The prospect of microorganism in the silver nanoparticles biosynthesis to enhance antibiotic drug activity as an alternative solution to combat resistances

M F Warsito

1Research Center for Biotechnology, Indonesian Institute of Sciences (LIPI), Komplek CSC-LIPI Jl. Raya Bogor Km 46, Cibinong-Bogor 16911, West Java, Indonesia.

E-mail: mega009@lipi.go.id

Abstract. Antimicrobial resistance (AMR) has become a major global concern. Nanotechnology is an alternate solution to combat these emerging problems, through the formulation of antibiotic drugs with nanoparticle to enhance the activity and reduce toxicity. Interaction between nanoparticle and bacteria can cause membrane disruption and toxicity to pathogenic microorganisms. Thus the combination of silver nanoparticle and antibiotic substances hopefully can increase therapeutic efficiency. Several microorganisms, such as actinomycetes, Escherichia coli, Pseudomonas sp, Aspergillus flavus, Bacillus sp., Penicillum, and Saccharomyces cerevicae have been known to be able to synthesis silver nanoparticle. It is an alternative method for chemical and physical synthesis processes, which is more environmentally friendly. The biological synthesis process is also considered easy and efficient compared to the conventional one. Furthermore, the biogenic nanoparticle has been proved to have board spectrum activity against gram-negative and gram-positive bacteria, including the pathogenic fungi. This review will discuss the microbial agent that has been known for its silver nanoparticle (AgNPs) synthesis ability and the AgNPs antimicrobial activity either as the sole agent or in combination with antibiotic drugs.

1. Introduction
Antimicrobial resistance (AMR) becomes a major concern worldwide since it dampers the effectivity of the prevention and treatment of infection caused by pathogenic bacteria, fungi, viruses, and parasites [1-3]. The drawbacks of the current therapies towards AMR lead to the exploration and development of drugs. One of the alternatives to overcome these problems is the development of silver nanoparticles (AgNPs) either as the potential antimicrobial drug [4] or by the combination with antimicrobial drugs.

Silver has been used as antimicrobial drugs since the ancient time [4, 5]. The previous studies proposed several mechanisms of antimicrobial activity of AgNPs through biophysical interaction between AgNPs with the cell. AgNPs causes cell wall disruption [6, 7], cellular components oxidation, the respiratory chain enzymes inactivation, reactive oxygen species (ROS) production, and cellular components decomposition [8, 9] that lead to cell death. It also weakens DNA replication and causes protein inactivation, which contributes to its antibacterial activity. It is harder for microorganisms to develop resistance against silver compared to antibiotics drugs due to the silver targets multiple components in the bacterial cell [10]. The particles size, shape, and particles size distribution affect the
physicochemical, magnetic, and optoelectronic properties of the nanoparticles. They lead to significant differences in biological and mechanical properties, for example, its antibacterial activity [11].

There are various physical, chemical, biological, and hybrid available in the nanoparticles synthesis method [12]. The physical synthesis could use arc-discharge [13], physical vapor condensation [14], or energy ball milling method [15] or direct current magnetron sputtering [16]. Meanwhile, the chemical approach used chemical reduction, electrochemical, irradiation assisted chemical, and pyrolysis methods [17]. The conventional chemical techniques involve expensive chemicals that often use toxic materials with potentially hazardous substances, such as organic solvents, reducing agents, and stabilizers used to prevent agglomeration of the colloids [18, 19]. At the same time, the downside of physical demerits is the consumption of high energy [16]. The residues of the toxic chemicals on the surface of the nanoparticles limit their application in the pharmaceutical and biomedical products. Fortunately, these factors can be controlled via biological mediated production, which is cleaner, more reliable, biologically compatible, benign, and environmentally friendly processes than the conventional methods [20, 21]. Microorganisms synthesis is one of the options to achieve this goal.

Biosynthesis uses environmental-friendly green chemistry processes utilizing biological entities, such as microorganisms, that will act as biological factories. It offers clean, biocompatible, non-toxic, and environmental-friendly methods, which are able to produce a wide range of shapes, sizes, compositions, and physicochemical properties [22]. Biological entities also act as templates in the synthesis, assembly, and organize nanometre-scale materials to fabricate well-defined micro and macro scale structures. The nanoparticle synthesis using microorganisms has several steps to be conducted, such as culturing and isolation techniques. Several microorganisms reported having the ability to synthesis AgNPs are Actinobacter [23], Bacillus endophyticus [24], Trichoderma longibrachiatum [12], Fusarium oxysporum [25], Neochloris oleoabundans [26], and Enteromorpha compressa [27]. This review aims to present a brief overview of the microorganisms and techniques that can be used for synthesizing AgNPs, and their application in the pharmaceutical development to combat AMR.

2. Mechanism of AgNPs biosynthesis by microorganisms

Green synthesis has become popular in recent years due to its eco-friendly approach. Green synthesis of nanoparticles using a biological microorganism, such as fungi, bacteria, yeast, and algae, also has advantages compared to the physical and chemical synthesis method, i.e., lower production cost due to the reduction of the usage of expensive and hazardous chemicals, higher energy efficiency, no need of high temperature, and easily scalable production process [21]. AgNPs biosynthesis by microorganism mostly involves reduction reactions by the microbial enzymes that have reducing properties on the Ag+ ion to form AgNPs [28-30], either through intracellular or extracellular routes [31]. There are three major components involved in the preparation of nanoparticles using biological methods, i.e., the solvent medium for synthesis, the environmentally friendly reducing agent, and a non-toxic stabilizing agent [28].

