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BIOSYNTHESIS OF NANOPARTICLES

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ABSTRACT

Biosynthesis of nanoparticles is reviewed in detail in this study. Comparison of different synthesis methods, namely physical, chemical and green methods giving emphasis to biological synthesis is documented here. This study also details limitations of the present techniques and envisages the future scope of nanoparticle biosynthesis. Important applications of nanoparticles are also discussed briefly in the present report.

INTRODUCTION: Nanotechnology has started leaving conforms of laboratory and conquering the new application to change our lives. The increased surfaces of these nanoparticles are responsible for their different chemical, optical, mechanical, megnatic properties as compared to large bulk materials [1]. Nanoparticles were used by the artisans of Mesopotamia to generate glittering effects to pots. The properties of nanoparticles were proved in 1857 in Faraday's famous paper "Experimental relations of gold (and other metals) to light" [2].

Due to incredible properties nanoparticles have become significant in many fields in the recent years, such as energy, health care, environment, agriculture, *etc*. The preparation of nanoparticles are carried out either by (i) Nanoparticles synthesis or by (ii) Processing of nanomaterials into nanostructure particles [3]. The silver nanoparticles are prepared by using physical, chemical and biological methods [4]. The physical and chemical methods are very expensive [5]. Biological methods of nanoparticles synthesis would help to remove harsh processing conditions by enabling the synthesis at physiological pH, temperature, pressure, and at the same time at lower cost. Large number of micro organisms have been found capable of synthesizing inorganic nanoparticles composite either intra or extracellularly [6].

In view of all these, a detail survey of available literature for various biosynthesis methods, their corresponding merits and demerits, numerous applications of silver nanoparticles and future aspects of synthesis and applications of nanoparticle are presented in this review.

Bio production of Nanoparticles: There are numerous methods available using various approaches including chemical, physical, and biological protocols for the synthesis of nanoparticles. Chemical method of synthesis is advantageous as it takes short period of time for synthesis of large quantity of nanoparticles. However, in this method capping agents are required for size stabilization of the nanoparticles. Moreover, chemicals reagents used generally for nanoparticles synthesis and stabilization are toxic and lead to byproducts that are not environment benign. The need for eco-friendly non-toxic methods for nanoparticles synthesis is developing interest in biological approaches which are free from the use of toxic chemicals as byproducts. A variety of natural sources are there for metal nanoparticle synthesis including plants, fungi, yeast, actinomycetes, bacteria *etc*. The unicellular and multicultural organisms can produce intracellular and extra cellular inorganic nanoparticles. An overview of biological synthesis of nanoparticles is focused in **Table 1**.

TABLE 1: BIOLOGICAL SYNTHESIS OF NANOPARTICLES

Sources	Name of the organisms	Localization	Types of nanoparticles produced	Size ranges (nm)	References
Plant	*Azadirachta indica* (Neem)	Extracellular	Ag, Au	50-100	7
	Geranium leaves plant extract	No	Ag	16-40	8
	Avena sativa (Oat)	Extracellular	Au	5-85	9
	Aloe vera	Extracellular	Au	50-350	10
Fungi sources	*Fusarium oxysporum*	Intracellular	Au	20-40	11
	Verticillium sp.	Intracellular	Ag	25-12	12
	Aspergillus fumigatus	Intracellular	Ag	5-25	13
	Schizosaccharomycepombe	Intracellular	CdS	200	14
	Fusarium oxysporum and *Verticillium* sp.	Intracellular	Magnetite	20–50	15
Yeast	Yeast strain MKY3	Extracellular	Ag	2-5	16
	Candida glabrata	Intracellular	CdS	200	17
	Schizosaccharomyce pombe	Intracellular	CdS	200	17
Bacteria	*Pseudomonas stutzeri*	Intracellular	Ag	200	18
	Lactobacillus strains	Intracellular	Ag, Au	No	19
	Escherichia coli	Intracellular	Cds	2-5	20
	Klebsiella pneumoniae	Extracellular	Au	5-32	18

