely cost-effective and less time-consuming (Gade et al. 2008; Ranjan and Joshi 2012; Prasad et al. 2016, 2017). Biosynthetic methods, in a renewable manner, ensure lower environmental impact and increase cost-effectiveness without the need of exogenous chemicals. Furthermore, biosynthetic mechanisms might produce nanoparticles of the desired shape, size, and distribution, given the highly specific interactions of the biomolecular templates and inorganic materials (Kitching et al. 2015).

Fungal endophytes are microorganisms that colonize living, internal tissues of plants without causing any immediate, negative effects (Shukla and Singh 2017). Endophytic fungi have been recognized as important sources of a variety of structurally novel active secondary metabolites with anticancer, antimicrobial, and other biological activities (Ranjan and Joshi 2012; Bose and Uma 2017; Sandhu et al. 2017). Endophytic-mediated synthesis of metal nanoparticles is gaining great importance owing to its simplicity; rapid rate of synthesis of nanoparticles of attractive, diverse morphologies; and eco-friendliness.

3.4 Applications of Nanotechnology

Current interest in metallic nanoparticles is due to their variable chemical, physical, and optical properties as well as the extremely small size which means very large surface area and increased reactivity per equivalent weight (Chaudhry 2016). Nanoscale, where less may be more, and nano-sizing may generate new properties and functionalities (Chaudhry 2016). Advantages of nanotechnology that can be obtained and exploited are as follows: *a*) lower doses and increased bioavailability (quick dissolution, improved penetration and permeation through membranes), *b*) controlled release and targeted bio-distribution, *c*) lower dose-dependent toxicity, and *d*) reduction of the influence of environment on bioavailability (Josef and Katarina 2015). However, it is important to address the ethical, social, and regulatory aspects of nanomedicine to minimize its adverse impacts on the environment and public health (Coles and Frewer 2013). Different applications of nanotechnology are shown in Fig. 3.2. At present, the most significant concerns for application of nanoparticles involve risk assessment, risk management of engineered nanomaterials, and risk communication in clinical trials (David and Tinkle 2007). In the future, education about the benefits and risks of nanomedicine is an urgent role and challenge to gain and maintain public support and ensure health care. Many studies have reported the pros and cons of applying nanotechnology (Gwinn and Val 2006; Johanna et al. 2016). Advantages and disadvantages of nanotechnology applications are represented in Table 3.1.

3.4.1 Antimicrobial Activity

Nanoparticles are proven to have novel antimicrobial effects which offer several advantages such as broad-spectrum activity. Fungi have become one of the main biological candidates for synthesizing nanoparticles because of their metabolic

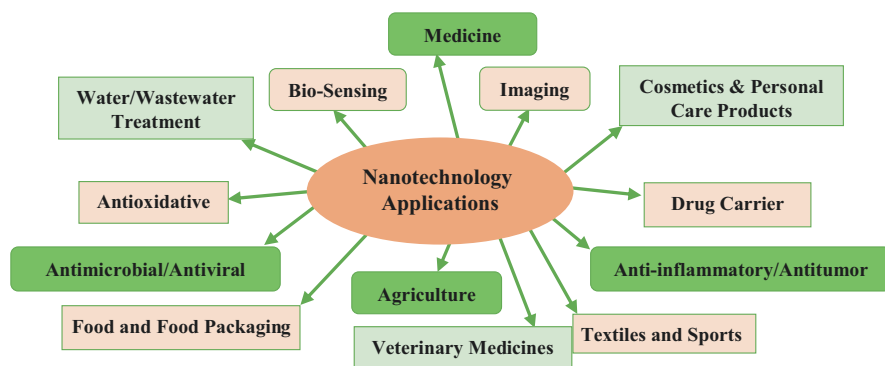


Fig. 3.2 Fields for applications of nanotechnology

Table 3.1 Advantages and disadvantages of nanotechnology applications

Pros	Cons
Nanotechnology can actually revolutionize a lot of electronic products, procedures, and applications	Nanoparticles are very small, and thus, problems can actually arise from the inhalation of these minute particles
Nanotechnology can benefit the energy sector, i.e., effective energy-producing, energy-absorbing, and energy storage products in smaller and more efficient devices	Nanotechnology production could develop unanticipated illness arising from their exposure
Nanotechnology can benefit the manufacturing sector that needs materials like nanotubes, aerogels, and nanoparticles	Inhalation of a sufficient doses can lead to lung ailments, including asbestosis and lung cancer, related to their size and chemistry as well as their ability to remain in lungs for a long time
Nanotechnology can benefit fields such as food, agriculture, cosmetics, and wastewater treatment	Exposure to much nanoparticles can weaken the natural defense systems
Nanotechnology, in the medical world, can help with creating smart drugs that help in faster cure and are without side effects that other traditional drugs have. Nanotechnology in medicine is now focusing on areas like tissue regeneration, bone repair, immunity, cancer, diabetes, and other life-threatening diseases	During the last few decades, there has been a continued increase in the morbidity and mortality attributed to air pollution in industrialized and developing countries

