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Review Article

Green Synthesis of Metal Nanoparticles for Drug Delivery

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With the rapid advancement in the field of nanotechnology, the use of toxic chemicals can be eliminated with the help of certain medicinal plants which has a significant role for a better future in terms of nanoparticle synthesis and are known for their potent activity due to the presence of bioactive components. Owing to the large surface to volume ratio of the nanoparticles, they have been of immense importance for their effective utilization in various sectors such as in medicine, pharmaceutical, food industry and pharmaceutical sector. Recently several research findings has suggested the role of plants as an excellent source for the formation of nanoparticles as it requires less time and impose no threat to the environment. Therefore, the present review focuses on the methods of synthesis of AgNPs, ZnNPs, AuNPs which are mostly mediated by bacteria, fungi and different parts of the plant extracts and their possibility of usage in the field of biomedical sector anddiscusses it role in the drug delivery process. Furthermore, more detailed research and an in depth understanding on the assays has to be performed for getting the information about the toxicity of these nanoparticles.

Introduction

The concept of nanotechnology was first debated in 1974 by Japanese scientist Professor Norio Taniguchi. Nanotechnology refers to dealing with atoms or molecules at the nanoscale. The range of atoms is in the nano-meter range which is approximately one modicum of a meter. Modification of atoms at the nanoscale encircles physics, biology, engineering, imaging, and chemistry and is the amalgamation of all taken together. Since it is not possible for the naked eye to visualize such a tiny object therefore specialized microscopes like atomic force microscope and scanning tunnel microscope were made to picture those tiny particles.[1]

There are basically two types of nanoparticles, namely natural and man-made nanomaterials. Natural particles are one which naturally occurs in the environment for example, haemoglobin in blood, smoke and ash. On the other hand, man-made nanoparticles are designed by people. It includes exhaust occurring because of vehicles or by burning fossil fuels.

Nowadays there is a great application of green pharmaceuticals including biotechnology and chemistry for acquiring the safest and environmentally friendly methodologies. Also, to offer the specific target cells, raise the transport of drugs that are entirely soluble in water, and even co-delivery of several drugs altogether. Green synthesis has very low chances of failure and even has ease to signalize. The strategy of using plant-based nanoparticles employs a green environment and moreover is convenient to take on just by synthesizing metallic salt with the herbal extract at room temperature which hardly takes a few minutes. The main principle behind utilizing the concept of green synthesis is to make the process cheaper, safer and simple. Engaging with physical or chemical methods increases toxicity and reactivity which is hazardous to human health. Ultimately by making use of green nanotechnology we are contributing to environmental health [2].

There are two approaches for developing a nanoparticle via bottom-up methods. Top-down is a procedure of breaking down the large particle into smaller fine particles by using physical methods like laser, grinding, spark ablation, and milling. On the other hand, the bottom-up approach is being followed for the nanoparticles which are prepared through chemical and biological procedures by

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inserting an atom into the nuclei thereby creating a nano-sized particle.

This review discusses about various methods for the development of nanoparticles using green synthesis, also the importance of nanoparticles in the drug delivery system. For example, in the treatment of cancer using copper nanoparticles or in treating genetic diseases by using gold nanoparticles.

Benefits of using Green Synthesis for Drug Delivery

Synthesis of nanoparticles by safer, eco-friendly and non-toxic methods is now being employed. This *"Green synthesis"* has multiple advantages like proper size and stability [3]. Due to the small size of the metal, it creates the ease to deliver the nanoparticles for delivering drug to the target site by easily penetrating inside the small capillaries. Also, by getting absorbed by the cells and thus increasing the efficiency of accumulating the drug on the target site. Furthermore, green synthesis helps in extending the period for the release of drugs to the target site [4]. There are various methods to produce nanoparticles including chemical and physical methods. But in comparison to the chemical methods, biological synthesis of nanoparticles is moreover considered to be the most reliable method due to its one-step bio reduction procedure and the usage of a minimal amount of energy [3].

