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GREEN BIOSYNTHESIS OF METALLIC NANOPARTICLE FOR MEDICAL DIAGNOSTIC

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ABSTRACT: Metal nanoparticles are garnering considerable attention owing to their high potential for use in various applications in biological, biomedical, and biosensing. Nanoparticle have unique Physical and Chemical Properties due to their high surface area and nanosized. The synthesis of metallic nanoparticle has the potential to deliver new source of novel metal that are stable, nontoxic, cost effective, environmental friendly and synthesized using green channel approach. By using microorganisms such as Bacteria, Fungi, Algae/Cyanobacteria and plant, for the production of nanoparticle is an economical, energy efficient and healthier work for human health and environment leading to lesser waste and make useful product, for example, cyanobacterial nanoparticle has been utilized in many medical areas such as hepatocellular carcinoma, nanomaterial-based biosensor, gene therapy, anti-bacterial agent and drug delivery system etc. The review emphasizes the strategies for biosynthesis of metallic nanoparticles using microorganism and plant which have potential to developed novel anti cancerous, antibacterial and nontoxic product.

KEYWORDS: Nanoparticles, Cyanobacteria, Green Synthesis, Drug delivery.

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1.INTRODUCTION

Metallic Nanoparticles research is currently of intense significance due to a wide variety of potential application in biomedical, drug design and delivery and Medical diagnostic. Nanoparticle are of great scientific interest as they are effectively a bridge between bulk material and atomic or molecular structure. However, nanomedicine present considerable challenges for preclinical application. Nanoparticle are wide class of material that include particulate substance which have one dimension less than 100 nm at least [1]. Depending on the overall shape these materials can be 0D,1D,2D, or 3D [2]. The nanoparticle can be employed for drug delivery [3], chemical and biological sensing [4] [5] and other related application [6]. Biological synthesis of nanoparticles is a one-step bio reduction method and less energy are used for synthesis of ecofriendly nanoparticles. [7]. Nanoparticles are gaining reputation as multifaceted material exhibiting novel or advanced characteristics compound to larger particles. [8]. Smaller size nanoparticles display higher surface to volume ratio a feature vital for catalytic reactivity, thermal conductivity, antimicrobial activity chemical steadiness and non -linear optical performance. [9] because of such characteristics nanoparticles playing significant role in medical diagnostics, antisense and gene therapy application and tissue engineering [10]. In order to provide a more environmental sound synthesis of nanoparticles various biological routes are considered including the use of plant extract [11], enzyme [12], bacteria [13], fungi [14] and algae [15, 8]. Mechanism and protocol for the synthesis of various inorganic metal nanoparticles and nanomaterial have been developed for a wide range of application including biosensor and chemical sensors, bioimaging, catalysis , optics, electronics , drug delivery and energy [16][17].For example various nanomaterials have been tested as specially controlled carries in drug delivery system for drug transport to the cellular target [18] and use to convert solar energy directly into stream for sanitation and water purification. Several microorganisms such as bacteria, algae, yeast, and fungi, are capable of reducing metal ions through metallo-regulatory mechanism upon exposure [19]. Formation of metal nanoparticles from heavy metal ions occurs through the reduction of the metal ions resulting in the formation of insoluble complexes. This mechanism is employed for the biosynthesis of diverse metal nanoparticles using microorganism engineered to express heavy metal binding protein and /or peptide [20]. The composition of a specific nanoparticles can be very complex, depending on interaction, it has had with other chemicals or particles and its lifetime. The chemical process taking place on surface of nanoparticles are also very complicated and remain largely unknown.

Biosynthesis of Nanoparticles

The principal parameter of nanoparticles is their shape, size, surface characteristics and inner structure. Nanoparticle can be encountered as aerosol [solid or liquid in air] suspension [solid in liquid] or as emulsion [liquid in liquid]. In the presence of certain chemicals properties of nanoparticles may be modified. Biological method for the synthesis of silver nanoparticles employing microorganism [21,22] and plant [23]. Microbial synthesis of nanoparticles does not encounter variation, although regular maintenance of culture and sterile condition for nanoparticles synthesis is required [23].