Plant in Nanoparticles Synthesis: Plants offer a better option for synthesis of nanoparticle as the protocols involving plant sources are free from toxic chemicals; moreover, natural capping agents are readily supplied by the plants. Sastry *et al*., reported the synthesis of gold and silver nanoparticles using geranium extracts [21]. Further, gold nanotriangles and silver nanoparticles were synthesized using Aloe Vera plant extracts [22]. Most reports available on the synthesis of silver or gold nanoparticles use broths resulting from boiling fresh plant leaves.

However, Huang *et al*., synthesized silver and gold nanoparticles using the sundried Cinnamomum camphora leaf extract [23]. A simple green synthesis method for production of well-defined silver nanowires was reported recently by Lin *et al*[24]. The method involves reduction of silver nitrate with the broth of sundried *Cassia fistula* leaf at room temperature without using any additive. Various plants/plant tissues, nanoparticles synthesized using them, their shape and size and the references are listed in Table 1.

Bacteria in Nanoparticles Synthesis: Bacteria have been most extensively researched for synthesis of nanoparticles because of their fast growth and relative ease of genetic manipulation. Slawson *et al.,* found the Silver producing bacteria isolated from the silver mines *Pseudomonas stutzeri AG259* where the silver nanoparticles were accumulated in the periplasmic space but the particles size ranges from 35 to 46 nm [25].

The Lactobacillus strains present in the milk were exposed to larger concentration of nanoparticles to produced silver, gold, and alloy crystals of defined morphology [26]. Bacteria have also been used to synthesize gold nanoparticles[27]. The PH was an important factory in controlling the morphology of bacteriogenic nanoparticles and location of the deposition. These nanoparticles were used in many application e.g. direct electrochemistry of proteins[28]. The most important application of bacterium would be in industrial silver recovery.

Yeast in Nanoparticle Synthesis: Kowshik *et al.,* have demonstrated that MKY3, a silver-tolerant yeast species, when challenged with soluble silver in the log phase of growth, majority of silver precipitate extracellularly as elemental nanoparticles. When challenged with soluble silver in the log phase of growth, based on differential thawing of the sample, for separation of the Metallic nanoparticles from the medium [29].

Fungi in Nanoparticle Synthesis: The fungi taking the center stage of studies on biological generation of nanopartilces because of the tolerance and bioaccumulation [30]**.** The advantages of using fungi in their scale up process (e.g., using a thin solid substrate fermentation method). Fungi are efficient secretor of extra cellular enzymes it can easily obtain large scale production of enzymes. Further advantages of using fungal mediated green approach for synthesis of metallic nanoparticles include economic viability and ease in handling biomass.

The main drawback of biosynthesis of nanoparticles synthesis in eukaryotic organisms lies in the problem of genetic manipulation of the organism as a mean to over express the enzymes which is relatively much more difficult in eukaryotes than that in prokaryotes. Mukherjee *et al* demonstrated "green synthesis" of highly stabilized nanocrystalline silver particles by a nonpathogenic and agriculturally important fungus, *Trichoderma asperellum* [31].

Algae in Nanoparticles Synthesis: Algae are similar to yeast for biosynthesis of nanoparticle, still very few reports used algae as a "Biofactory" for the nanoparticles synthesis [32]. The marine algae used for the biosynthesizing highly stable extracellular gold nanoparticles in a relatively short time period compare to other biosynthesizing process [32]. Palladium and platinum nanoparticles starting with their corresponding metallic chloride- containing salts have been investigated [32].

