Plant Mediated Green Synthesis of Metal Nanoparticles for Applications in Medicine

Syed Md Humayun Akhter[1,] Faiz Mohammad[1,*] and Shamim Ahmad[2]

[1]*Department of Applied Chemistry, Faculty of Engineering and Technology, AMU, Aligarh, India*

[2]*Microbiology Section, Institute of Ophthalmology, Faculty of Medicine, AMU Aligarh, India*

Abstract: The infectious diseases are one of the leading causes of death of children, adolescents and olds worldwide. Antimicrobial agents are commonly used to kill or inhibit the growth of these microorganisms. To date, herbal medicines are in great demand because of their efficacy, safety and fewer adverse effects as compared with prevailing antibiotics. However, a big challenge is to deliver the herbal formulations in a sustained manner to the infected region at the lowest effective level. Besides the development of alarming resistance of microbes towards antimicrobial agents is a major global public health problem. Nanomaterials seems to be effective alternative antimicrobials to combat such resistant bugs. Various physio-chemical methods have been employed for nanometal synthesis. Biosynthesis of nanometals using different parts of plants is now an emerging field of research in order to overcome the high cost and to minimize the use of hazardous chemicals in the traditional methods of synthesis. The nanometals synthesized using different parts of plants have been proven to be effective antibacterial agents. This review will describe the recent advancement in the green synthesis of nanometals using different parts of various plants and their antibacterial efficacy.

Keywords: Antibacterial efficacy, biosynthesis, nanometals, plant extracts.

1. INTRODUCTION

Infectious diseases claim 16.2 per cent deaths every year worldwide. More than 1000 epidemics of infectious diseases including avian flu, swine flu, polio, and cholera are reported in the past five years. Infectious diseases are the second leading cause of deaths worldwide and are responsible for more deaths annually than cancer. The global burden of infectious diseases is rising, affecting masses viz. number of people with influenza in 1918, HIV/AIDs in 1981, SARS in 2003, H1N1 in 2009 and recently Ebola in 2014. Antibiotics have played a very important role in combating such infectious diseases. The rising antimicrobial resistance in increasing number of pathogens limits the therapeutic options. Furthermore, due to the lack of financial support and incentives, the pharmaceutical companies are losing interest in antibiotic research and development [1]. So the need of the hour is to develop new antimicrobial agents to contest with the infectious diseases.

The use of herbs for treating various diseases dates back several eras. According to WHO, it is estimated that 80% of the world population use herbal medicines for primary health care. To date, the growing concerns of herbal drugs are their lower bioavailability, increased systemic clearance and elucidation of the metabolic pathways making them the poor candidates for therapeutic use. Nano-sized herbal drugs have potential future eliminating the problems associated with plant medicines. Due to their nanosize, they will help to cross all the barriers increasing the time for prolonged circulation in blood-making it fit for effective drug delivery system [2, 3]. To date, various toxic chemicals are being used either in the form of reducing agents or stabilizing agents for nanoparticle synthesis [4]. Green synthesis of metal nanoparticles has been an emerging highlight of the research in the field of nanobiotechnology and chemistry due to growing need for the development of the environmentally benign technologies, especially in material science and medicine. A lot of efforts have been invested into the synthesis of inorganic materials especially metal nanoparticles using microorganism and plants [4, 5, 6]. The rate of reduction of metal ions using plant extracts has been observed to be much faster as compared to that with microorganisms besides microorganisms being bio hazardous and expensive [7,8,9]. The reduction method using plant extracts is a one step, low cost and eco-friendly process, hence considered as the most preferred way for the synthesis of metal nanoparticles [10]. Thus, this method may be included in the class of green technology. Among various nanometals explored so far, nanoparticles of silver, gold, copper, zinc, palladium, titanium, nickel, indium etc. have been prepared by using a wide variety of plant extracts.

2. SYNTHESIS OF METAL NANOPARTICLES FROM PLANT EXTRACTS

Nanoparticles can be synthesized either through “top-down” process or a “bottom-up” process [11].

*Address correspondence to this author at Department of Applied Chemistry, Faculty of Engineering and Technology, Aligarh Muslim University, ALIGARH-202002, India; Tel: 0091-9412623533;
E-mail: faizmohammad54@rediffmail.com

E-ISSN: 2311-8792/16

Table 1: Green Synthesis of Nanometals from Different Parts of Plants

Trivial Name	Plant's Part/ Botanical Name	Nanoparticles	Morphology/ size	References
Alfalfa	Shoot, Root/ *Medicago sativa*	Ag^0	Icosahedral/ 2-4nm	[16]
Indian mustard	Shoot/ *Brassica juncea*	Au^0	- / 5-50nm	[17]
Alfalfa	Shoot/ *Medicago sativa*	Au^0	Icosohedron/ 4nm Twinned structures/ 6-10nm	[18]
Desert willow	Stem, Leaves *Chilopsis linearis*	Au^0	-/ 1.1nm	[19]
Rattlebush	Shoot, Root/ *Sesbania drummondii*	Au^0	Spherical/cytoplasm/ 6–20 nm	[20]
Common reed	Root/ *Phragmites australis*	Cu^0	Spherical cuboctahedron/ 10–15 Å	[21]
Soyabean	Sprouts/ *Glysine max*	Fe_3O_4	Spherical/ 8 nm	[22]
Common osier	Stem/ *Salix viminalis*	ZnO	-	[23]
Common osier	Stem/ *Salix viminalis*	$LaMnO_3$	-	[24]

Green synthesis of nanoparticles applies "bottom up" approach and it mainly relies on chemical and biological methods of production. Since ancient times different parts of the plants like root, stem, leaf, latex, seed etc. were used as a medicinal herb. To date, biological methods mainly rely on the plants for nanoparticles synthesis. The major classes of antibacterial compounds found in plants are phenolics, terpenoids, alkaloids, lectins, polypeptides and flavonoids. Medicinal plants mainly having high phenolic contents have drawn increasing attention due to their potent antioxidant properties. Recently, these plant parts have become the potential candidates for green synthesis of metal nanoparticles.

