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**3 authors:**

Panchanathan Manivasagan

Pukyong National University



Seung Yun Nam

Pukyong National University



Junghwan Oh

Pukyong National University

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REVIEW ARTICLE

# Marine microorganisms as potential biofactories for synthesis of metallic nanoparticles

Panchanathan Manivasagan[1], Seung Yun Nam[2], and Junghwan Oh[1,2]

[1]*Marine-Integrated Bionics Research Center, Pukyong National University, Busan, Republic of Korea and* [2]*Department of Biomedical Engineering and Center for Marine-Integrated Biotechnology (BK21 Plus), Pukyong National University, Busan, Republic of Korea*

**Abstract**

The use of marine microorganisms as potential biofactories for green synthesis of metallic nanoparticles is a relatively new field of research with considerable prospects. This method is eco-friendly, time saving, and inexpensive and can be easily scaled up for large-scale synthesis. The increasing need to develop simple, nontoxic, clean, and environmentally safe production methods for nanoparticles and to decrease environmental impact, minimize waste, and increase energy productivity has become important in this field. Marine microorganisms are tiny organisms that live in marine ecosystems and account for >98% of biomass of the world's ocean. Marine microorganisms synthesize metallic nanoparticles either intracellularly or extracellularly. Marine microbially-produced metallic nanoparticles have received considerable attention in recent years because of their expected impact on various applications such as medicine, energy, electronic, and space industries. The present review discusses marine microorganisms as potential biofactories for the green synthesis of metallic nanoparticles and their potential applications.

**Keywords**

Biosynthesis, gold, marine microorganisms, metallic nanoparticles, silver

**History**

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## Introduction

In recent years, the biosynthesis of metallic nanoparticles has received a greater interest as a novel platform for biomedicine and bionanotechnology (Shim et al., 2008). Metallic nanoparticles provide solutions to scientific and ecological challenges in diverse areas such as medicine, energy, electronics, coatings, packaging, cosmetics, and bionanotechnology (Płaza et al., 2014). Research in this area has dramatically been developing worldwide. The development of novel nanomaterials, including nanoparticles, is on a rise because their unique properties in medicine, electronics, and optics have led to an increasing attention to their biosynthesis (Zhang et al., 2011). Nanoparticles have been synthesized by several methods, such as physical and chemical methods. However, some chemical processes cannot avoid the use of toxic chemical in the biosynthesis method (Sau & Rogach, 2010). Hence, there is an urgent need to develop a process for the biosynthesis of metallic nanoparticles using marine microorganisms.

Marine microorganisms, such as bacteria, cyanobacteria, actinobacteria, yeast, and fungi, are tiny organisms that live in marine ecosystems. Marine microorganisms are the best sources of metabolite producers and are very important from an industrial point of view. Microbial synthesis of metallic nanoparticles has a good potential to develop simple, cost-effective, eco-friendly methods and is an important aspect of green chemistry approach that interconnects microbial biotechnology and nanotechnology (Manivasagan et al., 2014c). Microbial biotechnology has traditionally used microorganisms and their products in several applications, such as pharmaceutical, agriculture, food production, and bioremediation technologies. In recent years, many studies are concentrating on the potential use of marine microorganisms as ''nanofactories'' for the production of metallic nanoparticles (Villaverde, 2010). At present, very limited reports are available for the biosynthesis of metallic nanoparticles by marine microorganisms functioning consecutively as reducing, capping, and stabilizing agents (Shankar et al., 2004; Xie et al., 2007). This review critically evaluated the recent findings on marine microorganisms as potential biofactories for the green synthesis of metallic nanoparticles such as gold, silver, lead sulfide, and cadmium sulfide.

Address for correspondence: Junghwan Oh, Department of Biomedical Engineering and Center for Marine-Integrated Biotechnology (BK21 Plus), Pukyong National University, Busan 608-737, Republic of Korea. E-mail: jungoh@pknu.ac.kr

## Marine microorganisms

Marine microorganisms such as bacteria, cyanobacteria, actinobacteria, yeast, and fungi are prokaryotic and eukaryotic cells that live in the ocean and account for >98% of ocean biomass. Marine microorganisms are ubiquitous in the marine environment as well as extreme environments (e.g. hypersaline) and thrive at a wide range of acidity, alkalinity, temperatures, and salinity (Satpute et al., 2010). The formation of nanomaterials by marine microbial cells is a promising approach for the biosynthesis of metallic nanoparticles. The marine microbial cells are considered as potential biofactories for the green synthesis of metallic nanoparticles either intracellularly or extracellularly (Hulkoti & Taranath, 2014). In recent years, using marine microorganisms for the green synthesis of nanoparticles is still frequently emerging to understand the molecular mechanisms of biosynthesized nanoparticles. Biosynthesis of metallic nanoparticles using bacteria and fungi has attracted a special interest compared with biosynthesis of metallic nanoparticles using actinobacteria and yeast because a well-developed technology is available for biosynthesis using bacteria and fungi than actinobacteria and yeast (Zhang et al., 2011). Therefore, using marine microorganisms to synthesis nanoparticles is safer because they are not pathogenic to humans. However, marine microorganisms remain relatively unexplored for metallic nanoparticles synthesis with a human perspective (Karthik et al., 2013). An overview on the marine microbial synthesis of metallic nanoparticles is given in Table 1.

## Marine bacteria

Marine bacteria are the most abundant microorganisms on earth and play critical roles in the ocean environments. Marine bacteria have received considerable attention in the area of metallic nanoparticle synthesis (Hulkoti & Taranath, 2014). Marine bacteria synthesize metallic nanoparticles either intracellulary or extracellularly. The potential role of bacteria in the green synthesis of metallic nanoparticles has been studied in the literature suggesting their further exploration in several applications, such as biological and biomedical as well as diagnostic, therapeutic, and bio-imaging technology. The primary report for the microbial synthesis of gold nanoparticles (AuNPs) was investigated in *Bacillus subtilis* (Beveridge & Murray, 1980). The biological synthesis of silver-based crystalline nanoparticles was first conducted by exploiting *Pseudomonas stutzeri* AG259 (Klaus et al., 1999). Later, metallic nanoparticles, such as gold, silver, iron, lead, silicon, copper, titanium, palladium, and platinum nanoparticles, were biosynthesized using several bacteria that were primarily isolated from terrestrial sources (Thakkar et al., 2010). Marine ecosystems can be an excellent resource of metal-tolerant microorganisms because metals are continuously released into the marine ecosystems by volcanoes, natural weathering of rocks, and numerous anthropogenic activities, namely industrial, mining, combustion of fuels and urban sewage, and agricultural practices. In recent years, they are being explored as the potential biofactories of metal-tolerant microorganism with the capability to synthesis metallic nanoparticles (Agnihotri et al., 2009). AuNPs have been biosynthesized by *Marinobacter pelagius* to achieve a fast rate of nanoparticles synthesis (Sharma et al., 2012). Seshadri et al. (2012) have studied the intracellular biosynthesis of silver nanoparticles (AgNPs) by a marine bacterium, *Idiomarina* sp. PR58–8 which was found to be highly silver tolerant.

Most of these earlier reports have concentrated on soil microflora being a good candidate for the production of silver and gold nanoparticles. However, Sharma et al. (2012) investigated that marine environments can also be exploited to identify the organisms responsible for the green synthesis of AuNPs. Because marine organisms can easily adapt themselves to extreme environmental conditions, it is very essential to explore marine bioresource for the green synthesis of different types of metallic nanoparticles. Malhotra et al. (2013) reported the biosynthesis of gold and silver nanoparticles by extracellular secretion of a novel strain of *Stenotrophomonas*, isolated from the Mandapam coast, Bay of Bengal, India. Salunke et al. (2015) investigated the potential of two microorganisms, *Saccharophagus degradans* and *Saccharomyces cerevisiae*, for the synthesis of manganese dioxide nanoparticles.