Some microorganisms have resistance to silver metal. Thus they can survive in the environment at certain metal ion concentrations, and they also can grow under those conditions. The resistance mechanisms involve efflux systems, solubility, and toxicity alteration via reduction or oxidation reaction, biosorption, bioaccumulation, the formation of extracellular complex or metals precipitation, and lack of specific metal transport systems [32]. Microorganisms that have been reported to have the capability to synthesize AgNPs with antimicrobial properties are listed in Table 1.

Bacterial cells have been employed as AgNPs nano factories, using both the extracellular and intracellular approaches. An extracellular approach occurs outside the bacterial cell, while the intracellular approach occurs inside the cell. Techniques that have been used in the process of AgNPs biosynthesis extracellularly can be done using either (a) bacterial biomass, (b) supernatant of bacterial cultures, or (c) cell-free extracts [33]. Extracellular synthesis is preferred over intracellular synthesis because it is devoid of complex downstream processing [34]. The complete understanding of AgNPs biosynthesis mechanism in bacteria is yet to be fully understood. The most widely accepted theory is the presence of nitrate reductase enzyme, which is generally involved in the cellular nitrogen cycle. It will induce the conversion of nitrate into nitrite, and then the electron is transferred to the silver ion;
hence, the silver ion is reduced to silver (Ag\(^+\) to Ag\(^0\)) [35]. Nicotinamide adenine dinucleotide (NADH)-dependent nitrate reductase enzyme in bacteria is responsible for the reduction of Ag ions to metallic Ag via an electron transfer mechanism. Besides, it is also responsible for the subsequent formation of stabilized Ag nanoparticles, thus it would remove the downstream processing step that is required in other cases [36]. The intracellular synthesis process requires the Ag\(^+\) ions to be transported into the microbial cell to be catalyzed by the enzyme to form AgNPs. While in the extracellular synthesis, the Ag\(^+\) ions are trapped on the cells surface. Moreover, the nanoparticles are formed through the reduction of the ion in the presence of the enzyme [37]. Another biosynthesis mechanism reported by Fu et al. was through the interaction of the silver ions with the groups on the microbial cell wall in dried cells of *Lactobacillus* sp. A09 can also reduce silver ions without the presence of enzymes [38].

Fungi are a viable alternative in AgNPs biosynthesis due to their ability to produce larger amounts of nanoparticles compared to bacteria. It is because of their ability to produce larger amounts of proteins that are directly correlated with the enhancement of AgNPs production [39, 40]. Fungi also have better tolerance and possess higher metal-bioaccumulation property, which is responsible for the high accumulation of AgNPs [41-43], and the synthesized particles also tend to be smaller in size [44, 45]. AgNPs synthesis in fungi can occur at both in intracellular and extracellular locations [18]. The synthesis mechanism is based on the reduction of the Ag\(^+\) ions by the nitrate reductase present in the fungal system [46]. In extracellular synthesis, the surface of the fungal cells traps the Ag\(^+\) ions. Then, it is followed by the reduction of the Ag\(^+\) ions by the enzymes, such as naphthoquinones and anthraquinones [46]. The enzymes released by the fungal biomass also present in the solution and is bound to the surfaces of nanoparticles [47-49]. The NADPH-dependent nitrate reductase and a shuttle quinone extracellular process are also believed to be responsible for nanoparticle formation [50]. In the intracellular synthesis, extraction procedures have low yields. In contrast, extracellular synthesis produces nanoparticles at the cell surface or at the cell periphery where they can be easily recovered during downstream processing [51, 52]. It is assumed that chemical composition from the fungal compounds and their media components potentially has role as the stabilization of the nanoparticles [53].

Yeasts also can absorb and accumulate significant amounts of metals from the environment [54, 55] because they have detoxification mechanisms such as chelation, bio-precipitation, bio-sorption, and extracellular sequestration. The AgNPs size, location, and properties are variable due to different mechanisms used by yeast organisms to form and stabilize the nanoparticles during synthesis [56]. The metal nanoparticle size and shape were regulated by several factors such as the growth rate, cellular activities of the yeast culture [57], biomass and metal salt concentration [58, 59].

Algae, a diverse group of aquatic microorganisms, is also increasingly popular for the nanoparticle biosynthesis, including AgNPs. *Gelidium amansii* was reported to be able to synthesize AgNPs, which had excellent antimicrobial properties by forming a biofilm to combat bacterial strains [60]. There was a blue shift in the UV absorption after the concentration of *S. crassifolium* increased, which was attributed to smaller size particles due to the increased of nucleation centers in the reductant [61].