A good number of works have been reported for the green synthesis of nanometals from different parts of the plants (Table **1**). The first step of the synthesis is extraction from plant parts which can be done by the various methods like maceration, infusion, digestion, decoction. Hot continuous extraction by soxhlet apparatus is a general method of extraction from the plants [12]. Nanoparticles are synthesized from plant parts by mixing plant extract with metal salt solution at room temperature. (Figure **1**) shows a general method for green synthesis of metal nanoparticles. The reaction is complete within short period of time. Nanoparticles of silver, gold, iron, copper, palladium,

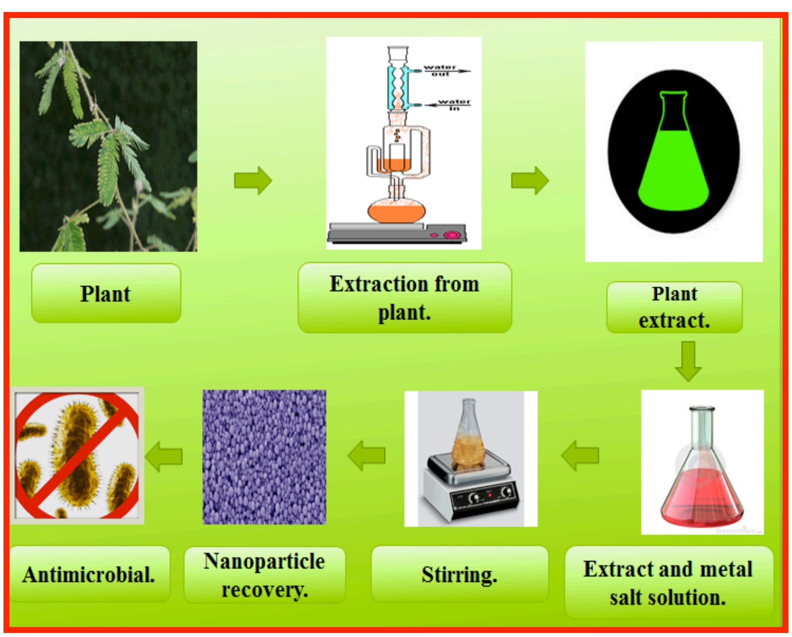


Figure 1: Green synthesis of metal nanoparticles.

platinum and many other metals have successfully been synthesized using plant extracts.

3. FACTOR INFLUENCING THE RATE OF NANOPARTICLES PRODUCTION

The rate of production of nanoparticles is affected by several factors like the nature of the plant extract, its concentration, the concentration of the metal salt, the pH, temperature and contact time etc. [13]. It was reported that changing the concentration of dried biomass changes the shape of the nanoparticles. For example, when Huang *et al*. synthesized the gold nanoparticles by varying the concentration of sundried *Cinnamomum camphora* leaves, the nanoparticles changed shape from nanotriangles to spherical [14]. In the case of *Medicago sativa*, an increase in reduction of metal salts is reported with the corresponding increase in the exposure time and substrate concentration [16]. In an experiment, Jae Yong Song and Beom Soo Kim reported that with an increase in temperature, rate of conversion by persimmon leaves broth into metal nanoparticles increases achieving 60% conversion at 250°C and 100% at more than 600°C [15]. The pH of medium affects the size and distribution of the nanoparticles. At low pH, coalescing of particles occurs, forming larger nanoparticles while at high pH values smaller particles are formed. This is due to the presence of different functional groups in the plant extracts.

4. CHARACTERIZATION OF NANOPARTICLES

Characterization refers to study the material's features such as its composition, structure, and various properties. Nanometals are in nanorange so they can be observed under the powerful microscope rather than with naked eyes. The basic information about the size and shape can be obtained by transmission electron microscope (TEM), scanning electron microscope [SEM], atomic force microscopy (AFM). The techniques of utmost significance in nanoscience are x-ray diffraction (XRD), energy dispersive spectroscopy (EDS), uv-visible spectrophotometry, dynamic light scattering (DLS) etc. Each and every characterization technique has its own importance, for example, uv-visible spectrophotometry is used to give qualitative and quantitative information of a given compound or molecule. The uv-vis spectroscopic analysis is generally carried out in the range of wavelength 300-700nm. A good number of works have been done to synthesize the silver nanoparticles and most of them reported the peak of absorption in the range of 350-500nm. Recently in our lab we have synthesized copper nanoparticles from leaves of *Swertia chiryta* plant. A small aliquot of diluted sonicated sample was used for detection of surface plasmon resonance property (SPR) of copper nanoparticles at the range of 200-700nm. The absence of sharp peak as shown in the Figure **2**(**a**) may be due to copper nanoparticles having diameters less than 10nm. However, large nanoparticles and clusters of small nanoparticles shows a surface plasmon peak at 550-575nm. The diverse absorbance intensities as shown by copper are due to vary particle size. Figure **2**(**b**) shows the EDS spectrum having the signals corresponding to copper nanoaparticles which confirms the presence of copper nanoparticles synthesized from *Swertia chiryta*. The peak of carbon and oxygen is also reported in the spectra. The carbon peak is due to carbon tape based attachment. The oxygen peak supports the presence of an oxygen containing functional group in the extract. Kirthika P *et al*. synthesized the silver nanoparticles

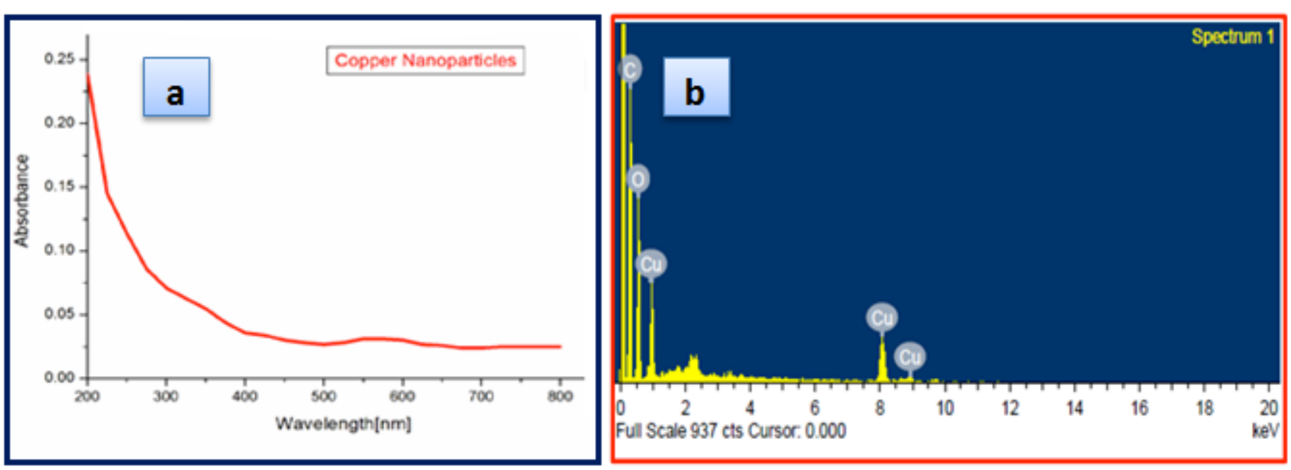


Figure 2: (a) Uv-visible spectrum of copper nanoparticles and **(b)** EDS spectrum of copper nanoparticles [our unpublished work].