## Marine cyanobacteria

Marine cyanobacteria (blue–green algae) are one of the major and most primitive ancestral groups of photoautotrophic bacteria in the marine ecosystem. They offer great potential as a resource of fine pharmaceuticals, chemicals, and biofuels, and are a rich source of pigments/proteins. They may be a good candidate for the biosynthesis of metallic nanoparticles because they produce high amounts of water-soluble fluorescent pigment and phycobiliproteins (Mubarak Ali et al., 2012). Ali et al. (2011) studied the extracellular biosynthesis of AgNPs by marine cyanobacterium *Oscillatoria willei* NTDM01 (Ali et al., 2011). *Phormidium tenue*, a marine cyanobacterium, is a rich source of the phycoerythrin, C-phycoerythrin, and was used for the biosynthesis and characterization of cadmium sulfide nanoparticles (CdS NPs). The main advantages of C-phycoerythrin are that its content in the cyanobacterium is approximately 70% of the total protein, and it can be easily isolated from the cell.

## Marine actinobacteria

Marine actinobacteria are considered an important constituent of bacterial communities in marine ecosystems (Stevens et al., 2007), particularly marine sediments where they can reach up to 13% of the bacterial abundance (Maldonado et al., 2005). Marine actinobacteria plays a pivotal ecological role in the carbon cycle with their ability to break down organic compounds and recycle the organic matter as their terrestrial counterparts (Haefner, 2003). They have generated a strong interest for the bioprospecting of novel metabolites with high bionanotechnological value (Lam, 2006; Manivasagan et al., 2014d). Marine actinobacteria products have useful applications in medicine (Manivasagan et al., 2014a; Simmons et al., 2005), aquaculture (Das et al., 2008; Manivasagan et al., 2013b), enzyme production (Manivasagan et al., 2014b, 2015d), and environmental bioremediation processes (Dash et al., 2013). Marine actinobacteria are efficient producers of metallic nanoparticles that show a range of biological activities such as antimicrobial, antioxidant, and antimalarial effect. Recently, marine actinobacteria isolated from marine ecosystems have been recognized as the potential synthesizers of metallic nanoparticles, and green synthesis of metallic nanoparticles has been reported in *Streptomyces* sp. (Karthik et al., 2013, 2014; Manivasagan et al., 2015b) and *Nocardiopsis* sp. (Manivasagan et al., 2013a, 2015a).

Table 1. Biosynthesis of metallic nanoparticles by different researchers using marine microorganisms.

| Metallic nanoparticles | Marine microorganisms | Name of the species | Average size (nm) | Morphology/ localization | Mechanism | Activity | References |
|---|---|---|---|---|---|---|---|
| AuNPs | Bacteria | *Marinobacter pelagius* | 2–6 | Spherical | Ext | ND | Sharma et al. (2012) |
| | | *Stenotrophomonas* | 10–50 | Spherical | Ext | ND | Malhotra et al. (2013) |
| | | *Klebsiella pneumoniae* | 35–65 | Spherical | Ext | ND | Malarkodi et al. (2013) |
| | Cyanobacteria | *Lyngbya majuscule* | <20 | Spherical | Ext | ND | Chakraborty et al. (2009) |
| | Actinobacteria | *Streptomyces* sp. LK-3 | 5–50 | Polygonal | Ext | Antimalarial | Karthik et al. (2013) |
| | | *Streptomyces* sp. MBRC-82 | 40 | Spherical | Ext | ND | Manivasagan et al. (2015a) |
| | | *Nocardiopsis* sp. MBRC-48 | 11 | Spherical | Ext | Antimicrobial; antioxidant; cytotoxic | Manivasagan et al. (2015a) |
| | Yeast | *Yarrowia lipolytica* NCIM 3589 | 15 | Hexagonal and triangular | Int | ND | Agnihotri et al. (2009) |
| | Fungi | *Rhizopus oryzae* | 28–52 | Spherical | Int/Ext | ND | Vala (2014) |
| | | *Aspergillus sydowii* | 10 | Spherical | Int/Ext | ND | Vala (2015) |
| AgNPs | Bacteria | *Idiomarina* sp. PR58-8 | 26 | Spherical | Int | ND | Seshadri et al. (2012) |
| | | *Stenotrophomonas* | 40–60 | Spherical | Ext | ND | Malhotra et al. (2013) |
| | | *Vibrio alginolyticus* | 50–100 | Spherical | Int/Ext | ND | Rajeshkumar et al. (2013) |
| | | *Escherichia coli* | 5–20 | Spherical | Ext | Antimicrobial | Kathiresan et al. (2010) |
| | | *Pseudomonas* sp. | 20–100 | Spherical | Ext | ND | Rammohan and Balakrishnan (2011) |
| | | *Bacillus subtilis* | 25–50 | Spherical | Ext | Antifungal | Vijayaraghavan et al. (2012) |
| | | *Pseudomonas fluorescens* | 1–10 | Spherical | Ext | Antimicrobial | Prabhawathi et al. (2012) |
| | | *Shewanella algae* | 5–30 | Spherical | Ext | Pest control | Yokesh Babu et al. (2014) |
| | Cyanobacteria | *Oscillatoria willei* NTDM01 | 100–200 | Spherical | Ext | ND | Ali et al. (2011) |
| | Actinobacteria | *Thermoactinomyces* sp. | 20–40 | Spherical | Ext | Antibacterial | Deepa et al. (2013) |
| | | Nocardiopsis sp. MBRC-1 | 45 | Spherical | Ext | Antimicrobial; cytotoxic | Manivasagan et al. (2013a) |
| | | *Streptomyces* sp. MBRC-91 | 35 | Spherical | Ext | Antibacterial | Manivasagan et al. (2015d) |
| | | *Streptomyces* sp. LK3 | 5 | Spherical | Ext | Acaricidal | Karthik et al. (2014) |
| | | *Streptomyces* sp. BDUKAS10 | 21–48 | Spherical | Ext | Antimicrobial | Sivalingam et al. (2012) |
| | | *Streptomyces albidoflavus* | 14.5 | Spherical | Int/Ext | Antibacterial | Shetty & Kumar (2012) |
| | Yeast | *Pichia capsulata* | 50–100 | Spherical | Ext | ND | Subramanian et al. (2010) |
| | | *Candida* sp. VITDKGB | 87 | Spherical | Ext | Antimicrobial | Kumar et al. (2011) |
| | Fungi | *Penicillium fellutanum* | 5–25 | Spherical | Ext | ND | Kathiresan et al. (2009) |
| | | *Aspergillus niger* | 5–35 | Spherical | Ext | Antimicrobial | Kathiresan et al. (2010) |
| | | *Aspergillus flavus* | 2–22 | Spherical | Ext | ND | Vala et al. (2014) |
| PbS NPs | Yeast | *Rhodosporidium diobovatum* | 2–5 | Spherical | Int | ND | Seshadri et al. (2011) |
| CdS NPs | Bacteria | *Pseudomonas aeruginosa* | 20–40 | Spherical | Ext | Bioremediation | Raj et al. (2016) |
| | Cyanobacteria | *Phormidium tenue* NTDM05 | 5 | Spherical | Ext | ND | Mubarak Ali et al. (2012) |
| $MnO_2$ NPs | Bacteria | *Saccharophagus degradans* | 34 | Hexagonal | Ext | ND | Salunke et al. (2015) |
| | Yeast | *Saccharomyces cerevisiae* | 34 | Spherical | Ext | ND | Salunke et al. (2015) |

Int, intracellular; ext, extracellular; ND, not determined.