diversity (Rai et al. 2009). The first report of using fungi to synthesize nanoparticles dates back to a letter in *Nature* in 1989, reporting the production of cadmium sulfide nanoparticles by *Candida albicans* (Dameron et al. 1989). Silver nanoparticles are more effective against Gram-negative bacteria due to the different construction of cell walls. Gram-negative bacteria have lipopolysaccharide layer on the outside of the cell wall beneath, where a thin layer of peptidoglycan is located. The lipopolysaccharide layer structure is characterized by a lack of rigidity and strength (Pulit-Prociak and Banach 2016). A negative charge, located on lipopolysaccharides, attracts the positively charged particles of silver nanoparticles. The main component of cell walls of Gram-positive bacteria is a thin layer of peptidoglycan, which creates a rigid three-dimensional structure. Its structure comprises polysaccharide cross-linked short chains of protein molecules (Pulit-Prociak and Banach 2016). The stiffness and geometry of these layers are not conducive to penetration of silver nanoparticles through the cell wall of Gram-positive bacteria. However, some studies have reported that silver nanoparticles are able to penetrate both types of cell wall and enter into the cell, resulting in the uncontrolled tyrosine phosphorylation (Pulit-Prociak and Banach 2016).

Most antimicrobial agents inhibit microbial growth through several mechanisms such as cell wall inhibition and lysis, inhibition of protein synthesis, alteration of cell membranes, inhibition of nucleic acid synthesis, and antimetabolite activity (Yah and Simate 2015). Two main hypotheses can explain the toxic effects of

Table 3.2 Antimicrobial applications of nanotechnology

Field	Effect	Reference
Antibacterial activity	Silver interacts with sulfhydryl groups of proteins and with DNA, altering hydrogen bonding, respiratory processes, DNA unwinding, cell wall synthesis, and cell division, resulting in bacterial death. Induces denaturation and oxidization for cell wall and modulates the phosphotyrosine profile of putative bacterial peptides, which could inhibit protein synthesis and cell growth. Interaction with thiol (-SH) groups in bacteria and production of reactive oxygen species	Rai et al. (2014), Banerjee et al. (2010), Azmath et al. (2016), Ottoni et al. (2017), and Aziz et al. (2015, 2016)
Antifungal activity	Attacking membranes and inhibition of normal budding process in yeasts due to the destruction of the membrane integrity. Affect membrane dynamics and transmembrane pores are formed, thus causing a leakage of cell constituents and eventually cell death. Leakage of ions and other materials as well as dissipating the electrical potential of the membrane. Interaction between nano-Ag and the membrane structure leading to cell death	Kim et al. (2009), Rai et al. (2009), Scorzoni et al. (2017), Xue et al. (2016), and Aziz et al. (2016)
Antiviral activity	Nanoparticles show antiviral target human immunodeficiency virus type-1 (HIV) and inhibit replication of HIV in a dose-dependent manner. Might inhibit postentry stages of infection by blocking other functional HIV-1 proteins or reducing reverse transcription or proviral transcription rates by directly binding to the RNA or DNA molecules	Malik et al. (2017) and Sandhu et al. (2017)

nanoparticles on living organisms. The first is the harmful activities of nanoparticles due to the release of metal ions (Li et al. 2011). The second states that toxicity is induced by formation of free radicals, i.e., reactive oxygen species (Li et al. 2011). These free radicals are able to damage any components of the cell and initiate the production of increasing numbers of reactive oxygen species (Klaine et al. 2008). For example, generated free radicals are able to oxidize the double bonds of fatty acids in cell membranes, resulting in increased permeability of membranes, which contributes to the osmotic stress. The free radicals may also inhibit the activity of enzymes by binding to them and changing the helix of DNA, leading to cell death (Pulit-Prociak and Banach 2016). Formation of larger amounts of reactive oxygen species is induced by the higher surface area of nanoparticles as compared to their larger analogues. One of the most common mechanisms of silver nanoparticles is their natural affinity for bonding with a thiol group that is present in cysteine, which is a building block of the protein in bacterial cell wall (Pulit-Prociak and Banach 2016). Consequently, the enzymatic function of proteins is disturbed, and the chain of cellular respiration is interrupted. The spectrum antimicrobial activity of nanotechnology applications in food science and technology is given in Table 3.2.

3.4.2 Food Industry

Food-biocatalysts and bioprocessing industries face great challenges to develop high-quality and safe foods. Food processing aids to improve texture, flavor, taste, and consistency as well as improved delivery of bioactive compounds and nutrients through the integration of nanocomposites, nano-encapsulation, nano-emulsion, and edible nano-coatings in food technology (Sharma and Singh 2016). However, it is particularly important to ensure and assess the benefits and risks of nano-food products with urgent need for international regulation system for use of nanoparticles (Trujillo et al. 2016). Nanotechnology's success in the food industry depends on the social acceptance and awareness with possible toxicity of nanoparticles to the environment and potential risks to human health as well as the different mechanisms of action of nanoparticles in biological systems (Stark 2011).