and reported its surface plasmon resonance at 350-500nm range [25]. X-ray powder diffraction (XRD) is a rapid analytical technique for phase identification of a crystalline material and can provide information on unit cell dimensions. The studied material is finely ground, homogenized, and average bulk composition is determined. Yongqiang Zhang *et al*. biosynthesized silver nanoparticles from aqueous aloe leaves extract and reported that the diffraction peaks comes at 2θ=38.420,44.530 and 64.590 conforming the (fcc) lattice of silver nanoparticles [26]. Energy dispersive spectroscopy is used to study the elemental composition of metal nanoparticles. Figure **3**(**a**) shows IR spectrum of copper nanoparticles synthesize in our lab from the leaves of *Swertia chiryta*. The broad band observed near 3416cm^{-1} is likely due to O-H stretch from hydroxyl group expected to be present in biomolecules of plant material such as polyphenols. The band may also be at least partly due to attachment of water molecules. The band at 2935 cm^{-1} may be due to C-H stretching mode of hydrocarbon chain. The amide band from protein carbonyl stretch appears at 1622 cm^{-1} and has been noted elsewhere in similar plant based in analysis of nanoparticles, 1404 cm^{-1} is due to polyphenol present O-H, 1276 cm^{-1} shows aromatic primary amine. The SEM technique reveals information about the surface morphology, chemical compostion and orientation of materials. Figure **3**(**b**) shows the SEM image of copper nanoparticles where copper ions were reduced by biomolecules present in extract of *Swertiachiryta* [Our unpublished work]. Shanker *et al*. observed FTIR analysis peaks for silver nanoparticle at 1608cm^{-1}, 1384cm^{-1}, and 1076cm^{-1} and suggested the presence of flavanones and terpenoids adsorbed on the surface of metal nanoparticles which act as reducing agent [27].

5. PLANT PARTS USED IN THE SYNTHESIS OF METAL NANOPARTICLES [28]

5.1. Silver (Ag) Nanoparticles

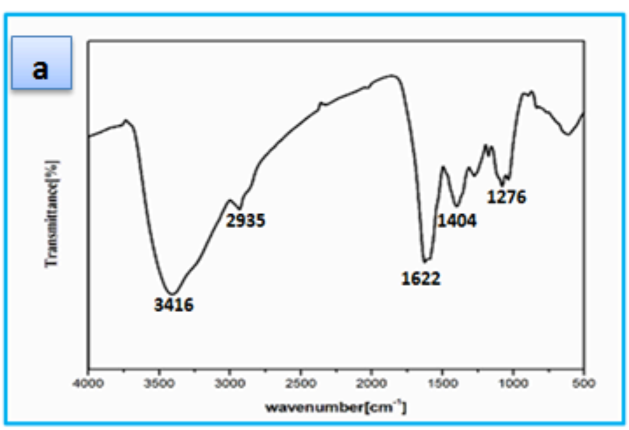
Plants leaves are widely used for the biosynthesis of nanoparticles. Some of the example of leaf mediated synthesis of silver nanoparticles are *Azadirachta indica, Aloe barbadensis, Cinnamomum camphora, Camellia sinensis, Lawsonia inermis, Phyllanthus amarus, Aloe ferox, Hibiscus rosa sinensis, Pinus desiflora, Ginko biloba, Platanus orientalis, Magnolia kobus, Diospyros kaki, Tanacetum vulgare, Syzygium aromaticum, Chenopodium album, Hevea brasiliensis, Capsicum annuum, Mentha piperita, Parthenium hysterophorus, Gliricidia sepium, Pelargonium graveolens, Acalypha indica, Eucalyptus hybrid, Cochlospermum gossypium, Ocimum sanctum, Murraya koenigii, Swietenia mahogany, Anacardium occidentale, Sesuvium portulacastrum, Enhydra fluctuans, Ludwigia adscendens, Garcinia mangostana, Nelumbo nucifera, Eclipta, Elaeis guineensis, Clerodendrum inerme, Lippia citriodora, Svensonia hyderabadensis, Coriandrum sativum, Moringa oleifera, Coleus amboinicus and Aloe barbadensis.*

The stem of *Desmodium triflorum, Calotropis procera,* and *Vitex negundo* were also used for the eco-friendly synthesis of silver nanoparticles.

Fruits of *Solanum lycopersicum*, *Allium cepa*, *Citrus limon*, *Helianthus annuus* and *Sorbus aucuparia* are being used for the silver nanoparticles synthesis.

5.2. Gold (Au) Nanoparticles

Leaf mediated green synthesis of gold nanoparticles using plants of *Pelargonium graveolens, Cymbopogon flexuosus, Azadirachta indica, Tamarindus indica, Aloe*



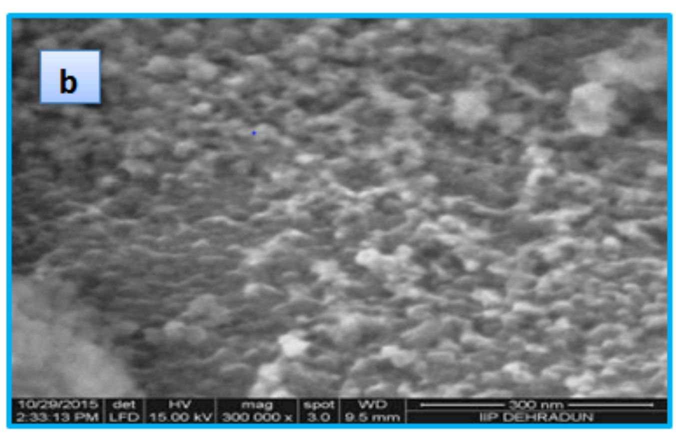


Figure 3: **(a)** FTIR spectrum of copper nanoparticles and **(b)** SEM image of copper nanoparticles [our unpublished work].

barbadensis, Cinnamomum camphora, Coriandrum sativum, Coleus amboinicus, Eucalyptus camaldulensis, Podospermum roseum, Camellia sinensis, Lawsonia inermis, Phyllanthus amarus, Aloe ferox, Hibiscus rosa-sinensis, Psidium guajava, Magnolia kobus, Diopyros kaki, Centella asiatica, Sorbus aucuparia, Rosa rugosa, Camellia sinensis, Olea europaea, Callistemon viminalis, Stevia rebaudiana, Magnifera indica, Ocimum sanctum, Murraya koenigii, Cinnamomum zeylanicum, Swietenia mahogany, Anacardium occidentale, Semecarpus anacardium and Solanum nigrum is a significant tool for the eco-friendly synthesis.