Bacteria/Fungi Mediated Nanoparticles

The biosynthesis of nanoparticle depends on the cell [24]. Acinetobacter has been shown to exhibit biocompatibility with its own metal nanoparticles however exposure to the corresponding metal, salt decrease their cell count [25]. Fusarium oxysporum has been reported to produce a wide variety of metal nanoparticles including Ag-Au, Ag, cds, cdSe, Co3O4, Sio2, Tio2, ZrO2, BuTio3 and Fe3O4 approximately size 50 to 200 nm [26, 27]. Extra cellular synthesis of nanoparticles occurs outside the bacterial cell such as spherical, disk, cuboidal, hexagonal, triangular etc. have been synthesized using cell culture supernatant or aqueous cell free extract [28]. The intracellular silver nanoparticles depend on the culture medium used to grow the cell, [24]. Individually encapsulated recombinant E. coli cells were able to synthesize homogeneous nanoparticles through concentrated treated metal precursors [16]. Lactobacillus strain has been described to mediated biosynthesis of silver and titanium nanoparticles [29] and gold, silver, and titanium nanoparticle. Vibacterium casei and Aeromonas SH10 silver nanoparticle were synthesized by biomass accumulation as well as Bacillus subtilis, Bacillus licheniformis, Corynebacterium and Pseudomonas studzeri reduced AgNo3 yielding silver nanoparticle produce under atmospheric condition and in size range is 10 and 5 nm, 200 nm respectively [30]. The bacterial strain is used for the synthesis of silver nanoparticles which is isolate from the soil which are identified by Pneumoniae [31]. The synthesis of circular and triangular crystalline silver nanoparticles by solar irradiation of cell free extract of Bacillus amyloliquefaciens and silver nitrate [32], staphylococcus aureus produced biogenic silver nanoparticles against a range of resistant bacteria [33]. The green synthesis of silver nanoparticles from Bacillus sp. Were collected from the periplasmic region of the bacterial cell [34]. Geobacter ferrireducens was also produce gold nanoparticles intracellularly in periplasmic space [35]. In the biological synthetic process for metal nanoparticle soluble sulfate act as the source of sulfur. The formation mechanism of metal nanoparticle by biological transformation mechanism of Rhodobacter spheroids is explained by soluble sulfate which enter into immobilized beads via diffusion and later is carried to the interior membrane of Rhodobacter. Cell facilitated by sulfate permease then the sulfate is reduced to sulfite by ATP sulfurylase and phosphodenamine. Phosphosulfate reductase and next sulfide react with O acetyl serine to synthesize cystine which are solubilize with metal and synthesized metallic nanoparticle. [36].

Algae mediated nanoparticles

Spirulina plantensis synthesized nanoparticles of silver, gold, and gold core, silver shell [Au core-Ag shell]. [37]. An extract of the unicellular green alga Chlorella vulgaris synthesized single crystalline Ag nanoparticles at room temperature extract of the brown alga Chlorella monliformis were shown for the synthesis of silver nanoparticles with size range of 50-100 nm spherical and small particles at low temperature [38,39]. Filamentous cyanobacterium strain i.e. Anabena, Calothrix and Leptolyngbya have the capability to synthesize Au, Ag, Pd and Pt nanoparticles, the microorganism will use for these metallic nanoparticle's formation is Calothrix, Leptolyngbya and Anabena spi. [40]. The mechanism of gold nanoparticles synthesis by cyanobacteria is describe by the interaction of cyanobacteria with aqueous gold chloride initially promoted the precipitation of nanoparticles of amorphous gold sulfide at the cell wall and finally deposited metallic gold in the form of octahedral platelets near cell surface and in solution. This process is based on enzymatic reduction of the metal ions leading to their aggregation and the formation of nanoparticles. [41]. Nanoparticles production using Plectonema boryanum of spherical silver nanoparticles of up to 200 nm is solution [42]. The production of ZnO nanoparticles by the Anabena-flas aquae photosynthetic microorganism [40]. Silver nanoparticles using the leaf extract of Bacillus monosperna were synthesized and observed that at a concentration of 1% leaf extract [43]. Cds nanoparticles were synthesized using C. Phycoerythrin as the capping agent [44]. Silver nanoparticle was synthesized by cyanobacterial and green algae strain in BG 11 medium [45]. Filamentous cyanobacteria strain i.e. Anabena, Calothrix and Leptolyngbya have the capability to form metallic nanoparticles of well controlled size such as silver, gold, platinum, palladium. The algal cell of Spirulina platensis was chosen because it also possessed pharmaceutical and nutraceutical properties for the silver nanoparticles synthesis [37].

Plant Mediated Nanoparticles

Synthesis of gold and silver nanoparticles using dried powder of Catharanthus camphora leaf which are used to check antiplasmodial activities [46]. The extract of the Microbilis jalapa flower work as reducing agent and gold nanoparticles with ecofriendly method [47]. By ecofriendly synthesis of metallic nanoparticles of Piper nigrum leaves and Ag Nps have effective drug in Cancer medicine to cure various oncology and dreadful disease. A green synthesis of silver nanoparticles using the leaves of Artemisia nilagirica plant extract [48]. An ecofriendly method synthesis of gold nanoparticles by using Rose plant is described by Noruzi.et.al., [2011] [49]. Catharanthus -raseus and Cilitora ternate diverse group of flowers are used for the metallic nanoparticle's synthesis with desired size and shape. Nyctanthues arbortristis flower of gold nanoparticles extract are synthesized by green chemical method [50].