Nano-biocatalyst is considered an innovative branch of the nanosciences. Several nanomaterials are currently used in nano-biocatalyst for enzyme immobilization or encapsulation. Such immobilized enzymes could be recovered and reused in a large-scale continuous process, reducing the overall cost of the biocatalytic process (Misson et al. 2015). When immobilized on nanocarriers, enzyme activity significantly increases, and mechanisms of enzyme action are enhanced. Enzyme activity increases when physical adsorption onto nanocarriers, through hydrophobic interactions, is carried out (Trujillo et al. 2016). The food and beverage industry is a focus for nanomaterial applications and strategies. Potential applications of nanotechnology in food include (a) nano-sensors for food quality control and smart packaging; (b) nanocomposites, nanocoating, and nanofilms for foodstuffs; (c) antimicrobial, hygiene coatings, detection of pathogens in food and beverages, self-sanitizing surfaces, and polymeric films for food packaging with high antibacterial properties; and (d) nanoscale freshness indicators and nano-emulsions for fat reduction (Magnuson et al. 2011; Aguilera 2014; Prasad et al. 2017).

3.4.2.1 Nanocomposites

Nanocomposites provide advantages in food packaging techniques; prevent growth of bacteria, fungi, or any pathogens; improve barrier abilities; provide resistive packaging; maintain the quality of foods; and increase the shelf life (Sharma and Singh 2016). Incorporation of the nanocomposites within the packaging material has been reported to increase the strength and thermal stability.

In many reports, it has been determined that silver metal nanoparticles can breach into the membranes of the bacterial cells. Antimicrobial properties against *E. coli* and *Staphylococcus aureus* have been reported with lots of nanocomposite systems, comprising polymer and silver nanoparticles (Sharma and Singh 2016). Significant antibacterial activity, shown against the food-borne pathogen by the nanocomposite film, will help to compete with and eradicate the bacterial invaders and to improve the shelf life and food quality (Sharma and Singh 2016).

3.4.2.2 Nano-encapsulation

Nano-encapsulation aids as a strategy to control a delivery system for food ingredients and additives in food processing. Food industry claimed that addition of nanocapsules to processed foods will improve both the availability and delivery of nutrients, thereby enhancing the nutritional status of food (Neethirajan and Jayas 2011). In nanotechnology, during various food processing operations, encapsulation of nanoparticles can deliver a material to the targeted site, enhance the flavor and shelf life during storage, and integrate antimicrobial agents with the nanoparticles in food (Sharma and Singh 2016). Encapsulated protective coating and advanced packaging system prevent spoilage and improve food quality (Sharma and Singh 2016; Souza and Fernando 2016). Nano-encapsulation system presents various benefits together with ease of handling, improved stability, withholding volatile components, controlled moisture release, pH-triggered controlled release, and enhanced bioavailability and efficacy (Sharma and Singh 2016). Nano-encapsulation has been tested for the safe and controlled discharge of favorable live probiotic cells to boost healthy gut function.

3.4.2.3 Nano-emulsion

Operations such as the targeted delivery of lipophilic products (i.e., nutraceuticals, medicines, flavor, antioxidants, and antimicrobial agents) are accomplished by carriers, named nano-emulsions. Due to their comparatively miniature size, nano-emulsion is very stable to gravitational separation (McClements et al. 2009). Bioavailability of the captured components can be enhanced through the non-emulsion-assisted delivery systems due to their relative smaller size as well as more surface area-to-volume ratio (Acosta 2009). Particles that are trapped within the nano-emulsions scatter light waves weakly, which make them suitable for integration with products like carbonated drinks, soups, ketchups, and dips (Sharma and Singh 2016). The highly viscous or gel-like product in food products can be formed from nano-emulsion. The nano-emulsion in many studies is stated as a most prominent way for capturing and transporting antimicrobial agent to the targeted site (Sharma and Singh 2016). Even the decontamination of food packaging equipment and function associated with varieties of food surfaces are accomplished with antimicrobial nano-emulsions (Sekhon 2010).

3.4.2.4 Edible Nano-coatings

Edible films are defined as a thin layer that can be safely consumed and provides a barrier against moisture, oxygen, and solute movement for the food. An edible film can be coated on food or placed between the food and the surrounding environment (Donhowe and Fennema 1993). In particular, safety and physical properties of the edible film-forming materials and coating are carefully examined. However,

technical information is still needed to develop films for food application. Edible films and coatings have received considerable attention in recent years because of their advantages over synthetic films (Bourtoom 2008). Nanoparticles are used on the packaging material cover, incorporated as nano-sensors in the packaging system or as a nano-laminate layer (Sharma and Singh 2016). The edible nano-laminates are applied to fresh fruits and vegetables, confectionary products, and formulation due to their ability to provide barrier against water, lipids, gases, odors, and off-taste (Sharma and Singh 2016). Besides, many nanomaterials provide extensive properties to the packaging material like antimicrobial activity, oxygen-reducing activity, and immobilization of enzymes.

Nanostructured coatings should (a) exhibit antimicrobial capability, (b) extend the shelf life and enhance food quality, (c) reduce packaging wastes, (d) integrate with eco-friendly and biodegradable polymer used for active food packaging, and (e) not affect the development of beneficial bacteria that are present in the digestive tracts like probiotics (Kuzma et al. 2008). Knowledge and awareness related to nanomaterials, regarding side effects for human health and environmental risk, is scarce (Sharma and Singh 2016). To what extent usage of natural biodegrading material and recycling of nanomaterial is prohibited is not well defined (Kuzma et al. 2008). The British Standards Institution and International and European Committee for Standardization have undertaken all the ethical, social, and demand issues related to nano-safety. Assessment of nanomaterials safety is entirely based on the chemistry and toxicity details (Sharma and Singh 2016). Significantly, accomplishment of nanotechnology in the food and bioprocessing industry is determined by alertness in the society and consumers. Non-degrading food packaging materials such as plastic enhance severe environmental problems. Novel bio-nanotechnology-based materials are being designed to develop cost-effective packaging materials and formulate edible films and eco-friendly biodegradable biopolymers that possess antimicrobial activity to extend shelf life of food (Sharma and Singh 2016).

