Chapter 2

Fungal-Derived Nanoparticles as Novel Antimicrobial and Anticancer Agents

Muhammad Waseem and Muhammad Atif Nisar

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/66922

Abstract

In order to control microbial resistance against commonly used antibiotics, it is indispensable to develop novel and efficient antimicrobial agents. For this purpose, metallic nanoparticles (mainly inorganic) with their antimicrobial activites represent an effective solution for this global problem. However, synthesis of nanoparticles involves the use of expensive, poisonous and dangerous chemicals responsible for different biological and environmental hazards. This fact increases the necessity of developing environment-friendly procedure by means of green synthesis (using plants) and extra-biological methods (using microbes such as bacteria and fungi). More recently, metallic nanoparticles, derived from fungal sources, have demonstrated their potential not only as a new-generation antimicrobial agents but also as anticancer agents. Therefore, this chapter is aimed to explore the various nanoparticles producing fungi with ultimate objective of elucidating the possible (i) mechanism of biosynthesis of metallic NPs by various fungi and (ii) mode of action of these mycosynthesized NPs on bacterial cell. This chapter would certainly increase our knowledge about interaction of nanoparticles with bacterial cell for their use in health biotechnology.

Keywords: nanoparticles, silver, myconanosynthesis, fungi, cancer, antibacterial activities

1. Introduction

In the field of nanotechnology and nanomaterial, more specifically, nanoparticles are extremely important because of their unique optical, physicochemical, and biological facets. Though their biological synthesis is still at early stages and many material scientists around the globe are working on the production of nanoparticles from different sources including plants, animals, microbes, and metallic compounds like gold, silver, platinum, etc. Various studies on biosyn-

thesis of nanoparticles have been carried out using a wide array of microorganisms such as algae, bacteria, actinomycetes, fungi, yeasts, and viruses [1, 2]. Among the many possible bioresources, biologically active products from fungi and yeast represent excellent scaffolds for this purpose. Since fungi and yeast are very effective secretors of extracellular enzymes and number of species grow fast and therefore culturing and keeping them in the laboratory is very simple [3]. They are able to produce metal nanoparticles and nanostructure via reducing enzyme extracellularly [3, 4]. Not only the harvesting of extracellularly synthesized nanoparticles from fungi is easy and inexpensive [2, 5], they can also be manipulated by controlling the pH, temperature, substrate concentration (metal ions), and reaction time [6, 7]. Therefore, the biosynthesis could be ideally used for large-scale production of nanoparticles for several industrial applications [3]. Importantly, fungi have also secreted fairly large amount of proteins and secondary metabolites extracellularly, and hence, the fungal biomass could reduce the metal ions more easily leading to the rapid formation of nanoparticles [8]. Because of these advances, the myco-based extracellular synthesis method is often considered as a better resource for higher productivity of nanoparticles [4].

On the other hand, increasing incidence of microbial resistance to clinically approved classes of antibiotics has emerged in recent years and is a major health problem, requiring to develop novel and effective antimicrobial agents [4, 9–11]. Owing to their antibacterial activities, metallic nanoparticles (mainly silver and gold) represent a novel and an effective solution for overcoming bacterial resistance. In general, nanoparticles are divided into two groups, i.e., organic and inorganic, where the later one being significant biomedical agents [12]. These silver and gold nanoparticles, derived from microbial sources, have demonstrated their potential not only as a new generation antimicrobial [13] agents against a broad spectrum of Gram-positive and Gram-negative bacteria including multidrug-resistant human pathogens, but also as anticancer agents [3]. They have also significantly enhanced the bactericidal activity when used in combination with standard antibiotics [14]. However, synthesis of nanoparticles involves the use of expensive, poisonous, and dangerous chemicals responsible for different biological and environmental hazards. This fact increases the necessity of developing environment-friendly procedure by means of green synthesis (using plants) and extra biological methods (using microbes such as bacteria and fungi) [15]. Therefore, as a part of our continuing search to identify microorganisms with the potential to synthesize nanoparticles with amazing biological properties, interest has spurred on microbes [11], especially fungi. Indeed a few fungal species around the globe have been reported to secrete nanoparticles. Therefore, the present chapter is aimed to provide an overview of nanoparticles producing fungi, with the ultimate objective of producing effective antimicrobial agents.

2. Biosynthesis of nanoparticles by fungi

In the last decade, biomineralization has been developed as an emerging and attractive technique for the synthesis of metallic nanoparticles. In which microbial cells are preferably being used for the synthesis of nanosized material involving the oxidation/reduction of metallic ions (like silver, gold, platinum, etc.) giving rise to nanostructures and nanoparticles [16].

http://dx.doi.org/10.5772/66922

This green synthesis of metallic nanoparticles undergo three necessary steps (**Figure 1**) that are (i) choice of appropriate solvent medium, (ii) choice of appropriate reducing agent (environment friendly), and (iii) stabilizing agents or substances for silver nanoparticles stability [17]. Generally, this reduction is carried out by means of microbial enzymes (**Figure 1**), present in microbes, and considered to be responsible for synthesis of nanoparticles by those organisms [18, 19].

For this purpose, various fungi have been used as novel and assuring resources for manufacturing of nanoparticles extracellularly as well as intracellularly, such as *Aspergillus*, *Pencillium*, *Fusarium*, and *Verticillium*. Though synthesis of metallic nanoparticles (NPs) having defined size, shape, and composition by fungi are major challenges in this field [20, 21]. In general, fungal enzymes with reducing capabilities are mostly responsible for reduction of metal ions (**Figure 1**) to their corresponding nanoparticle(s) as described earlier [22]. We will discuss biosynthesis of NPs from various fungi one by one.

