Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 8 [11] October 2019 : 10-21

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.876
Universal Impact Factor 0.9804
NAAS Rating 4.95

REVIEW ARTICLE **OPEN ACCESS**

A review on phytogenic synthesis of silver Nano- Particles and their future application with multifaced impacts

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ABSTRACT
Recent development in nano technology has explored various ways for biosynthesis of silver nano particles. A number of plants have been explored and found capable to synthesize silver nano particles. Biomolecules (like Polyphenols, terpenoids, alkaloids etc) present in plant parts (stem, routes, flower, shoots, fruits etc) act as capping and reducing agent to synthesize nano particles. Eco friendly plant based nano particles are anti-bacterial, anti cancer, anti-inflammatory, anti viral and anti fungal which enable them a benign option to improve environmental health. These silver nano particles have widely applied in solving environmental problems, health issues and substitute industrial processes. This review summarizes recent developments in synthesis, cytotoxicity and possible environmental consequences as well as health concerns of silver nano particle.
Keywords*: Nano particles, plant material, applications, toxicity*

Received 29.05.2019 Revised 20.07.2019 Accepted 24.09. 2019

INTRODUCTION

PLANT EXTRACTS AS REDUCTANT TO SYNTHESIZE NANO PARTICLES

Green chemistry and eco-friendly approaches for sustainable development are emerging, because of global concern of environmental pollution. The green routes of chemical processes have been explored and many books have been published to produce the Nano- materials in recent years[9; 71; 2; 8]. Former methods ultra-sonic fields, UV irradiation, laser ablation, lithography and reduction via photochemical reaction were used to synthesize Nano-materials, but these methods used harmful and toxic chemicals, thus these processes were eradicated.

Use of plant material for synthesis of silver nanoparticles has drawn much attention, because this method is comparatively fast, environment friendly, non-pathogenic, economically efficient and is single step procedure [46]. Enormous section of flora had been used for fabrication of silver nanoparticles and reported in literature. Table 1 is showing the plants extracts and their respective significance.

Nano materials have extensive and wide application in different fields, which are related to their manufacturing, size and shape. Nano particles yield is dependent on the nature and amount of extract/quantity of metal extract, pH, temperature and reaction time 26.

To produce less toxic and eco-friendly silver nano particles, plant based raw materials are used; that require less energy and water [17].

Plants based biomolecules (like flavonoids, phenol, alkaloids and terpenoids) reduce metallic ions into Nano materials of different sizes and shapes 11. Different researches related to silver Nano particles associated to effect the genotoxicity, oxidative stress and changes related to apoptosis are reported [44].