## Marine yeast

Marine yeasts are ubiquitous in the marine ecosystems and they provide a unique potential for the synthesis of metallic nanoparticles. Yeasts are easy to culture and maintain compared with bacteria (Zaky et al., 2014). Marine yeasts are able to produce several bioactive compounds namely, enzymes, phytase, toxins, amino acids, glucans, glutathione, and vitamins, with potential applications in the pharmaceutical, cosmetic, food, and chemical industries as well as in marine culture and environmental protection (Sarkar et al., 2010). In recent years, *Yarrowia lipolytica* has emerged as a potential non-conventional yeast with significant biological and bionanotechnological applications. *Y. lipolytica* is a promising candidate for metallic nanoparticle synthesis (Agnihotri et al., 2009; Pimprikar et al., 2009).

## Marine fungi

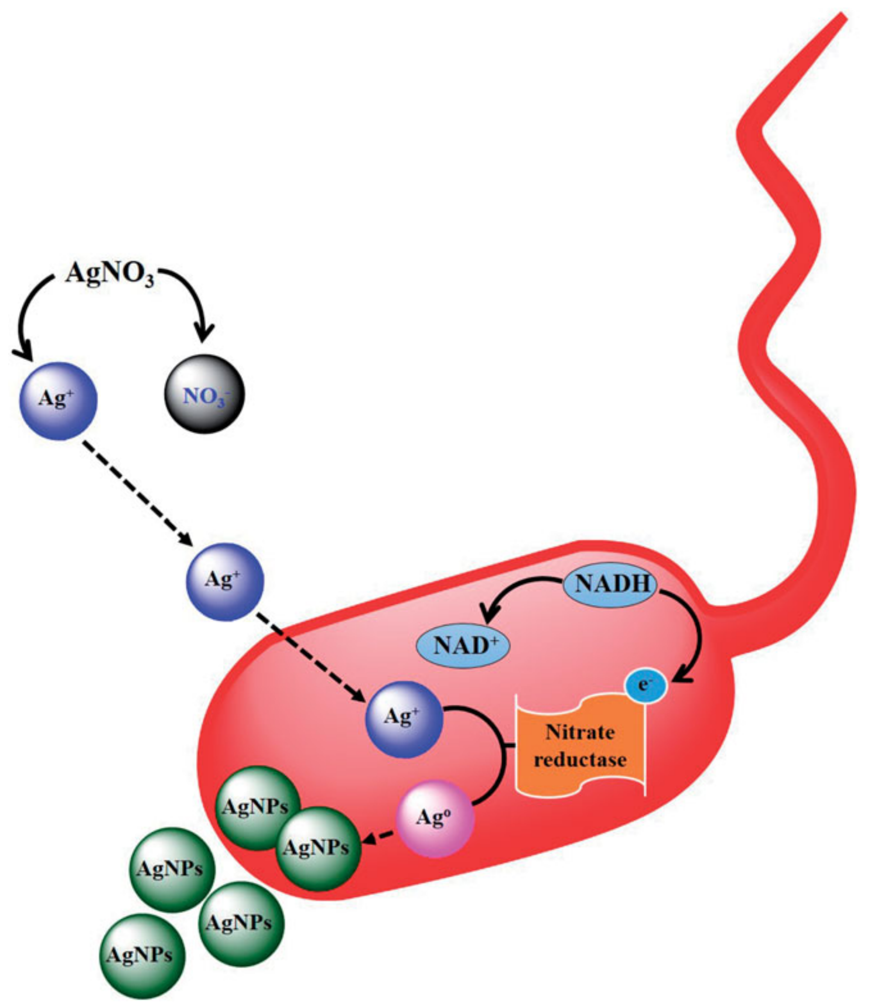
Marine fungi are eukaryotic organisms that live in marine ecosystems. Marine fungi have proved to be a rich source of bioactive compounds that show a range of biological properties such as antibacterial, anticancer, antiviral, anti-inflammatory, and antiplasmodial effects (Bhadury et al., 2006). Marine fungi are considered as excellent candidates for the green synthesis of metallic nanoparticles because a variety of enzymes are present in their cells and they are very easy to culture and maintain in the laboratory (Longoria et al., 2012). Compared with bacteria, fungi synthesize a lot of metallic nanoparticles. Fungi secrete a high amount of proteins, resulting in the higher productivity of metallic nanoparticles (Mohanpuria et al., 2008). Kathiresan et al. (2009) studied the biosynthesis of AgNPs by a marine fungus *Penicillium fellutanum* isolated from coastal mangrove sediment.

## Mechanism of nanoparticle synthesis by marine microorganisms

Biosynthesis is a phenomenon that takes place by means of biological processes or enzymatic reactions. These eco-friendly processes are referred to as green and clean technology, and can be used for better synthesis of metallic nanoparticles from marine microbial cells (Mandal et al., 2006). Marine microorganisms can survive and grow at a high concentration of metal ion because of their capability to fight stress (Moghaddam, 2010). The precise mechanism of the biosynthesis of metallic nanoparticles using biological agents remains unknown because several biological agents react differently with metal ions, and in addition, there are various biological molecules responsible for the synthesis of metallic nanoparticles. In addition, the mechanism of intracellur and extracellular biosynthesis of metallic nanoparticles is different in several biological agents. The intracellular method involves a special ion transportation in microbial cells. The microbial cell wall also plays an important role in the intracellular biosynthesis of metallic nanoparticles. The cell wall being negatively charged electrostatically interacts with the positively charged metal ions. The enzymes present within the cell wall bioreduce the metal ions to smaller-sized nanoparticles, which diffuse through the cell wall. A stepwise mechanism of the intercellular biosynthesis of metallic nanoparticles by *Verticillium* sp. explains that the mechanisms of the biosynthesis of metallic nanoparticles involve trapping, bioreduction, and capping (Mukherjee et al., 2007).

The mechanism of extracellular biosynthesis of AgNPs by microorganisms is generally found to be a nitrate reductase-mediated synthesis (Figure 1). The enzyme nitrate reductase secreted by the fungi helps in the bioreduction of metal ions and green synthesis of metallic nanoparticles. In recent years, many studies have been conducted on nitrate reductase for the extracellular synthesis of AgNPs (Durán et al., 2005; Gade et al., 2008; Karthik et al., 2014; Manivasagan et al., 2013a).

Figure 1. Proposed mechanism for the biosynthesis of silver nanoparticles.



The nitrate reductase activity test through the reaction of nitrate with 2,3 diaminophthalene was conducted. Thus, it was determined that the enzyme nitrate reductase is responsible for the bioreduction of $Ag^+$ ions and the subsequent formation of AgNPs. In this study, commercially available nitrate reductase disks were used; the color of the disc turned reddish from white when challenged with fungal filtrate signifying the presence of nitrate reductase (Ingle et al., 2008). Thus, it can determine that the enzyme an NADH-dependent reductase is associated with the reduction of $Ag^+$ to $Ag^{(0)}$ in the case of fungi. A similar mechanism was also studied in the case of extracellular biosynthesis of AgNPs by marine actinobacterium *Streptomyces* sp. LK3 (Karthik et al., 2014).