2.1. Biosynthesis of nanoparticles by *Fusarium*

Several fungal strains belonging to genera *Fusarium* have been studied for the production of metallic nanoparticles. Dias and coworkers [23] have screened different *Fusarium* species to be used as potential candidate(s) for biosynthesis of silver NPs. They have obtained the tiniest size silver-nanoparticles (Ag-NPs) by *Fusarium oxysporum* through extracellular reduction of Ag^+ ions in aqueous medium [24–26]. Generally, two methods were used to evaluate the synthesis of silver nanoparticles by *Fusarium* species involving (i) silver reduction method that involve the fungus biomass in conical flask containing $AgNO_3$ solution and distilled water. In other method, fungal filtrate were obtained by keeping fungal biomass in distilled water for 72 h at 28°C that was further challenged with $AgNO_3$ solution (10^{-3} M). In this study, several strains of *Fusarium oxysporum* were exposed to $AgNO_3$ solution (10^{-3} M) leading to the reduction of silver ions and thereby formation of silver hydrosol. The silver nanoparticles produced

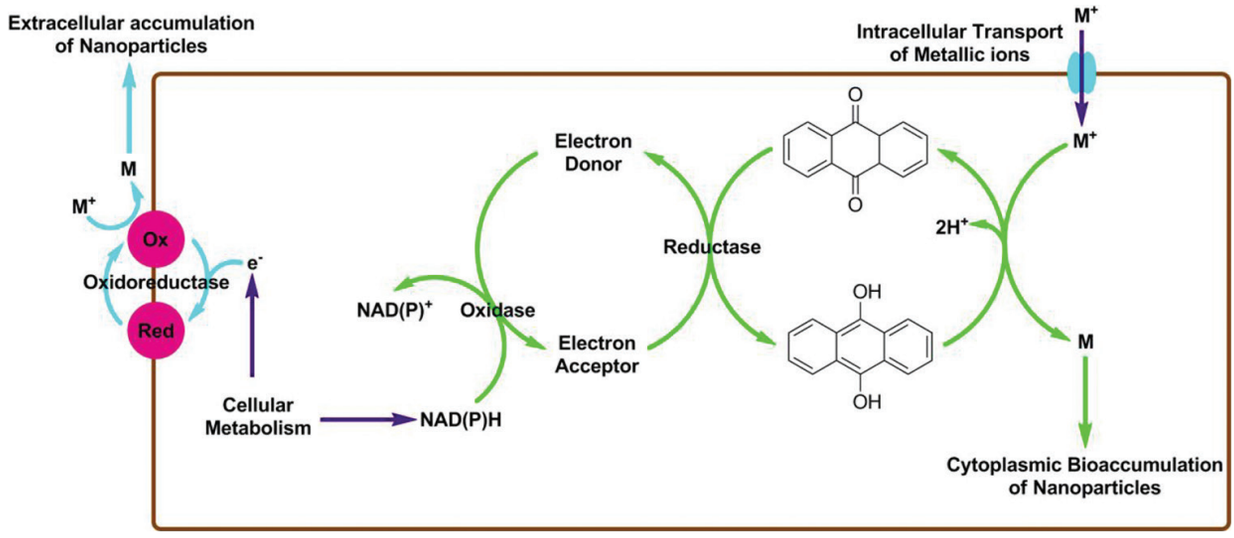

Figure 1. Intracellular and extracellular biosynthesis of metallic nanoparticles (NPs) by fungi.

were in range of 20–50 nm in diameter as a result of nitrate-dependent reductase and shuttle quinone extracellular activities [27]. Similar study was also performed using similar fungal species, i.e., *Fusarium oxysporum* by Mohammadian et al. [28] who observed that synthesis of silver nanoparticles was extremely rapid even at ambient conditions that can compete with chemical synthesis, highly stable even for months in darkness (without light). To date, various *Fusarium* species have been reported to produce metallic nanoparticles for silver [13, 29–33], zirconia [34, 35], platinum NPs intra- and extracellularly [13, 32].

2.2. Biosynthesis of nanoparticles by *Penicillium*

Certain filamentous fungi such as *Penicillium* were also investigated for the synthesis of metallic nanoparticles. For this purpose, various studies have been carried out using different species of *Penicillium* including (but not limited to) *P. brevicompactum* [36], *P. fellutanum* [37], *Penicillium* sp. [38], *P. citrinum* [39], *P. fellutanum* [36], and *P. purpurogenum* [40]. Nanoparticles produced by *Penicillium* spp. are relatively more stable at neutral pH (>8.0) due to repulsion as they possess zeta potential (negative) [41]. In another study, where *P. fellutanum* was challenged with silver ions, it could reduce metallic ions in 10 min, when it came in contact with fungus filtrate [37]. Presence of single protein having molecular weight of about 70 kDa was observed in gel electrophoreses. The authors supposed that nitrate reductase enzymes could possibly be responsible for the reduction of silver ions (**Figure 1**). In addition, the whole reduction process could be manipulated by controlling concentration and exposure time to Ag^+ ions, pH, and temperature [37, 42]. Although exact mechanism commanding the Ag^+ ions reduction is not yet comprehended, however, authors have assumed that reducing agents are secreted by fungi as a response to stress posed by metal ions [40, 42]. Moreover, these silver NPs were uniformly distributed over fungal mycelium (*Penicillium* sp.) suggesting that silver NPs were bound with cells of fungal surface. This was further confirmed by FTIR spectroscopy. In which it was described that both carbonyl groups from amino acid residues and peptides of protein(s) had strong affinities for binding with Ag^+ ions in order to form protective covering around silver NPs to avoid their clustering [36].

2.3. Biosynthesis of nanoparticles by *Aspergillus*

Biosynthesis of NPs from species belonging to genera *Aspergillus* is more desirable and economically important due to its occurrence in natural habitat along with easy culturing on growth media [43]. In the same study, five species belonging to genus *Aspergillus*, i.e., *A. nidulans, A. flavus, A. terreus, A. fumigatus*, and *A. niger*, were synthesized, in which *A. terreus* was proved to be more potent NPs producer among all and was further investigated. It was observed that silver NPs were highly stable even after 4 months due to the presence of stabilizing agents mostly "protein" that would allow functionalizing the NPs with other biological molecules [44]. Their proper functionalizing is an important factor for appropriate antimicrobial activities of these metallic nanoparticles (NPs). In addition, FTIR analyses revealed amide linkages between amino acid residues and NPs. Most active functional groups involved in the reduction of silver ions being the hydroxyl, carboxyl, and carbonyl groups [10, 43, 45–48]. Depending on the biological system used, different sizes and shapes of NPs had been reported ranging from 5 to 45 nm [49] with spherical NPs being the dominant [43].