Microorganism and Plant derived Metallic Nanoparticles **S. No.**	**Types of microorganism**	**Metal**	**Reference**
	Bacteria		
1.	*Enterobacter aureus*	Ag	[51]
2.	*Bacillus subtilis*	Ag	[52]
3.	*Bacillus subtilis*	Au	[53]
4.	*Cupriavidus metallidurans*	Au	[54]
5.	*Rhodopseudomans capsulate*	Au	[55,56]

6.	*Bacillus selenitireducens*	Te	[57]
7.	*Serratia sps*	Cu, Cuo	[58]
8	*P. aeruginosa*	Ag, Co, Fe, Li, Ni, Pd, Pt, Rh, Ru	[59]
9.	*Escherichia coli*	Au, Cu, Cuo, Cds	[60], [61]
10.	*Sulfate reducing Bacteria*	Fe_3S_4, Fe_3O_4	[62], [63]
11.	*Cobalt resistant bacteria*	Co_3O_4	[64]
12.	*Recombinant E. coli*	Au, Ag, Fe, Te, Cds Br, Cd, Zn	[65], [66], [67], [68] [69]
13.	*Enterobacter aerogens*	Au, Ag	[70]
14.	*Geobacter sufurredicen*	Ag	[71]
15.	*Gluconobacter roseus*	Ag	[72]
16.	*Idiomarina sps*	Ag	[73]
17.	*Klebsiella pneumoniae*	Ag	[74]
18.	*Morganella sps*	Ag	[75]
19.	*Proteus Microbilis*	Ag	[76]
20.	*Pseudomonas aeruginosa*	Ag	[59]
21.	*Yersinia enterocolitis*	Ag	[78]
22.	*Bacillus thuringenesis*	Ag	[79]
23.	*Rhodococcus sps.*	Ag	[80]
24.	*Holococcus salifodi*	Ag	[81]
	Fungi		
25.	*Trichoderma viride*	Ag	[82]
26.	*Coriolus versicolor*	Ag	[83]
27.	*Volvariella volvacea*	Ag	[84]
28.	*Penicillium strain*	Ag	[85]
29.	*Verticillium sps.*	Au	[86]

30.	*Phanerochaete chrysosporium*	Ag	[87]
31.	*Aspergillus fumigatus*	Ag	[88]
32.	*Aspergillus flavus*	Ag	[89]
33.	*Fusarium solani*	Ag	[90]
		Algae	
34.	*Shewanella sps.*	Au	[91]
35.	*Shewanella oneidensis*	Au	[92]
36.	*Plectonema boryanum*	Au, Ag, Pd	[93]
37.	*Anabena*	Fe, Mn	[42]
		Plant	
38.	*Acalypha indica*	Au, Ag	[94]
39.	*Aloe vera*	In_2O_3	[95]
40.	*Andrographis paniculata*	Ag	[96]
41.	*Alternanthera sessilis*	Ag	[97]
42.	*Alternanthera Mexicana*	Ag	[60]
43.	*Caria papaya*	Ag	[98]
44.	*Cassia fistula*	Au	[99]
45.	*Cinnamon zeylanium*	Ag	[100]
46.	*Citrullus colocynthis*	Ag	[101]
47.	*Citrus sinensis*	Ag	[102]
48.	*Dillenia indica*	Ag	[103]
49.	*Dioscorea bulbifera*	Ag	[104]
50.	*Euphorbia prostrata*	Ag	[105]
51.	*Gelsemium sempervirens*	Ag	[49]
52.	*Lippia citriodora*	Ag	[61]
53.	*Microbilis jalapa*	Ag	[47]
54.	*Helicobacter canadensis*	Ag	[49]

55.	*Iresina herbstii*	Ag	[108]
56.	*Melia azedarach*	Ag	[109]
57.	*Tinospora cordifolia*	Ag	[110]
58.	*Trigonella foenum-graecum*	Au	[111]
59.	*Withania somnifera*	Ag	[112]
60.	*Mentha Piperita*	Ag, Au	[44]