Actinomycetes in Nanoparticles Synthesis: The monodispersity of the silver and gold nanoparticles produced either intracellular or extracellularly is of interest to scientists. But it was not very high and was far inferior to that obtained by conventional methods. Most of the actnimycetes especially the thermophilic actinimycetes, *Thermomonospora sp* was exposed to gold and silver irons and the metals got reduced extracellularly [33]. These micro-organisms have developed numerous special adaptations to survive in such extreme habitats which include new mechanism of enzyme transduction, regulating metabolism, maintaining the structure and function of the membrane. Actinomycetes are micro organisms that can share important characteristics of fungi and bacteria [34]. Even though the Actinomycetes have close relation with the mycobacterium and coryneforms, they were originally designated with 'ray fungi' (*Strahlenpilze*). These actinomycetes are able to produced secondary metabolites. The nanoparticles were also found to be non-toxic to the cells which continued to multiply even after the formation of the nanoparticles.

Viruses in Nanoparticle Synthesis: Biological synthesis of nanoparticles has been extended to biological particles like viruses, proteins, peptides and enzymes. Cowpea chlorotic mottle virus and cowpea mosaic virus have been used for the mineralization of inorganic materials [35]. Tobacco mosaic virus has shown to direct successfully the mineralization of sulphide and crystalline nanowires. One step further, peptides capable of nucleating Nano crystal growth have been identified from combinatorial screens and displayed on the surface of M13 bacteriophage [36].

Applications: Silver nanoparticles have been used extensively in anti bacterial agents in the health industry, food storages, textile coating and number of environmental applications. Important to note, despite and decades of use, the evidence of toxicity of silver is not still clear [37]. The antibacterial property of silver nanoparticles has allowed its wide range of application from disinfecting devices and home appliances to water treatment [37]. Catalytic activities of nanoparticles differ from chemical properties.

Silver Dressing: Dressings play a major part in the management of wounds [38]. The antibacterial properties and the toxicity of silver to micro-organisms is well known, thus, now a days, silver is used in different kinds of formulations like surface coating agents, wound dressing, etc [39]. The nanocrystalline silver dressings, creams, gel effectively reduce bacterial infections in chronic wounds.

Silver Toxicity: The toxicity from the silver is observed in the form of argyria when there is a large open wound and large amount of silver ions are used for dressing. There are no regular reports of silver allergy[40]. Important to note despite and decades of use the evidence of toxicity of silver is not still clear. Wide applications of nanotechnology are possible in the fields like electronics, engineering, medicine, *etc*., but the possible side effects of nanoparticles have not been much studied. Hence, detailed study needs to carry out before the introduction of products related to nano medicine in the market [41].

Environmental Applications: The silver nanoparticles can be used for the treatment of water to avoid contamination of the environment [42]. Environmental-friendly antimicrobial nanopaint can be developed [42]. Inorganic composites are used as preservatives in various products [43]. Silver nanoparticles can be used for water filtration [44]. The silver nanoparticles used as a Anti bacterial agents and wide range of application from disinfecting devices and home appliances to water treatment [45].

Future Prospects: Nanoparticles are widely used to improve the various catalytic reactions due to their novel physico-chemical properties as compared to there bulk size components. Because of its their wide applications, there is need to produce nanoparticles in industries. As stated above the physical and chemical methods of nanoparticle synthesis are having many disadvantages. Biological synthesis would be a preferred method because of its environmental friendly approach [46].

However, very limited studies have been reported on the factors affecting or responsible for biosynthesis of metal nanoparticles. Synthesis of nanoparticles by using microorganisms has been developed over the last decades. It is known that the synthesis of nanoparticles using microorganisms is a quite slow process compared to physical and chemical approaches. Synthesis using microorganism is still on the laboratory scale. Efforts should be made to investigate the practical application of microorganism in nanoparticles production [47].

The use of nanoparticles already established for some medical applications like wound infections, dressing, and treatment of preclinical stages. Recent research has revealed exciting new biological properties of NS that could be translated into new therapeutic and pharmacological treatments [48]. The full potential of this technology has yet to be discovered. The antibacterial, antifungal and antiviral properties of silver ions, silver compounds and silver nanoparticles have been extensively studied.