In another study, AgNP were synthesized using aqueous supernatant of *A. niger*. Synthesized silver NPs were mainly round shape ranging in size from 1 to 20 nm [50]. Various studies have shown the mycosynthesis of silver nanoparticles extracellularly through the reduction of Ag+ ions using different species belonging to genus *Aspergillus*, such as *A. niger* [51], *A. flavus* [52], *A. terreus* [53], *A. clavatus* [54, 55], *A. fumigatus* [56], and *A. tamari* [57]. Majority of these NPs were in the range of 1–20 nm with spherical shape.

2.4. Biosynthesis of nanoparticles by other fungi

Various other fungal genera were also exploited for the synthesis of silver nanoparticles. Metallic NPs can be synthesized using fungal biomass and cell-free supernatant. Among eukaryotes, yeast was repeatedly explored for the formation of metallic nanoparticles. Since then, many studies were carried out in order to evaluate the fungal potential as potent producer of silver nanoparticles. For example, cadmium nanoparticles (CdS) were synthesized intracellularly by *Schizosaccharomyces pombe* and *Candida glabrata* when challenged with Cd^{+2} ions [42, 58–60]. The authors proposed that these NPs were covered with phytochelatin [42]. Similarly, other studies have also reported the biosynthesis of metallic nanoparticles using fungi such as Toluropsis sp. for Pb nanocrystals [60] and for Cu NPs using *Humicola* sp. [61]. Formation of gold nanoparticles was described in yeast Yarrowia lipolytica NCIM 3589 that were highly stable [62, 63]. As described earlier, shape and size of NPs mainly rely on the reaction conditions like temperature, pH, metal concentrations, and reaction time [16].

However, first example of intracellular mycosynthesis of silver and gold NPs was demonstrated using *Verticillium sp*. biomass, challenged with aqueous silver ions [64, 65]. Although the mechanism of biosynthesis was not clearly understood, however, it was assumed that metal ions (silver or gold) either (i) adsorbed on cell surface or enter into cytoplasm via diffusion. In both cases, these metallic ions were reduced by enzymes present on the cellular membrane and/or cytoplasm [64, 65]. Similarly, different species belonging to genus *Trichoderma* and *Phoma* were also screened for the synthesis of metallic NPs with dimensions ranging from 8 to 60 nm [66, 67] for the selection of potential species as a new synthesizer of silver NPs.

3. Application of mycosynthesized nanoparticles in biomedics

Mycosynthesized nanoparticles are of extreme importance because of their unique optical, physicochemical and biological facets. These nanosized particles are continuously being used in different fields including electronics [68], catalytic processes [69], optical devices [12], sensor technology [70], biological labeling [71], and may suppress the expression of proteins associated with adenosine triphosphate production [72], agriculture, pharmacology, and environmental monitoring [73]. More recently they are being used as novel antimicrobial and anticancer agents [61, 74–82]. Antimicrobial mediators can be either synthetic and/or partially modified natural compounds [82, 83]. Type of antimicrobials agent(s) may vary according to targeted pathogens, e.g., antibacterial (for bacteria), antifungal (for fungi), and antiviral (for virus). Similarly, their mechanism of action on microbial cell varies according to the nature of the antimicrobial agents and pathogens. Main targets for antimicrobial compounds could be

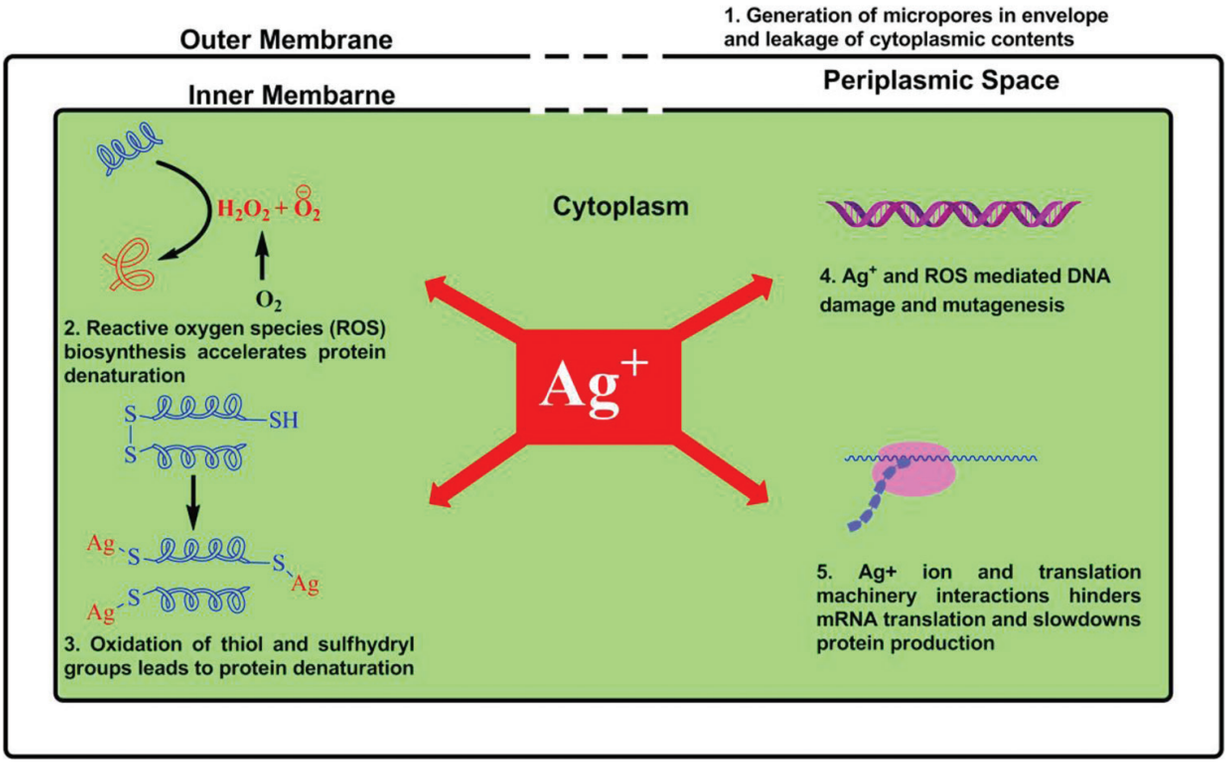

Figure 2. Possible mechanism of action of silver NPs on bacterial cell.