Fruits of *Emblica officinalis*, *Tanacetum vulgare*, *Pyrus sp*, *Citrus sinensis* and *Hovenia dulcis* were also used for the synthesis of gold nanoparticles.

5.3. Copper (Cu) Nanoparticles

Seeds of Soy beans, latex of *Calotropis procera*, leaves of *Tridax procumbens*, *Magnolia kobus, Ocimum sanctum*, Flowers and Buds of *Syzygium aromaticum*, Rhizomes *of Zingiber officinale* and Gum of *Gum karaya* have been used in the bio-reduction reaction for synthesis of copper nanoparticles.

5.4. Zinc (Zn) Nanoparticles

Leaf of *Coriandrum sativum, Calotropis Gigantea, Acalypha Indica* and Latex of *Calotropis procera* have been used for the biosynthesis of zinc nanoparticles.

5.5. Iron (Fe) Nanoparticles

Biosynthesis of iron nanoparticles using leaves of *Camellia sinensis*, *Tridax procumbens*, *Plantago majus*, *Dodonaea viscosa*, *Melaleuca nesophila*, dry fruits of *Terminalia chebula*, pericarp of *Eucalyptus globus* and peel of *Musa paradisiaca* were also reported in the literature.

6. THE ANTIBACTERIAL PROPERTY OF METAL NANOPARTICLES

The discovery of oligodynamic effect in 1893 by Karl Wilhelm von Nägel opened a new chapter of the toxic effect of metal ions on the microorganisms. This antimicrobial effect is shown by ions of mercury, silver, copper, iron, lead, zinc, bismuth, gold, aluminum and several other metals. Müller HE *et al*. investigated on oligodynamic action of the pure metal aluminium, antimony, bismuth, cadmium, cobalt, copper, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tin, titanium, and zinc on *Bacillus subtilis* (1 strain) *Enterobacteriaceae* (26 strains), *Legionellaceae* (13 strains), *Micrococcaceae* (6 strains) and *Pseudomonas aeruginosa* (4 strains) using the agar diffusion tests [29].

Apart from these metals, antimony, cobalt, gold and platinum also show antimicrobial effect. However, the synthesis of metal nanoparticles from the plant extracts and inorganic metal salts opened a new dimension in the field of microbiology. These nanoparticles show a better zone of inhibition against various microbes as compared to the plant extract alone. As the biological synthesis of nanoparticles opened a new area of research in the nanobiotechnology, a lot of work has already been done in this area.

6.1. Silver (Ag) Nanoparticles

Silver itself seems to be a potent candidate showing antibacterial property since ancient times. To date, the bottom-up approach for the synthesis of silver nanoparticles and its application as an antibacterial agent can be confirmed from a vast number of literature data. The biological reduction method using plant extracts is one step, low cost and eco-friendly, hence considered as the most preferred way for the synthesis of metal nanoparticles. The XRD pattern conforms that the silver nanoparticles formed by the reduction of Ag^+ ions by Neem leaf broth are crystalline in nature. The observed surface plasmon resonance at 450nm confirms the silver nanoparticles formation. The formation of silver nanoparticles by reduction of the metal ions is possibly facilitated by reducing sugars present in the Neem leaf extract [27]. R. Mariselvam synthesized silver nanoparticles from the extract of the inflorescence of *Cocos nucifera* and showed them to be active against the human bacterial pathogens viz., *Klebsiella pneumoniae*, *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Salmonella paratyphi* [30]. In the synthesis of silver nanoparticles at room temperature using aqueous aloe leaves extract, the particles formed are spherical with an average diameter of 20nm. The TEM micrograph showed that the silver nanoparticles were spherical with an average diameter of about 20nm. XRD showed the faced center cubic (fcc) lattice of silver nanoparticles [26]. The inhibition zone diameter of aloe leaves extract and silver nanoparticles against *Escherichia coli* was reported to be 6.7mm and 8.0mm respectively whereas inhibition zone diameter of aloe leaf extract and silver nanoparticles against *Staphylococcus aureus* was reported to be 6.1mm and 7.5mm respectively making silver nanoparticles as an encouraging candidate showing an antibacterial property.

The extract of olive leaf are rich in oleuropein and its derivatives such as hydroxytyrosol and tyrosol as well as cafeic acid, *p*-coumaric acid, vanillic acid, vanillin, luteolin, diosmetin, rutin, luteolin-7-glucoside, apigenin-7-glucoside and diosmetin-7-glucoside [31, 32] which are said to be responsible for reduction of silver ions to nanoparticles. The nanoparticles formed using the olive leaf extract were found to be less sensitive to gram-negative bacteria *Escherichia coli* and *Staphylococcus aureus* [33]. The extract of *Tinospora cordifolia* stems reported to be responsible for the reduction and stabilization of silver ions to silver nanoparticles. The nanoparticles synthesized were spherical in shape and their size was reported to be 36±9nm [34]. The synthesized nanoparticles have distinct antibacterial activity at the different concentrations of 6.25-200µg/mL. The zone of inhibition ranges from 10±0.58 to 21±0.25mm. A comparative study on bactericidal effect of silver nanoparticles, synthesized using green technology, in combination with antibiotics on *Salmonella typhi* was done and it was reported that the combination of silver nanoparticles and ampicillin is more effective than the combination of silver nanoparticles and gentamicin for *Salmonella typhi* having mean zone of inhibition 17mm and 15mm respectively [35].