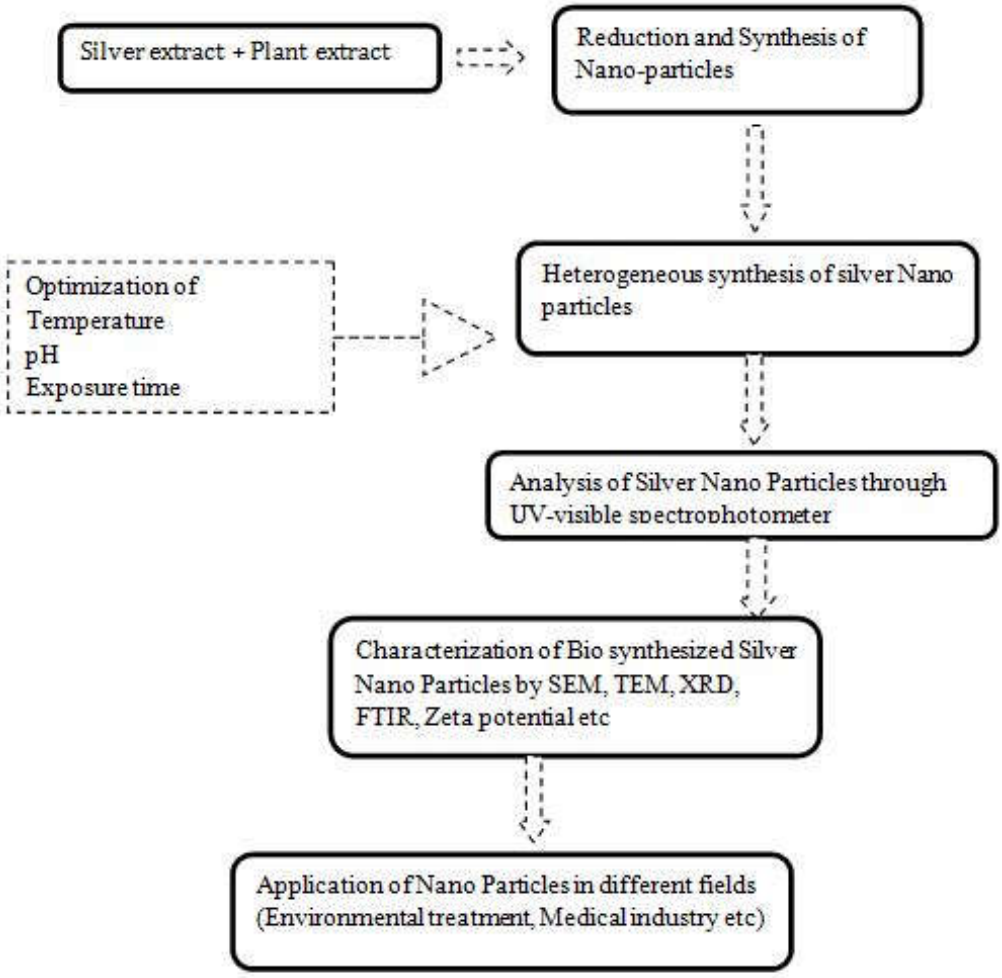

Fig: 1 General protocol for plant based bio synthesis of Silver Nano Particles

LEAVES EXTRACTS AS REDUCING AGENT

Variety of plants have been explored and utilized to synthesize the Nano particles. The aqueous leaf extract of *Alternanthera dentate* was used to synthesize spherical shape silver Nano product with 50-100 nm dimensions, by completing the reducing reaction within 10 minutes. The silver Nano-particles were tested against the *Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecal* and *Klebsiella pneumonia* [47]. The research conducted by Vijayakumar *et al.*, 103utilized *Artemisia nilagirica* leaves extract to synthesize siver Nano particles, by using silver nitrate as metal source, and hydrazine hydrate as reducing agent. *Boerhaavia diffusa* leaves extract was used to synthesize silver nano particles and their anti microbial property was tested against *Aeromonas hydrophila, Pseudomonas fluorescens* and *Flavobacterium branchiophilum [64*;65]. Many plant leaves are used as mediator to synthesize silver nano particle, for example *Alternanthera sessilis, Centella asiatica andMurraya koenigii*. *P. nigrum* leaves extract have important bioactive compound responsible for the synthesis of nano particles. The resulted nano particles were tested against cancer cells.

*Polyalthia longifolia*and *Cinnamomum camphora* leaf extract were also used to synthesize silver nano materials [41; 30]. *Polyalthia longifolia, Acorus calamus* and *Morinda citrifolia L*. leaf extract were also used to manufacture nano crystals both at room temperature and 60^{o}C. Their anti microbial property was also analyzed [39; 84; 65]. *Pelargonium graveolens* and *Crossandra infundibuliformis* leaves extracts were studied to synthesize silver nano particles [89;41].

Sesuvium portulacastrum L. plants leaves are also used to formulate the silver nano particles by changing the extract concentration during the incubation time [62]. Extremely stable nano material was formulated by leaf extract of *Datura metel.* The bimolecular identification of extract represented the wide variety of proteins, enzymes, alkaloids and polysaccharides. The presence of Quinol and chlorophyll

stabilized silver ions for synthesizing nano materials [43]. NAD+,H+ ions and ascorbic acid are present in extract, are used to reduce the silver ions to silver nano particles [3].

Nano particles were also synthesized by varying the incubation period of plants extracts. *Ficuscarica* leaf extract used to synthesize the silver nano particles with in the 3 hours of incubation period 98. Leaf broth of *Acalypha indica* was used to synthesize nano particles of silver within 30 minutes of incubation period 45.

Size of nano particle is main challenge to overcome and goal to achieve. Using variety of biomaterial effects size of particles, because of complex molecules that vary plant to plant, but they also enhance their possible applications [18; 60; 22].

Ocimum sanctum and Ziziphora tenuior leaves extract used to synthesize silver nano particles within size range of 3 to 20 nm and 8-40 nm respectively 56; 83. Leaves extract of tree *Cocous nucifera* generated silver nano particles of size 22 nm. Their extracts were prepared in ethyl acetate and methanol [57]. Leaf extract of *Ocimum tenuiflorum* synthesized silver nanocrystals ranging from 25–40 nm 72.The leaves extract of *Azadirachta indica* resulted silver nano particles within range of 10-35 nm [75]. *Ficus benghalensis* leaves synthesized the nano particles within the size range of 16 nm 85.

