



APPLICATION AND BIOSYNTHESIS OF MEDICINALLY USEFUL NANOPARTICLES FROM BACTERIAL SOURCES: A REVIEW

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ABSTRACT

Nanoparticles has attracted a great interest in recent years due to its expected impact on medicines like treatment of disease and their diagnosis. This review provides the state-of-art knowledge on the green synthesis of nanoparticles by bacterial sources. The available bacterial sources and their predicted nanoparticles biosynthesis mechanisms and medical applications.

KEYWORDS: Green synthesis of nanoparticles, Biosynthesis mechanism, Applications of nanoparticles, Drug delivery, Diagnosis.

INTRODUCTION

Nanotechnology has attracted a great interest in recent years due to its applications on many areas such as energy, medicine, electronics, and space industries. Research in this field has been growing dramatically throughout the world over the last decade. It has been known now that synthesis of nanoparticles from chemical and physical method cannot avoid the use of toxic chemicals and their side effect of on human body and environment (Azim et al., 2009; Tapan and Andrey, 2009). Therefore there is urgent need to adopt alternative ways for the synthesis of nanoparticles to avoid its harmful effects on environment and human body. The alternative ways for the synthesis of nanoparticles is green synthesis that is their biosynthesis from microbial sources and plant extract. It is well fact known that microorganisms have been used in bioremediation of toxic metals through reduction of metal ions, but the interest in green synthesis of nanoparticles using bacteria has emerged quite recently. Biosynthesis of nanoparticles is accomplished by using bacteria which grabs target ions from their solutions or nutrient media, and then accumulates the reduced metal in its element form through enzymes generated by their cellular activities.

Biosynthesis of nanoparticles can be categorized into intracellular and extracellular synthesis according to the place where nanoparticles are formed (Simkiss and Wilbur, 1989; Mann, 1996). The intracellular method consists of transporting ions inside the microbial cell while the extracellular method involves trapping the metal ions on cell envelop and reducing ions to form the nanoparticles in the presence of specific enzymes. So far, bacteria's, such as magnetotactic bacteria (Blackmore, 1982), S-layer bacteria (Pum and Sleytr, 1999) have been used to generate the nanoparticles. This paper provides a brief overview on green synthesis of nanoparticles using bacteria as source, and their predicted nanoparticles biosynthesis mechanism. Many bacteria's, fungi, have been found to be capable of intracellularly or extracellularly synthesizing nanoparticles, mineral crystals and metallic nanoparticles.

Biosynthesis of the nanoparticles using bacteria

Table 1 contain the number of bacteria reported which are used for biosynthesis of nanoparticles.

Table 1: Biosynthesis of nanoparticles from bacterial sources.

Microorganism	Nanoparticle	Size (nm)	Reference
<i>Acetobacter xylinum</i>	Ag	ND	Barud et al., 2008
<i>Actinobacter sp.</i>	Magnetite	10–40	Bharde et al., 2005
<i>Aeromonas sp SH10</i>	Ag	6.4	Mouxing et al., 2006
<i>Aquaspirillum Magnetotacticum</i>	Fe ₃ O ₄	40–50 nm	Mann et al., 1984
<i>B. licheniformis</i>	Ag	~50	Deepak et al., 2008
<i>B. megatherium D01</i>	Au	1.9±0.8	Wen et al., 2006
<i>B. selenitireducens</i>	Te	~10	Baseman et al., 2007
<i>Bacillus sp.</i>	Ag	5-15	Pugazhenthiran et al., 2009
<i>Bacillus subtilis 168</i>	Au	5-25	Beveridge et al., 1980
<i>Brevibacterium casei</i>	Co ₃ O ₄	5-7	Kumar et al., 2008
<i>Clostridium Thermoaceticum</i>	CdS	ND	Cunningham et al., 1993
<i>Desulfobacteriaceae</i>	ZnS	2–5	Labrenz et al., 2000
<i>Desulfosporosinus sp.</i>	UO ₂	1.5–2.5	Suzuki et al., 2002
<i>Desulfovibrio desulfuricans NCIMB 8307</i>	Pd	~50	Yong et al., 2002
<i>Enterobacter cloacae, Klebsiella pneumonia, E. coli</i>	Ag	52.5	Shahverdi et al., 2007
<i>Escherichia coli</i>	CdS	2–5	Sweeney et al., 2004
<i>Escherichia coli</i>	Au	<10	Konishi et al., 2004
<i>Escherichia coli</i>	Au	20-50	Deplanche et al., 2007
<i>Escherichia coli DH5α</i>	Au	ND	Liangwei et al., 2007
<i>Geobacter metallireducens</i>	Magnetite	10-15	Lovely et al., 1987
<i>Gluconoacetobacter xylinus</i>	CdS	30	Li X et al., 2009
<i>Klebsiella aerogenes</i>	CdS	20–200	Holmes et al., 1995
<i>Klebsiella pneumonia</i>	CdS	5–200	Smith et al., 1998