3.4.3 Nanotechnology in Medicine

Owing to their unique chemical and physical properties and high surface area-to-volume ratio, nanoparticles are found to possess many important biological activities. An important feature is the structural stability of nanoparticles to effectively deliver the drug over a long period of time without degradation occurring before it reaches the cellular target (Rai et al. 2012; Duran and Marcato 2013; Anderson et al. 2016). Nanoparticles for biomedical application should be prepared only with biocompatible chemicals to minimize their toxic effect and increase their safe usage (Kitching et al. 2015). Applications of nanomaterials in medicine include fluorescent biological labels, drug and gene delivery, tumor destruction via heating (hyperthermia), phago-kinetic studies, and separation and purification of biological molecules and cells (Salata 2004; Acosta 2009). Important recent advantages

include tissue engineering, probing of DNA structure, bio-detection of pathogens, detection of proteins, and the drug delivery system (Pedro et al. 2015). For instance, biologic treatments such as insulin and calcitonin that cannot be delivered by conventional methods as an oral treatment have successfully been packaged in hollow nanoparticles that protect it from degradation in the gastrointestinal tract allowing for systemic delivery of the drug and avoiding alternative methods of delivery such as subcutaneous injection (Pridgen et al. 2015). The advantages of using nanoparticles for the drug delivery result from their two main basic properties (Parveen et al. 2016). First, due to their small size, nanoparticles can penetrate through smaller capillaries and are taken up by cells, which allow efficient drug accumulation at the target sites. Second, use of biodegradable materials for nanoparticle preparation allows sustained drug release within the target site over the period of days or even weeks.

Nanoparticles are being advanced as novel and more targeted treatments for difficult to manage diseases such as cancers. One of the main problems in anticancer treatments is the continuous growth of tumor cells resistant to a broad range of anticancer agents (Abraham et al. 2012). Use of engineered nanoparticles offers the ability to transport therapeutics to specific sites of a disease, thus reducing the off-target toxicity of many drugs. This is especially true in the use of chemotherapeutics where off-target reactions cause serious side effects in cancer patients (Anderson et al. 2016). It is crucial to deliver a drug to a desired target site in a controlled manner while not causing additional adverse health effects to the patient. In particular, gold nanoparticles have unique features that make them excellent nanomaterials, enabling the integration of targeting, imaging, therapeutics, and applicability in management of heterogeneous diseases such as cancer (Pedro et al. 2015). However, in contrast to their beneficial effects, use of nanoparticles for drug delivery can raise various risks to human health. The small size is beneficial, but it could have negative effects due to the following: (a) some nanoparticles can cause inflammation and fibrosis as a result of causing phagolysosomal membrane permeability and formation of reactive oxygen species; (b) the small size indicates a large surface area which could be harmful by exposing more surface molecules to cellular components; (c) preparation and stabilization processes of the nanoparticles for drug delivery can cause negative effects, since chemical reducing agents and radiation can stimulate cytotoxicity (Anderson et al. 2016). Some benefits, risks, and toxicity of nanoparticle applications in medicine are represented in Table 3.3.

3.4.4 Nanotechnology in Cosmetics

“Silver and gold nanoparticles” applied as preservatives in cosmetics have been found to be very stable and did not exhibit sedimentation for over 1 year. In cosmetics, nanoparticles exhibit sufficient preservation efficacy against mixed bacteria and mixed fungi and did not penetrate normal human skin (Raj et al. 2012). Nanoparticles

Table 3.3 Medicinal applications of nanoparticles

Field	Benefit	Risk/toxicity	Reference
Wounds and burns	Can induce tissue regeneration and prevent fibrosis of the injured tissue such as surgical incisions, ischemic heart muscle, and severed nerves. Dried nanoparticles, suspensions, aerosols, hydrogels, or incorporated into sheets of biodegradable scaffold materials such as collagen, all can easily be used in wound dressings, restores normal structure of the injured skin before onset of the fibrosis process and scar formation	Toxicity from silver is observed in the form of argyria that is caused by silver ions release from the dressing in large open wounds. Silver nanoparticles show toxic effect on fibroblasts and human lung adenocarcinoma epithelial cell line	Rigo et al. (2013), Galili (2017), Konop et al. (2016), Yang and Hong (2015), and Kamoun et al. (2017)
Cancer	Nanotechnology represents possibility to enhance the diagnosis and treatment of cancer, multifunctional targeted devices capable of bypassing biological barriers to deliver therapeutic agents to the biological target involved in cancer, nano-biosensors for predicting the disease, minimizing the growth of cancer cells, and reducing the cost of treatments	Toxicity is dose-dependent and causes cellular damage in human epidermoid larynx cell line through reactive oxygen species formation	Jacob et al. (2012) and Liu and Jiang (2017)
Dental practice	Silver nano-solution has been used as a caries inhibitor. Fluoride and silver interact synergistically to form fluorapatite showing slower bacterial growth. Silver nanoparticles provide self-cleaning against plaque biofilm	Potential toxicity to the central nervous system	Feng et al. (2015)
Drug delivery	Using nanoparticles, it may be possible to achieve improved delivery of poorly water-soluble drugs by delivering drugs in small particle size and increasing the total surface area of the drugs allowing faster dissolution in blood stream and faster absorption by human body-targeted delivery of drugs in a cell- or tissue-specific manner. Size of nanoparticles opens the potential for crossing the various biological barriers within the body	Risk assessment reveals great carcinogenic potential; acute toxic response can accumulate in the body and over time result in the development of nanopathologies, such as granulomas, lesions (areas of damaged cells or tissue), cancer, or blood clots	Gatti and Rivasi (2002), Gatti (2004), and Srinivas (2015)