### Table 1. AgNPs synthesized by microorganisms.

| Microorganisms | Size (nm) | Shape | Ref. | Microorganisms | Size (nm) | Shape | Ref. |
|----------------|----------|-------|------|----------------|----------|-------|------|
| **Bacteria**   |          |       |      |                |          |       |      |
| Actinobacter    | 13.2     | Spherical | [22] |                |          |       |      |
| Bacillus endophyticus | 5.1 | Spherical | [23] |                |          |       |      |
| Bacillus brevis  | 41-68    | Spherical | [62] | *Rhodotorula glutinis* | 15.45 | Spherical | [70] |
| Streptomyces griseolueans | 19.5-20.9 | Spherical | [63] | *Rhodotorula maculaginoa* | 13.70 | Spherical | [71] |
| Micrococcus yunnanensis | 53.8 | Spherical | [64] | *Nemania* sp. | 33.52 | Spherical | [72] |
| **Fungi**      |          |       |      |                |          |       |      |
| Trichoderma longibrachiatum | 10 | Spherical | [12] | *Neochloris oleoabundans* | 40 | Spherical | [26] |
| Fusarium oxysporum | 21.3-37 | Spherical | [25] | *Entomorpha compressa* | 4-24 | Spherical | [27] |
| Aspergillus terreus | 16-57 | Spherical | [65] | *Nostoc lineksi* | 5-60 | Spherical | [73] |
| Ganoderma sessiliforme | ~45 | Spherical | [66] | *Nostoc* sp | 51-100 | Spherical | [74] |
| Phenerochaete chrysosporium | 34-90 | Spherical-Oval | [67] | *Leptolyngbya* | 5-50 | Spherical | [75] |
| **Algae/Cyanobacteria** |          |       |      |                |          |       |      |
| Neochloris oleoabundans | 40 | Spherical | [26] |                |          |       |      |
| *Entomorpha compressa* | 4-24 | Spherical | [27] |                |          |       |      |
| *Nostoc lineksi* | 5-60 | Spherical | [73] |                |          |       |      |
| *Nostoc* sp | 51-100 | Spherical | [74] |                |          |       |      |
| *Leptolyngbya* | 5-50 | Spherical | [75] |                |          |       |      |
3. Effect of AgNPs physicochemical properties on antimicrobial activity

AgNPs unique physicochemical properties, i.e., shape, size, concentration, and colloidal state, strongly influence their bactericidal activity [76,77]. Thus, it is important to have suitable sized, shaped nanoparticles with desirable surface properties. The stability and biocompatibility will increase when the particle size of AgNPs is smaller [78]. The effective size of nanoparticles should be no larger than 50 nm. Accurately, the AgNPs size between 10 and 15 nm reported having good stability, biocompatibility, and enhancing antimicrobial activity [79]. AgNPs with size <30nm showed better antibacterial activity against S. aureus and K. pneumoniae [80]. Apparently, the smaller particle size has superior penetration ability into bacteria, especially in Gram-negative [81]. AgNPs size of 5–10 nm display bacteriostatic and bactericidal effects against S. aureus, Methicillin-sensitive Staphylococcus aureus (MSSA) and Methicillin-resistant Staphylococcus aureus (MRSA) [82].

The AgNPs shape also affects its interaction with microorganism [83, 84, 78], that can be due to variations in the effective surface areas and active facets of AgNPs [9]. It was reported that truncated triangular shaped AgNPs show enhanced antibacterial action compare to the spherical AgNPs [85]. However, there is limited information about the particle shape effect on its biological activity.

The antibacterial activity of AgNPs is also concentration-dependent. In lower concentration, gram-negative bacteria, such as E. coli and S. typhi, is more susceptible to AgNPs than Gram-positive bacteria, such as S. aureus, P. aeruginosa, and V. cholera. Meanwhile, at the higher concentration (>75 µg/mL), both classes of bacteria display complete growth inhibition [86].

Colloidal form of AgNPs has shown an enhanced antimicrobial potential [87, 88], compared to AgNPs in the liquid system because of its low colloidal stability [89, 90]. It is because it works as a catalyst that destabilizes the enzymes of the pathogenic drug-resistant microorganisms mostly needed for their oxygen utilization [89, 91]. It also regulates signal transduction pathways in bacteria by altering the phosphotyrosine profile of the proteins, which leads to growth inhibition in bacteria [92]. AgNPs colloidal form also has enhanced bactericidal activity against drug-resistant bacteria, such as MRSA [87, 88].

4. AgNPs antibacterial activity

AgNPs have antimicrobial activity against a wide range of microorganisms, including bacteria, fungi, and viruses [9, 93], it is even effective against multidrug-resistant bacteria [82, 94]. Although the exact mechanism is not clearly known, there are several antimicrobial mechanisms of the proposed AgNPs action, such as (a) disruption of membrane potential and integrity caused by the adhesion of AgNPs onto the surface of cell wall and membrane, (b) the host immune responses activation, (c) inhibition of biofilm formation, (d) generation of (ROS), lipid peroxidation, inhibition of cytochromes in the electron transport chain, (e) inhibition of cell wall synthesis, (f) damaging the intracellular structure (mitochondria, vacuoles, and ribosomes) and biomolecules (protein, lipids, and DNA) caused by AgNPs penetration to the cells and (g) inhibition of RNA and protein synthesis through the induction of intracellular effects [9, 22, 95, 96].