Silver is also found to be non-toxic to humans in minute concentrations. The microorganisms are unlikely to develop resistance against silver as compared to antibiotics as silver attacks a broad range of targets in the microbes [49]. Experimental trials are needed to understand the toxicity. There are some questions, which need to be addressed, such as, the exact mechanism of interaction of silver nanoparticles with the bacterial cells, how the surface area of nanoparticles influence its killing activity, use of animal models and clinical studies to get a better understanding of the antimicrobial efficiency of silver dressings, the toxicity if any of the silver dressings, *etc.*

REFERENCE:

1. Mazur M., (2004) Synthesis of silver nanoparticles by chemical reduction method and their antibacterial activity *Electrochemistry Communications* 6, 400-403.
2. Faraday, M. (1957) Experimental relations of gold (and other metals) to light. Philosophical Transactions of the Royal Society of London, Volume 147, pp. 145-181.
3. Raveendran P, Fu J, Wallen SL. J Am Virender K. Sharma, Ria A (2003); Silver nanoparticles: Green synthesis and their antimicrobial activities. *Chem Soc*; 125:13940M.
4. C. Roco, J. (2005). Trends in nanotechnology patents, Nanopart Res., 7, 707–712.
5. Li Y, Duan X, Qian Y, Li Y, Liao H (1999). Nanocrystalline silver particles: Synthesis, agglomeration, and sputtering induced by electron beam. J Colloid *Interface Sci*; 209:347-349.
6. Raveendran P, Fu J, Wallen SL. J Am Virender K. Sharma, Ria A (2003); Silver nanoparticles: Green synthesis and their antimicrobial activities. *Chem Soc*;125:13940
7. Shiv Shankar S, Rai A, Ahmad A, Sastry M (2004). Rapid synthesis of Au, Ag, and bimetallic Au core–Ag shell nanoparticles using Neem (Azadirachta indica) leaf broth. J. Colloid Interface Sci; 275: 496-502.
8. Shiv Shankar S, Rai A, Ahmad A, Sastry M (2004). Biosynthesis of silver and gold nanoparticles from extracts of different parts of the Geranium plant. Applied Nanoscience; 1: 69-77.
9. Armendariz V, Herrera I, Peralta-Videa JR, Jose-Yacaman M, Troiani H, Santiago P, Gardea-Torresdey JL (2004). Size controlled gold nanoparticle formation by Avena sativa biomass: use of plants in nanobiotechnology. J Nanoparticle Res; 6:377-82.
10. Chandran SP, Chaudhary M, Pasricha R, Ahmad A, Sastry M. (2006) Synthesis of gold nano triangles and silver nanoparticles using Aloe vera plant extract. Biotechnol Prog; 22:577-83.
11. Ahmad A, Mukherjee P, Senapati S, Mandal D, Khan MI, Kumar R, Sastry M. (2003) Extracellular biosynthesis of silver

nanoparticles using the fungus Fusarium oxysporum. Colloids Surf B; 28:313-8.