can be attached to the cell membrane, penetrate inside the bacteria, and disrupt the membrane structure of bacterial cells (Kokura et al. 2010; Swati and Satish 2016).

Antimicrobial mechanisms of nanoparticles are related to the formation of free radicals. In the field of cosmetics, it is very important to protect the products against

microbial contamination which may occur during production of cosmetics or their storage. Before nanotechnology permanently penetrated the cosmetic industry, organic compounds such as parabens and phenoxyethanol had been used to control unwanted microbial flora (Pulit-Prociak and Banach 2016). Studies revealed the irritant effects of these types of preservatives, especially parabens, in relation to epidermis and cancer (Darbre et al. 2004; Cross and Roberts 2000). The harmful preservatives have been partially replaced by metal nanoparticles, in particular silver nanoparticles (Kokura et al. 2010). By introducing nanoparticles in the structure of materials, it is possible to give products antibacterial and anticorrosion properties and protection against UV radiation, and the resultant structures can be easily cleaned. Careful studies regarding toxicity of applying nanoparticles in cosmetics must be considered. Toxicity of nanoparticles, due to their smaller size, chemical composition, surface structure, solubility, and shape, can easily gain access to the blood stream via skin or inhalation and transport to the various organs and can lead to their dysfunction (Yevgen et al. 2012; Swati and Satish 2016).

3.4.5 Nanotechnology in Agriculture

The current world population of 7.3 billion is expected to reach 8.5 billion by 2030, 9.7 billion in 2050, and 11.2 billion in 2100, according to a new UN DESA report, World Population Prospects (World Population Project). Agriculture is the backbone of most developing countries, and it is widely recognized that global agricultural productivity must increase to feed a rapidly growing world population (Sekhon 2014). Nanotechnology has the potential to positively protect plants, monitor plant growth, detect plant and animal diseases, and increase global food production. Agriculture and food production capacity is faced with many challenges, and agriculture as a source of food is becoming increasingly important (Fraceto et al. 2016; Singhal et al. 2017). Thus, it is necessary to use the modern technologies such as nano-biotechnology in the form of nanopesticides or nanofertilizers, later referred to as nanoagrochemicals (Sekhon 2014; Kah 2015; Prasad et al. 2017; Bhattacharyya et al. 2017). There are major points for incorporating biosynthesized nanoparticles in agriculture (Mishra et al. 2017). These include the following:

- Alleviating the toxicity of nanoparticles by assessment of risk factors (evaluation for fate, transport, behavior, bioavailability, and toxicity).
- Optimizing the permissible level of nanoparticle dose within the safety limits by performing dose-dependent studies.
- Designing the experiments in natural habitat and avoiding in vitro assays for accurate interpretation.
- Most importantly, applying biosynthesized nanoparticles from laboratory to field conditions and using nanomaterials for sustainable agriculture production that allows risk-free environment in the near future to reduce their impact on human health (Arif et al. 2016; Mishra et al. 2017).

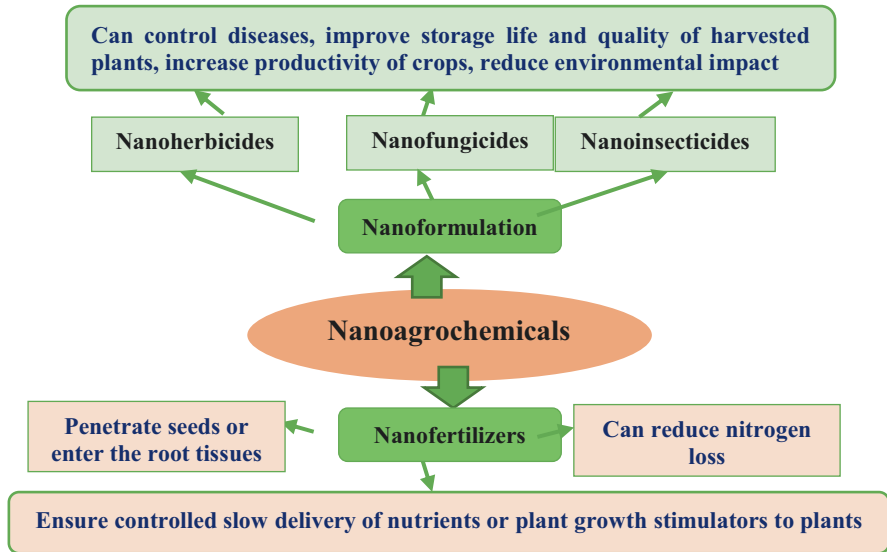


Fig. 3.3 Application of nanoparticles for plant growth stimulation and crop protection