Green Methods of Developing Nanoparticles

Since ages, India has been the core of herbal studies. Now, in the era of technologies, our scientists are trying to incorporate herbal science with nanotechnological sciences for abetter yield and safest outcome. Few years back herbal medicines were not considered acceptable however, phytopharmaceutical research had made this possible. For example, in recent times exceptional attention is gained by SLN i.e. solid lipid nanoparticles in drug delivery systems with the help of the nanotechnology concepts. SLNs are submicron carrier lipids which are biodegradable and biocompatible moreover can deliver both hydrophilic and lipophilic drugs. SLNs are peculiarly used in central nervous system (CNS) disorders.

A great example of this research was carried out using *Hibiscus rosa sinensis* extract in curing depression, infertility in males and respiratory health. The loaded extract of the flower was inserted in SLN using glycerol monostearate. Firstly, the flower extract was transferred to liquefied glycerol monostearate which was further stored at a temperature of 70°C. The molten lipid extract mixture was homogenized for 5 minutes with an isothermal aqueous dispersion of soy lecithin and Tween 80. Afterwards, using ultrasonication this emulsion was converted into nanosized particles [5].

Green Synthesis of Silver Nanoparticles

Pertaining to the productive results of nanoparticles for drug delivery, this method is regarded as an effective means in transferring folic acid and doxorubicin, where folic acid in nanoparticles identifies the folate receptors in the cancer cells and attached doxorubicin helps in killing the cancerous cells [11].

By bacteria

Most of the bacteria are resistant to silver and therefore aids in making a clump of silver on the cell wall. Thus, this is known as the best biocompatible substance. Moreover, bacteria such as *Bacillus cereus* produces silver nanoparticles [12].

Silver nanoparticles by *Pseudomonas stutzeri* AG259. J. T. Trevors generously provided *Pseudomonas stutzeri* AG259 for this study. In Lennox L (LB) broth, the silver-resistant *Pseudomonas stutzeri* AG259 strain was kept alive. Bacteria were cultivated at 30°C for 48 hours in the dark on Lennox L (LB) agar substrate using 50 mM silver nitrate. This bacterial cell piles up the silver nanoparticles in large quantities that are up to 200 nm in *Pseudomonas stutzeri* culture supernatant. Developing cells were collected and fixed for 2 hours in distilled water containing 2.5 per cent glutaraldehyde. TEM was utilized to show that the silver-resistant bacteria strain *Pseudomonas stutzeri* AG259 can collect significant amounts of silver when grown in the presence of high concentrations of silver salts 50 mM $AgNO3$ [13]. Aqueous solution of silver nitrate was added to *Bacillus licheniformis*for the production of silver nanoparticles. The formation of AgNPs was stabilized by the enzymatic action of