cell wall (cephalosporins, bacitracin, penicillins, etc.) and protein synthesis, DNA replication (tetracyclines, chloramphenicol, lincosamides, etc.) and metabolism (intermediary) processes (valinomycin, Gramicidin A, etc.), and DNA-synthesis (rifampicin, sulfonamides, quinolones, etc.) as described in **Figure 2** [82]. However, abusive use of antimicrobials against various pathogens has evolved into the development of highly adapted and resistant microbes. In addition, these resistant microbes are now being spread globally, challenging the treatment to common infections, and posing significant health threat around the globe. Multidrug-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci, have emerged as a symbol of global health hazard during the last decade.

4. Antibacterial activity of mycosynthesized nanoparticles

Uses of nanoparticles in medicine, particularly in the treatment of bacterial infections, have proved them as effective and novel healing tools against microorganisms. Though for centuries, natural silver has already been considered as one of the most safe and nontoxic inorganic antimicrobial agents [84]. Even silver nanoparticles have also exhibited broad-spectrum antimicrobial properties due to its unique physiochemical and biological characteristics [85]. Recently, silver NPs have shown excellent antimicrobial efficacy against certain bacterial pathogens such as *Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Staphylococcus epidermis, Leuconostoc mesenteroides, Klebsiella pneumonia*, and *K. mobilis* [84]. Reason for their higher antimicrobial efficacy lies with higher surface area-to-volume ratio of AgNPs that enables

them to bring large portion of Ag atoms in contact with the environment (i.e., microbial cell). However, mechanism of antibacterial activity of silver NPs has not been completely understood [84–88].

Silver nanoparticles have shown inhibitory effect on growth in both Gram-positive and Gram-negative bacteria. As described earlier, larger surface area of silver nanoparticles are believed to be key player in interaction with bacterial cell wall and would have resulted in more antibacterial activity. Although mechanism of action of silver NPs on bacterial cell is debatable; however, assumed mechanism include (i) adherence of AgNPs with bacterial cell wall causing membrane lysis, ultimately releasing cellular contents leading to destruction of cell structure and death [89–91], (ii) interaction of Ag ions with free thiol groups (−SH) and disulfide bridges (-S-S-) of cellular enzymes and membrane of bacteria to downregulate or inactivate the cellular protein synthesis by interfering the translation [72, 91, 92], (iii) blocking DNA replication [93], and (iv) inhibition of signal transduction by dephosphorylation of peptide substrates on tyrosine residues (**Figure 2**) [91]. Furthermore, inhibitory effect of AgNPs varied for different bacterium, e.g., Gram-positive bacteria were more susceptible to silver nanoparticles as compared to Gram-negative one [84]. The authors have found larger inhibition zone (diameter) in case of *S. aureus* than that of *E. coli* suggesting that variation in inhibitory response could be attributed to difference in cell wall and capsular composition, S-layer thickness, cellular metabolism and its byproducts, or a combination of these [84].

5. Anticancer potential of mycosynthesized nanoparticles

About 10 million people are being diagnosed with cancer annually, with higher mortality rate around the globe [94]. It is generally developed due to disturbance in various physiological processes like cell signaling and apoptosis [94]. In this disease, continuous growth of cancer cell due to resistance to wide range of anticancer agents has become the major challenge to pharmacist while treating the disease [95, 96]. Certain factors such as insufficient drug concentrations approaching tumor cells, intolerable cytotoxicity, nonspecific distribution of anticancer agents, and poor monitoring of drug responses particularly in developing countries has made cancer incurable [97, 98].

Recently, the emerging field of nano-biomedicine has highlighted the possibility of metallic NPs to be used for disease diagnosis and cancer treatment in humans [94]. Among various metallic NPs, silver nanoparticles are considered as novel and promising nanoproducts that can be exploited in the field of nanomedicine due to their unique and distinctive properties. Although antibacterial activity of Ag nanoparticles is well established, however, their anticancer activities have recently been reported against various cancerous cell lines [94, 99], and mechanism of action of AgNPs are still under evaluation and there are many ambiguities that should be addressed in future research.

It is well established that silver nanoparticles when interacting with various biomolecules, such as DNA, proteins, and carbohydrates, may cause cell death due to apoptosis or cytotoxicity

probably through reactive oxygen species (ROS) [32, 94]. Various factors influencing cytotoxicity of silver nanoparticles include dosage, contact time, and size of particles. For example, in case of human epidermoid larynx (Hep-2) cell line, cellular damage was dose dependent, causing cell death through ROS [96, 100, 101]. In another study, silver nanoparticles have shown cytotoxic effect through loss of mitochondrial integrity and activation of caspase-cascade exhibiting the apoptotic effect leading to cell death. In a recent study, AgNPs from plant extract, inhibited proliferation of human colon cancer cell line HCT15 while suppressing its cellular growth, inhibiting the G_0/G_1-phase, interfering DNA synthesis, and ultimately causing cell death through apoptosis [102]. Another important criterion for efficient anticancer drug is its ability to induce apoptosis cancer cell since they generally escape from programed cell death [103]. In recent studies it has been shown that silver nanoparticles possess this property [104]. The authors have treated the tumor-bearing mice (*in vivo*) with AgNPs that have reduced the tumor weight and increased its life span. The hematologic studies revealed reduced white blood cell (WBC) and platelet count in diseased mice as compared to control (disease free) suggesting that silver NPs were relatively nontoxic and did not produce any change in hematologic parameters and controlled the WBC that were important constituent of immune system of body. The authors further proposed that silver NPs could be used as potent therapeutic agents in order to delay the tumor progression in DLA cell lines through growth suppression and cytotoxic effects that increased vascular permeability leading to tumor cell death that could be linked to caspase enzyme activation. However, mode of action of silver NPs due to which they inhibit cell proliferation and viability causing tumor cell death has not been clearly understood.