- Costs for escalating production of nanoparticles and devices must be affordable, and safety of nanotechnology must be addressed before its spreading into the environment (Alejandro 2017).
- Nanoparticle-plant interactions, availability of soil microorganism, macro- and micro-nutrient availability, and effect of different abiotic stress factors on plant should be considered (Arif et al. 2016).
- Release and behavior of nanoparticles with the living systems are a major threat that must be analyzed before their wide applications to avoid their harmful impact on human health and the environment (Arif et al. 2016)

Nanoparticles can be applied in plants, through nanoagrochemicals, by (a) nanoformulations (i.e., nanoherbicides, nanofungicides, nanoinsecticides) and (b) nanofertilizers. Nutrients in nanofertilizers are delivered to crops within nanoparticles, whereby nutrients can be encapsulated inside nanomaterials, coated with thin protective polymer film, and delivered as particles or emulsions of nanoscale dimensions (Josef and Katarina 2015). Nanofertilizers can reduce nitrogen loss due to leaching, emissions, and long-term assimilation by soil microorganisms (Josef and Katarina 2015). Applications of nanoparticles for plant growth stimulation and crop protection are represented in Fig. 3.3.

The ability of some nanoparticles to penetrate seeds or enter the root tissue indicates the possibility to develop new nutrient delivery systems that exploit the nanoscale porous domains on plant surfaces and show sustained release of nutrients (Josef and Katarina 2015). On the other hand, the ability to incorporate genetic materials such as plasmid DNA, RNA, and siRNA into functionalized nanoparticles with little toxicity demonstrates a new era in delivering genes selectively to tissues

and cells (Jin et al. 2009). Nanoparticle-mediated DNA delivery involves coating DNA molecules onto the nanoparticles to be delivered directly into plant cells. After entering into the plant cells, DNA molecules will be released by nanoparticles and integrate into the host genome (Josef and Katarína 2015). Nanoformulations and nanofertilizers are smart delivery systems to plants.

Biotechnology of nanoparticles finds a broad range of uses for plant growth, defense, and nutrients. Nowadays nanomaterials like metal and metal oxide nanoparticles can be used to improve crop yield and alleviate toxicity (Arif et al. 2016). Currently, there is a common assumption that the small size of nanoparticles allows them to easily enter tissues, cells, and organelles and interact with functional biomolecular structures (i.e., DNA, ribosomes) since the actual physical size of an engineered nanostructure is similar to many biological molecules (e.g., antibodies, proteins) and structures (e.g., viruses) (Solanki et al. 2015). Nanofertilizer can be used for delivery to the plants. Uptake, translocation, and fate of nanoparticles in plant system are unknown, resulting in rise of various ethical and safety issues regarding the use of such nanofertilizers in plant productivity.

Public awareness about the advantages and challenges of nanotechnology will lead to better acceptance of this emerging technology. “Nanotechnology” has great potential for sustainable agriculture, improving and enriching food, and enhancing the quality of life. All over the world, nanotechnology has become the future of any country (Prasad et al. 2014). Combination of nanotechnology, food, and pesticides has high potential regarding public concern. Phytotoxicity cannot be neglected because nanotechnology will significantly affect the agricultural ecosystem by the increasing release of nanoparticles into the environment which will subsequently generate nano-wastes (Thul et al. 2013; Kah 2015). Nanoparticles are now introduced at all stages of the food chain, and public awareness about nanoagrochemicals seems generally low. Biological control agents are generally regarded as safe for humans and the environment. However, increased exposure of consumer population to fungal substances (mycotoxins) and fungal nanoparticles can affect the immune system and human body (Kah 2015). Particular attention should be devoted to non-biodegradable materials due to risks of accumulation and persistence in soil, plants, and mammals, which may subsequently result in various pathological processes (Handy et al. 2008; Josef and Katarina 2015).

3.5 Commercialization of Nanoparticles

The market for nanotechnology products is already huge and is predicted to grow rapidly in the coming years. Most nanoparticles are produced in multiton volumes in varying sizes, shapes, and surface coatings. Nanoparticles cover a range of materials such as inorganic metal and metal oxide nanomaterials, carbon-based nanomaterials, and polymeric particulate materials in a variety of forms (The global market 2015). Complete understanding of nano-bio interactions and the challenges regarding chemistry, manufacturing, and controls is required for clinical translation and

commercialization. Today, nanotechnology is used in a broad spectrum of scientific fields such as biotechnology, medicine, pharmacy, ecology, electronics, clothing, agriculture, veterinary medicine, food industry, and cosmetology. Nanomaterials of particular interest include nanoparticles of silver, gold, zinc, selenium, titanium dioxide, and carbon nanotubes (Pulit-Prociak and Banach 2016). According to a statement issued by the European Commission, the global amount of manufactured nanomaterials is close to 11.5 million tons, which is equivalent to their market value reaching 20 billion per year. It is estimated that the current global market for nanomaterials is from 300,000 tons to 1.6 million tons. The Asian region accounts for the largest market share (approx. 34%), followed by North America (approx. 31%) and Europe (approx. 30%) (The global market 2015). Silver nanoparticles market size was over \$ 1 billion in 2015 by application (health care, life sciences, textiles, electronics, food, and beverage) with industry analysis report, regional outlook (USA, Canada, Germany, UK, France, Italy, Spain, Poland, Russia, Netherlands, China, India, Japan, South Korea, Australia, Indonesia, Malaysia, Brazil, Argentina, Mexico, Saudi Arabia, UAE, South Africa), growth potential, price trends, competitive market share, and forecast, from 2016 to 2024 (Global Market Insight 2017).