Spherical and stable silver nano particles were obtained by using leaf extract of *Abutilon indicum*. The leaf extract of *Coleus amboinicu* was used to synthesize silver nano particles of spherical, triangular, hexagonal and decahedral shape [66].

Melia azedarach leaf extract was used to fabricate the silver nano particles 95. Plant extract based nano particles were also formulated by *Eclipta prostrate* leaf extract 34. Leaves of *Eucalyptus hybrid*were also used in reducing silver ions to nano particles, by the presence of flavonoids and terpenoids 25.The leaves extracts of *Piper longum* were used to fabricate the nano materials [32]. Leaf the extract of *sorgassum polysystum* was used to synthesize silver nano particles [112].

In another study green routes for the synthesis of silver nanoparticles (Ag NPs) were explored with the combination of graphene oxide nanocomposites 68.

Ajitha *et al.,*(2016) synthesized silver Nano particles from leaf extract of*Ocimum tenuiflorum* and characterized these particles by using UV-visible spectrophotometer, X-ray analysis and FTIR analysis. These nano paticles were proved anti pathogenic against tested organisms 4. *Nigella arevensis* leaf extracts were used to synthesize the Ag Nano particles and they were characterized by using UV-visible spectrophotometer, TEM and FTIR analysis. Their catalytic activity was also checked against dye methylene blue [113].

STEM EXTRACTS AS REDUCING AGENT

Silver nano particles can also be synthesized from the stem extract of *Callicarpa maingayi.* The aldehydes present in stem extract reduce the ions into metallic nano particles. Other functional groups like amide and poly peptides act as capping agent in synthesis of silver nano particles 88. *Cissus quadrangularis* stem extracts were used to phytosynthesize the silver nano particles. Specifically amine, carboxyl and phenolic compounds were present [99]. Silver nanoparticles were synthesized by using lab made carboxymethyl cellulose utilizing bamboo. The characterization of the silver nano particles was finished by FTIR, SEM, TEM, particle estimate analyzer and EDX [48].

FLOWER EXTRACTS AS REDUCING AGENT

Beside other parts of plants flower petals are also explored for the synthesis of silver nano particles. *Rosa damascena* petals extract was utilized to synthesize silver nano particles and resultant nano particles were confirmed by using UV-visible spectroscopy and FTIR and spherical shape/biomolecules presencewas confirmed by X-ray diffraction and FTIR analysis. Their anti-cancer activity was also checked on human cell line [102].

Petals of *Rosa macdub* and *Calendula officinalis* flower were used for green fabrication of silver nano particles. Formation of silver nano-particles was confirmed by UV-visible spectrophotometer and FTIR analysis showed presence of proteins, alkaloids, amino acids and terpenoids. Nano-products were also assessed for their antibacterial properties [20; 92; 21]. Other floral groups *Catharanthus roseus* and *Clitoria ternatea* are also used to synthesize silver nano particles synthesis of different size and shape [50].

Floral extract of *Tagetes erecta*are also used to synthesize silver nano particles. Which were characterized by using zeta potential, FTIR, UV-visible spectrophotometer, X-bam diffraction, energy dispersive X-beam diffraction, transmission electron microscope and selected area deflected design. Their synergistic anti

microbial strength was tested against different gram positive bacteria, gram negative bacteria and some parasites [69].

FRUIT EXTRACTS AS REDUCING AGENT

Fruits are also being studied for the synthesis of silver nano particles. Fruit extracts of *Emblica officinalis* was use to synthesize the silver nano particles, by varying pH and extraction concentration. Their shape and size was analyzed by SEM and XRD analysis. Nano particles were more effective against gram positive bacteria, by diffusion disc method [77]. Fruit plants of *Tribulus terrestris* and *Rumex hymenosepalus* extract synthesized spherical and crystalline shaped silver nanoparticles [27]. *Citrus limon* fruit were used to synthesize 50 nm sized of spherical silver nanoparticles [76].

Extract of peels as reducing agent:

The biosynthesis of silver nanocrystals from peel extract is also studied. Citrus fruits like lime, orange, lemon, tangelo and grape fruit were used to synthesize silver nano particles 41; 36). Use of banana peels to synthesize eco friendly silver nano particles was reported by Ibrahim 31. These nano particles from banan peels were tested against microbes and yeast to analyze anti microbial activity. *Musa paradisiaca* peels used to synthesize silver nano particles, whose antifungal and antibacterial properties were tested against different fungi and bacteria [13]. Orange peels *Citrussinensis* was used to synthesize spherical shaped silver nano particles with in size range of 3-12 nm [100]. *Citrus sinensis* extract was also used to synthesize silver nano particles [40].

