Green-synthesis of metallic nanoparticles & their biomedical utilizations: 
An illustrative review
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Abstract
In modern days the study and research of metallic nanoparticles is one of the important fields of science due to its important application in the field of catalysis, bio-medical, sensors, antimicrobials, catalysis, agricultural field etc. The green synthesis of nanoparticles have proved to be better than the chemical method due to the large amount of capital involved in production in chemical method and it can solve the difficult environmental challenges like solar energy conservation, agricultural production, catalysis etc. These biocompatible nanoparticles exists in the form of mono-metallic nanoparticles or in two or more metals as alloys found extremely beneficial applications as antioxidant, anticancer, antimicrobial, antidiabetic, anticoagulant agents. In this review, an attempt is made to project the different routes of bio-synthesized processes to obtain metallic nanoparticles and their biomedical utilizations.
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1. Introduction
Nanoparticles are fundamental building block of nano technology, which is a interdisciplinary field of both science and technology that increase the scope of investing and regulating at cell level between synthetic material and biological system. The first person who talked about the nanoparticle was Richard Feynman. In 1959, he gave a description about the field of nano technology. This branch of science influences intensely and plays a major role in daily life as a result of their vast applications in all circles of human life. It is a branch of science that deals with several structures of matter that have sizes in the order of a billionth (10⁻⁹) of a meter, that is it deals with production, manipulation and use of materials in nano meter dimensions.
Nanomaterials represent the major tools of nanotechnological applications such as nanotubes, nanowires, nanoflowers and nanoparticles which are extensively studied and fabricated to various sizes and shapes as desire to fit into different applications. Nanomaterials have great importance in biological labeling, biosensing, catalysis, antibacterial activity, drug delivery, antioxidant applications, DNA sequencing and gene therapy in recent years[1].
Existing nanoparticles are mainly classified as metallic and non-metallic nanoparticles. Some widely investigated metallic nanoparticles are silver, gold, palladium, magnesium, manganese, platinum, titanium etc.
1.1 Reason to be considered as green
Various routes of synthesis to prepare the metallic nanoparticles are physical, chemical, and bio synthesis. The metallic nanoparticles can be effectively synthesize through the biological route. Moreover, the bio synthesis of metallic nanoparticles is eco friendliness and compatibility for
the pharmaceuticals and other biomedical applications like drug delivery. Also, green synthesis of metallic nanoparticles using biological molecules as means of bioreduction has received wide approval and patronage due to the wide availability of probable biological raw agents.

2. Bio-synthesis of nanoparticles

Bio-synthetic methods involves naturally occurring reducing agents such as polysaccharides, biological microorganism such as bacteria and fungus or plants extract, i.e. the environmental challenges towards green chemistry, have emerged as a simple and viable alternative to more complex chemical synthetic procedures to obtain metallic nano-particles.

The bark of *Cassia fistula* was used to synthesize gold nanoparticles by phytochemical method. Finely coarse powder of Carbon. *fistula stem* bark was used for phytochemical mediated synthesis of the gold nanoparticles. The synthesis was carried by Daisy and Saipriya (2012). Here bark powder was added to distilled water and continuously stirred; aqueous HAuCl4 was subsequently added to the mixture whilst stirring. Here the change of colour from brown to ruby red confirms the formation of gold nano-particles.[3]

In many studies fungi was used as a raw materials for the preparation of silver nano-particles. Wahabi et al(2011) used fungus *Trichoderma Reesei* to synthesize silver nanoparticles. Here the fungus *mycelium* is exposed to silver nitrate solution. As a result, the fungus produces enzymes and metabolites for its survival. These enzymes and metabolites convert the toxic silver nitrate into non-toxic silver nanoparticle by the process of reduction.[4]

*He et al. (2008), studied about Rhodopsseudomonas capsule* and synthesized different sizes of gold nanowires (10-20 nm).In this experiment, he used cell free extract of the plant *Rhodopsseudomonas capsule*. The positive point about this experiment is that the procedure used offered control in shapes when the concentration of HAuCl4 was altered in the mixture resulting in reduction of gold ions in the solution and biosynthesis of morphologies of gold nanostructures. It was found that the shape of the nanoparticle was spherical at lower concentration of gold ions in the aqueous solution where as at higher concentration nanowires were produced.[5]

Safiuddin et al.(2009), studied and used a combination technique of microwave irradiation and bacteria to synthesize silver nanoparticles. The conclusion was that by combining both these techniques, the production of nanoparticle was very rapid.[6]

In a study, extract of leaves of *Pongamia pinnata Pierre* was used for the synthesis of silver nanoparticles. Here the oven dried leaves were used. These extract was mixed with silver nitrate solution and it was then reduced by the extract to form silver nano-particles (Raut et al, 2010)

In a another research, an onion (*Allium cepa*) extract was used to synthesize silver nanoparticles. The rate of the formation was so rapid in this procedure because onion extract increases the reaction rate (Saxena et al. 2010). Here the silver nitrate solution was reduced by onion extract .