<i>Klebsiella pneumonia</i>	Ag	5-32	Shhverdi et al., 2007
<i>Lactobacillus sp.</i>	Au, Ag, Au–Ag	20–50	Nair et al., 2002
<i>Lactobacillus sp.</i>	Au	>100	Nair et al., 2002
<i>Lactobacillus sp.</i>	Ti	40–60	Prasad et al., 2007
<i>M. magnetotacticum (MS-1)</i>	Fe ₃ O ₄	~50	Lee et al., 2004
<i>Magnetospirillum Magnetotacticum</i>	Fe ₃ O ₄	47.1	Philipse et al., 2002
<i>Magnetotactic bacterium MV-1</i>	Fe ₃ O ₄	40×40×60	Bazyliniski et al., 1998
<i>Magnetotactic Bacterium</i>	Fe ₃ S ₄ , FeS ₂	7.5	Maan et al., 1990
<i>Morganella sp.</i>	Ag	20±5	Parikh et al., 2008
<i>P. aeruginosa SNT1</i>	Se	ND	Yadav et al., 2008
<i>Plectonema boryanum (Cyanobacteria)</i>	Ag	1–10	Lengke et al., 2007
<i>Plectonemaboryanum UTEX485</i>	Au	10	Lengke et al., 2006
<i>Pseudomonas Aeruginosa</i>	Au	15-30	Husseiney et al., 2007
<i>Pseudomonas stutzeri AG259</i>	Ag, Ag ₂ S	<200	Joerger et al., 2000
<i>R. sphaeroides</i>	PbS	10.5±0.15	Bai HJ et al., 2009
<i>Rhodobacter sphaeroides</i>	ZnS	8	Bai HJ et al., 2007
<i>Rhodobactercapsulatus</i>	Au	ND	Lovely et al., 1987
<i>Rhodococcus sp.</i>	Au	5-15	Ahmad et al., 2003
<i>Rhodopseudomonas capsulate</i>	Au	10–20 50–400 50–60	Shinying et al., 2007
<i>Rhodopseudomonas palustris</i>	CdS	8.01±0.25	Lovely et al., 1991
<i>S. algae</i>	Pt	~5	Konishi et al., 2007
<i>S. oneidensis MR-1</i>	UO ₂	1–5	Marshall et al., 2006
<i>S. oneidensis MR–1</i>	Pd	ND	De Windt et al., 2005
<i>Shewanella algae</i>	Au	10-20 15-200	Konishi et al., 2007
<i>Shewanella algae</i>	Au	10-20	Konishi et al., 2004
<i>Shewanella algae ATCC 51181</i>	Au	10-20	Kashefi et al., 2001
<i>Shewanella oneidensis</i>	Uranium (iv)	ND	Marshall et al., 2007
<i>Stenotrophomonas maltophilia</i>	Au	40	Nangia et al., 2009
Sulfate-reducing Bacteria	FeS	2	Watson et al., 1999
Sulfate-reducingbacteria	Au	<10	Lengke et al., 2009
<i>Sulfurospirillum barnesii</i>	Te	<50	Baseman et al., 2007
<i>Sulfurospirillum barnesii</i> , <i>B. selenitireducens</i> , <i>Selenihalanaerobacter shriftii</i>	Se	~300	Oremland et al., 2004
<i>Thermoanaerobacter ethanolicus (TOR-39)</i>	Co, Cr, Ni-substituted	ND	Roh Y et al., 2001
<i>Thermomonospora sp.</i>	Au	30-60	Chavolla et al., 2010