Extracts of Rhizome as reducing agent:

Dioscorea batatas and various other plant's rhizome were used to synthesize nano-particles 63. Parts of *Acorus calamus* (rhizome), *oleifera* (leaves) and *Cucurbita maxima* (petals) were used to synthesize silver nano particles [67]. Plant root extract of *Diospyros paniculata* were used to synthesize silver nano particles and their anti fungal anti bacterial activity was tested 80. *Pelargonium endlicherianum Fenzl* rhizome was used to synthesize silver nano particles [38]. The roots of *Diospyros sylvatica* were used to synthesize nano particles. Their anti fungal property against selected fungal strains was tested [74].

SEED EXTRACTS AS REDUCING AGENT

Seeds consist of flavnons, lignins, saponins and vitamins and many other compounds, which are useful for the production of silver nano particles. *Artocarpus heterophyllus Lam*. seed extracts were used to synthesize silver nano particles and they have high efficiency against gram positive and gram negative bacteria [33]. Extracts of jambul seeds *Syzygium cumini* were also used for production of silver nanoparticles [49]. *Trachyspermum ammi* and *Papaver somniferum* seed extracts were used to synthesize silver nano particles of size 87–998 nm and 3–8 μm respectively [104]. *Coffea Arabica* roasted seeds were used to synthesize silver nano particles and they were tested against bacteria [23].

Gum and latex Extract as reducing agent:

Neem gum (*Azadirachta indica L.*) also used to synthesize silver nano particles and they showed antimicrobial properties against *Bacillus cereus* [101]. Rubber latex of *Hevea brasilensis* was used to synthesize spherical silver nano particles with in size range of 2nm to 10nm [79].

Use of Coffee, tea or nuts in fabrication reaction:

Tea extract with silver nitrate solution are also investigated to synthesize silver nano particles at different concentration 61;96, also conducted experiments on tea extract and synthesized silver Nano-particles of 20-90nm size. Soap nuts were also studied to synthesize silver nano particles and resulted particles showed growth inhibition of microbes [78].

Table: 1 Plants extracts and their respective significance

Plant part	Plant	Significance	Reference
Leaves	*Alternanthera dentate*	Antibacterial activity	Kumar *et al.,* 2014
	Artemisia nilagirica	Medicinal and industrial uses	Vijayakumar *et al.*, 2013
	P. nigrum	Anti cancer activity	Jacob *et al.,* 2012
	Polyalthia longifolia	Anti bacterial activity	Kaviya *et al.,* 2011
	Sesbania grandiflora	Antifungal and anti bacterial activity	Ajitha *et al.,* 2016
	Ocimum sanctum	----------	Mallikarjuna *et al.,* 2011
	Morinda citrifolia L.		Sathishkumar *et al.,* 2012

	Acorus calamus	Anti cancer, anti oxidant, anti bacterial	Nakkala *et al*., 2014
	Boerhaavia diffusa	Antibacterial activity	Nakkala *et al*., 2014
	Ziziphora tenuior	-	Sadeghi and Gholamhoseinpoor 2015
	Ficuscarica	-	Ulug *et al.,* 2015
	Acalypha indica		Krishnaraj *et al.,* 2010
	Chenopodium album		Dwivedi and Gopal 2010
	Ocimum tenuiflorum	Anti bacterial activity	Patil *et al.,* 2012
	Cornus officinalis	Anti cancer activity	He *et al.,* 2017
	Matricaria chamomile	Anti bacterial activity	Ocsoy *et al.,* 2017
	Sargassum polysystum	Anti oxidant and anti cancer activity	Palanisamy *et al.,* 2017
	Nigella arevensis	Catalytic activity against dye	Chahardoli *et al.,* 2018
	Agave tequilana Weber var. *azul*	Anti bacterial activity	López-Naranjo *et al.,* 2018
Stem	*Cissus quadrangularis*	Anti bacterial activity	Vanaja *et al.,* 2013
	Bamboo stem	Anti bacterial activity	Kumar *et al.,* 2019
	Callicarpa maingayi	Anti bacterial activity	Shameli *et al*., 2012
Flower	*Rosa damascena*	Ant cancer activity	Venkatesan *et al.,* 2014
	Rosa macdub	Antibacterial activity	Shete *et al.*, 2014
	Clitoria ternatea and *Catharanthus roseus*	Anti pathogenic activity	Kuppusamy *et al.,* 2015
	Tagetes erecta	Anti microbial and antifungal activity	Padalia *et al.,* 2015
Fruit	*Emblica officinalis*	Antibacterial activity	Ramesh *et al.*, 2015
	Tribulus terrestris	Antimicrobial activity	Gopinath *et al*. 2012
	Citrus limon	----------	Prathna *et al.,* 2011
Peels	Citrus fruit peels	Antibacterial activity	Kaviya *et al*., 2011
	Musa paradisiaca	Antibacterial activity	Ibrahim, 2015, Bankar *et al.,* 2010
	Citrus sinensis	Antibacterial activity	Veeraputhiran, 2013
Rhizome	*Dioscorea batatas*	antimicrobial	Nagajyothi and Lee, 2011
	Acorus calamus	Anticancer activity	Nayak *et al.,* 2015
	Diopyros paniculata	Anti bacterial and anti fungal activity	Rao *et al.,* 2016
	Pelargonium endlicherianum Fenzl.	Anti bacterial activity	Karatoprak *et al.,* 2017
	Diospyros sylvatica	Anti fungal and anti bacterial activity	Pethakamsetty *et al*., 2017
Seed	*Artocarpus heterophyllus Lam*	Antibacterial activity	Jagtap and Bapat, 2013
	Syzygium cumini	----------	Kumar *et al.,* 2010
	Coffea arabica	Anti bacterial activity	Dhand *et al.,* 2016
Gum	*Azadirachta indica L*	Antimicrobial activity	Velusamya *et al.*, 2015