AgNPs can be tailored and packaged with various antimicrobial drugs, such as kanamycin, rifampicin, ciprofloxacin, streptomycin, gentamicin, amoxicillin, ampicillin, polymyxin, chloramphenicol, penicillin-G, amikacin, tetracycline, cephalothin, amoxiclav, cepiprome, clotrimazole, etc. [97]. AgNPs antibacterial activity works multiple targets on microorganisms, and they have a unique mechanism. Thus, antimicrobial resistance may be possible to develop if AgNPs are combined with antibiotics since multiple simultaneous mutations are required in the same microorganism [98, 99]. The other advantages of this combination are AgNPs can deliver antimicrobial drugs to or target the infected sites. Therefore, it can reduce the dosage and toxicity of antibiotics [100], and it can also prevent biofilm formation. This combination can promote the reversal of antimicrobial resistance and enhance the antimicrobial effects of several antibiotics, such as polymyxin B, ciprofloxacin, ceftazidime, ampicillin, clindamycin, vancomycin, or erythromycin, against MDROs, including antibiotic-resistant A. baumannii, P. aeruginosa, E. faecium; vancomycin-resistant Enterococcus (VRE); and MRSA [100].
5. Conclusion

Biosynthesis of AgNPs using microorganisms is an eco-friendly synthesis process. It offers clean, biocompatible, and non-toxic methods that can produce a wide range of shapes, sizes, compositions, and physicochemical properties. These synthesis processes can utilize various microorganisms such as fungi, bacteria, yeast, and algae. It is due to the capability of microorganisms to gain resistance to silver metal through efflux systems, solubility, and toxicity alteration via reduction or oxidation reaction, biosorption, bioaccumulation, the formation of extracellular complex or metals precipitation, and lack of specific metal transport systems. AgNPs biosynthesis by microorganism mostly involves reduction reactions by the microbial enzymes that have reducing properties on the Ag⁺ ion to form AgNPs, either through intracellular or extracellular routes. The synthesis process can be using either (a) bacterial biomass, (b) supernatant of bacterial cultures, or (c) cell-free extracts.

AgNPs unique physicochemical properties, i.e., shape, size, concentration, and colloidal state, strongly influence their antimicrobial activity. Thus, it is important to have suitable sized, shaped nanoparticles with desirable surface properties that will conform their stability, biocompatibility, and biological activity. The antimicrobial mechanism of action of the AgNPs are through (a) disruption of the cell membrane (b) the host immune responses activation, (c) inhibition of biofilm formation, (d) generation of ROS, lipid peroxidation, inhibition of cytochromes in the electron transport chain, (e) inhibition of cell wall synthesis, (f) damaging the intracellular structure (mitochondria, vacuoles, and ribosomes) and biomolecules (protein, lipids, and DNA) and (g) inhibition of RNA and protein synthesis through the induction of intracellular effects. The combination of AgNPs with antibiotics can be a promising regimen to combat AMR.

6. References

[1] Prestinati F, Pezzotti P and Pantosti A 2015 Antimicrobial resistance: a global multifaceted phenomenon Pathog Glob Health 109: 309–318
[2] Nahrgang S, Nolte E and Rechel B 2018 Antimicrobial resistance (Health Policy Series, No. 51.) ed Rechel B, Maresso A, Sagan A, Hernández-Quevedo C, Richardson E, Jakubowski E, McKee M and Nolte E (Copenhagen: European Observatory on Health Systems and Policies) chapter 4 pp. 67-74
[3] Aslam B, Wang W, Arshad M I, Khurshid M, Muzammil S, Rasool M H, Nisar M A, Alvi R F, Aslam M A, Qamar M U, Salamat M K F and Baloch Z 2018 Antibiotic resistance: a rundown of a global crisis Infect Drug Resist 11: 1645—1658
[4] Reidy B, Haase A, Luch A, Dawson K A and Lynch I 2013 Mechanisms of silver nanoparticle release, transformation and toxicity: a critical review of current knowledge and recommendations for future studies and applications Materials (Basel) 6: 2295–2350
[5] Yan X, He B, Liu L, Qu G, Shi J, Hu L and Jiang G 2018 Antibacterial mechanism of silver nanoparticles in Pseudomonas aeruginosa: proteomics approach Metallomics 10: 557-564
[6] Lok C N, Ho C M, Chen R, He Q Y, Yu W Y, Sun H, Tam P K, Chiu J F and Che C M 2007 Silver nanoparticles: partial oxidation and antibacterial activities J Biol Inorg Chem 12: 527-34
[7] Bondarenko O M, Sihtmäe M, Kuzmičiova J, Rageliēnē L, Kahrū A, and Daugelavičius R 2018 Plasma membrane is the target of rapid antibacterial action of silver nanoparticles in Escherichia coli and Pseudomonas aeruginosa Int J Nanomedicine 13: 6779-6790
[8] Rizzello L and Pompa P P 2014 Nanosilver-based antibacterial drugs and devices: Mechanisms, methodological drawbacks, and guidelines Chem Soc Rev 43: 1501-18
[9] Dakal T C, Kumar A, Majumdar R S and Yadav V 2016 Mechanistic basis of antimicrobial actions of silver nanoparticles Front Microbiol 7: 1831
[10] Zhou Y, Kong Y, Kundu S, Cirillo J D and Liang H 2012 Antibacterial activities of gold and silver nanoparticles against Escherichia coli and bacillus Calmette-Guérin J Nanobiotechnology 10: 19
[11] Lee S H and Jun B H 2019 Silver nanoparticles: synthesis and application for nanomedicine Int J Mol Sci 20: 865
[12] Elamawi R M, Al-Harbi R E and Hendi A A 2018 Biosynthesis and characterization of silver nanoparticles using Trichoderma longibrachiatum and their effect on phytopathogenic fungi *Egypt. J. Biol. Pest Control* **28**: 28