6.2. Gold (Au) Nanoparticles

Shanker *et al*. reported the rapid synthesis of Au, Ag and bimetallic Au–Ag core shell nanoparticles using Neem (*Azadirachta indica*) leaf broth. λ_{max} for the gold nanoparticles was observed at 550nm. The XRD pattern thus clearly reports that the gold nanoparticles formed by the reduction of $AuCl_4^-$ by Neem leaves broth are crystalline in nature [27]. In a typical experiment, extract of tamarind was used for the reduction of Au^{3+} ions to Au^o. The TEM image appeared to be predominantly triangular and hexagonal in morphology. This study thus shows that films of the gold nanotriangles may be used with important implications for vapour sensing [36]. The leaf extract of *Mentha piperita* was used for the synthesis of gold nanoparticles and it was reported that they are also spherical in shape in the range of 150nm. The gold nanoparticles showed antibacterial activity against *Escherichia coli* whereas it didn’t show any antibacterial activity against *Staphylococcus aureus* [37]. In another experiment, A. Muthuvel *et al*. used *Solanum nigrium* leaf extract to biosynthesize Au-nanoparticles which inhibited the growth of medically important pathogenic gram-positive bacteria (*Staphylococcus saprophyticus* and *Bacillus subtilis*) and gram-negative bacteria (*Escherichia coli and Pseudomonas aeruginosa*) [38]. In the synthesis of gold nanoparticles using *Salicornia brachiata* plant, the particles are in the size range of 25-35nm as appeared under TEM. The aqueous extract contains polyphenols, glycosides, flavonoids, carbohydrates and proteins which are said to be responsible for the reduction of gold ions. A comparative study of antibacterial property of Au-nanoparticles and ofloxacin was made individually as well as the combined effect of Au-nanoparticles and ofloxacin antibiotic was also observed. It was reported that the combined effect of Au-nanoparticles and ofloxacin antibiotic shows higher antibacterial activity than individuals having a zone of inhibition 27mm against *Escherichia coli* as compared to12mm for Au nanaoparticles and 21mm for oflaxacin respectively [39].

6.3. Copper (Cu) Nanoparticles

Copper and its alloys brasses, bronzes, cupronickel, copper-nickel-zinc and several others are natural antimicrobial materials. Yoon *et al*. have made a comparative study of silver and copper nanoparticles and reported that copper nanoparticles seem to be surpassing silver on antibacterial activity using *Escherichia coli* and *Bacillius subtilis* [40]. S.C.G. Kiruba Daniel *et al*. reported on the use of fresh *Dodonaea viscosa* leaves as an effective reductant for making copper nanoparticles with size ranging from 30 to 40nm. The typical XRD spectra of the as-synthesized Cu nanoparticles confirms the resultant particles consists of face-centred cubic (FCC) copper nanoparticles. Different zone of inhibitions of synthesized Cu nanoparticles (10g) were reported against *Escherichia coli* (9mm), *Klebsiella pneumonia* (14mm), *Pseudomonas fluoro Terminalia arjuna scens* (8mm), *Bacillus subtilis* (9mm), *Staphylococcus aurous* (10mm) [41]. In another report microwave was used for the biogenic synthesis of stable copper nanoparticles using *Terminilia arjuna* bark extract which reduces $Cu^{2+} \rightarrow Cu$. The characterization techniques, XRD and uv-visible confirm the formation of copper nanoparticles. The antibacterial activity was done by disc diffusion method and it was found that Cu nanoparticles dried at room temperature show the better antibacterial property as compared to Cu dried at 700°C [42]. Recently, we have biosynthesized the copper nanoparticles from plant extract. TEM image (Figure **4**) show of copper nanoparticles in which majority of particles are of spherical shape and well distributed. The average diameter is within the range of 9-15nm.

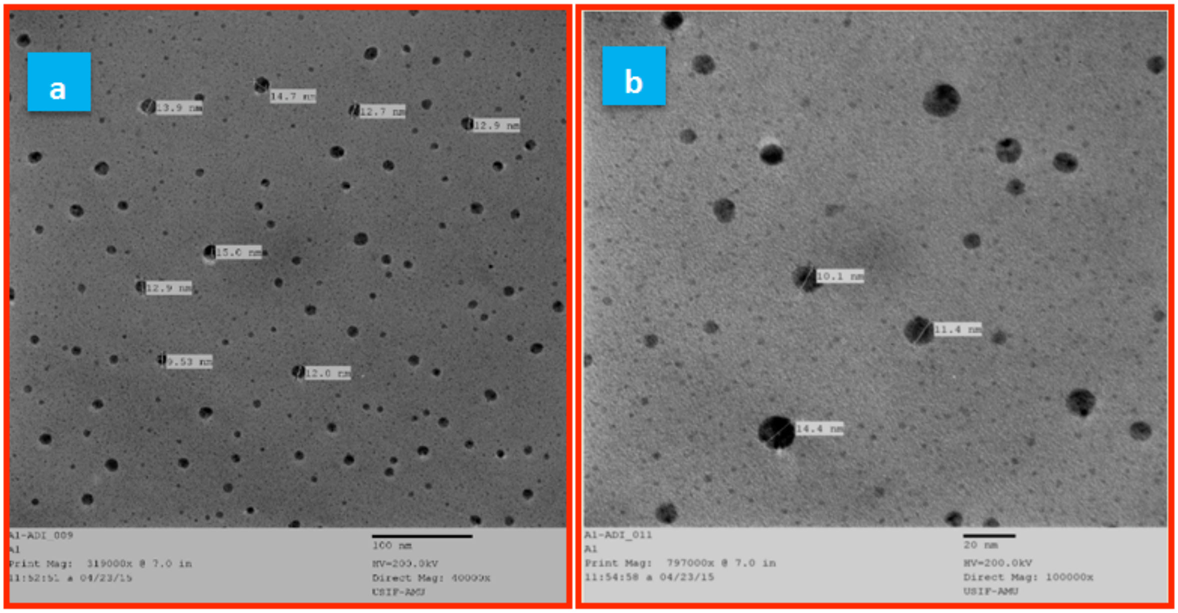


Figure 4: TEM images of biosynthesized copper nanoparticles [our unpublished work].

6.4. Iron (Fe) Nanoparticles

Monalisa Pattanayak and PL. Nayak *et al*. used extracts from 10 plant parts that include mango leaves, clove buds, black tea, green tea leaves, coffee seeds, rose leaves, cumin seeds, oregano leaves, thymol seeds, curry leaves for reducing ferric ions. The SEM image confirms the size of iron nanoparticles having diameter 50-100nm [43]. C. Narendhar *et al*. synthesized iron nanoparticles by using the extracts of *Cuminum cyminum* and *Ocimum tenuiflorum* in the ratio 2:1. The size of these nanoparticles obtained by green synthesis was 239.7nm as detected by particle size analyzer. Iron nanoparticles formed were reported to have high antimicrobial activity [44]. An *in vitro* comparative antibacterial efficacy of iron nanoparticles, plant extract and iron nanoparticles treated with plant extract was reported against *Escherichia coli* MTCC 443, *Proteus mirabilis* MTCC 425 and *Bacillus subtilis* MTCC 441. The results showed a striking zone of inhibition on *Proteus mirabilis* and *Escherichia coli* with iron nanoparticles [45].