AuNPs are formed by different types of microorganisms. Although the common underlying mechanism involved in biosynthesis is the reduction of gold ions ($Au^{+3}$) to form AuNPs (Figure 2), it has been postulated that the enzymes secreted by microorganisms play an important role in the bioreduction of metal ions, leading to nanoparticle nucleation and growth (He et al., 2007). Despite the enormous number of reports on microbially mediated AuNPs synthesis, the mechanistic characteristics have not been established and need to be reported in depth (Das & Marsili, 2010). A similar mechanism was studied in the extracellular biosynthesis of AuNPs by *Rhodopseudomonas capsulate* (Kumar et al., 2007). The bacterium *R. capsulata* is identified to secrete cofactor NADH and NADH-dependent enzymes. The bioreduction of gold ions was found to be initiated by the electron transfer from NADH to NADH-dependent reductase as an electron carrier. $Au^{3+}$ obtain electrons and get reduced to $Au^{(0)}$ resulting in the formation of AuNPs.

## Synthesis and characterization of metallic nanoparticles

The procedures for making nanoparticles can commonly involve either a ''top–down'' approach or a ''bottom–up'' approach (Figure 3). In top–down synthesis, metallic nanoparticles are produced by size reduction from an appropriate starting material (Meyers et al., 2006). Size reduction is reached by several physical and chemical treatments. In bottom–up synthesis, the metallic nanoparticles are built from smaller entities, such as by joining atoms, molecules, and smaller particles (Mukherjee et al., 2001). The bottom–up synthesis mostly relies on chemical and biological methods of production. Of the biological methods of synthesis, the methods based on microorganisms have been widely reported (Gade et al., 2008; Manivasagan et al., 2015c; Prabhawathi et al., 2012). The formation of bionanomaterials by marine microbial cells is promising approach for the biosynthesis of metallic nanoparticles. Metallic nanoparticles have possible applications in diverse areas such as biomedicine, cosmeceuticals, pharmaceuticals, electronics, environmental monitoring and bioremediation, biocatalysis, and biomaterial sciences, because of the relative ease with which they can be prepared and manipulated, their commonly high reactivity and surface area, and the tunable nature of their optical and other properties (Donaldson et al., 2004; Hamouda, 2012). Most studies that focused on the biosynthesis of metallic nanoparticles, such as gold, silver, lead sulfide, and cadmium sulfide, have been constantly applied and modified to enable the use of these nanoparticles as a diagnostic and therapeutic agent.

Biosynthesis of metallic nanoparticles is generally characterized by their size, shape, surface area, and dispersity (Jiang et al., 2009). A homogeneity of these properties is important in various applications. The general techniques of characterizing metallic nanoparticles are as follows: UV–visible spectrophotometry, dynamic light scattering, X-ray diffraction, Fourier transform infrared spectroscopy, field emission scanning electron microscopy (SEM), energy dispersive X-ray analysis, and transmission electron microscopy (TEM; Figure 4; Shahverdi et al., 2011).

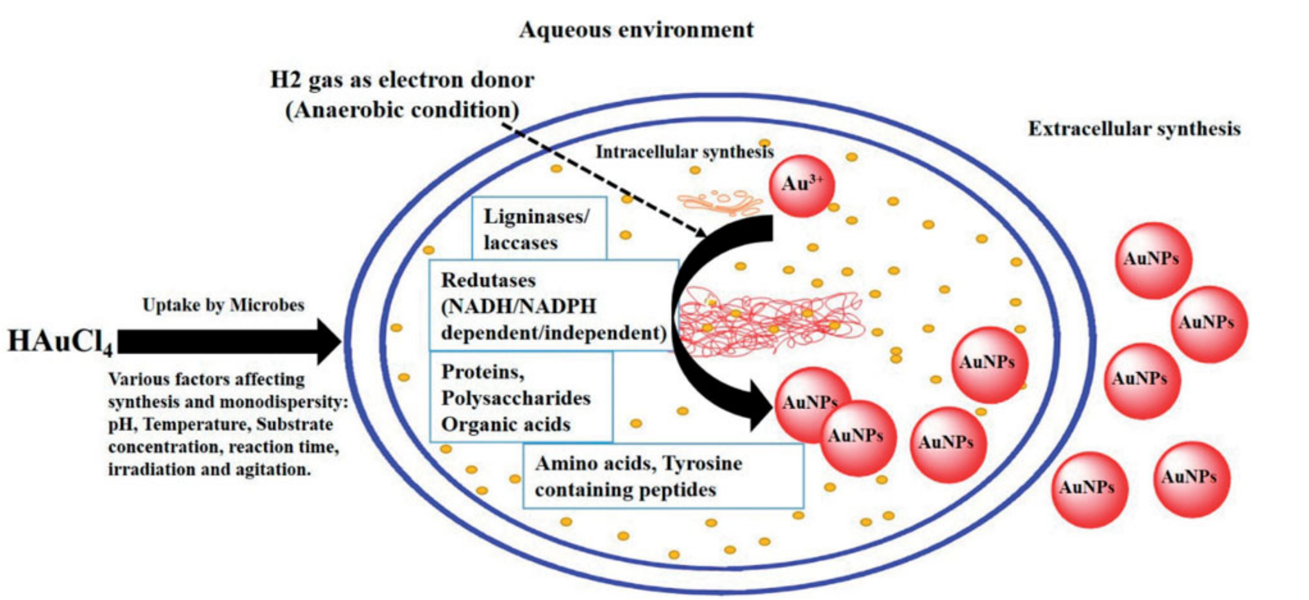



Figure 2. Mechanism of biosynthesis of gold nanoparticles.

## Gold nanoparticles

AuNPs are a novel biomedical application and are considered as nanomedicine presenting a high potential for diagnosis and a therapeutic agent (Zhang et al., 2008). In recent years, AuNPs have attracted importance in research due to their unique properties such as electrical, optical, and photothermal properties, and they are highly stable to oxidation (Kemp et al., 2009). There is an increasing need to develop clean, nontoxic, eco-friendly, inexpensive, time saving, and easily scaled-up large-scale synthesis processes. Development of high yield and low-cost techniques for nanoparticle production is an important challenge (Das & Marsili, 2010). Accordingly, many studies in nanoparticle synthesis have focused on biological methods because of its rich diversity (Rao et al., 2000).