6. Conclusion

The use of nanoparticles in the field of medicine is proving to be a novel and promising technique in order to treat various infections. Among various NPs, silver NPs have proved to possess therapeutic alternative that can be exploited in diagnostic and treatment of certain bacterial infections and cancer. To date, various fungi have been reported to biosynthesize the silver nanoparticles. A few among them have been evaluated for the treatment of infection(s) caused by bacterial pathogens providing evidence for their potential role as a new generation antimicrobial agents against a broad spectrum of Gram-positive and Gram-negative bacteria including multidrug-resistant human pathogens. In addition, monodispersed silver NPs can be synthesized by controlling various parameters (such as pH, temperature, etc.) to avoid toxic effects on human cells. Furthermore, biosynthesized silver NPs have successfully exhibited the anticancer activities against different cancer cell lines through inhibiting cell progression (cell proliferation), ROS formation, blockage of DNA synthesis, and apoptosis. However, further research work is required to understand possible mechanism of action of antibacterial and anticancer activities of silver NPs on microbial cell. Various factors (physiochemical and biological) affecting bioavailability, biocompatibility, and cellular toxicity of silver NPs at molecular level should also be addressed in future research that will open new insight for their application alone or in combination with other bioactive agents to control and treat the microbial infections and cancer.

Author details

Muhammad Waseem* and Muhammad Atif Nisar

*Address all correspondence to: muhammad.waseem@gcuf.edu.pk

Department of Microbiology, Government College University, Faisalabad, Pakistan

References

[1] Narayanan, K.B. and N. Sakthivel, Biological synthesis of metal nanoparticles by microbes. Advances in Colloid and Interface Science, 2010. 156(1–2): 1–13.

[2] Thakkar, K.N., S.S. Mhatre, and R.Y. Parikh, Biological synthesis of metallic nanoparticles. Nanomedicine: Nanotechnology, Biology and Medicine, 2010. 6(2): 257–262.

[3] Mishra, A., et al., Microbial synthesis of gold nanoparticles using the fungus Penicillium brevicompactum and their cytotoxic effects against mouse mayo blast cancer C2C12 cells. Applied Microbiology and Biotechnology, 2011. 92(3): 617–630.

[4] Muhsin, T.M. and A.K. Hachim, Mycosynthesis and characterization of silver nanoparticles and their activity against some human pathogenic bacteria. World Journal of Microbiology and Biotechnology, 2014. 30(7): 2081–2090.

[5] Fayaz, A.M., et al., Biogenic synthesis of silver nanoparticles and their synergistic effect with antibiotics: a study against gram-positive and gram-negative bacteria. Nanomedicine: Nanotechnology, Biology and Medicine, 2010. 6(1): 103–109.

[6] Sathishkumar, M., K. Sneha, and Y.S. Yun, Immobilization of silver nanoparticles synthesized using Curcuma longa tuber powder and extract on cotton cloth for bactericidal activity. Bioresource Technology, 2010. 101(20): 7958–7965.

[7] Krishnaraj, C., et al., Synthesis of silver nanoparticles using Acalypha indica leaf extracts and its antibacterial activity against water borne pathogens. Colloids and Surfaces B: Biointerfaces, 2010. 76(1): 50–56.

[8] Gade, A.K., et al., Exploitation of Aspergillus niger for synthesis of silver nanoparticles. Journal of Biobased Materials and Bioenergy, 2008. 2(3): 243–247.

[9] Goffeau, A., Drug resistance: The fight against fungi. Nature, 2008. 452(7187): 541–542.

[10] Jain, N., et al., Extracellular biosynthesis and characterization of silver nanoparticles using Aspergillus flavusNJP08: A mechanism perspective. Nanoscale, 2011. 3(2): 635–641.

[11] Elbeshehy, E.K.F., A.M. Elazzazy, and G. Aggelis, Silver nanoparticles synthesis mediated by new isolates of Bacillus s, nanoparticle characterization and their activity against Bean Yellow Mosaic Virus and human pathogens. Frontiers in Microbiology, 2015. 6: 453.

[12] Jain, J., et al., Silver nanoparticles in therapeutics: Development of an Antimicrobial gel formulation for topical use. Molecular Pharmaceutics, 2009. 6(5): 1388–1401.

[13] Ingle, A., et al., Mycosynthesis of silver nanoparticles using the fungus fusarium acuminatum and its activity against some human pathogenic bacteria. Current Nanoscience, 2008. 4(2): 141–144.

[14] Dar, M.A., A. Ingle, and M. Rai, Enhanced antimicrobial activity of silver nanoparticles synthesized by Cryphonectria sp. evaluated singly and in combination with antibiotics. Nanomedicine: Nanotechnology, Biology and Medicine, 2013. 9(1): 105–110.

[15] Balakumaran, M.D., et al., Mycosynthesis of silver and gold nanoparticles: Optimization, characterization and antimicrobial activity against human pathogens. Microbiological Research, 2016. 182: 8–20.

[16] Gericke, M. and A. Pinches, Biological synthesis of metal nanoparticles. Hydrometallurgy, 2006. 83(1–4): 132–140.

[17] Raveendran, P., J. Fu, and S.L. Wallen, Completely "green" synthesis and stabilization of metal nanoparticles. Journal of the American Chemical Society, 2003. 125(46): 13940–13941.

[18] Kalimuthu, K., et al., Biosynthesis of silver nanocrystals by Bacillus licheniformis. Colloids and Surfaces B: Biointerfaces, 2008. 65(1): 150–153.