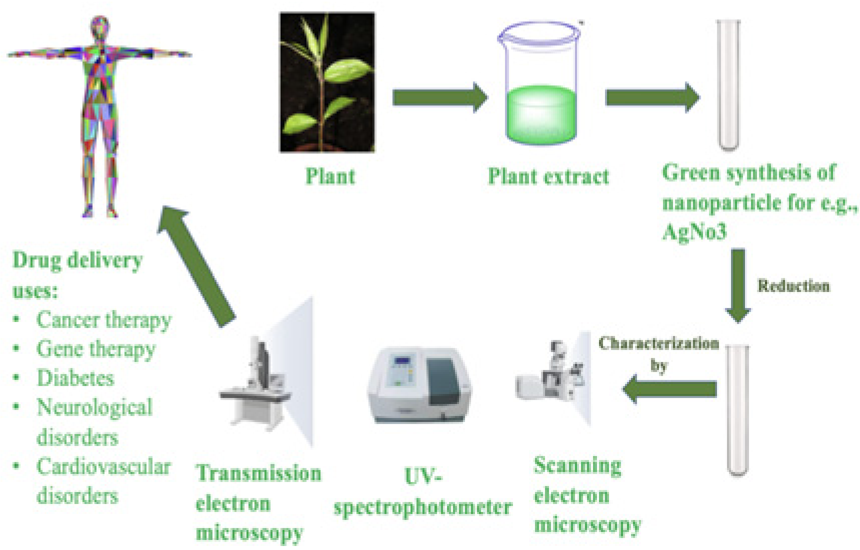

Figure 1: Green synthesis of nanoparticle for drug delivery

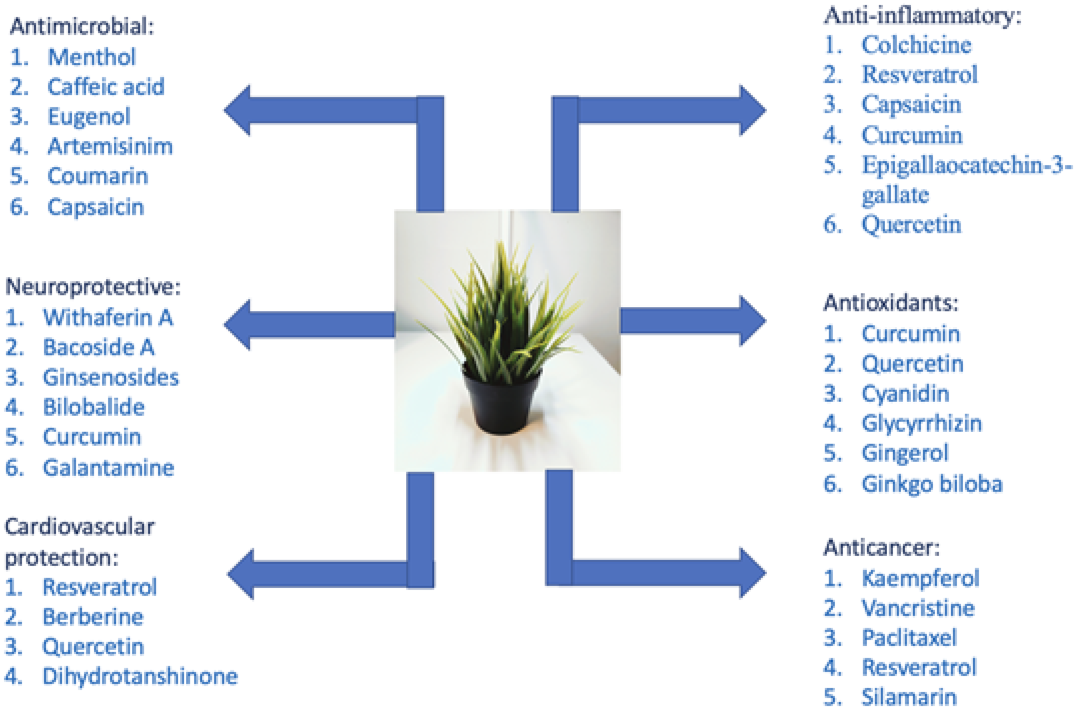

Figure 2: Natural phytocomponents used in green synthesis for drug delivery

nitrate. The size range of the resulting nanoparticles was found to be 50 nm. Completion of the process was indicated by a change in the coloration from white yellow to brownish colour.

The utilization of different types of broth aids in the advancement of the synthesis of intracellular and extracellular silver nanoparticles. The selection of bacteria makes the green synthesis method suitable for the large-scale production of nanoparticles. Despite numerous advantages, it has a few limitations which depicts that the preparation of nanoparticles by bacteria is a time taking process and thus can result in theformation of nanoparticles of various shapes and sizes. To overcome this problem, fungal strains are being used for the production of silver nanoparticles.

By fungi

Fungi have comparatively higher biocompatible space and binding capacity as compared to the bacteria and are the eukaryotic species,

Table 1: Peel extracts used for the green synthesis of nanoparticles

Peel Extract	Metal Nanoparticles	Functions	Ref.
Citrus sisnensis	Silver Nanoparticle	Photocatalytic activity Used in water purification systems.	[6]
Allium cepa	Zinc Oxide nanoparticle	Phytotoxicity on mung beans and wheat plant growth Chemical absorbent Polymer additives	[7]
Citrus limon	Silver nanoparticle	Antidermatophytic activity Resistant to Drugs	[8]
Punica granatum	Silver nanoparticle	Antibacterial activity Antimicrobial agents Acts as antioxidants	[9]
Musa	Gold nanoparticle	Antioxidant properties Antibacterial properties Catalytic properties	[10]
Phyllanthus emblica	Copper oxide nanoparticle	Anticancerous activity Antibacterial efficiency	[9]
Psidium guajava	Gold nanoparticles	Antioxidant property Anticancerous property	[9]

as they have membrane-bound organelles and clearly defined nuclei in their cells. They are considered as one of the most widely disseminated creatures on this globe and are vital to the environment and medicine. Most of the fungi live freely in the soil or water, while others have parasitic or symbiotic connections with plants or animals. The following are a few examples of the silver nanoparticles obtained from fungi.