Dubey et al. 2009, synthesized silver nanoparticles from the extract of *Eucalyptus hybrida* leaf. In this procedure, methanolic biomass of Eucalyptus hybrida leaf was mixed with aqueous solutions of silver nitrate[7].

Another research was done by Ankanna et al. (2010), where highly dispersed silver nanoparticles were synthesized by using a dried stem bark of *Boswellia ovalifoliolata* (Anendemic plant) extract as the reducing agent. Here also silver nitrate solution was reduced by this extract. When silver ions are mixed to bark extract, rapid reduction of the silver ions was observed as a result silver nanoparticles was formed.This type of silver nanoparticles was used for the anti-bacterial treatment in modern days [8].

In a research, *euphorbia hirta* were used to form silver nanoparticles (Elumalai et al. 2010). Here the leaves of the plant were dried at first and then mixed with AgNO3 solution at room temperature. Then the supernated was centrifuge and exposed at high temperature to forming nano-particles. Selenium nano-particle is another type of important class which has a great impact in modern days. Initially selenium nano-particle was synthesize using *klebsiella pneumoniae* in selenium chloride solution (Fesharaki et al, 2010). Here *k. pneumoniae* was sterilized with selenium nanoparticles. It was noticed that the elemental selenium can be recover from the bacteria by they wet heat sterilization process [9].

Varshney et al.(2009) was reported about the
previously unexploited fungus *Hormoconis resinae* was exploited for synthesise of silver nanoparticle. On treatment of aqueous solution of silver with this extract, the resulting silver was fabricated within an hour. The resulting nanoparticle is polydisperse and have different morphologies and size ranging from 20 to 80 nm.[10]

Green synthesis of platinum nanoparticle was done by using naturally occurring polyphenols. In this procedure, this polyphenol was obtained from aqueous extract of *terminalia chebula*. The advantage of this method is no use of surfactant or stabilizing agent in the procedure. The resulting platinum nano-particle is found to be approximately 4 nm in size. Here the the oxidised polyphenols reduced platinum from Pt$^{4+}$ to Pt$^0$ [10].

3. Characterization techniques of nanoparticles

To understand particle size, size distribution, morphology, composition, surface area, surface chemistry, particle reactivity in solution etc extensive characterization of nanoparticles are required. The characterization can be done with the help of UV-Vis absorption spectroscopy, Scanning Electron Microscopy (SEM), transmission electron microscopy (TEM), Energy Dispersive x-ray Spectrometry (EDX), dynamic light scattering, X-ray diffraction technique, X-ray photoelectron spectroscopy. These methods were done over metals, metal oxides and different carbon based materials in cell culture media and aqueous media.

By the use of uv-vis spectroscopy, the optical properties of a solution can be determined. The spectrophotometer shows different absorption peak for various types of metallic nano particles. For example, in a study silver nitrate solution was mixed to *nerium obander* plant extract and the absorption peak comes at 410 nm (Subbaiya et al., 2014). For the synthesis of Iron nano-particles from *Azadirchta indica*, the absorption peak comes at 216-265 nm gold nanoparticles (Mishra et al., 2010). The surface Plasmon resonance band for the gold nano-particles synthesized by using *Klebsiella pneumonia* comes at 400-700 nm (World J. Sci. Technol., 2012). Again the gold nano-particles synthesized using marine *Entrococcus sp*. Produced absorption band at 540 nm (Nanomed. J., 2015). The stability of nano-particle with increase of time can also be determined by this peak observed.

With the help of XRD analysis, we can get information about the crystallographic structure of the nano particles. XRD analysis for various nanoparticles were done in so many research works to determine the high crystallinity of the sample. For example, the synthesis of gold nanoparticles of various shapes like hexgon, triangles etc were synthesized by reduction of gold chloride with the help of leaf extract of *Stevia rebaudiana*. The crystallinity nature of the gold nano-particles was confirmed by X-ray diffractometer (Mishra et al., 2010).