12. Mukherjee P, Ahmad A, Mandal D, Senapati S, Sainkar SR, Khan MI, *et al*. (2001) Fungus mediated synthesis of silver nanoparticles and their immobilization in the mycelial matrix: a novel biological approach to nanoparticle synthesis. Nano Lett; 1:515-519.
13. Bhainsa KC, D'Souza SF. (2006) Extracellular biosynthesis of silver nanoparticle using the fungus Aspergillus fumigates. Colloids Surf B Biointerfaces; 47:160-4.
14. Kowshik M, Ashtaputre S, Kharrazi S, Vogel W, Urban J, Kulkarni SK, Paknikar KM (2003) Extracellular synthesis of silver nanoparticles by a silver-tolerant yeast strain MKY3. Nanotechnology 14:95–100
15. Bharde A, Rautaray D, Bansal V, Ahmad A, Sarkar I, Yusuf SM, *et al*. (2006) Extracellular biosynthesis of magnetite using fungi. Small; 2(1):135-41.
16. Kowshik M, Ashtaputre S, Kharrazi S, Vogel W, Urban J, Kulkarni S,Paknikar K. (2003) Extracellular synthesis of silver nanoparticles by a silvertolerant yeast strain MKY3. Nanotechnology; 14:95-100.
17. Dameron CT, Reese RN, Mehra RK, Kortan AR, Carroll PJ, Steigerwald ML, et al. (1989) Biosynthesis of cadmium sulphide quantum semiconductor crystallites. Lett Nat; 338:596-7.
18. Klaus T, Joerger R, Olsson E, Granqvist CG (1999) Silver based crystalline nanoparticles, microbially fabricated. Proc Natl Acad Sci USA 96:13611–13614.
19. Nair B, Pradeep T. (2002) Coalescence of nanoclusters and formation of submicron crystallites assisted by Lactobacillus strains. Cryst Growth Des; 2:293-8.
20. Sweeney RY, Mao C, Gao X, Burt JL, Belcher AM, Georgiou G, et al. (2004) Bacterial biosynthesis of cadmium sulfide nanocrystals. Chem Biol; 11:1553-9.
21. Shahverdi AR, Fakhimi A, Shahverdi HR, Minaian S. (2007) Synthesis and effect of silver nanoparticles on the antibacterial activity of different antibiotics against Staphylococcus aureus and Escherichia coli. Nanomedicine; 3:168-71.
22. Singaravelu G, Arockiamary J, Ganesh K, Govindaraju K. (2007) A novel extracellular synthesis of monodisperse gold nanoparticles using marine alga, Sargassum wightii Greville. Colloids Surf B Biointerfaces; 57:97-101.
23. Shankar SS, Rai A, Ahmad A, Sastry M (2004) Rapid synthesis of Au, Ag, and bimetallic Au core–Ag shell nanoparticles using neem (Azadirachta indica), leaf broth. J Colloid Interf Sci 275:496–502.
24. C Pedit, E. Dickson, J. Magn Magn, (1999), In situ synthesis of silver nanocluster in AOT reverse micelles. Mater203, 46–49.
25. Loveley J. F, Stolz G. L, Nord, E. J. P. Phillips, Mechanisms for chelator stimulation of microbial Fe(III)-oxide reduction *Nature* (1987) 330, 252-254.
26. S. Shankar, A. Ahmad, M. Sastry, (2003*)* Geranium Leaf Assisted Biosynthesis of Silver Nanoparticles *Biotechnol. Prog*. 19 1627–1631.
27. S.P. Chandran, M. Chaudhary, R. Pasricha, A. Ahmad, M. Sastry(2006), Synthesis of Gold Nanotriangles and Silver Nanoparticles Using *Aloevera* Plant Extract *Biotechnol. Prog*. 22 577–583.
28. J Huang, Q Li, D. Sun, Y Lu, Y Su, X. Yang, H. Wang, Y. Wang, W. Shao, N. He, J. Hong, C. Chen (2007), Biosynthesis of silver and gold nanoparticles by novel sundried *Cinnamomum camphora* leaf. *Nanotechnology* 18 105104–105114.
29. Liqin Lin, Wenta Wang, Jiale Huang, Qingbiao Li, Daohua Sun, Xin Yang, Huixuan Wang, Ning He, Yuanpeng Wang, (2010). Nature factory of silver nanowires: Plant-mediated synthesis using broth of *Cassia fistula* leaf, *Chemical Engineering Journal* 162 852–858.