Antibacterial effect on textile fabrics has been observed in silver nanoparticles from the extracellular synthesis of *Fusarium oxysporum*. In Petri plates, the fungal inoculum was made with 2% malt extract and 0.5 per cent yeast extract at 28°C. The liquid fungal growth was carried out for 6 days at 28°C in the presence of 0.5 per cent yeast extract. Before being used, cotton textiles were cleaned, sterilized, and dried. Final filtrate obtained was ultra-centrifuged for 5 minutes, and half of the filtrate was removed for the processing of silver nanoparticles in a more concentrated form. Cotton textiles were submerged in an Erlenmeyer flask of 50 ml volume and were shaken at 600 rpm for 24 hours before being dried at 70°C. *Staphylococcus aureus* (ATCC 6538), a Gram-positive pathogen, was used to test the antibacterial properties oftextiles. Cotton textiles were infected on *Staphylococcus aureus* inoculated agar plates. The concentration of the inoculum ranged between 1.3 and 1.6105 microliters per millilitre. Examination of the cotton textiles were performed using scanning electron microscopy [14]. Uniformly sized particles were formed by the fungi *Aspergillus flavus*. One of the research reports focuses on the creation of AgNPs in the presence of sunlight by utilizing the extract of *Aspergillus flavus* CR500. Their size dispersion varies from 60 to 130 nm, with a high concentration of silver, as indicated by the characterization techniques. This was validated by an energy-dispersive X-ray spectroscopy examination. For silver nanoparticles, X-ray diffraction and Fourier transform infrared studies revealed the crystalline character and active functional group availabilityfor the synthesized nanoparticles [15]. Synthesis of silver nanoparticles isbeing carried out under in-vitro conditions using *Penicillium fellutanum*which is extracted from the coastal mangrove sediments. After few minutes, the silver ion was found to come into the contact with the cell filtrate thereby accelerating the biosynthetic machinery. The presence of silver nanoparticles in the culture filtrate was verified by transmission electron microscopy in which a sharp absorption peak was observed at 430 nm. When the culture filtrate was treated with 1.0 mM AgNO3, by adding 0.3 per cent NaCl and its pH was maintained at 6.0 and was further incubated at 5 °C for 24 hours which indicated the biogenesis of nanoparticles at its peak level. Polyacrylamide gel electrophoresis was used to show that the culture filtrate, which had been precipitated with ammonium sulphate, had a particular protein band with a molecular weight of 70 kDa [16]. The formation of highly stable silver hydrosol took place by adding silver in *Fusarium oxysporum*. As a result, size of the nanoparticles wasin the range of 5-15 nm which was further stabilized by protein secreted fungus [5].

By Plant Extracts

Nowadays, nanoparticles synthesis via the plants extract is gaining much importance due to the presence of secondary metabolites which particularly aid in the process of greener synthesis. One such study has targeted the eco-friendly method of silver nanoparticle synthesis using the aqueous leaf extract of *Cucumis prophetarum*. The characterization techniques depicted the antibacterial property of biosynthesized silver nanoparticles against *Staphylococcus aureus* and *Salmonella typhi*. The antiproliferative potential of the Cp-AgNPs was evaluated for the obtained nanoparticles on A549, MDA-MB-231, MCF-7 and HepG2cell lines for cancer were found to be in the range of 105.8, 81.1, 94.2, and 65.6 ìg/mL respectively. The study inferred the potent activity of Cp-AgNPs for MCF-7 in comparison with the other different cell lines. Hence the study reveals it as a potential candidate for antibacterial, antiproliferative and antioxidant agent [28]. Similarly, the other group of researchers have reported the synthesis of silver nanoparticles using the leaf extract of *Tridax procumbens* which serve as an important capping agent for the process. The absorption spectra of the Tr-AgNPs were found at 370nm and the nanoparticles were observed in the spherical shape. Also, the antibacterial effect of Tr-AgNPs was evaluated against the multidrug resistant bacteria such as *E. coli*, *Shigella*, *Candida tropicalis*, *Aeromonas* and *P. aeruginosa*. Hence the study presented the role of the synthesized silver nanoparticles with a remarkable antibacterial property and an effective agent for the treatment of cells of lung carcinoma [17].