3.6 Cytotoxicity of Nanotechnology

Nano-toxicology is a branch of bio-nanoscience that includes the study of toxicity of nanomaterials. Due to the small size of nanoparticles, nano-toxicological studies are planned to determine whether and to what level these particles may pose a risk to the environment and human health (Salaheldin et al. 2016). In general, toxicity of nanoparticles is determined by their particle size, shape, and biodegradability. The small size of nanoparticles allows them to easily enter tissues, cells, and organelles and interact with functional biomolecular structures (i.e., DNA, ribosomes) (Kah 2015; Pulit-Prociak and Banach 2016). The actual physical size of an engineered nanostructure is similar to many biological molecules (e.g., antibodies, proteins) and structures (e.g., viruses) (Xia et al. 2009).

Based on the particle size and biodegradability, nanoparticles can be classified into four classes: (1) size >100 nm and biodegradable, (2) size >100 nm and non-biodegradable, (3) size <100 nm and biodegradable, and (4) size <100 nm and non-biodegradable (Josef and Katarina 2015). Non-biodegradable materials which remain in the body, of course, can accumulate and affect the immune system and represent an increased risk of toxicity (Keck and Muller 2013). Nanotechnology is incorporated into a large variety of goods, such as food, food packaging, sunblock, chemical fertilizers, and animal feed. However, little is currently known about the possible effects of nanotechnology on human or environmental health. Nanoparticles can enter in the human system through several ways: (a) via the lungs where a rapid translocation through the blood stream to vital organs is possible, including crossing the blood-brain barrier, (b) absorption by the intestinal tract, or (c) the skin (Josef and Katarina 2015). Nanoparticles can affect cell membranes and causing DNA

damage, which could be harmful to the human health (Solanki et al. 2015). Nano-size materials change their physical and chemical properties in comparison with bulk materials and can become toxic when they reach nano-size (Josef and Katarína 2015). Therefore, an increased attention must be devoted to the impact of risks associated with their usage:

- Nanoparticles usually aggregate after entering an environment, and therefore, investigation of mechanisms of toxic effects/impacts and toxicity trials should be performed.
- Use of nanotechnology in medicine, more specifically as a drug delivery, spreads rapidly. The pharmaceutical sciences are using nanoparticles to reduce toxicity and side effects of drugs. However, these carrier systems themselves may impose risks to the patient (Jong and Borm 2008).
- Cytotoxicity studies show that nanoparticles can easily penetrate DNA and the cells of the lungs, skin, and digestive system, thereby causing harm to living organisms (Oberdorster et al. 2005). One example of a commonly used but potentially harmful nanoparticle can be found in the beverage industry. Beverage companies have been using plastic bottles made with nanocomposites, which minimize the leakage of carbon dioxide out of the bottle. This increases the shelf life of carbonated beverages without using heavy glass bottles or more expensive aluminum cans (Adam 2012).
- Nanoparticles are now being engineered, thereby increasing the risk of causing irreversible damage to living organisms. It is important to proactively address the ethical, social, and regulatory aspects of engineered nanoparticles in food, medicinal, pharmaceutical, and agricultural fields to minimize the adverse impacts on the environment and public health and to avoid a public backlash (Oberdorster et al. 2005).
- Penetration of nanoparticles into an environment and its specific reactivity can cause dangerous effects. Therefore, there is a need to develop techniques to monitor their potential risks. Understanding the life cycle of nanoparticles in the environment and their chemical stability is an important step in the process of determining their influence on living organisms.

3.7 Regulation of Nanoparticles

Nanoparticles tend to accumulate in various organs, especially in the liver, kidneys, and lungs. Presence and accumulation of silver nanoparticles in these organs may be particularly dangerous and can have negative effects in the future (Pulit-Prociak and Banach 2016). Toxic effects of nanoparticles are mostly connected with the damage of membranes and DNA, generation of reactive oxygen species, and genotoxicity. Some toxicological studies have reported that the effect of nanoparticles can be cytotoxic, genotoxic, neurotoxic, and ecotoxic (Pulit-Prociak and Banach 2016). Based on these facts, regulation requirements for nanotechnology, preparation, and

application are strongly needed, especially in relation to nature, environment, and human health (Josef and Katarina 2015). It is very important to know the whole life cycle of products containing nanomaterials. Full scientific information is not yet available, and developed conclusions are incomplete. It is necessary to perform tests to determine the degree of nano-accumulation in a living matter (Pulit-Prociak and Banach 2016). If alarming data are confirmed, it will be necessary to provide methods for environment protection against a possible threat of nanomaterials that may accumulate in the future.

The most significant ethical issues relating to nanomedicine involve risk assessment, risk management, and risk communication in clinical trials. Before a nanomedicine product can be used in diagnosis and prevention or treatment of disease, extensive clinical testing must be first achieved to explore the toxicological, pharmacological, and immunological properties of different nanomaterials (David et al. 2007). Educating members of society about the benefits and risks of nanomedicine is important to gain and maintain public support. The problem of nanomedicine products could be a significant concern in countries that do not have guaranteed health-care coverage (David et al. 2007). New technologies such as genetically modified foods and nanomedicine are likely to be considered as dangerous or disruptive.