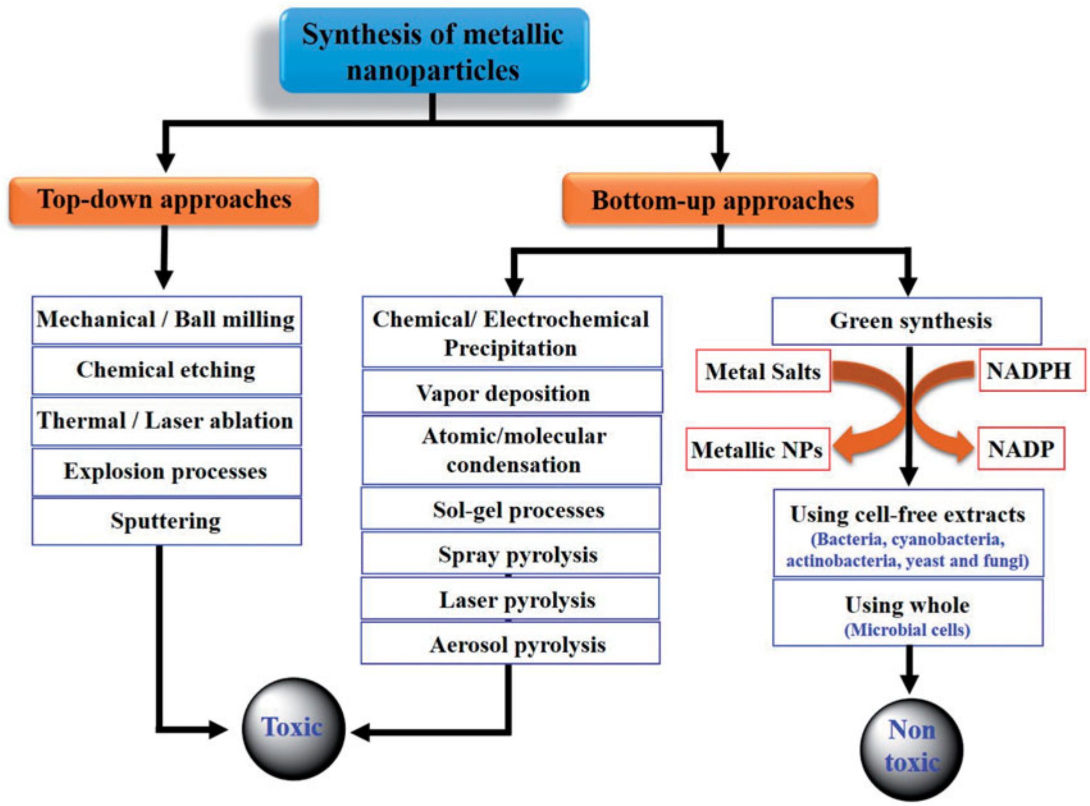



Figure 3. Different approaches of synthesis of metallic nanoparticles.

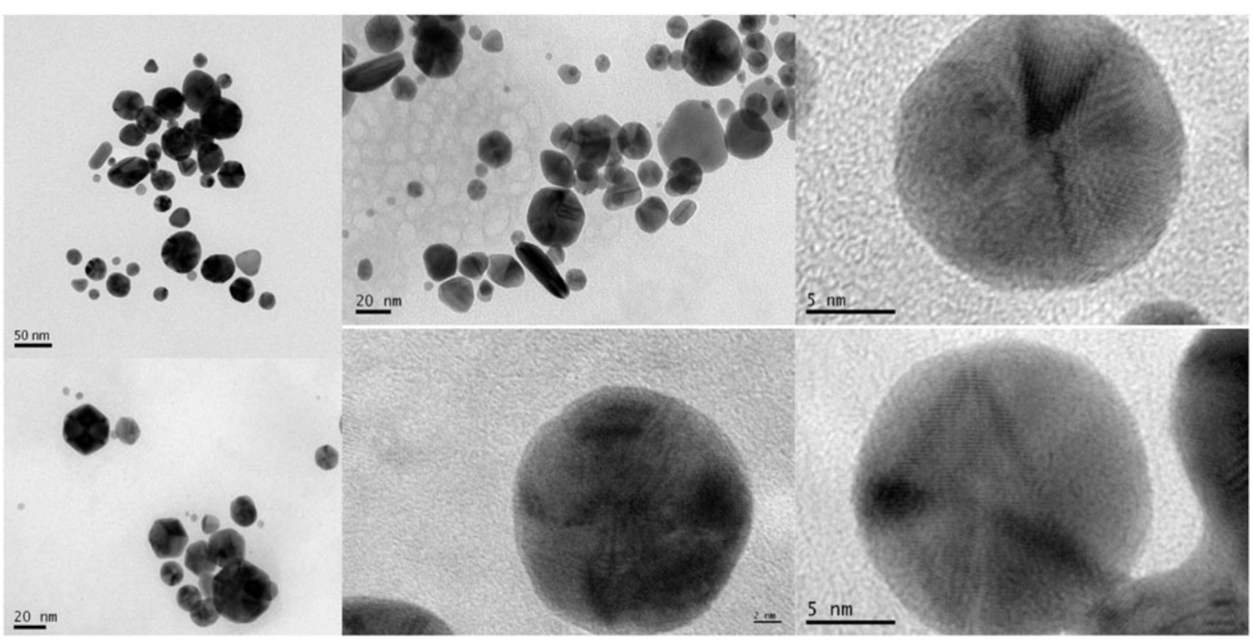



Figure 4. TEM images of metallic nanoparticles formed by marine microorganism.

The marine ecosystems are remains relatively unexplored; they are a huge treasure trove of marine bacteria resources. Sharma et al. (2012) have studied the production of AuNPs by a novel marine bacterium, *M. pelagius*. The particles were spherical and ranged from approximately 2 to 6 nm. Marine bacterium, *Pocillopora damicornis* isolated from a coral sample, collected from Mandapam coast, Bay of Bengal, India, was found to be a novel strain of *Stenotrophomonas*. TEM micrograph for AuNPs was observed after 16 h of incubation, and the average particle size ranged between 10 and 50 nm (Malhotra et al., 2013). Malarkodi et al. (2013) studied the eco-friendly method for the marine bacteria-mediated synthesis of AuNPs by the bioreduction of $HAuCl_4$ ions using the culture broth of *Klebsiella pneumoniae* isolated from the saltpan soil from Tuticorin, India. TEM of the AuNPs indicated that they were well dispersed and ranged in sizes from 35 to 65 nm. Chakraborty et al. (2009) reported the biorecovery of gold using marine cyanobacterium *Lyngbya majuscula* collected from the National Facility for Marine Cyanobacteria, Tiruchirapalli, Tamil Nadu, India. On TEM of *Lyngbya* biomass, a number of small gold particles (<20 nm) were observed within the cells particularly at peripheral cytoplasmic regions and on the sheath material as extracellular depositions.

Karthik et al. (2013) have reported the biosynthesis of AuNPs using *Streptomyces* sp. LK-3 isolated from the marine sediment samples collected from the Nicobar Islands, India. Gold nanoparticles were found within the size range of 5–50 nm. AuNps treatment in *Plasmodium berghei* ANKA (PbA)-infected mice delayed the parasitemia rise (approximately 6%) compared with *PbA* infection on day 8 post infection. The results obtained suggest that the AuNPs possess antimalarial activity and could be considered as a potential resource for antimalarial drug development. Manivasagan et al. (2015c) studied the optimization of α-amylase for the biosynthesis of AuNPs by *Streptomyces* sp. MBRC-82 isolated from the marine sediment samples collected from the Busan coast, South Korea. TEM also confirmed the size of the nanoparticles, which were in the range of 20–80 nm with an average particle size of 40 nm. The same group also studied the synthesis and characterization of gold bionanoparticles by *Nocardiopsis* sp. MBRC-48 isolated from the marine sediment samples collected from the Busan coast, South Korea. The particle size distribution of the AuNPs ranges from 7 to 15 nm with an average particle size of $11.57 \pm 1.24$ nm. The biosynthesized AuNps showed excellent antimicrobial activity against pathogenic microorganisms. It showed antioxidant activity as well as cytotoxicity against HeLa cell line (Manivasagan et al., 2015a).

Agnihotri et al. (2009) have reported the green synthesis of AuNPs by marine yeast *Y. lipolytica* NCIM 3589. TEM showed small particles of gold organized on the walls of the cells. AuNPs were found within the size of 15 nm. Vala (2014) reported the intracellurar and extracellular biosyntheses of AuNps by a marine-derived fungus *Rhizopus oryzae*. The particles were in the size range of 28–52 nm. Vala (2015) studied the biosynthesis of AuNPs by a marine-derived *Aspergillus sydowii* isolated from seawater samples collected from the Gulf of Khambhat, west coast of India. The particles were found to be in the size range of 8.7–15.6 nm with an average particle size of 10 nm.