[19] Kalishwaralal, K., et al., Extracellular biosynthesis of silver nanoparticles by the culture supernatant of Bacillus licheniformis. Materials Letters, 2008. 62(29): 4411–4413.

[20] Mukherjee, P., et al., Green synthesis of highly stabilized nanocrystalline silver particles by a non-pathogenic and agriculturally important fungus *T. asperellum*. Nanotechnology, 2008. 19(7): p. 075103.

[21] Gaikwad, S.C., et al., Screening of different Fusarium species to select potential species for the synthesis of silver nanoparticles. Journal of the Brazilian Chemical Society, 2013. 24: 1974–1982.

[22] Boroumand Moghaddam, A., et al., Nanoparticles biosynthesized by fungi and yeast: A review of their preparation, properties, and medical applications. Molecules, 2015. 20(9): 16540–16565.

[23] Dias, M.A., et al., Removal of heavy metals by an Aspergillus terreus strain immobilized in a polyurethane matrix. Letters in Applied Microbiolology, 2002. 34(1): 46–50.

[24] Ahmad, A., et al., Extracellular biosynthesis of silver nanoparticles using the fungus Fusarium oxysporum. Colloids and Surfaces B: Biointerfaces, 2003. 28(4): 313–318.

[25] Bansal, V., et al., Biosynthesis of zirconia nanoparticles using the fungus Fusarium oxysporum. Journal of Materials Chemistry, 2004. 14(22): 3303–3305.

[26] Birla, S.S., et al., Rapid synthesis of silver nanoparticles from *Fusarium oxysporum* by optimizing physicocultural conditions. The Scientific World Journal, 2013. 2013: p. 12.

[27] Durán, N., et al., Mechanistic aspects of biosynthesis of silver nanoparticles by several Fusarium oxysporum strains. Journal of Nanobiotechnology, 2005. 3(1): p. 8.

[28] Mohammadian, A., S. Shojaosadati, and M. Habibi Rezaee, Fusarium oxysporum mediates photogeneration of silver nanoparticles. Scientia Iranica, 2007. 14(4): 323–326.

[29] Sadowski, Z., et al., Synthesis of silver nanoparticles using microorganisms. Materials Science-Poland, 2008. 26(2): 419–424.

[30] Khosravi, A. and S.A. Shojaosadati, Evaluation of silver nanoparticles produced by fungus Fusarium oxysporum. International Journal of Nanotechnology, 2009. 6(10–11): 973–983.

[31] Bawaskar, M., et al., A new report on mycosynthesis of silver nanoparticles by Fusarium culmorum. Current Nanoscience, 2010. 6(4): 376–380.

[32] Durán, N., et al., Potential use of silver nanoparticles on pathogenic bacteria, their toxicity and possible mechanisms of action. Journal of the Brazilian Chemical Society, 2010. 21: 949–959.

[33] Deepa, K. and T. Panda, Synthesis of gold nanoparticles from different cellular fractions of Fusarium oxysporum. Journal of Nanoscience and Nanotechnology, 2014. 14(5): 3455–3463.

[34] Bharde, A., et al., Extracellular biosynthesis of magnetite using fungi. Small, 2006. 2(1): 135–141.

[35] Riddin, T., M. Gericke, and C. Whiteley, Analysis of the inter-and extracellular formation of platinum nanoparticles by *Fusarium oxysporum* f. sp. lycopersici using response surface methodology. Nanotechnology, 2006. 17(14): p. 3482.

[36] Shaligram, N.S., et al., Biosynthesis of silver nanoparticles using aqueous extract from the compactin producing fungal strain. Process biochemistry, 2009. 44(8): 939–943.

[37] Kathiresan, K., et al., Studies on silver nanoparticles synthesized by a marine fungus, Penicillium fellutanum isolated from coastal mangrove sediment. Colloids and surfaces B: Biointerfaces, 2009. 71(1): 133–137.

[38] Singh, D., et al., Optimization and characterization of silver nanoparticle by endophytic fungi Penicillium sp. isolated from Curcuma longa (turmeric) and application studies against MDR E. coli and S. aureus. Bioinorganic Chemistry and Applications, 2014. 2014: p. 8.

[39] Honary, S., et al., Green synthesis of silver nanoparticles induced by the fungus Penicillium citrinum. Tropical Journal of Pharmaceutical Research, 2013. 12(1): 7–11.

[40] Maliszewska, I., A. Juraszek, and K. Bielska, Green synthesis and characterization of silver nanoparticles using ascomycota fungi Penicillium nalgiovense AJ12. Journal of Cluster Science, 2014. 25(4): 989–1004.

[41] Zhang, X., et al., Biosynthesis of size-controlled gold nanoparticles using fungus, Penicillium sp. Journal of Nanoscience and Nanotechnology, 2009. 9(10): 5738–5744.

[42] Maliszewska, I., *Microbial Synthesis of Metal Nanoparticles*, in *Metal Nanoparticles in Microbiology*, M. Rai and N. Duran, Editors. 2011, Springer Berlin Heidelberg: Berlin, Heidelberg. 153–175.

[43] Khalil, N.M., Biogenic silver nanoparticles by Aspergillus terreus as a powerful nanoweapon against Aspergillus fumigatus. African Journal of Microbiology Research, 2013. 7(50): 5645–5651.

[44] Hennebel, T., et al., Biogenic metals in advanced water treatment. Trends in Biotechnology, 2009. 27(2): 90–98.

[45] Xie, J., et al., Silver nanoplates: From biological to biomimetic synthesis. ACS Nano, 2007. 1(5): 429–439.

[46] Gajbhiye, M., et al., Fungus-mediated synthesis of silver nanoparticles and their activity against pathogenic fungi in combination with fluconazole. Nanomedicine: Nanotechnology, Biology and Medicine, 2009. 5(4): 382–386.