6.5. Zinc Oxide (ZnO) Nanoparticles

It has wide application in medicine, electronics, rubber manufacture, ceramic industry etc. The fine particles of zinc oxide have deodorizing and antibacterial properties and for that reason are added into materials including cotton fabric, rubber, oral care products and food packaging etc. The antibacterial property of ciprofloxacin is enhanced on adding zinc oxide nanoparticles into it. ZnO nanoparticles of spherical and hexagonal shapes with an average particle size ranging between 20 and 50nm have been produced using *Plectranthus amboinicus* leaf extract. It was reported that the zinc nanoparticles synthesized from plant extract show zone of inhibition 11mm and 13mm observed at 8µg/mL and 10µg/mL MRSA ATCC 33591 [46]. M. Ramesh *et al*. synthesized 29.79nm Zinc Oxide Nanopaticles nanoparticles using *Solanum nigrum* leaf extract. The formed nanoparticles had considerable antibacterial property against *Staphylococcus aureus, Escherichia coli, Salmonella paratyphi, Vibrio cholerae* as compared to the standard tablet with highest antibacterial property against *Staphylococcus aureus* MIC having (17mm) [47].

7. MECHANISM OF BACTERIAL ACTION

A number of studies have been done on the mechanism of interaction of nanoparticles with microbes especially that of silver nanoparticles, but still it remains a debated topic for further study. Ag nanoparticles may cause cell damage by interacting with the sulfur rich protein and DNA. The data available suggest that antibacterial activity may be due to both the nanoparticles and ions having the similar mechanism of action [48]. Klasen reported that the respiration process in bacteria is inhibited when silver nanoparticles interact with the thiol groups found in the respiratory enzyme [49]. Figure **5** shows schematic action of Ag nanoparticles, Ag^+ and ROS inducing damage to mitochondria and DNA of bacterium.

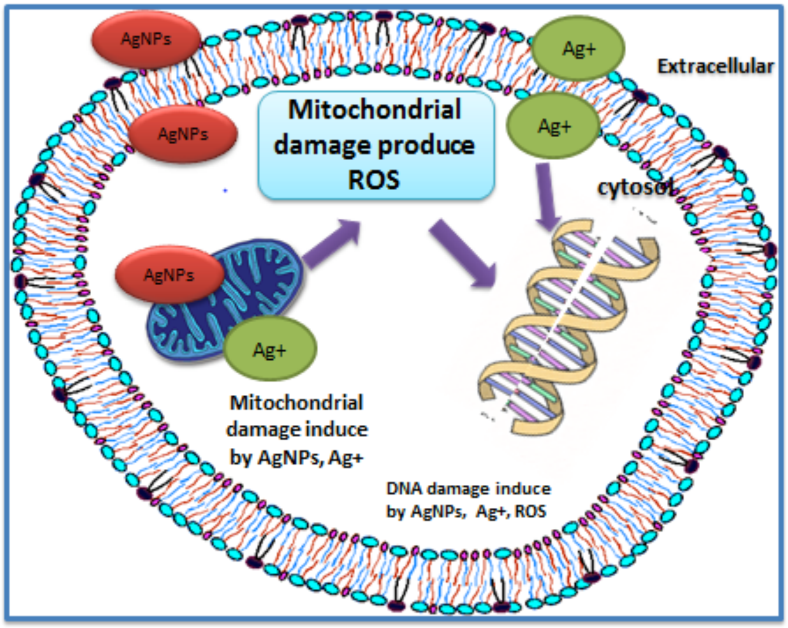


Figure 5: Schematic action of Ag nanoparticles, Ag^+ and ROS inducing damage to mitochondria and DNA of bacterium.

8. CHALLENGES AND FUTURE PROSPECTS

To date, biosynthetic methods reported in the literature so far have been devoted mainly to the production of nanoparticles itself while little work has been done for the mechanistic pathways of the synthesis reaction. Biogenic synthesis involves the use of an extract from some natural plant or microbial source, which itself is a cocktail of several different compounds actually act as a reducing and stabilizing agents. In most of the reported cases, little attention has been given to identifying these active compounds. Yet such information is essential for large scale of production. Most of the literature has reported only spherical mono-metallic nanoparticles. However, emphasis should be given to the synthesis methods which yields regular non-spherical shapes like rods, prisms or polyhedra, as well as bimetallic or trimetallic nanoparticles with alloy or core–shell morphology, in a strictly exclusive and deterministic manner.

CONCLUSIONS

Biogenic synthesis of nanoparticles from plant extracts is a promising area of research because it is one step, rapid, eco-friendly and economically viable. There are various applications of metal nanoparticles in various fields like in medicine as an antimicrobial agent. Silver and another metal synthesized from plant extracts seem to be an effective antimicrobial agent against the various pathogens. Being a panacea of all technical ills, nanoparticles have also wide applications in electronics as biosensors, in agriculture as pesticides, in food packaging, treating waste water effluent etc. It is expected that traditional medicines along with nanocarriers will overcome the existing problem of effective drug delivery systems. Nanocarriers along with herbal drugs will reach the site of action directly and will increase the prolonged circulation of the drug into the blood.

ACKNOWLEDGEMENT

The author, Syed Md Humayun Akhter gratefully acknowledges financial support from the University Grants Commission (New Delhi) in the form of Maulana Azad National Fellowship For Minority Students.

REFERENCES

[1] Freire-Moran L, Aronsson B, Manz C, Gyssens IC, So AD, Monnet DL, *et al*. Critical shortage of new antibiotics in development against multidrug-resistant bacteria—Time to react is now. Drug Resistance Updates 2011; 14(2): 118-124. http://dx.doi.org/10.1016/j.drup.2011.02.003

[2] Yadav D, Suri S, Choudhary A, Sikender M, Hemant BN. Novel approach: Herbal remedies and natural products in pharmaceutical science as nano drug delivery systems. Int J Pharm Tech 2011; 3(3): 3092-3116.

[3] Bairwa NK, Sethiya NK and Mishra SH. Protective effect of stem bark of *Ceiba pentandra* Linn. Against paracetamol-induced hepatotoxicity in rats. Pharmacognosy Research 2010; 2(1): 26-30. http://dx.doi.org/10.4103/0974-8490.60584

[4] Nadagouda MN, Hoag G, Collins J and Varma RS. Green synthesis of Au nanostructures at room temperature using biodegradable plant surfactants. Crystal Growth and Design 2009; 9(11): 4979-4983. http://dx.doi.org/10.1021/cg9007685

[5] Luangpipat T, Beattie IR, Chisti Y and Haverkamp RG. Gold nanoparticles produced in a microalga. Journal of

Nanoparticle Research 2011; 13(12): 6439-6445. http://dx.doi.org/10.1007/s11051-011-0397-9

[6] Rajesh S, Raja DP, Rathi JM and Sahayaraj K. Biosynthesis of silver nanoparticles using *Ulva fasciata* (Delile) ethyl acetate extract and its activity against *Xanthomonas campestris* pv. *malvacearum*. Journal of Biopesticides 2012; 5: 119-128.