## Silver nanoparticles

AgNPs have emerged as an important class of bionanomaterials for a wide range of biomedical and industrial applications such as antibacterial, catalyst, biosensor, bone cement, surgical instruments, and surgical masks. Silver is considered relatively harmless to humans and is a strong antibacterial agent, nontoxic, and a natural inorganic metal (Fabrega et al., 2011). AgNPs are the particles of silver with a particle size between 1 and 100 nm. Furthermore, it has also been revealed that ionic silver, in right quantities, is suitable for treating wounds. In fact, AgNPs are now replacing silver sulfadiazine as an effective agent in the treatment of wounds. Moreover, Samsung has produced and marketed a nanomaterial called Silver Nano, which contains AgNPs on the surfaces of household appliances. Recently, many studies have focused on the antibacterial and multifunctional properties of AgNPs (Jeong et al., 2005; Nersisyan et al., 2003; Rai et al., 2009). AgNPs have attracted considerable attention in biomedical imaging using surface-enhanced raman scattering (SERS) due to their attractive physicochemical properties (Mody et al., 2010). In addition, the surface plasmon resonance and large effective scattering cross section of individual AgNPs make them an excellent candidate for molecular labeling (Schultz et al., 2000).

Kathiresan et al. (2010) synthesized AgNPs using the coastal strains of *Escherichia coli* isolated from the coastal mangrove sediment of southeast India. The particles synthesized were generally spherical, ranging in size from 5 to 20 nm. The biosynthesized AgNPs inhibited certain clinical pathogens, with antibacterial activity being more distinct that antifungal activity. Rammohan & Balakrishnan (2011) studied the rapid synthesis of AgNPs using a novel marine bacterium, *Pseudomonas* sp. SEM revealed that AgNPs are polydispersed, ranging in size from 20 to 100 nm. Vijayaraghavan et al. (2012) biosynthesized AgNPs using a marine bacterium *B. subtilis*. The nanoparticles were in the size range of 25–50 nm. These nanoparticles showed strong antifungal activity against pathogenic fungi. Prabhawathi et al. (2012) reported the green synthesis of protein stabilized AgNPs by the marine bacterium *P. fluorescens* PMMD3 isolated from Chennai Harbor, India. The AgNPs are spherical in shape and are 1–10 nm in size. AgNPs-coated polycaprolactam exhibited 89.7% and 92.4% reduction in colony-forming units compared with bare polymer against *Staphylococcus aureus* and *E. coli*.

Seshadri et al. (2012) have studied the intracellular biosynthesis of AgNPs using the marine bacterium *Idiomarina* sp. PR58–8. The average particle size as per TEM analysis was found to be 26 nm. Malhotra et al. (2013) have studied the green synthesis of AgNPs using a novel marine strain of *Stenotrophomonas*. The AgNPs were in the size range of 40–60 nm. Youssef & Abdel-Aziz (2013) prepared AgNPs using marine bacterial isolate (MER1) culture filtrate as biosynthesis by microorganisms, which is considered as eco-friendly nanofactories that meet many bionanotechnological applications. Rajeshkumar et al. (2013) reported the intracellular and extracellular biosynthesis of AgNPs by the marine bacterium *Vibrio alginolyticus* isolated from the marine water sample collected from Kanyakumari coast, India. SEM also confirmed the size of the AgNPs, which were in the range of 50–100 nm. Yokesh Babu et al. (2014) biosynthesized AgNPs from marine bacterium *Shewanella algae* to control pests. The synthesized AgNPs were spherical, crystalline, and 5–30 nm in diameter. They were found to have both larvicidal and bactericidal activities.

Ali et al. (2011) have reported the extracellular biosynthesis of AgNPs by marine cyanobacterium *O. willei* NTDM01 isolated from Kurusadai Island at Gulf of Mannar, Tamil Nadu, India. SEM studies exhibited the formation of agglomerated AgNPs because of the capping agent in the range of 100–200 nm. Biosynthesis nanoparticles would have greater commercial viability, if the nanoparticles were synthesized more rapidly in the reaction vessel. Kiran et al. (2010) developed a cost-effective biosurfactant production method under solid-state culture, which was ultimately useful for the biosurfactant-mediated synthesis of AgNPs. The glycolipid biosurfactant was produced from sponge-associated marine *Brevibacterium casei* MSA19 under solid-state fermentation using the agro-industrial and industrial waste as substrate.

Sivalingam et al. (2012) have investigated the biosynthesis of bactericidal AgNPs using a novel *Streptomyces* sp. BDUKAS10, isolated from the mangrove sediment samples from Pitchavaram, Tamil Nadu, India. TEM indicated spherical AgNPs in the size range of 21–48 nm. These nanoparticles showed strong antimicrobial activity against bacterial strains. Shetty & Kumar (2012) studied the biosynthesis of AgNPs by *Streptomyces albidoflavus*. The strain revealed production of AgNPs, both extracellulary and intracellularly. The produced particles were spherical and monodispersive and exhibited a single surface plasmon resonance peak at 410 nm. Size distribution histograms indicated a production of 10–40 nm nanoparticles with a mean size of 14.5 nm. The nanoparticles produced were proteinaceous compounds as capping agents with −8.5-mV zeta potential and revealed antibacterial activity against both Gram-negative and Gram-positive bacterial strains.

Deepa et al. (2013) investigated the extracellular biosynthesis of AgNPs using *Thermoactinomyces* sp. isolated from the marine sediment samples collected from Vellappallam coast, Nagapattinam, India. The biosynthesized AgNPs were spherical, ranging in size from 20 to 40 nm. These particles showed good antibacterial against *Staphylococcus aureus* and *B. subtilis*. Manivasagan et al. (2013a) biosynthesized AgNPs using a novel *Nocardiopsis* sp. MBRC-1, isolated from the marine sediment samples collected from Busan coast, South Korea. These particles were spherical with an average particle size of $45 \pm 0.15$ nm. They exhibited good antimicrobial activity against pathogenic bacteria and fungi. Cytotoxicity of biosynthesized AgNPs against *in vitro* HeLa cell line exhibited a dose-response activity. $IC_{50}$ value was found to be 200 μg/ml of AgNPs against HeLa cells.

Karthik et al. (2014) investigated the actinobacteria-mediated biosynthesis of AgNPs using *Streptomyces* sp. LK3 isolated from the marine sediments of the island of Nicobar, India. TEM showed that the synthesized AgNPs were spherical with an average size of 5 nm. The synthesized AgNPs exhibited significant acaricidal activity against *Rhipicephalus microplus* and *Haemaphysalis bispinosa* with $LC_{50}$ values of 16.10 and 16.45 mg/l, respectively. Manivasagan et al. (2015b) reported the optimization of polysaccharide-based bioflocculant for the biosynthesis of AgNPs using *Streptomyces* sp. MBRC-91. Optimization of the culture medium and growth conditions decreased the cost of medium constituents and improved the feasibility of commercial production. These nanoparticles were spherical with particle in size ranging from 10 to 60 nm and an average particle size of 35 nm. The biosynthesized AgNPs have great potential as antibacterial activity in sewage water, and this result could make a new avenue in the wastewater treatment.

Subramanian et al. (2010) investigated the synthesis of AgNPs using a marine yeast, *Pichia capsulata* isolated from the mangrove sediment samples from Pitchavaram, Tamil Nadu, India. *Pichia capsulata* showed the most efficient production of AgNPs in culture filtrate, at a faster rate within minutes. The particles were spherical with particle size ranging from 50 to 100 nm. Kumar et al. (2011) reported the biosynthesis of AgNPs from marine yeast *Candida* sp. VITDKGB isolated from Nicobar Islands, India. These particles were spherical in nature with an average particle size of 87 nm. Biosynthesized AgNPs exhibited good antimicrobial activity against multidrug-resistant pathogens such as *Staphylococcus aureus* and *K. pneumoniae*. An inhibition zone of $14.66 \pm 1.52$ mm for *S. aureus* with an MIC value of 20 μg/ml and an inhibition zone of $12.33 \pm 0.57$ for *K. pneumoniae* with MIC value of 40 μg/ml was observed.