Most of the research findings have suggested the use of plants for the nanoparticles synthesis as it does not involve the use of toxic chemicals and has been considered as an eco-friendly method when talking in terms of sensitivity and its usage in medical field [18]. One such study has disclosed the development of nanoparticles using the aqueous leaf extract of *Azadirachta indica* which act as a capping agent. Various characterization techniques including UV spectroscopy, FTIR, TEM & DLS studies revealed the size and diameter of the nanoparticles formed which was reported to be in the range of 34nm and the UV spectra absorbance range of the formed nanoparticles was found at 436 nm. The nanoparticles formed were found to be effective against *S. aureus* which is a gram-positive bacteria and *E. coli* which is agram negative bacteria. Hence the results support the methodology of adopting the nanoparticles synthesis as a very efficient process as the reaction undergoes the completion process after 15mins and thus avoids the use of hazardous chemicals [19]. Many such studies have been conducted for the biogenic synthesis of silver nanoparticles using the leaf extract of *Buchanania lanzan* which is an endemic tree and contains lots of bioactive components in the form of tannins, saponins, flavonoids, glycosides, alkaloids, glucosides etc. Here the reduction process has been undergone with the 0.5mM concentration of silver nitrate solution. The color change of the solution was mediated from translucent to a brown color indicating the formation of Bl-AgNPs. The nanoparticles obtained were brought for the characterization where the UV- spectra of the nanoparticles obtained were recorded in between the 300- 600nm ranges. The assessment of the antifungal activity against *Rhizoctonia solanum* and wilt *Fusarium oxysporum* where the 47% inhibition was observed in case of *F. oxysporum* after the 5 days of incubation period observed at a concentration of 150ppm. Therefore, the study opens up the broader area for the usage of nanoparticles in the control of plant diseases. Moreover, the studies have been successful in presenting the valuable data for studying the phytopathogenic and antibacterial effects of the Bl-AgNPs [20]. But still the question lies in terms of effects and toxicity assays they may pose on soil, plants and onto the environment due to the long-term exposure. Therefore, there is a need for setting up certain guidelines for ensuring the better use of the advancement in the field of nanotechnology.

Green Synthesis of Zinc Nanoparticle

The emergence of metallic and metal oxide nanoparticles is gaining more attention due to their eco-friendly nature. Zinc oxide is of utmost importance in industrial as well as from the economic point of interest. The main characteristic that makes zinc oxide important is its antimicrobial activity, semi-conductivity, ultraviolet absorption and vulcanisation activator [16]. Copper nanoparticles high air sensitivity necessitates highly cautious and forbidding techniques to elude the development of copper oxide in the final making of the product. For example, cancer is one of the serious health issues all around the world. The standard approach includes surgery and chemotherapy. But this approach delivers only a restricted quantity of drug to the tumour site which leads to detrimental effects in the future. Therefore, localised drug delivery is important that includes the controlled delivery of drug to the target site hence improving patients' health. Intravenous thermosensitive hydrogels have drawn more attention and is one of the viable methods for delivering local anticancer drugs. To get a high drug loading, past biological membranes are drawn from the site of injection to the targeted site, or for both drug-loaded nanoparticles in a hydrogel without impairing the formation process, however, is difficult for this type of system. Hinderance in the delivery includes internalisation by cancer cells, accumulation at tumour locations, and deep penetration into the tumour interstitial and intracellular release of drugs [21]. In drug delivery zinc nanoparticles are doped with magnesium ferrite, coated with polyethylene glycol for biomedical applications. Further, the antimicrobial activity was evaluated against *E. coli* bacteria [17].