[7] Ankamwar B, Damle C, Ahmad A and Sastry M. Biosynthesis of gold and silver nanoparticles using *Emblica officinalis* fruit extract, their phase transfer and transmetallation in an organic solution. Journal of Nanoscience and Nanotechnology 2005; 5(10): 1665-1671.

[8] Bar H, Bhui DK, Sahoo GP, Sarkar P, De SP and Misra A. Green synthesis of silver nanoparticles using latex of *Jatropha curcas*. Colloids and Surfaces A: Physicochemical and Engineering Aspects 2009; 339(1): 134-139. http://dx.doi.org/10.1016/j.colsurfa.2009.02.008

[9] Sathishkumar M, Sneha K, Kwak IS, Mao J, Tripathy SJ and Yun YS. Phyto-crystallization of palladium through reduction process using *Cinnamom zeylanicum* bark extract. Journal of Hazardous Materials 2009; 171(1): 400-404. doi:10.1016/j.jhazmat.2009.06.014

[10] Dhuper, Sandeep, Darshan Panda and Nayak PL. Green synthesis and characterization of zero valent iron nanoparticles from the leaf extract of Mangifera indica. Nano Trends: J Nanotech App 2012; 13(2): 16-22.

[11] Sepeur S. Nanotechnology: technical basics and applications. Vincentz Network GmbH and Co KG; 2008.

[12] Sukhdev SH, Suman PS, Gennaro L and Dev DR. Extraction technologies for medicinal and aromatic plants. United Nation Industrial Development Organization and the International Center for Science and High Technology 2008; 116.

[13] Dwivedi AD and Gopal K. Plant-mediated biosynthesis of silver and gold nanoparticles. Journal of biomedical nanotechnology 2011; 7(1): 163-164. http://dx.doi.org/10.1166/jbn.2011.1250

[14] Huang J, Li Q, Sun D, Lu Y, Su Y, Yang X, *et al.* Biosynthesis of silver and gold nanoparticles by novel sundried *Cinnamomum camphora* leaf. Nanotechnology 2007; 18(10): 105104-105115. http://dx.doi.org/10.1088/0957-4484/18/10/105104

[15] Song JY and Kim BS. Rapid biological synthesis of silver nanoparticles using plant leaf extracts. Bioprocess and Biosystems Engineering 2009; 32(1): 79-84. http://dx.doi.org/10.1007/s00449-008-0224-6

[16] Gardea-Torresdey JL, Gomez E, Peralta-Videa JR, Parsons JG, Troiani H and Jose-Yacaman M. Alfalfa sprouts: a natural source for the synthesis of silver nanoparticles. Langmuir 2003; 19(4): 1357-1361. http://dx.doi.org/10.1021/la020835i

[17] Marshall AT, Haverkamp RG, Davies CE, Parsons JG, Gardea-Torresdey JL and Van Agterveld D. Accumulation of gold nanoparticles in *Brassica juncea*. International Journal of Phytoremediation 2007; 9(3): 197-206. http://dx.doi.org/10.1080/15226510701376026

[18] Gardea-Torresdey JL, Parsons JG, Gomez E, Peralta-Videa J, Troiani HE, Santiago P, *et al*. Formation and growth of Au nanoparticles inside live alfalfa plants. Nano Letters 2002; 2(4): 397-401. http://dx.doi.org/10.1021/nl015673+

[19] Rodríguez E, Peralta-Videa JR, Sánchez-Salcido B, Parsons JG, Romero J and Gardea-Torresdey JL. Improving gold phytoextraction in desert willow (*Chilopsis linearis*) using thiourea: a spectroscopic investigation. Environmental Chemistry 2007; 4(2): 98-108. http://dx.doi.org/10.1071/EN06048

[20] Sharma NC, Sahi SV, Nath S and Parsons JG, Gardea-Torresde JL and Pal T. Synthesis of plant-mediated gold nanoparticles and catalytic role of biomatrix-embedded nanomaterials. Environmental Science and Technology 2007; 41(14): 5137-5142. http://dx.doi.org/10.1021/es062929a

[21] Manceau A, *et al*. Formation of metallic copper nanoparticles at the soil−root interface. Environmental Science and Technology 2008; 42(5): 1766-1772. http://dx.doi.org/10.1021/es072017o

[22] Cai Y, Shen Y, Xie A, Li S and Wang X. Green synthesis of soya bean sprouts-mediated superparamagnetic Fe_3O_4 nanoparticles. Journal of Magnetism and Magnetic Materials 2010; 322(19): 2938-2943. http://dx.doi.org/10.1016/j.jmmm.2010.05.009

[23] Lukaszewicz JP, Wesołowski RP and Cyganiuk A. Enrichment of *Salix viminalis* wood in metal ions by phytoextraction. Polish Journal of Environmental Studies 2009; 18(3): 507-511.

[24] Cyganiuk A, Klimkiewicz R, Olejniczak A and Lukaszewicz JP. Biotechnological fabrication of $LaMnO_3$-carbon catalyst for n-butanol conversion to ketones. Carbon 2010; 48(1): 99-106. http://dx.doi.org/10.1016/j.carbon.2009.08.034

[25] Kirthika P, Dheeba B and Sivakumar R. Plant Mediated Synthesis and Characterization of Silver Nanoparticles. International Journal of Pharmacy and Pharmaceutical Sciences 2014; 6(8): 304-310.

[26] Zhang Y, Cheng X, Zhang Y, Xue X and Fu Y. Biosynthesis of silver nanoparticles at room temperature using aqueous aloe leaf extract and antibacterial properties. Colloids and Surfaces A: Physicochemical and Engineering Aspects 2013; 423: 63-68.

[27] Shankar SS, Rai A, Ahmad A and Sastry M. Rapid synthesis of Au, Ag, and bimetallic Au core–Ag shell nanoparticles using Neem (*Azadirachta indica*) leaf broth. Journal of Colloid and Interface Science 2004; 275(2): 496-502. http://dx.doi.org/10.1016/j.jcis.2004.03.003

[28] Narayanan KB and Sakthivel N. Green synthesis of biogenic metal nanoparticles by terrestrial and aquatic phototrophic and heterotrophic eukaryotes and biocompatible agents. Advances in Colloid and Interface Science 2011; 169(2): 59-79. http://dx.doi.org/10.1016/j.cis.2011.08.004

[29] Łukaszewicz JP, Wesołowski RP and Cyganiuk A. Enrichment of *Salix viminalis* wood in metal ions by phytoextraction. Polish Journal of Environmental Studies. 2009; 18(3): 507-511.