[13] Tien D C, Tseng K H, Liao C Y, Huang J C and Tsung T T 2008 Discovery of ionic silver nanoparticle suspension fabricated by arc discharge method *J Alloys Compd.* **463**: 408-411

[14] Abou El-Nour K M M, Eftaiha A, Al-Warthan A and Ammar R A A 2010 Synthesis and applications of silver nanoparticles *Arab J Chem.* **3**:135-140

[15] Kosmala A, Wright R, Zhang Q and Kirby P 2011 Synthesis of silver nano particles and fabrication of aqueous Ag inks for inkjet printing *Mater Chem Phys.* **129**: 1075-1080

[16] Asanithi P, Chaiyakun S and Limsuwan P 2012 Growth of silver nanoparticles by DC magnetron sputtering *J Nanomater.* **2012**: 963609

[17] Zhang W, Qiao X and Chen J 2007 Synthesis of silver nanoparticles—Effects of concerned parameters in water/oil microemulsion *Mater Sci Eng B.* **142**: 1-15

[18] Siddiqi K S, Husen A and Rao R A K 2018 A review on biosynthesis of silver nanoparticles and their biocidal properties *J Nanobiotechnol* **16**: 14

[19] Shah M, Fawcett D, Sharma S, Tripathy S K and Poinern G E J 2015 Green synthesis of metallic nanoparticles via biological entities *Materials* **8**: 7278-7308

[20] Husen A and Siddiqi K S 2014 Phytosynthesis of nanoparticles: concept, controversy and application *Nanoscale Res Lett.* **9**: 229

[21] Siddiqi K S and Husen A 2016 Fabrication of metal nanoparticles from fungi and metal salts: scope and application *Nanoscale Res Lett.* **11**

[22] Mathur P, Jha S, Ramteke S and Jain N K 2018 Pharmaceutical aspects of silver nanoparticles *Artificial Cells, Nanomedicine, and Biotechnology* **46**: 115-126

[23] Wypij M, Golinska P, Dahm H and Rai M 2017 Actinobacterial-mediated synthesis of silver nanoparticles and their activity against pathogenic bacteria *IET Nanobiotechnol.* **11**: 336-342

[24] Gan L, Zhang S, Zhang Y, He S and Tian Y 2018 Biosynthesis, characterization and antimicrobial activity of silver nanoparticles by a halotolerant Bacillus endophyticus SCU-L *Prep. Biochem. Biotechnol.* **48**: 582-588

[25] Ahmed A A, Hamzah H and Maarof M 2018 Analyzing formation of silver nanoparticles from the filamentous fungus Fusarium oxysporum and their antimicrobial activity *Turk. J. Biol.* **42**: 54-62

[26] Ramkumar V S, Pugazhendhi A, Gopalakrishnan K, Sivagurunathan P, Saratale G D, Dung T N B and Kannapiran E 2017 Biofabrication and characterization of silver nanoparticles using aqueous extract of seaweed Enteromorpha compressa and its biomedical properties *Biotecnol. Rep. (Amst)* **14**: 1-7

[27] Vanlalveni C, Rajkumari K, Biswas A, Adhikari P P, Lalfakzuala R and Rokhum L 2018 Green synthesis of silver nanoparticles and their activity against pathogenic bacteria *BioNanoScience* **8**: 624-631

[28] Prabhu S and Poulou E K 2012 Silver nanoparticles: mechanism of antimicrobial action, synthesis, medical applications, and toxicity effects *International Nano Letters* **2**: 32

[29] Anil Kumar S, Majid K A, Gosavi S W, Kulkarni S K, Pasricha R, Ahmad A and Khan M I 2007 Nitrate reductase mediated synthesis of silver nanoparticles from AgNO3 *Biotechnol. Lett.* **29**: 439-445

[30] Mukherjee P, Ahmad A, Mandal D, Senapati S, Sainkar S R, Khan M I, Parischa R, Ajaykumar P V, Alam M, Kumar R and Sastry M 2001 Fungus-mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: a novel biological approach to nanoparticle synthesis *Nanopart. 1*: 515-519

[31] Li X Q, Xu H Z, Chen Z S and Chen G F 2011 Biosynthesis of nanoparticles by microorganisms and their applications *Journal of Nanomaterials* **2011**: 270974

[32] Hussein M I, Aziz M A E, Badr Y and Mahmoud M A 2007 Biosynthesis of gold nanoparticles using Pseudomonas aeruginosa *Spectrochim Acta A Mol Biomol Spectrosc* **67**: 1003-1006
[33] Ovais M, Khalili A T, Ayaz M, Ahmad I, Nethi S K and Mukherjee S 2018 Biosynthesis of metal nanoparticles via microbial enzymes: a mechanistic approach Int. J. Mol. Sci. 19: 4100

[34] Singh R, Wagh P, Wadhwan S, Gaidhani S, Kumbhar A, Bellare J and Chopade B A 2013 Synthesis, optimization, and characterization of silver nanoparticles from Acinetobacter calcoaceticus and their enhanced antibacterial activity when combined with antibiotics Int. J. Nanomed. 8: 4277-4290

[35] Korbekandi H, Iravani S, Abbasi S 2009 Production of nanoparticles using organisms Crit. Rev. Biotechnol. 29: 279-306