By Bacteria

The production of metal nanoparticles in bacterial culture can occur in an external or an internal environment. The pH of the solutions and the electrokinetic potential of microorganisms also play an important role in the reduction of metal ions. The study proposed that in the case of extracellular condition the proteins and the enzymes released by the bacteria in the process reduces the metal ion and also stabilizes the atom. **For example**, Tripathi *et al.* earlier reported nanoflower-shaped nanoparticles of zinc with average dimensions of 600 nm, which were biosynthesized via *Bacillus licheniformis* cell biomass. The rod-like agglomerated structures formed a nano-flower shape [22]. It is very much clear that on modifying the reaction conditions the form of biosynthesized nanoparticles could be customized. Previously, it was suggested that flower-shaped nanoparticles might be made with zinc nitrate as a precursor, which is consistent with the findings of this investigation. Similarly, *Staphylococcus aureus* was used to obtain zinc nanoparticles. Gram-positive, *Staphylococcus aureus*, and facultative anaerobic *cocci* are the most significant genus of *Staphylococcus* from a scientific standpoint [23]. Zinc oxide nanoparticles having a purity of more than 99 per cent, ranging in size from 10 to 30 nm are formed by this bacterium. In addition, activated ammonia from *Serratia ureilytica*was successful in the formation of zinc nanoparticles under thermal decomposition at 50 degrees Celsius. The fabric designed from cotton was submerged in a biogenic zinc ammonium complex medium and was subjected to heat treatment for varying period of time at an ideal temperature of 50°C (30, 60, 90min). The adhesion of zinc nanoparticles on the cotton fabric was verified by the crystal growth and morphological analyses. With increasing time length from 30 to 90 minutes, spherical to nanoflower-shaped particles were formed.

Simultaneously, the formation of zinc nanoparticles from intracellular synthesis is a much more complicated process. This is due to the composition and complexity of the living cell. Intercellular biosynthesis is probably the convincible method for the formation of zinc nanoparticles since it could internalize zinc [24].

Moreover, intracellular processes require a subsidiary step of cell lysis. This is to release the nanoparticles formed inside the bacteria. Thus, this technique is a bit more expensive and time-consuming than extracellular synthesis where the metal ions directly chelate themselves by the enzymes and the proteins present outside the cell.

By Fungi

Formation of metal nanoparticles by fungi and bacteria is almost similar. Zinc nanoparticle synthesis was produced using *Aspergillus fumigatus* by Raliya and Tarafdar. At room temperature, zinc oxide nanoparticles were made by reducing an aqueous zinc sulphate solution with cell-free filtrates from the fungus *Aspergillus fumigatus*. Even they proposed that the enzyme secreted by the fungi is important for the encapsulation of nanomaterial. [25]

The fungus is given more priority than bacterial culture due to its capability of producing higher amounts of metabolites. Moreover, fungal cells are more resistant to pressure, and the flow rate aids in the enhanced and the large-scale production.

By Plant Extracts

Plants are the best-suited substrate for nanoparticle production using non-toxic methods which are environmentally friendly pertaining to their cost-effective and less toxic nature. Furthermore, the plant extract is easily obtained by exposing the plant part to the solvent i.e., water or ethanol. Different parts of the plants are chosen for carrying out the experiment such as roots, fruits, seeds, and leaves.

There are many antioxidants present in the plants like phenolic acid, saponins, methylxanthines and flavonoids which are majorly responsible for the bio reduction of the metal ions and also in stabilising the green synthesis of metal nanoparticles. This mechanism was studied in *Moringa oleifera* leaves to chelate the metals from antioxidants at higher temperatures. This was then analyzed by using Fourier Transform Infrared Spectroscopy (FTIR). Once zinc metal is reduced, it reacts with the oxygen present in the solution to form zinc oxide [16].

Depending on the synthesis conditions, most scientists formulated different plant extracts to make copper nanoparticles of various sizes and forms. Copper-nanoparticles are known to be highly oxidant, and several difficulties with stability, oxidation resistance, and aggregation have been identified. As a result, the synthesis of CuNPs has not received as much attention as that of other elements. According to literature reported, copper nanoparticles are simply oxidized from the surfaces at ambient temperature. The use of different overlaying agents, such as polymers, and natural ligands, might resolve the concerns of clumping and oxidation [26].