Application

Metal nanoparticles have widely and commonly been used in biological, biomedical, and biosensing application. In biological system a large variety of organism from organic/inorganic composites with ordered structure by the use of biopolymers such as protein and microbial cells. Several different approaches for the synthesis of metal nanoparticles based on the different system such as whole live cell versus cell extract, wild type versus recombinant microorganism strain and bulk phase versus microdroplet can be examined such novel metal nanoparticles that have not yet been synthesized can potentially serve as new nanoparticles for exciting industrial application. There are also various ecofriendly nanoparticles product available in commercial market with high efficiency such as Water purifier, bone and teeth cement, facial cream and home-made product [113]. Silver, silica and platinum nanoparticles have various application in personal care and cosmetics and biologically synthesized nanoparticles are used as biological ingredient in various product such as sunscreen, antiaging cream, toothpaste, mouthwash, hair care product and perfume [114]. In medical field tentative evidence support a clearance risk of urinary tract infection, when alloy catheter is used silver nanoparticles synthesized by bacteria exhibit excellent larvicides potency against the dengue vectors, Ades aegypti [115] and Hemophysalis bispinosa [116] indicating their application as a patent insecticide as well as nanomedicine is a field of research with tremendous prospect for the improvement of the diagnosis and treatment of human disease. Dispersed nanoparticles are usually employed in Nano biomedicine as fluorescent biological labels [117], drug and gene delivery agent [118] and in application such as bio detection of pathogens [119], tissue engineering tumor destruction via heating ,MRI contrast enhancement and phagokinetic studies [120],delivering the drug precisely and safely to their target sites at the right time to have a controlled release and achieve the maximum therapeutic effect is a key issue in design and development of novel drug delivery system. Nanoparticles such as silver [121,122], zinc oxide [123,124] and polyethyleneimines nanoparticles [125] are incorporated into dental adhesive [126] or dental composite [127].The mechanism of action of these antibacterial nanoparticles may vary and include a generation of ROS [128] active transport metabolism of sugar [129] disruption of cell envelope disturbance in membrane electron transport [122]. The application of the biosensing field are known to be ecofriendly and less toxic. It has become a novel and very promising material for nanoelectronics, nanocomposites, opto-electronic devise, electrochemical super capacitor devise, fabricated field effect transistors, drug delivery system, solar cells, memory devices and constructed ultra-sensitive chemical sensors such as PH sensors, gas sensors and biosensors [130,131]. An ultrasensitive electrochemical immunosensor based on nano gold particles [Au-GN-HRP] is used as the label for the immunosensors. An electrochemical immunosensor for the sensitive detection of carbohydrate antigen was fabricated based on ionic liquid functionalized graphene and Cd+2 nanoparticles Tio2 drug biosensors using graphene and Na ion film modified GEC is fabricated for the detection codeine displaying [132].

1.	***Aquaspirillum magnetatactium***	Au	Biosensors Drug delivery Bioremediation	[133][69] [93]
2.	***Cupriavidus***	Ag	Biosensors Drug delivery Bioremediation Antibacterial agents	[133] [53] [134] [91] [135]
3.	***Fusarium oxysporum***	Au, Ag	Microscopy, catalysts	[136]
4.	***Fusarium oxysporum***	Ag2S BaTiO3	Biofilm Imaging microelectric device	[137] [138]
5.	***Plant stercullia***	Cu, CuO	Biosensors Antibacterial agent Cancer therapy Bioremediation	[139] [140] [141]
6.	***Clostridium aceticum***	Co	Bioremediation Surface modification	[142]
7.	***Pseudomonas aeruginosa***	Fe	Cleaning of contaminated land and water	[143]

8.	***Fusarium oxysporum***	Cds	Biosensors Drug delivery Electronic devices Biomarker, cell labeling agent	[144,145] [146] [147] [148]
9.	***Pseudomonas aeruginosa***	Li	Catalysts	[143]
10.	***Plant***	Ni	Catalysts Bioremediation	[144] [143]
11.	***Bacterial Sps.***	Pd	Catalysts Bioremediation	[145] [146]
12.	***Plant***	Pt	Biosensors Antibacterial agent Cancer therapy Bioremediation	[147] [148]
13.	***Bacillus subtilis***	Se	Biosensors	[149] [147]
14.	***Fusarium oxysporum***	SiO2	Biomedical therapy	[150]
15.	***Bacillus sps.***	Te	Antibacterial agent	[151]

2. CONCLUSION

This review provide a glimpse to some simpler nanoparticles which are being currently modified for their potential application are so beneficial to increase the production which are zero energy consuming and low cost .The synthesis of metallic nanoparticles using biological entities has the potential to deliver , new source of novel material that are stable , nontoxic , cost effective , environment friendly and synthesized using green approach .An increasing awareness towards green chemistry and use green route for the synthesis of metal nanoparticles lead a desire to develop environment friendly technique . Benefit of synthesis of metallic nanoparticles using plant and microorganism is that it is an economical, energy efficient, cost effective provides healthier work place and communities protecting human health and environment leading to lesser waste and safer product. It seems that several important technical challenges must be overcome before this green bio-based method will be a successful and competitive alternative for industrial synthesis of nanoparticles.

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