[36] Vaidyanathan R, Gopalram S, Kalishwaralal K, Deepak V, Pandian S R and Gurunathan S 2010 Enhanced silver nanoparticle synthesis by optimization of nitrate reductase activity Colloids Surf. B BioInterfaces 75: 335-341

[37] Zhang X, Yan S, Tyagi R D and Surampalli R Y 2011 Synthesis of nanoparticles by microorganisms and their application in enhancing microbiological reaction rates Chemosphere 82: 489-494

[38] Fu J K, Liu Y, Gu P, Tang D L, Lin Z Y, Yao B X and Weng S 2000 Spectroscopic characterization on the biosorption and bioreduction of Ag(I) by Lactobacillus sp. A09 Acta. Physico-Chimica. Sinica. 16: 779 -782

[39] Narayanan K B and Sakhthivel N 2010 Biological synthesis of metal nanoparticles by microbes Adv. Colloid Interface Sci. 156: 1-13

[40] Mohanpuria P, Rana K N and Yadav S K 2008 Biosynthesis of nanoparticles: technological concepts and future applications J. Nanopart. Res. 10: 507–517

[41] Singh P, Kim Y J, Zhang D, Yang, D C 2016 Biological Synthesis of Nanoparticles from Plants and Microorganisms Trends Biotechnol. 34: 588-599

[42] Alghuthaymi M A, Almoammar H, Rai M, Said-Galiev E and Abd-Elsalam K A 2015 Myconanoparticles: synthesis and their role in phytopathogens management Biotechnol Biotechnol Equip 29: 221-236

[43] Castro-Longoria E, Vilchis-Nestor A R and Avalos-Borja M 2011 Biosynthesis of silver, gold and bimetallic nanoparticles using the filamentous fungus Neurospora crassa Colloids Surf B BioInterfaces 83: 42-48

[44] Mukherjee P, Senapati S, Mandal D, Ahmad A, Khan M I, Kumar R and Sastry M 2002 Extracellular synthesis of gold nanoparticles by the fungus Fusarium oxysporum ChemBioChem 3: 461-463

[45] Volesky B and Holan Z R 1995 Biosorption of heavy metals Biotechnol. Prog. 11: 235–250

[46] Mohanpuria P, Rana K N and Yadav S K 2008 Biosynthesis of nanoparticles: technological concepts and future applications J. Nanopart. Res. 10: 507–517

[47] Kumar A, Mandal S, Selvakannan P R, Parischa R, Mandale A B and Sastry M 2003 Investigation into the Interaction between Surface-Bound Alkylamines and Gold Nanoparticles Langmuir 19: 6277–6282

[48] Kumar C V and McLendon G L 1997 Nanoencapsulation of cytochrome c and horseradish peroxidase at the galleries of α-Zirconium Phosphate Chem. Mater. 9: 863–870

[49] Macdonald I D G and Smith W E 1996 Orientation of cytochrome c adsorbed on a citrate-reduced silver colloid surface Langmuir 12: 706-713

[50] Ahmad A, Mukherjee P, Senapati S, Mandal D, Khan M I, Kumar R and Sastry M 2003 Extracellular biosynthesis of silver nanoparticles using the fungus Fusarium oxysporum Colloids Surf. B BioInterfaces 28: 313-318

[51] Dhillon GS, Brar S K, Kaur S and Verma M 2012 Green approach for nanoparticle biosynthesis by fungi: current trends and applications Crit. Rev. Biotechnol. 32: 49-73

[52] Kathiresan K, Manivannan S, Nabeel MAand Dhivya B 2009 Studies on silver nanoparticles synthesized by a marine fungus, Penicillium fellutanum isolated from coastal mangrove sediment Colloids Surf. B 71: 133-7

[53] Molnár Z, Bódai V, Szakacs G, Erdélyi B, Fogarassy Z, Sáfrán G, Varga T, Kónya Z, Tóth-Szeles E and Sz‘ucs R 2018 Green synthesis of gold nanoparticles by thermophilic filamentous fungi Sci. Rep. 8: 3943
[54] Bhattacharya D and Gupta R K 2005 Nanotechnology and potential of microorganisms *Crit. Rev. Biotechnol.* **25**: 199-204

[55] Mandal D, Bolander M E, Mukhopadhyay D, Sarkar G and Mukherjee P 2006 The use of microorganisms for the formation of metal nanoparticles and their application *Appl. Microbiol. Biotechnol.* **69**: 485-492

[56] Hulkoti N I and Taranath T C 2014 Biosynthesis of nanoparticles using microbes- a review *Colloids Surf. B Biointerfaces* **121**: 474-483

[57] Gericke M and Pinches A 2006 Microbial production of gold nanoparticles *Gold Bull.* **83**: 22–28

[58] Agnihotri M, Joshi S, Kumar A R, Zinjarde S S and Kulkarni S K 2009 Biosynthesis of gold nanoparticles by the tropical marine yeast Yarrowia lipolytica NCIM 3589 *Mater. Lett.* **63**: 1231–1234

[59] Pimprikar P S, Joshi S, Kumar A R, Zinjarde S S and Kulkarni S K 2009 Influence of biomass and gold salt concentration on nanoparticle synthesis by the tropical marine yeast Yarrowia lipolytica NCIM 3589 *Colloids Surf B Biointerfaces* **74**: 309-316

[60] Ovais M, Raza A, Naz S, Islam N U, Khalil A T, Ali S, Khan M A and Shinwari Z K 2017 Current state and prospects of the phytosynthesized colloidal gold nanoparticles and their applications in cancer theranostics *Appl. Microbiol. Biotechnol.* **101**: 3551-3565

[61] Maceda A F, Ouano J J S, Que M C O, Basilia B A, Potestas M J and Alguno A C 2018 Controlling the Absorption of Gold Nanoparticles via Green Synthesis Using *Sargassum crassifolium* Extract *Key Engineering Materials* (Clausthal-Zellerfeld: Trans Tech Publ) pp. 44–48.