The study conducted depicts the production of copper nanoparticles from leaves extracted from *Capparis zeylanica*using aqueous copper sulphate solution as a reducing agent[27**]**. The nanoparticles obtained after 12 hours were cubical in form and its size was found to be in the range of 50 to 100 nm. The microbicidal action of copper nanoparticles was examined against gram-negative and gram-positive microorganisms.Other investigations carried out green synthesis by utilizing the leave extract of *Hibiscus rosa-sinensis*by decreasing the copper nitrate solution. In the dark chamber, after few hours, the solution was maintained for 48 hours and spherical shaped copper nanoparticles were produced[28]. Researchers have reported the strong antimicrobial efficacy of copper nanoparticles against pathogens including *Bacillus subtilis* and *Escherichia coli*, which are both therapeutically relevant. Similar studies have shown the production of copper nanoparticles by utilizing the aqueous extract of cloves*Syzygiumaromaticum* in whichCopper sulphate was reduced in one hour thus, yielding spherical copper nanoparticles of size 5–40 nm [29]. Other group of researchers discovered that on adding the leave extract of *Ocimumsanctum*in 1mM in copper sulphate solution may help in reducing copper cations to copper nanoparticles in 8–10 minutes. As a result, this approach may be used to make copper nanoparticles in a quick and environmentally benign manner [30].

Green Synthesis of Gold Nanoparticles

The non-toxic nature and distinct optical, physicochemical, and biological characteristics of gold nanoparticles have been investigated for different nanotechnology-related medical aspects. The electric charge of gold nanoparticles, characterized by the electrokinetic potential, aids in the stability of their physicochemical properties, as well as their subsequent incorporation into cellular processes and bioaccumulation. As per the studies conducted, the toxicity level attributed to gold nanoparticles is largely proportional to the surface charge of particles. Therefore, positive-charged metal NPs lead to apoptosis at a significantly lesser dose, whereas neutral-charged NPs cause cell suicide in a much greater proportion [**31**].

By Bacteria

Owing to the less hazardous ingredients or harmful derivatives, the necessity for a cost-effective and environmentally acceptable synthesis of gold Nanoparticles utilizing microorganisms is taken into consideration. Enzymes such as laccases, peptides, ligninases and reductases are thought to be tangled in the development and gelation of nanoparticles. Several variables impact the synthesis and stability of gold nanoparticles during synthesis, including temperature, substrate concentration, pH, and static conditions. Nevertheless, research has been carried on how to improve these methods. Research indicates that*Klebsiella pneumoniae* promoted the production of gold nanoparticles and had a synergetic antibacterial impact against *Escherichia coli, Staphylococcus epidermidis, Staphylococcus aureus, Pseudomonas aeruginosa, and Bacillus subtilis* **[21]**. Another research displayed the bio-reduction of *Actinomycetes*in producing gold nanoparticles. The biosensor for the overall cells was constructed and described by utilizing glucose as the substrate analog and *Gluconobacteroxydans*immobilized on the graphite electrode using sol-gel (tetraethyl ortho silicate)/chitosan hybrid composite gold nanoparticles[32].

Extracellular Preparation of Colloidal Gold

In the occurrence of cells, a reduction-based technique of chloroauric ions is the strategy for extracellular synthesis of gold nanoparticles, and the biosynthesis is effective due to the essential involvement of the non-living components of the cell and its amino acid residues [6].

The metallic gold reduction process was effectively aided by oxidoreductase enzymes, yeast-mediated nano-gold production and quinones. The nitro-reductase enzyme, which is tangled in the bacterial-interceded production of suspended gold, is abundant in *Enterobacteriaceae* culture supernatants. A vast number of extracellular enzymes with diverse activities can be secreted by fungal strains. Externally released fungal proteins such as various hydrolases and amylases, -NADPH-dependent sulphite reductase, proteases and different cellulases have all stood to be efficient in the reduction of metallic gold ions [7].