[47] Ghaseminezhad, S.M., S. Hamedi, and S.A. Shojaosadati, Green synthesis of silver nanoparticles by a novel method: Comparative study of their properties. Carbohydrate Polymers, 2012. 89(2): 467–472.

[48] Priyadarshini, S., et al., Synthesis of anisotropic silver nanoparticles using novel strain, Bacillus flexus and its biomedical application. Colloids and Surfaces B: Biointerfaces, 2013. 102: 232–237.

[49] Alani, F., M. Moo-Young, and W. Anderson, Biosynthesis of silver nanoparticles by a new strain of Streptomyces sp. compared with Aspergillus fumigatus. World Journal of Microbiology and Biotechnology, 2012. 28(3): 1081–1086.

[50] Sagar, G. and B. Ashok, Green synthesis of silver nanoparticles using Aspergillus niger and its efficacy against human pathogens. European Journal of Experimental Biology, 2012. 2: 1654–1658.

[51] Kumar, A., et al., Silver-nanoparticle-embedded antimicrobial paints based on vegetable oil. Natural Matererial, 2008. 7(3): 236–241.

[52] Ranjbar Navazi, Z., M. Pazouki, and F.S. Halek, Investigation of culture conditions for biosynthesis of silver nanoparticles using Aspergillus fumigatus. Iranian Journal of Biotechnology, 2010. 8(1): 56–61.

[53] Jaidev, L.R. and G. Narasimha, Fungal mediated biosynthesis of silver nanoparticles, characterization and antimicrobial activity. Colloids and Surfaces B: Biointerfaces, 2010. 81(2): 430–433.

[54] Verma, V.C., R.N. Kharwar, and A.C. Gange, Biosynthesis of antimicrobial silver nanoparticles by the endophytic fungus Aspergillus clavatus. Nanomedicine, 2009. 5(1): 33–40.

[55] Li, G., et al., Fungus-mediated green synthesis of silver nanoparticles using Aspergillus terreus. International Journal of Molecular Sciences, 2011. 13(1): 466–476.

[56] Saravanan, M. and A. Nanda, Extracellular synthesis of silver bionanoparticles from Aspergillus clavatus and its antimicrobial activity against MRSA and MRSE. Colloids and Surfaces B: Biointerfaces, 2010. 77(2): 214–218.

[57] Raliya, R. and J.C. Tarafdar, Biosynthesis and characterization of zinc, magnesium and titanium nanoparticles: An eco-friendly approach. International Nano Letters, 2014. 4(1): 93.

[58] Reese, R. and D.R. Winge, Sulfide stabilization of the cadmium-gamma-glutamyl peptide complex of Schizosaccharomyces pombe. Journal of Biological Chemistry, 1988. 263(26): 12832–12835.

[59] Dameron, C.T., et al., Biosynthesis of cadmium sulphide quantum semiconductor crystallites. Nature, 1989. 338(6216): 596–597.

[60] Kowshik, M., et al., Microbial synthesis of semiconductor PbS nanocrystallites. Advanced Materials, 2002. 14(11): 815.

[61] Ahmad, A., et al., Fungus-based synthesis of chemically difficult-to-synthesize multifunctional nanoparticles of $CuAlO_2$. Advanced Materials, 2007. 19(20): 3295–3299.

[62] Agnihotri, M., et al., Biosynthesis of gold nanoparticles by the tropical marine yeast Yarrowia lipolytica NCIM 3589. Materials Letters, 2009. 63(15): 1231–1234.

[63] Pimprikar, P.S., et al., Influence of biomass and gold salt concentration on nanoparticle synthesis by the tropical marine yeast Yarrowia lipolytica NCIM 3589. Colloids and Surfaces B: Biointerfaces, 2009. 74(1): 309–316.

[64] Mukherjee, P., et al., Fungus-mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: A novel biological approach to nanoparticle synthesis. Nano Letter, 2001. 1: 515–519.

[65] Mukherjee, P., et al., Bioreduction of AuCl4- ions by the fungus, Verticillium sand surface trapping of the gold nanoparticles formed. Angewandte Chemie International Edition, 2001. 40(19): 3585–3588 .

[66] Devi, T.P., et al., *Biosynthesis of silver nanoparticles from Trichoderma species*. Indian J Exp Biol, 2013. **51**(7): p. 543-7.

[67] Gade, A., et al., Screening of different species of Phoma for the synthesis of silver nanoparticles. Biotechnology and Applied Biochemistry, 2013. 60(5): 482–493.

[68] Zhang, W., et al., Biosynthesis and structural characteristics of selenium nanoparticles by Pseudomonas alcaliphila. Colloids Surf B Biointerfaces, 2011. 88(1): 196–201.

[69] Rauter, H., et al., Nanotechnology for smart polymer optical devices. Macromolecular Symposia, 2004. 217(1): 109–134.

[70] Schrand, A.M., et al., Can silver nanoparticles be useful as potential biological labels? Nanotechnology, 2008. 19(23): 235104.

[71] Jin, R., The impacts of nanotechnology on catalysis by precious metal nanoparticles. Nanotechnology Reviews, 2012. 1(1): 31–56.

[72] Yamanaka, M., K. Hara, and J. Kudo, Bactericidal actions of a silver ion solution on Escherichia coli, studied by energy-filtering transmission electron microscopy and proteomic analysis. Applied and Environmental Microbiology, 2005. 71(11): 7589–7593.

[73] Navarro, E., et al., Toxicity of silver nanoparticles to Chlamydomonas reinhardtii. Environmental Science & Technology, 2008. 42(23): 8959–8964.

[74] Aymonier, C., et al., Hybrids of silver nanoparticles with amphiphilic hyperbranched macromolecules exhibiting antimicrobial properties. Chemical Communications, 2002(24): 3018–3019.

[75] Schabes-Retchkiman, P.S., et al., Biosynthesis and characterization of Ti/Ni bimetallic nanoparticles. Optical Materials, 2006. 29(1): 95–99.

[76] Ping, G., et al., Preparation and antibacterial activity of Fe_3O_4@Ag nanoparticles. Nanotechnology, 2007. 18(28): 285604.