[62] Saravanan M, Barik S K, MubarakAli D, Prakash P and Pugazhendhi A 2018 Synthesis of silver nanoparticles from *Bacillus brevis* (NCIM 2533) and their antibacterial activity against pathogenic bacteria *Microb. Pathog.* **116**: 221–226

[63] Vijayabharaathi R, Sathyia, A and Gopalakrishnan S 2018 Extracellular biosynthesis of silver nanoparticles using *Streptomyces griseoplanus* SAI-25 and its antifungal activity against *Macrophomina phaseolina*, the charcoal rot pathogen of sorghum *Biocatal. Agric. Biotechnol.* **14**: 166-171

[64] Jafari M, Rohkhakhsh-Zamin F, Shakibaie M, Moshaﬁ M H, Ameri A, Rahimi H R and Forootanfar H 2018 Cytotoxic and antibacterial activities of biologically synthesized gold nanoparticles assisted by *Micrococcus yunnanensis* strain J2 *Biocatal. Agric. Biotechnol.* **15**: 245-253

[65] Singh P S and Vidyasagar G 2018 Biosynthesis of antibacterial silver nano-particles from *Aspergillus terreus* *World News Nat. Sci.* **16**: 117–124

[66] Mohanta Y K, Nayak D, Biswas K, Singdevsachan S K, Abd_Allah E F, Hashem A, Alqarawi A A, Yadav D, Mohanta T K 2018 Silver Nanoparticles Synthesized Using Wild Mushroom Show Potential Antimicrobial Activities against Food Borne Pathogens *Molecules* **23**: 655

[67] Saravanan M, Arokiyaraj S, Lakshmi T and Pugazhendhi A 2018 Synthesis of silver nanoparticles from *Phenerochaete chrysosporium* (MTCC-787) and their antibacterial activity against human pathogenic bacteria *Microb. Pathog.* **117**: 68-72

[68] Neethu S, Midhun S J, Sunil M, Souyma S, Radhakrishnan E and Jyothy M 2018 Efﬁcient visible light induced synthesis of silver nanoparticles by *Penicillium polonicum* ARA 10 isolated from *Chetomorpha antennina* and its antibacterial efﬁcacy against *Salmonella enterica* serovar Typhimurium *J. Photochem. Photobiol. B* **180**: 175-185

[69] Jalal M, Ansari M, Alzohairy M, Ali S, Khan H, Almatroudi A and Raees K 2018 Biosynthesis of silver nanoparticles from oropharyngeal *Candida glabrata* isolates and their antimicrobial activity against clinical strains of bacteria and fungi *Nanomaterials (Basel)* **8**: 586

[70] Cunha F A, da C S O Cunha M, da Frota S M, Mallmann E J, Freire T M, Costa L S, Paula A J Menezes E A and Fechine P B 2018 Biogenic synthesis of multifunctional silver nanoparticles from *Rhodotorula glutinis* and *Rhodotorula mucilaginosa*: antifungal, catalytic and cytotoxicity activities *World J. Microbiol. Biotechnol.* **34**: 127
[71] Farsi M and Farokhi S 2018 Biosynthesis of Antibacterial Silver Nanoparticles by Endophytic Fungus Nemania sp. Isolated From Taxus baccata L. (Iranian Yew) Zahedan J. Res. Med. Sci. 20: e57916

[72] Bao Z and Lan CQ 2018 Mechanism of light-dependent biosynthesis of silver nanoparticles mediated by cell extract of Neochloris oleoabundans Colloids Surf. B : Biointerfaces 170: 251-257

[73] Sonker A S, Pathak J, Kannauiyia V and Sinha R 2017 Characterization and in vitro antitumor, antibacterial and antifungal activities of green synthesized silver nanoparticles using cell extract of Nostoc sp. strain HKAR-2 Can. J. Biotechnol. 1: 26-37

[74] Zada S, Ahmad A, Khan S, Yu X, Chang K, Iqbal A, Ahmad A, Ullah S, Raza M and Khan A 2018 Biogenic synthesis of silver nanoparticles using extracts of Leptolyngbya JSC-1 that induce apoptosis in HeLa cell line and exterminate pathogenic bacteria Artif. Cells Nanomed. Biotechnol. 46: S471-S480

[75] Murugesan S, Bhuvaneswari S and Sivamurugan V 2017 Green synthesis, characterization of silver nanoparticles of a marine red alga Spyridia fusiformis and their antibacterial activity Int. J. Pharm. Sci. 9: 192-197

[76] Nateghi MR and Hajimirzababa H 2014 Effect of silver nanoparticles morphologies on antimicrobial properties of cotton fabrics J. Text. I. 105: 806-813

[77] Raza M A, Kanwal Z, Rauf A, Sabri A N, Riaz S and Naseem S 2016 size- and shape-dependent antibacterial studies of silver nanoparticles synthesized by wet chemical routes Nanomaterials (Basel) 6: 74