Kathiresan et al. (2009) biosynthesized AgNPs using a marine fungus *P. fellutanum*. The biosynthesis was faster, occurring within minutes after silver ion contacted the cell filtrate. The micrograph displayed nanoparticles with variable shape; most of them were spherical. The size of the particle ranged from 5 to 25 nm. Kathiresan et al. (2010) biosynthesized AgNPs using *Aspergillus niger* isolated from coastal mangrove sediments, southeast India. The particles synthesized were mostly spherical, ranging in size from 5 to 35 nm. Vala et al. (2014) have reported the biosynthesis of AgNPs by marine-derived fungus *Aspergillus flavus* from Bhavnagar coast, Gulf of Khambhat, India. The particles were found to be in the size range of 2–22 nm. Hence, the test isolate is a potential candidate for the green, inexpensive synthesis of AgNPs.

## Lead sulfide nanoparticles

Green synthesis of metallic nanoparticles using marine microorganisms has received considerable attention in recent years as this route has the potential to lead to the biosynthesis of nanoparticles (Seshadri et al., 2011). Marine microorganisms are useful for synthesizing nanoparticles. Marine microorganisms interact with metal ions because marine environment is continuously exposed to metal pollution (Hulkoti & Taranath, 2014). These microorganisms may reduce the metallic ions or convert them into sulfides, phosphates, and carbonates and/or intracellularly sequester them with low molecular weight, cysteine-rich proteins. Lead sulfide nanoparticles (PbS NPs) of the quantum dot size range has been applied in solar concentrators to enhance solar harvesting, and also as bioconjugates with antibodies for near-infrared molecular imaging (Kango et al., 2013). Controlled synthesis of semiconductor nanoparticles of well-defined size, shape, and composition is a big challenge. The capability of microbial cells to use highly structured compartments and biosynthetic activities to precisely direct the size, shape, and crystallinity of the materials has emerged as a novel approach for the synthesis of inorganic nanoparticles. Seshadri et al. (2011) have studied the intracellular biosynthesis of PbS NPs using a marine yeast, *Rhodosporidium diobovatum.* UV-visible absorption scan revealed a peak at 320 nm, a characteristic of the nanosize range. Crystallite size as determined from TEM was found to be in the range 2–5 nm.

## Cadmium sulfide nanoparticles

CdS NPs are among the widely studied in semiconductor nanoparticles that possess unique, photochemical, and photophysical properties. CdS Nps have successfully been synthesized using a wide range of marine microorganisms such as bacteria, cyanobacteria, yeast, and fungi (Flenniken et al., 2004). Apart from the synthesis of such CdS NPs, the stabilization of synthesized particles is also important. Several stabilizing agents such as enzymes, starch, chitosan, 3-mercaptopropionic acid, mercaptosuccinic acid, and glutathione, have also been used to synthesize CdS NPs. These stabilizing agents provide the thiol group that would bind Cd through the S-H group (Sobhana et al., 2011); R-phycoerythrin also has this property (Brekhovskikh & Bekasova, 2005). There are three types of phycoerythrin: R-phycoerythrin and B-phycoerythrin in the Rhodophyta, and C-phycoerythrin in the Cyanophyra. *Phormidium tenue*, a marine cyanobacterium, is a rich source of C-phycoerythrin. The major advantages of C-phycoerythrin are that its content in the cyanobacterium is approximately 70% of the total protein, and it can be easily extracted from the cell. The pigment, C-phycoerythrin isolated from the marine cyanobacterium, *Phormidium tenue* NTDM05 was used to synthesize CdS NPs. The size of the CdS NPs was found to be approximately 5 nm (Mubarak Ali et al., 2012). Raj et al. (2016) have developed a novel methods for the synthesis of CdS NPs using the bacterial extracellular polymeric substances (EPS) that also helps in removal of toxic metal pollutant cadmium from aqueous solution.

## Manganese dioxide nanoparticles

Marine microorganisms are one of the most attractive and simple sources for the green synthesis of different types of metal nanoparticles. The unique physical and chemical properties, and the wide range of applications, make manganese oxide nanoparticles ($MnO_2$ NPs) as one of the most attractive nanomaterials. $MnO_2$ NPs are useful for medicine, catalysis, ion exchange, molecular adsorption, biosensors, and energy storage (Jaganyi et al., 2013; Raj et al., 2014). Marine bacteria and yeasts are the most celebrated for the green synthesis of various types of metallic nanoparticles (Nishat Sharma et al., 2012). Salunke et al. (2015) reported the green synthesis of $MnO_2$ NPs by marine bacterium *Saccharophagus degradans* and marine yeast *Saccharomyces cerevisiae*. The microbial supernatants of the bacterium and yeast showed positive reactions to the synthesis of $MnO_2$ NPs by displaying a change of color in the permanganate solution from purple to yellow. TEM micrographs revealed the presence of uniformly dispersed hexagonal and spherical-shaped particles with an average size of 34.4 nm.

## Applications of metallic nanoparticles

Development of nanodevices using marine biomaterials and their use in the wide array of various applications on living organisms have recently attracted the attention of biologists toward bionanotechnology. Below mentioned are very few applications of this technology which would help in understanding the use of diverse living organisms in nanodevices production and also the use of these nanoproducts in several applications (Mohanpuria et al., 2008). AuNPs and AgNPs produced either intracellularly or extracellularly using marine microorganisms could be of great value. AuNPs have become the focus of intensive research due to their wide range of applications such as catalysis, optics, and antimicrobial and biomaterial production (Venkatesan et al., 2014). AgNPs have large number of applications, such as in nonlinear optics, spectrally selective coating for solar energy absorption, biolabeling, intercalation materials for electrical batteries, optical receptors, catalyst in chemical reactions, and antibacterial (Durán et al., 2005).

Metallic nanoparticles offer a promise for the development of novel nanomedicines. Nanomedicines should be able to overcome the limitations of human diseases at the nanoscale level at which biomolecules are acting (Akhtar et al., 2012). Metallic nanoparticles are usually applied to the antibacterial drug carriers. Nano-based formulations of various antimicrobial drugs have been shown to improve either pharmacokinetics or antibacterial efficiency by achieving sustained release directly at the infection site (Aboutaleb et al., 2012). Drug encapsulation and delivery via nanoparticles may also help prevent adverse effects (Cover et al., 2012).