Intracellular synthesis of colloidal gold

The research involved in cultivating Alfalfa plants in an environment which is rich in chloroauric acid, and the results indicated that the herbs had a remarkable capacity in generating inorganic nanoparticles in-situ within the vegetal cells. Growing *Sesbania drummondii* seedlings in chloroaurate solution resulted in the creation of stable gold nanoparticles inside various plant tissues due to the result of shoot-guided transport phenomena of root-located reduction activities. It has been observed that the cultures of *Brassica juncea* grown in gold pulverized based soil that has the capacity to limit the number of nanoparticles integrated into the vegetal tissue by chemically reducing gold ions [8].

By Plant Extract

Amalgamation of the plant's inorganic nanoparticle offers several benefits over the synthesis of microbes together with the elimination of onerous cell culture and the ability to generate vast quantities of NPs on a huge engineering gauge. The mechanism-guided synthesis method involves augmenting polyphenol-based secondary metabolites from plants as effective reductants for metal precursors [9]. The hydroxyl radical groups contained in plant-derived polyphenols were shown to be successful in the reduction of gold ions, promoting the oxidation reaction and the particular production of quinine forms. Electrostatic interactions prevent the further development of the formed gold nanoparticles, ensuring their stability. Theleaf extract of *Magnolia kobus* has been effectively utilized for the eco-friendly manufacture of gold nanoparticles**[10].** Scientists discovered a negative relationship between the forms and dimensions of the nanoparticles and the temperature required for the synthesis in the experiment. Findings suggests the execution of the synthesis procedure at 25° C would result in the creation of gold nanoparticles with a mean size of 5-300 nm, whereas doing the same experiment at 95 degrees Celsius resulted in the formation of 5-7 nm-sized nanogold.

Risk Factors Involving Green Synthesis

In heterogeneous processes, the advantages of utilising a high surface-to-mass ratio have been well proven, and the massive abilities of small particles that are suitable to function at the microscale have been discovered in nanotechnology about the actions of nanoparticles. Moving from the micro to the nanoscale has resulted in new uses for existing materials, as well as the discovery of novel nanomaterials. As a result, there is a ton of research going on with the prospective uses in most of the analytical and industrial sectors, as well as in the scientific applications in the medical grounds of disease detection, treatment, and drug administration.

However, there is a social obligation associated with the manufacturing and usage of nanomaterials, as well as their potential negative environmental impacts. The question on the widespread usage of nanomaterials might lead to a new population of nano pollutants which are distinct from those produced by retained macroscopic or microscopic particles thus, sharing numerous characteristics in association with the volatile chemicals and fumes. The uncontrolled release of nanoparticles containing heavy metals like cadmium which when combined with toxic components as overlaying constituents may serve to boost the accessibility of perilous substances in the atmosphere and can results in the formation of a new type of nano-pollutant with high reactivity and extremely small size, suitable for passing it through living cells.

The uncontrolled release of nanoparticles containing heavy metals like cadmium combined with toxic components as capping materials may serve to boost the accessibility of dangerous substances in the atmosphere and results in the formation of a new type of nano pollutant with high reactivity and extremely small size, suitable for passing it through living cells.

Working with nanomaterials that are free from any sort of toxic material from the start could be a good starting point for shifting from chemical synthesis to a greener nanotechnology approach with a strong focus on constituents and procedures that are not harmful to the environment or disastrous consequences dangers for operations so that our study does not come to a halt, and we can safely transit from the bench to the actual world. The development of sustainable nanotechnology is not just a moral concern, but also a practical one, but also a method to broaden the scope of our research, because not a single thing that begins with inappropriate hazardous ingredients can be expected to provide accurate results with a broad therapeutic or industrial use. As a result, we must be cautious in our study, taking into consideration its possibly dangerous parts in order to improve safety in our own research and potential uses, stepping away from just practical and successful outputs and toward environmental compatibility [29].

Conclusion

The greener approach towards the synthesis of metal nanoparticles via plant, microbial, polymer mediated methods has been discussed. Mostly research findings have reported the ability of various metals such as silver, gold, copper and Zinc with the potential of reduction by following the process of fabrication using the leaves, plant, seed and root extractshaving medicinal importance. The biocompatibility of the biological reagents does not require the use of the toxic chemicals as compared to the methods adopted using classical approach. Therefore, the eco-friendly approaches used for the synthesis of nanoparticles have a much greater and a possible future demand towards the biomedical sector in many forms thereby escalating its role for the less noxious environment.

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