[78] Kim S H, Lee H S, Ryu D S, Choi S J and Lee D S 2011 Antibacterial activity of silver-nanoparticles against Staphylococcus aureus and Escherichia coli Korean J. Microbiol. Biotechnol. 39: 77-85

[79] Yacaman M J, Ascencio J A, Liu H B and Gardea-Torrejón J 2001 Structure shape and stability of nanometric sized particles J. Vacuum Sci. Technol. B. Microelectron. Nanomater. Struct. 19: 1091-1103

[80] Collins T L, Markus E A, Hassett D J and Robinson J B 2010 The effect of a cationic porphyrin on Pseudomonas aeruginosa biofilms Curr. Microbiol. 61: 411-416

[81] Morones J R, Elechiguerra J L, Camacho A, Holt K, Kouri J B and Ramírez J T 2005 The bactericidal effect of silver nanoparticles Nanotechnology 16: 2346-2353

[82] Ansari M A, Khan H M, Khan A A, Malik A, Sultan A, Shahid M Shujatullah F and Azam A 2011 Evaluation of antibacterial activity of silver nanoparticles against MSSA and MRSA on isolates from skin infections Biol. Med. 3: 141–146

[83] Tamayo L A, Zapata P A, Vejar N D, Azócar M I, Gulppi M A and Zhou X 2014 Release of silver and copper nanoparticles from polyethylene nanocomposites and their penetration into Listeria monocytogenes Mater Sci Eng C Mater Biol Appl 40: 24-31

[84] Wu D, Fan W, Kishen A, Gutmann J L and Fan B 2014 Evaluation of the antibacterial efficacy of silver nanoparticles against Enterococcus faecalis biofilm J. Endod. 40: 285-290

[85] Pal S, Tak Y K and Song J M 2007 does the antibacterial activity of silver nanoparticles depend on the shape of the nanoparticle? a study of the gram-negative bacterium Escherichia coli Appl. Environ. Microbiol. 73: 1712-1720

[86] Kim J S, Kuk E, Yu K N, Kim J H, Park S J and Lee H J 2007 Antimicrobial effects of silver nanoparticles Nanomed. Nanotechnol. Biol. Med. 3: 95-101

[87] Panáček A, Kvítek L, Pruček R, Kolar M, Vecerova R and Pizurova N 2006 Silver Colloid Nanoparticles: Synthesis, Characterization, and Their Antibacterial Activity J. Phys. Chem. B 110: 16248–16253

[88] Lkhagvajav N, Yasab I C, Elike E, Koizhaiganova M and Saria O 2011 Antimicrobial activity of colloidal silver nanoparticles prepared by sol-gel method Dig. J. Nanomater. Biostruct. 6:149–154

[89] Kumar S, Singh M, Halder D and Mitra A 2014 Mechanistic study of antibacterial activity of biologically synthesized silver nanocolloids Colloids Surfaces A : Physicochemical and Engineering Aspects 449: 82-86
[90] Shi Z, Tang J, Chen L, Yan C, Tanvir S and Anderson W A 2014 Enhanced colloidal stability and antibacterial performance of silver nanoparticles/cellulose nanocrystal hybrids J. Mater. Chem. B 3: 603-611

[91] Suganya K S U, Govindaraju K, Kumar V G, Dhas T S, Karthick V and Singaravelu G 2015 Size controlled biogenic silver nanoparticles as antibacterial agent against isolates from HIV infected patients Spectrochim. Acta A Mol. Biomol. Spectrosc. 144: 266–272

[92] Shrivastava S, Bera T, Roy A, Singh G, Ramachandrarao P and Dash D 2007 Characterization of enhanced antibacterial effects of novel silver nanoparticles Nanotechnology 18: 225103

[93] Ahmed S, Ahmad M, Swami B L, Ikram S 2016 A review on plants extract mediated synthesis of silver nanoparticles for antimicrobial applications: A green expertise Journal of Advanced Research 7: 17-28

[94] Lee N Y, Ko W C and Hsueh P R 2019 Nanoparticles in the treatment of infections caused by multidrug-resistant organisms Frontiers in Pharmacology 10: 1153

[95] Duran N, Duran M, de Jesus M B, Seabra A B, Favaro W J and Nakazato G 2016 Silver nanoparticles: A new view on mechanistic aspects on antimicrobial activity Nanomedicine 12: 789-799

[96] Beyth N, Houri-Haddad Y, Domb A, Khan W and Hazan R 2015 Alternative antimicrobial approach: nano-antimicrobial materials Evid. Based. Complement Alternat. Med. 2015: 246012

[97] Ruddaraju L K, Pammi S V N, Guntuku G S, Padavala V S and Kolapalli V R M 2020 A review on anti-bacterials to combat resistance: From ancient era of plants and metals to present and future perspectives of green nano technological combinations AIPS 15: 42-59

[98] Fischbach M A 2011 Combination therapies for combating antimicrobial resistance Curr. Opin. Microbiol. 14: 519-523

[99] Zhao Y and Jiang X 2013 Multiple strategies to activate gold nanoparticles as antibiotics Nanoscale 5: 8340-8350

[100] Hemeg HA 2017 Nanomaterials for alternative antibacterial therapy Int. J. Nanomed. 12: 8211-8225