AuNPs have been considered as an important field of research because of their unique and intense plasmon resonance in the visible range and their application in biomedical sciences (Huang, 2006). AuNPs are excellent labels and have been primarily used for labeling and bioimaging applications for biosensors because they can be detected by several techniques, such as optic absorption fluorescence and electric conductivity. AuNPs are a very attractive contrast agent (Chen et al., 2008). Recently, metallic nanoparticles have found application in antimicrobial effects. The antimicrobial study of the bionanomaterials was performed because of the increase in novel strains of microorganisms that are resistant to most potent antibiotics resulting in novel research into the well-known activity of gold and gold-based compounds, such as AuNPs. The effect was size and dose dependent, and more distinct against pathogenic bacteria and fungi. It showed strong antioxidant activity as well as cytotoxicity against HeLa cell line. *Nocardiopsis* is an excellent marine microbial resource for the biosynthesis of AuNPs with several biomedical applications such as antimicrobial, antioxidant, and anticancer activities (Manivasagan et al., 2015a). Karthik et al. (2013) have studied the green synthesis of AuNPs by *Streptomyces* sp. LK-3 and revealed that AuNPs possess antimalarial

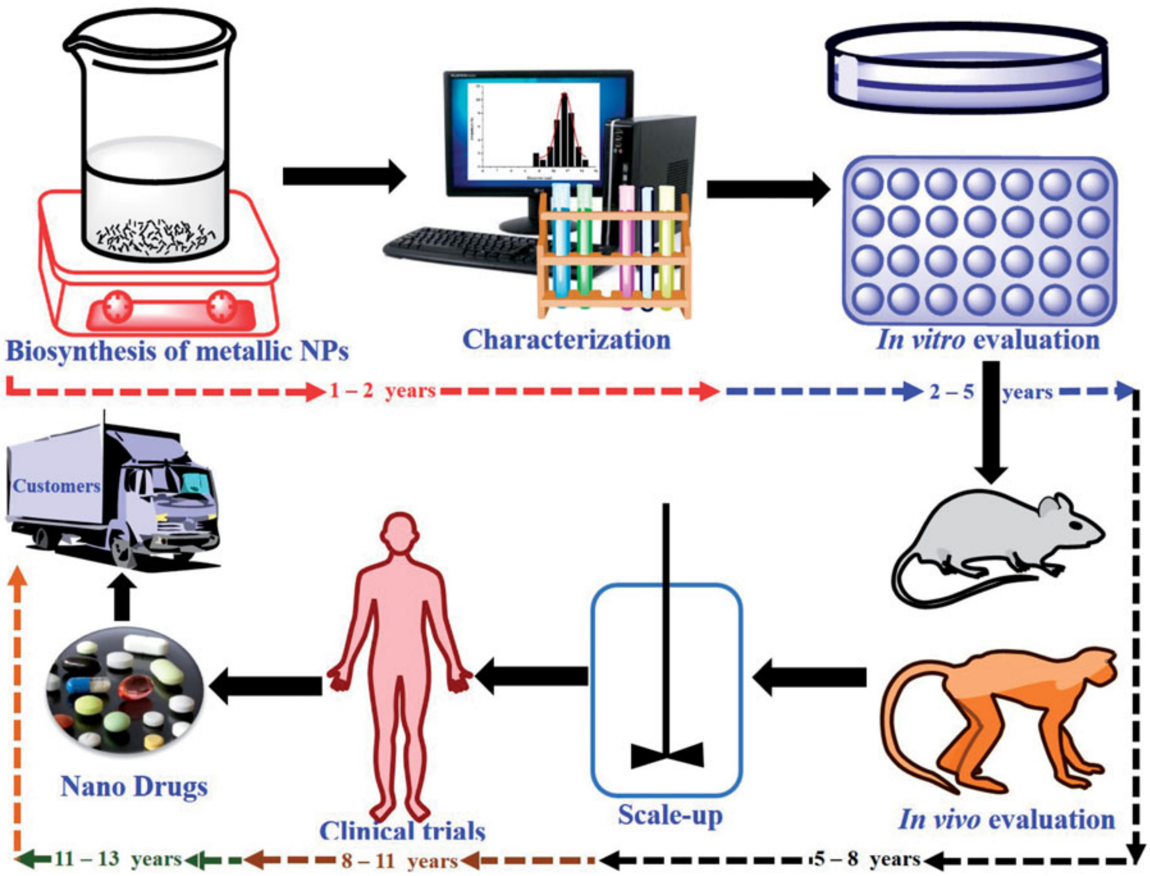



Figure 5. Flow chart depicting the main techniques of green synthesis, characterization, *in vitro*, *in vivo* studies and clinical trials leading to the development of nanoproducts.



activity, and these could be considered as an important resource for antimalarial drug development.

AgNPs have significant antibacterial activities and are used in fabrics and cosmetics. They have medical uses, such as healing wounds and ulcers, usually in the form of dressings and creams and are also applied to coat medical devices, such as catheters, dentures, or surgical masks (Cortivo et al., 2010). They are also used in the production of antimicrobial nanopaints. Furthermore, AgNPs are utilized for the preparation of antibacterial water filter (Roy et al., 2013). The biosynthesized AgNPs revealed strong antibacterial activity in sewage water, and this result could make a new avenue in wastewater treatment (Manivasagan et al., 2015b). The biosynthesized AgNPs showed significant acaricidal activity against *Rhipicephalus microplus* and *Haemaphysalis bispinosa* with $LC_{50}$ values of 16.10 and 16.45 mg/l, respectively. AgNPs could provide a safer alternative to conventional acaricidal agents in the form of a tropical antiparasitic formulation (Karthik et al., 2014). A schematic representation of steps followed to develop nanoproducts has been presented in Figure 5.

## Future research needs

There have been tremendous developments in the field of marine microorganism-produced metallic nanoparticles and their biological and biomedical applications over the last decade. However, much work is required to develop green synthesis, control of particle size, and morphology. The control of size, shape, and monodispersity is a major challenge of the green synthesis of metallic nanoparticles because the synthesis of nanoparticles using marine microorganisms is quite a slow process compared with physical and chemical approaches. The bioreduction of synthesis time will make this green synthesis route much more attractive. Therefore, the effective control on the size, shape and monodispersity must be explored. Thus far, there have been very limited studies on the green synthesis of metallic nanoparticles using marine microorganisms. Therefore, studies on the extracellular biosynthesis of metallic nanoparticles are definitely required. However, biosynthesis and their industrial applications are still at the laboratory level, and efforts are essential to enhance the practical application of marine microorganisms in the large-scale production of metallic nanoparticles. Elucidating the cellular, biochemical, and molecular mechanisms of nanoparticles, synthesis is important and urgent. If the mechanisms are understood, green synthesis of metallic nanoparticles will have a greater progress in commercial applications. Because of the very rich biodiversity of marine microorganisms, their potential as biomaterials for nanoparticle synthesis remains unexplored. At present, very limited patents are available on biosynthesis of metallic nanoparticles by marine microorganisms and their applications. In addition, *in vivo* studies and clinical applications are required to develop new commercial nanoproducts.

## Conclusion

Green synthesis of metallic nanoparticles has attracted attention in recent years due to its decreased environmental toxicity. Marine microorganisms, such as bacteria, cyanobacteria, actinobacteria, yeast, and fungi, have many opportunities for the utilization of nanobiotechnology, particularly in the development of a reliable and eco-friendly process for the green synthesis of metallic nanoparticles. The rich microbial biodiversity points to their innate potential for acting as potential biofactories for biosynthesis of metallic nanoparticles. Marine microorganisms appear to be potentially excellent candidates for nanoparticles synthesis because they produce copious amount of enzymes and thus, are usually nontoxic to animals and human, and are easily cultured in laboratories. However, very few aspects of nanoparticles synthesis require specific attention as they have not yet either been touched upon at all or are still in their infancy. Research focuses strongly on the potential application of eco-friendly synthesized metallic nanoparticles with the main focus on antimicrobial, antioxidant, antimalarial, and anticancer activities. This branch promises to further grow and explore many more possible applications such as optical devices, catalysis, cancer therapy, drug delivery, and biosensor. Hence, this review would provide standing information for the development of more useful metallic nanoparticles. In future, marine microbial nanoparticles will offer a better platform in several fields of science and medicine.

## Declaration of interest

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