Mechanism of nanoparticles synthesis

According to the research conducted by Beveridge in 1997 the mechanisms which are considered responsible for the biosynthesis of nanoparticles includes efflux system, alteration of solubility and toxicity via reduction or oxidation, bio-absorption, bioaccumulation, extracellular complexation or precipitation of metals, and lack of specific metal transportation system (Beveridge *et al.*, 1997). Studies have proved that the extracellular production of nanoparticles is more commercial as compare to intracellular process. List of bacterial species involve in biosynthesis of nanoparticles are given in table 1.

Metallic nanoparticles

Although number of bacteria's has been tested, only few bacteria were found to be capable of producing nanoparticles and their synthesis mechanism is not well understood yet. According to the studies, the electrons should be provided to the ions which are going to be converted to the corresponding elemental metals. Therefore, there must be a reducing agents generated due to the metabolic activities of bacteria to reduce ions to their metallic particles.

(Priyabrata *et al.*, 2001) observed that the while biosynthesis of silver nanoparticles the most of the particles were clearly attached on the surface of cytoplasmic membrane. Authors investigated that the silver ions, which were caught on the cell membrane through the electrostatic interaction, were firstly reduced to form silver nuclei in the cell wall because of the presence of certain unknown enzymes which is yet to be studied, and eventually nanoparticles were formed on the mycelia after accumulation of these nuclei. (Ahmad *et al.*, 2003a) has been observed that NADH-dependent reductase was probably resulting in the production of nanoparticles in the microbes. According to Gericke and Pinches (2006) besides enzyme, the growth phase of bacteria was also considered to be an important factor for nanoparticle biosynthesis. Authors investigated the cells of *Verticillium luteoalbum* and observed that different growth phase produced different numbers of particles. The cells obtained from early exponential phase produce one fifth numbers of more particles in compare to the late exponential phase.

As accepted, heavy metallic ions are found to be antimicrobial in nature with few exceptions. The bacteria will react to metallic ion protect themselves (Hallmann *et al.*, 1997). In order to accomplish that, first of all, the ions will be trapped by the cells. The ion can be trapped by two probable ways first via electrostatic interaction or the second one is by secretion of certain compound (protein/ complex extracellular polymeric solution/ substance) which

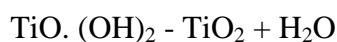
adhere the ions. It has been observed that most of the bacteria are negatively charged (Albert *et al.*, 1997; Manti *et al.*, 2008). Which provide base to the first theory of electrostatic interaction between the positively charged ion and negatively charged group (cellular compound for example carboxylate group). While, secretion of adhesion type of substances could probably stabilize the ions on the cells due to its stickiness.

For the process of intracellular synthesis of nanoparticles, the ions must travel inside the cell which may be happened in the nutrient exchange and/or substance diffusion. The enzymes present in cytoplasm like NADH-dependent reductase may involve in the reduction of these ions which are treat to the bacteria by metabolic reactions. Finally, the nuclei will further grow and subsequently intracellularly or extracellularly accumulate to form nanoparticles. In this entire process, enzyme plays the role of significant factor. On the other hand the ions adhere in the extracellular substance may involve the reduction process by the enzyme on the cell surface or may be the enzymes inside the cells aids the reduction reaction to occur. Since only some of the bacteria have shown the ability for the biosynthesize nanoparticles, it can be considered that particular enzyme(s) secreted by the very kinds of microbes will support the synthesis (Ahmad *et al.*, 2003a).