[30] Mariselvam R, Ranjitsingh AJ, Nanthini AU, Kalirajan K, Padmalatha C and Selvakumar PM. Green synthesis of silver nanoparticles from the extract of the inflorescence of *Cocos nucifera* (Family: *Arecaceae*) for enhanced antibacterial activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2014; 129: 537-541. http://dx.doi.org/10.1016/j.jcis.2004.03.003

[31] Bianco A and Uccella N. Biophenolic components of olives. Food Research International 2000; 33(6): 475-485. http://dx.doi.org/10.1016/j.saa.2014.03.066

[32] Farag RS, El-Baroty GS and Basuny AM. Safety evaluation of olive phenolic compounds as natural antioxidants. International Journal of Food Sciences and Nutrition 2003; 54(3): 159-174. http://dx.doi.org/10.1016/j.colsurfa.2013.01.059

[33] Khalil MM, Ismail EH, El-Baghdady KZ and Mohamed D. Green synthesis of silver nanoparticles using olive leaf extract and its antibacterial activity. Arabian Journal of Chemistry 2014; 7(6): 1131-1139. http://dx.doi.org/10.1016/S0963-9969(00)00072-7

[34] Selvam K, Sudhakar C, Govarthanan M, Thiyagarajan P, Sengottaiyan A, Senthilkumar B, *et al.* Ecofriendly biosynthesis and characterization of silver nanoparticles using *Tinospora cordifolia* (Thunb.) Miers and evaluate its antibacterial, antioxidant potential. Journal of Radiation

Research and Applied Sciences 2016. http://dx.doi.org/10.1080/0963748031000136306

[35] Rajawat S and Qureshi MS. Comparative study on bactericidal effect of silver nanoparticles, synthesized using green technology, in combination with antibiotics on *Salmonella typhi*. Journal of Biomaterials and Nanotechnology 2012; 3(4): 480-485. http://dx.doi.org/10.4236/jbnb.2012.34049

[36] Ankamwar B, Chaudhary M and Sastry M. Gold nanotriangles biologically synthesized using tamarind leaf extract and potential application in vapor sensing. Synthesis and Reactivity in Inorganic, Metal-Organic and Nano-Metal Chemistry 2005; 35(1): 19-26. http://dx.doi.org/10.1081/SIM-200047527

[37] MubarakAli D, Thajuddin N, Jeganathan K and Gunasekaran M. Plant extract mediated synthesis of silver and gold nanoparticles and its antibacterial activity against clinically isolated pathogens. Colloids and Surfaces B: Biointerfaces 2011; 85(2): 360-5. http://dx.doi.org/10.1016/j.colsurfb.2011.03.009

[38] Muthuvel A, Adavallan K, Balamurugan K and Krishnakumar N. Biosynthesis of gold nanoparticles using *Solanum nigrum* leaf extract and screening their free radical scavenging and antibacterial properties. Biomedicine and Preventive Nutrition 2014; 4(2): 325-332. http://dx.doi.org/10.1016/j.bionut.2014.03.004

[39] Ahmed KB, Subramanian S, Sivasubramanian A, Veerappan G and Veerappan A. Preparation of gold nanoparticles using *Salicornia brachiata* plant extract and evaluation of catalytic and antibacterial activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2014; 130: 54-58. http://dx.doi.org/10.1016/j.colsurfb.2011.03.009

[40] Yoon KY, Byeon JH, Park JH and Hwang J. Susceptibility constants of *Escherichia coli* and *Bacillus subtilis* to silver and copper nanoparticles. Science of the Total Environment 2007; 373(2): 572-575. http://dx.doi.org/10.1016/j.bionut.2014.03.004

[41] Daniel SK, Vinothini G, Subramanian N, Nehru K and Sivakumar M. Biosynthesis of Cu, ZVI, and Ag nanoparticles using *Dodonaea viscosa* extract for antibacterial activity against human pathogens. Journal of Nanoparticle Research 2013; 15(1): 1-10. http://dx.doi.org/10.1016/j.saa.2014.03.070

[42] Yallappa S, Manjanna J, Sindhe MA, Satyanarayan ND, Pramod SN and Nagaraja K. Microwave assisted rapid synthesis and biological evaluation of stable copper nanoparticles using *Terminalia arjuna* bark extract. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2013; 110: 108-115. http://dx.doi.org/10.1016/j.saa.2013.03.005

[43] Pattanayak M and Nayak PL. Ecofriendly green synthesis of iron nanoparticles from various plants and spices extract. International Journal of Plant, Animal and Environmental Sciences 2013; 3(1): 68-78.

[44] Narendhar C, Anbarasu S, Divakar S and Gunaseelan R. Antimicrobial activity of Chitosan Coated Iron Oxide Nanoparticles IJCRGG 2014; 6(3): 2210-2212. http://dx.doi.org/10.1016/j.saa.2013.03.005

[45] Arokiyaraj S, Saravanan M, Prakash NU, Arasu MV, Vijayakumar B and Vincent S. Enhanced antibacterial activity of iron oxide magnetic nanoparticles treated with *Argemone mexicana* L. leaf extract: an in vitro study. Materials Research Bulletin 2013; 48(9): 3323-3327. http://dx.doi.org/10.1016/j.materresbull.2013.05.059

[46] Vijayakumar S, Vinoj G, Malaikozhundan B, Shanthi S and Vaseeharan B. *Plectranthus amboinicus* leaf extract mediated synthesis of zinc oxide nanoparticles and its control of methicillin resistant *Staphylococcus aureus* biofilm and blood sucking mosquito larvae. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2015; 137: 886-891.

[47] Ramesh M, Anbuvannan M and Viruthagiri G. Green synthesis of ZnO nanoparticles using *Solanum nigrum* leaf extract and their antibacterial activity. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy 2015; 136: 864-870. http://dx.doi.org/10.1016/j.saa.2014.09.105

[48] Morones JR, Elechiguerra JL, Camacho A, Holt K, Kouri JB, Ramírez JT, *et al*. The bactericidal effect of silver nanoparticles. Nanotechnology 2005; 16(10): 23462353. http://dx.doi.org/10.1088/0957-4484/16/10/059

[49] Klasen HJ. Historical review of the use of silver in the treatment of burns. I Early Uses Burns 2000; 26(2): 117-130. http://dx.doi:10.1016/S0305-4179(99)00116-3

Received on 26-05-2016 Accepted on 09-06-2016 Published on 31-07-2016

DOI: http://dx.doi.org/10.12974/2311-8792.2016.04.3