[77] Jo, Y.K., B.H. Kim, and G. Jung, Antifungal activity of silver ions and nanoparticles on phytopathogenic fungi. Plant Disease, 2009. 93(10): 1037–1043.

[78] Kim, J.A., et al., Role of cell cycle on the cellular uptake and dilution of nanoparticles in a cell population. Nature Nanotechnology, 2012. 7(1): 62–68.

[79] Prabhu, S. and E.K. Poulose, Silver nanoparticles: Mechanism of antimicrobial action, synthesis, medical applications, and toxicity effects. International Nano Letters, 2012. 2(1): 32.

[80] Lemire, J.A., J.J. Harrison, and R.J. Turner, Antimicrobial activity of metals: Mechanisms, molecular targets and applications. Nature Reviews Microbiology, 2013. 11(6): 371–384.

[81] Saharan, V., et al., Synthesis of chitosan based nanoparticles and their in vitro evaluation against phytopathogenic fungi. International Journal of Biological Macromolecules, 2013. 62: 677–683.

[82] Rudramurthy, R.G., et al., Nanoparticles: Alternatives against drug-resistant pathogenic microbes. Molecules, 2016. 21(7): 836.

[83] von Nussbaum, F., et al., Antibacterial natural products in medicinal chemistry—exodus or revival? Angewandte Chemie International Edition, 2006. 45(31): 5072–5129.

[84] Rahimi, G., F. Alizadeh, and A. Khodavandi, Mycosynthesis of silver nanoparticles from *Candida albicans* and its antibacterial activity against *Escherichia coli* and Staphylococcus aureus. Tropical Journal of Pharmaceutical Research, 2016. 15(2): 371–375.

[85] Waghmare, S.R., et al., Ecofriendly production of silver nanoparticles using *Candida utilis* and its mechanistic action against pathogenic microorganisms. 3 Biotechology, 2015. 5(1): 33–38.

[86] Nanda, A. and M. Saravanan, Biosynthesis of silver nanoparticles from Staphylococcus aureus and its antimicrobial activity against MRSA and MRSE. Nanomedicine: Nanotechnology, Biology and Medicine, 2009. 5(4): 452–456.

[87] Marambio-Jones, C. and E.M.V. Hoek, A review of the antibacterial effects of silver nanomaterials and potential implications for human health and the environment. Journal of Nanoparticle Research, 2010. 12(5): 1531–1551.

[88] Bhati-Kushwaha, H., A. Kaur, and C. Malik, The synthesis and role of biogenic nanoparticles in overcoming chilling stress. Indian Journal of Plant Sciences, 2013. 2(4): 54–62.

[89] Feng, Q., et al., A mechanistic study of the antibacterial effect of silver ions on *Escherichia coli* and *Staphylococcus aureus*. Journal of Biomedical Materials Research, 2000. 52(4): 662–668.

[90] Guggenbichler, J.P., et al., A new technology of microdispersed silver in polyurethane induces antimicrobial activity in central venous catheters. Infection, 1999. 27(1): S16–S23.

[91] Gopinath, P.M., et al., Multi-functional nano silver: A novel disruptive and theranostic agent for pathogenic organisms in real-time. Scientific Reports, 2016. 6: 34058.

[92] Davies, R.L. and S.F. Etris, The development and functions of silver in water purification and disease control. Catalysis Today, 1997. 36(1): 107–114.

[93] Fox, C.L. and S.M. Modak, Mechanism of Silver Sulfadiazine Action on Burn Wound Infections. Antimicrobial Agents and Chemotherapy, 1974. 5(6): 582–588.

[94] Jeyaraj, M., et al., An investigation on the cytotoxicity and caspase-mediated apoptotic effect of biologically synthesized silver nanoparticles using *Podophyllum hexandrum* on human cervical carcinoma cells. Colloids Surf B Biointerfaces, 2013. 102: 708–717.

[95] Abraham, I., et al., Current status on Marine products with reversal effect on cancer multidrug resistance. Marine Drugs, 2012. 10(10): 2312–2321.

[96] Rai, M., et al., Broad-spectrum bioactivities of silver nanoparticles: The emerging trends and future prospects. Applied Microbiology and Biotechnology, 2014. 98(5): 1951–1961.

[97] Misra, R., S. Acharya, and S.K. Sahoo, Cancer nanotechnology: Application of nanotechnology in cancer therapy. Drug Discovery Today, 2010. 15(19–20): 842–850.

[98] Seigneuric, R., et al., From nanotechnology to nanomedicine: Applications to cancer research. Current Molecular Medicine, 2010. 10(7): 640–52.

[99] Joshi, P., et al., The anticancer activity of chloroquine-gold nanoparticles against MCF-7 breast cancer cells. Colloids and Surfaces B: Biointerfaces, 2012. 95: 195–200.

[100] Justin Packia Jacob, S., J.S. Finub, and A. Narayanan, Synthesis of silver nanoparticles using *Piper longum* leaf extracts and its cytotoxic activity against Hep-2 cell line. Colloids and Surfaces B: Biointerfaces, 2012. 91: 212–214.

[101] Satyavani, K., et al., Toxicity study of silver nanoparticles synthesized from Suaeda Monoica on Hep-2 cell line. Avicenna Journal of Medical Biotechnology, 2012. 4(1): 35–39.

[102] Prabhu, D., et al., Biologically synthesized green silver nanoparticles from leaf extract of *Vitex negundo* L. induce growth-inhibitory effect on human colon cancer cell line HCT15. Process Biochemistry, 2013. 48(2): 317–324.

[103] Mendoza, F.J., et al., Anti-tumor chemotherapy utilizing peptide-based approaches-apoptotic pathways, kinases, and proteasome as targets. Archivum Immunologiae et Therapiae Experimentalis, 2005. 53(1): 47–60.

[104] Sriram, M.I., et al., Antitumor activity of silver nanoparticles in Dalton's lymphoma ascites tumor model. International Journal of Nanomedicine, 2010. 5: 753–762.

IntechOpen