Compound nanoparticles

Klebsiella aerogenes was used to synthesis extracellular Cadmium sulfide nanoparticles on its cell surface. *Klebsiella aerogenes* was cultured under different buffer (Tris, Bistris propane, Tricine, Bes, ortho-phosphate compounds, TES (a solution made up of Tris, EDTA and NaCl), or 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (Holmes *et al.*, 1995). The results indicates that Tricine and phosphate buffered medium could extend *K. aerogenes* tolerance against cadmium concentration from 10 μ M (other medium) to 2 mM and 5 mM, respectively, and cadmium phosphates nanoparticles were appeared when the growth medium was phosphate-buffered. This study indicated that different medium fortified with different buffer exhibited effect on the production of cadmium sulfide and the nanoparticle formation also depended on the chemical composition of the medium. (Rozamond *et al.*, 2004) authors studied the formation of cadmium sulphide nanoparticles using *E.coli* and this time they found that the production of the nanoparticles was affected by growth phase of the bacteria. As accepted that various enzymes are generated during the different growth phase of microbes due to the different metabolic reactions (Alexander *et al.*, 2003). From all this data we can conclude that the, enzyme could be a key factor for the formation of compound

nanoparticle as in case of metallic nanoparticles biosynthesis (discussed above). Nano-sized particles of TiO₂ has been successfully formed by adding TiO(OH)₂ solution to the suspension of *Lactobacillus* sp. (Jha et al., 2009). The equation can be described as following:



However, so far, there is still no clear and thorough understanding mechanism had been discovered on the synthesis of nanoparticles by microbes. It was concluded that the Self-defence is the essential action to prevent from hazard for each single life in the ecosystem. In order to survive may be microbes releases specific enzymes, to protect themselves which is capable of removing toxic ions (hazard compound). The enzyme may produce extracellularly or intracellularly, and once the ions meet the enzyme, the reaction to form compound nanoparticles will occur and precipitate on the cell surfaces or in the cytoplasm. Briefly, it is mainly a hypothesis that the electrostatic interaction and specific enzyme(s) of microbes are significant factors in the formation of nanoparticles (discussed above), even though the real mechanism of biosynthesis of nanoparticles is still to be studied.

Medical application of nanoparticles

Nanotechnology has a great use in bio-medicine, like drug delivery, cancer treatment diagnosis of diseases etc. The characteristic features of nanoparticles such as their high volume/surface ratio, surface tail or ability, improved solubility and multi functionality open many new possibilities for biomedicine (Gou J *et al.*, 2009). Nano- silver particles have been widely used for diagnosis (Uchinara *et al.*, 2007), treatment (shibald *et al.*, 2007), drug delivery (shirtack *et al.*, 2006), medical device coating (Galiano *et al.*, 2008), wound dressings (Moore *et al.*, 2006), medical textiles (Vigeshwaram *et al.*, 2006) and contraceptive devices (Chen X *et al.*, 2008).

Gold nanoparticles

Gold nanoparticles have promising application in cancer treatment, drug delivery, nano biosensor, biomedicine (Paciotti et al., 2004), sensing (Liu J et al., 2004, Yanez- sedeno et al., 2005) and catalysis (Tikariha et al., 2012) biosensor and DNA label (Groning et al., 2001). The gold nanoparticles also used in heavy metal detection by colorimetric technique (Armendariz et al., 2002).

Sliver Nanoparticles

Silver nanoparticles have enormous applications in biomedicine because of its unique properties. A number of bacterial species have been reported for the synthesis of silver nanoparticles. It has been reported that Silver possess high antimicrobial activity against Gram positive and negative bacteria, fungi, protozoa, and certain viruses. Recently, the antitumor activity of AgNPs against various cancerous cell lines was also introduced (Jayaraj *et al.*, 2013). Various new biomedical applications of AgNPs have been reported, including diagnostic applicative biological tags and biosensors, as well as antibacterial agents in apparel, anti-fungal, anti-inflammatory, anti-angiogenic and anti permeability activity. It has also been found that silver nanoparticles have tremendous used in cosmetic (Kailashwarlal *et al.*, 2007, Gurunathan *et al.*, 2009, Sheikparnababu *et al.*, 2009), wound dressings and healing (Law N *et al.*, 2008).

CONCLUSION

The present study is concentrate on biosynthesis of nanoparticles from bacterial sources and their application in medical field. It has been observed that in the field of nanotechnology have tremendous developments in the field of microorganism-produced nanoparticles and their medical applications over the last decade and found to be very useful. However, much work is needed to improve the synthesis efficiency and the control of particle size and morphology.

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