30. Slawson RM, Van Dyke MI, Lee H, Trevor JT. (1992) Germanium and silver resistance, accumulation and toxicity in microorganisms. *Plasmid;* 27:73-79.
31. Konishi Y, Ohno K, Saitoh N, Nomura T, Nagamine S (2004). Microbial synthesis of gold nanoparticles by metal reducing bacterium. *TransMater Res Soc Jpn*; 29:2341-2343.
32. Liangwei D, Hong J, Xiaohua L, Erkang W (2007). Biosynthesis of goldnanoparticles assisted by Escherichia coli DH5α and its application on direct electrochemistry of hemoglobin. *Electrochem Commun*; 9:1165-1170.
33. Konishi Y, Ohno K, Saitoh N, Nomura T, Nagamine S (2004). Microbial synthesis of gold nanoparticles by metal reducing bacterium. *TransMater Res Soc Jpn*; 29:2341-2343.
34. Sastry M, Ahmad A, Khan I, Kumar R (2003). Biosynthesis of metal nanoparticles using fungi and actinomycete. *Curr Sci*; 85(2):162-170.
35. Mukherjee P, Roy M, Mandal B, Dey G, Mukherjee P, Ghatak J, et al (2008).Green synthesis of highly stabilized nanocrystalline silver particles by anon-pathogenic and agriculturally important fungus T.asperellum. *Nanotechnology*; 19:75 103-110.
36. Singaravelu G, Arockiamary J, Ganesh K, Govindaraju K (2007). A novel extra cellular synthesis of monodisperse gold nanoparticles using marine alga, Sargassum wightii Greville. *Colloids Surf B Biointerfaces*; 57:97-101.
37. Ahmad A., Senapati S, Khan M I, Kumar R, Sastry M, Langmuir, (2003), *Biosynthesis of nanoparticles* 19, 3550–3553.
38. Okami Y., Beppu T. and Ogawara H, (1988) (*eds*), Biology of Actinomycetes, Japan Scientific Societies Press, Tokyo, vol**.** 88**,** p. 508.
39. Douglas T, Young M. (1993) Host-guest encapsulation of materials by assembled Virus protein cages. *Nature*; 393:152-155.
40. Zhong L, Hu J, Cui Z, Wan L., Song W., (2007). Synthesis and applications of silver nanoparticles Chem. Mater. 19, 4557.
41. Bosetti M., Masse A., Tobin E., Cannas M., (2002). Silver coated materials for external fixation devices: In vitro biocompatibility and genotoxicity Biomaterials 23 (3), 887.
42. Leaper DL (2006). Silver dressings: their role in wound management. *Int Wound J*; 3(4): 282–294).
43. Duran N, Marcarto PD, De Souza GIH, Alves OL, Esposito E (2007). Antibacterial effect of silver nanoparticles produced by fungal process on textile fabrics and their effluent treatment. *J Biomed Nanotechnol*; **3:**203–208.
44. Chopra I .*et* al, (2007) the increasing use of silver-based products as antimicrobial agents: a useful development or a cause for concern? *J Antimicrob Chemother*; 59:587–590.
45. Leaper DL (2006). Silver dressings: their role in wound management. *Int Wound J*; 3(4): 282–294.
46. Kumar A, Vemula PK, Ajayan PM, John G (2008). Silver-nanoparticle-embedded Antimicrobial paints based on vegetable oil. *Nature Materials*; 7(3):236–241.
47. Gong P, Li H, He X, Wang K, Hu J, Tan W, *et al* (2007). Preparation and antibacterial activity of Fe3O4 @ Ag nanoparticles. *Nanotechnology*; 18:604–611
48. Gupta A, Silver S. (1998) Silver as a biocide: will resistance become a problem? *Nat Biotechnol*, 16: 888.
49. Jain P, Pradeep T (2005). Potential of silver nanoparticle-coated polyurethane foam as an antibacterial water filter. *Biotechnol Bioeng*; 90(1):59–63.
50. Oberdorster G, Oberdorster E, Oberdorster J (2005). Nan toxicology: an emerging discipline evolving from studies of ultra fine particles. *Environ Heal Perspect*; 113 (7): 823–939.