Existing data show how nanomaterials accumulate in the environment, and moreover, every year their number drastically increases (Pulit-Prociak and Banach 2016). For example, the amount of silver nanoparticles derived from various sources in 2005 was equal to 4 tons per year, while in 2008 it increased to 563 tons (Pulit-Prociak and Banach 2016). There are currently several food and beverage products with nanotechnology on the market. Governments and food companies in several countries are investing in hundreds of projects developing nanotechnology in food and agriculture (Bhagat et al. 2015). Nanotechnology can be applied in all aspects of the food chain, both for improving food safety and quality control and as novel food ingredients or additives, which may lead to unforeseen health risks. The Organisation for Economic Co-operation and Development's Working Party on Manufactured Nanomaterials, which is comprised primarily of regulators from various countries, is looking to share information among the countries about regulatory actions and voluntary programs and the data they have or need for discussions relating to regulatory decisions (Josef and Katarina 2015).

3.8 Challenges and Future Prospects

Bio-nanoparticles possess excellent biocompatibility and are, therefore, promising materials for several applications such as coatings, packaging, medicine, construction, electronics, as well as cosmetics, textile, and agriculture (Sohel et al. 2017). There has been increasing interest in the use of fungi for these processes, because fungi may have the potential to provide relatively quick and ecologically clean bio-factories for metallic nanoparticles (Sohel et al. 2017). Many industrial areas,

including food, enzyme, and pharmaceutical production and processing, currently use fungal biomass. Downstream handling and processing procedures for fungal material are already well established (Rai et al. 2009; Bose and Uma 2017; Sandhu et al. 2017). In relation to many other uses of fungi, production of metallic nanoparticles is a relatively new development. Fungi is a very effective secretor of extracellular enzymes and able to produce metal nanoparticles and nanostructure. Fungal nanotechnology would appear to be a considerable potential biotechnology to develop in the future (Rai et al. 2009; Li et al. 2017; Palanivel et al. 2017). A number of challenges, however, need to be undertaken before the full evaluation and application of myco-nanotechnology.

Despite the broad range of applications, cytotoxicity of nanoparticles and health risks cannot be neglected (Thul et al. 2013). The interactions of nanomaterials with biological systems may change the properties of nanomaterials and in return affect their biological responses. Therefore, studies on innovative methodologies on the surface chemistry, unique mechanisms of the nano-bio-interface, and relevant biological applications are challenges of great importance (Li et al. 2017). Release and behavior of nanomaterials with the living systems are a major threat that must be analyzed before their wide application to avoid their harmful impact on human health and the environment (Thul et al. 2013).

The future of nanotechnology provides an opportunity for positive economic development through effective and innovative products. However, there is a lack of in vitro validated tests and in vivo toxicity data and limited evaluation of risk assessment in this area (Solanki et al. 2015). Therefore, in this context, the following key points should be considered in the future:

- Nano-risks and nano-safety should be determined to control and monitor the development of such a new technology.
- Permissible levels of nanoparticles dose within safety limits need to be explored and clarified to gain comprehensive knowledge of nanotoxicity.
- A clear overview of soil physicochemical characteristics in the agricultural field, where nanoparticles are to be applied, may help in reducing their risk toward plant and soil biota (Mishra et al. 2017).
- Studies on nanoparticles should discuss what is known concerning their fate, behavior, toxicity, and effects on human health and agroecosystem. Several issues must be addressed to ensure safety of nanoparticles (Klaine et al. 2008; Mishra et al. 2017).
- It is believed that biosynthesized nanoparticles may possess relatively lesser or no toxicity, and hence future researches must precisely focus on their practical utility.
- Safety of nanoparticles regarding the human health is associated with great uncertainty. Governments across the world should form common and strict norms and monitoring, before commercialization and bulk use of nanomaterials (Agrawal and Rathore 2014).

3.9 Conclusion

Bio-nanotechnology involves the use of biological components and nanotechnology to support biotechnological processes on a nanoscale level. Bio-nanoparticles possess excellent biocompatibility and are, therefore, promising materials for several applications such as coatings, packaging, medicine, construction, and electronics as well as cosmetics, textile, and agriculture applications. In recent years, a lot of attention is being paid to bio-nanotechnology due to its amazing applications and beneficial effects. Numerous microorganisms have been shown to have potential for biosynthesis of metallic nanoparticles. There has been increasing interest in the use of fungi for these processes because fungi may have the potential to provide relatively quick and ecologically clean bio-factories for metallic nanoparticles. Fungal nano-biotechnology has scopes for solving some of the major problems faced by humans in today's world. The need for more safe alternatives in large-scale production of nanoparticles resulted in the development of eco-friendly methods. Industrial bio-nanotechnology takes advantage of biological-based approaches to produce nanoparticles using biological renewable resources to reduce hazardous waste production which is the main advantage of nanoparticle biosynthesis. However, as with all powerful tools of science, this rapidly evolving biotechnology needs to be handled with care. Considering the great benefits and risks as well, is bio-nanotechnology a novel green tool of the future?

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