FTIR spectroscopy determines the nature of functional groups attach to nano-particles and structural features of herbal extracts used for corresponding preparation. The synthesis of silver nano-particles by using various types of plant leaf extract, fungi, bacteria has shown characteristic peaks in FTIR spectroscopy (Amudha Murugan et al., 2014).

The TEM analysis provides information about the morphology, size, size distribution, crystallinity of the sample etc and TEM with SAED gives information about crystal structure (Shobha et al., 2014). For example, TEM image pattern for marine *Entrococcus sp.* Confirms the uniform spherically shaped structure having average size about 10 nm.

SEM gives information about the size, shape and morphology of the synthesized nano-particles. During the analysis SEM requires preparation of sample, this involves the formation of a carbon based thin films on copper grids. *Asim Umer et al., 2012* used SEM analysis for the characterization of gold nano-particles synthesized by using *Turbinaria conoides* and noticed that the various shapes of nano-particles are formed like rectangle, square, cubic etc. Also the average diameter of the nano-particles are found to be 60 nm.

4. Biomedical applications of metallic nanoparticles in modern days:

In modern days, the nanoparticles which are the building block of nanotechnology has great influence on medicinal field. Metallic nanoparticles like silver and gold nanoparticles have high importance on treatment of fatal disease like cancer, which have been spread and affecting almost everywhere now a days. They works as
anti-cancer agent and used for treatment of a variety of human cells like lung, cardio, colon, prostate and breast cancer etc. Gold nanoparticles have also electron transferring ability and adsorptive capacity for which they are widely used in the manufacturing of biosensor. Thus gold nanoparticles are used for sensing toxic metals from the environment. As an example, it is used for detection of copper, which is a toxic pollutant in environment, also involved in Wilson’s disorder where the copper level is above than normal (S. Baker, M.N. Nagendra, S.Satish Prasad, 2016).[7]

The antimicrobial activity of the nanoparticle is also a great factor. Due to the size, shape and surface-volume ratio of the nanoparticles, they can produce a gap or pits and hence changes the permeability of the cell membrane of the fungi or bacteria. This inhibits the enzymatic activity of the respiration which results in apoptosis of the cells (S. Baker, S. Satish, 2015).

The silver nano-particle was extracted from papaya fruit by the cost effective way and the resulting nano-particle is found to be more effective to control the bacterial microorganism and thus has a great potential in bio-medical application (Jain et al., 2009).

Again in a study, an onion extract was used to prepare silver nano-particles, further it was found that these nano-particles have great potential to resist the antibacterial activity against E.coli and Salmonella typhimurium (Saxena et al., 2010).[6] Pal et al., (2007) carried out a study that includes differently shaped silver nano-particles. The experiment was done against the gram negative bacteria Escherichia coli. This was the first treatment of silver nano-particles against bacterial contaminants. The result clearly showed about the shaped dependent interaction of silver nanoparticles against gram -negative bacterial organism,[8] Gopalakrishnan et al., (2012), synthesized Cu2O nano-particle by using ridax procumbens leaf extract. The anti bacterial activity was tested against Escherichia coli as a model for gram-negative bacteria. The result had shown that the growth of bacteria was inhibited by 65%. Thus the metallic nanoparticles synthesized via green routes are highly toxic against multidrug resistant bacteria, hence they have a great application in bio-medical application.[8]

Conclusions

In modern days, the research on nano-particles can carry a great deal of interest and importance from all science related disciplines. Specially the importance of metallic nano-particle is so high as they deals widely with biomedical applications like imaging, sensing, drug delivery and gene targeting. Now-a-days they also widely used in detection, diagnosis and human cancer treatment. Gold and silver nano-particles synthesized from green plants or organisms take a special role against bacterial contaminants and thus set to be use as the antibacterial drug in the medicinal field. The use of UV-Vis absorption spectroscopy, TEM, SEM, XRD, FTIR analysis etc for characterization produced to set improvement in the field of nanotechnology. Due to use of these technique for characterization, the actual size, shape, morphology, crystalinity of the surface of the nano-particle can be known and thus can be recognize to use for a particular application.

Despite these advantages, in some cases nanoparticles possesses unusually high toxicity, also carry human and ecological health risks. Government around the world are in a state of dilemma of choosing between economy and ecological health risks. In spite of these challenging issues, there are numerous probabilistic and statistical models to determine the risk. The aim to be spread the nanotechnology is not to feel inadequate or fear, but rather to give importance on improvement of this field so that nanotechnology can uplift our daily life.

References