Silver Nano particles in Nano medicine:

Nano particles have solved many problems, in the medical field, such as in treatment, surgical nano medicines, diagnosis and commercial biomedicine formation 14. Plasmonic nano antennas have been applied in subfield of nano medicine, it includes nano-electronics, molecular imaging and biomedicine. They used enhanced electromagnetic fields on and near the silver nano particles 52.By increasing intensity of local electromagnetic field (Ramon spectroscopy), molecule identification is performed by the molecular vibration. Plasmonic nano antennas enhance the amplification of Ramon signals and surface. Enhanced ramon scattering helps in identifying the critical biomolecules and proteins, like cancer bio markers and drug level in blood 19.

Sliver nano particles serve as probes to image and target the small molecular DNA, tissue and tumor cells 24. Silver nanoparticles with stronger Plasmon resonance have extensively applied in cellular imaging, like cancer cells and can be analyzed through photochemical therapy to destroy cancer cells 54. The longumine and piper longminine present in *P. nigrum* leaf extract act as capping agent and caused cytotoxicity in tumor cells. There future perspectives are much needed to explore to analyze the various clinical aspects 32. Kang *et al* 37 studied the uses of NIR sensitive nano particles to detect and identify the aromatic compounds.

Silver nano materials with dense layer of Y_2O_3 and separating silica gel, analyze metals on nanoscale and used as fluorescent labels in bioassays 109. Silver nano particles assisted multiplexed lateral flow assay has been used to identify the various pathogens and can be tuned into easily distinguished color. These nano particles conjugated with antibodies helped in identifying the dengue virus proteins, Ebola virus glycol proteins and yellow fever virus proteins. The limit for detecting biomarkers in single channel is 150ng/l 106.They also used in selective identification of lead even in the presence of other interacting and interfering. This technique is cost effective and time effective, used to detect lead poisoning in water samples 12.

Silver nano particles used in anticancer medicine and their surface charge very important in retention time of the nano material in luminal or blood vessel (important route for anti cancer agents) 86. The intrinsic property of silver nano particles helps in treating different types of cancers like breast, cervical cancer 42. They have ability to disrupt DNA and cause genomic instability and also the calcium homeostasis that stops cell cycle blocking the division of cancer cells 51.

PHOTOCATALYTIC ACTIVITY OF SILVER NANO-MATERIAL

In textile industries regulations regarding wastewater release into water channels have become progressively rigorous. The synthetic dye stuff consumed in the textile and other dyeing industries produce dangerous waste products daily. Dye decolourization is significant but difficult area of wastewater treatment. Photocatalytic approaches for destructive oxidation of toxic dyes have lately received substantial consideration. Photocatalysis reaction results in complete mineralization of toxic dyes into non hazardous CO_2 and H_2O and inorganic compounds, or sometimes transform them into biodegradable or nontoxic products 35.

Ag-Nps /TiO_2 Composite thin films produced by molecular precursor technique were used by 53to enhance their phtocatalytic activity. The Ag-NPs/TiO_2 composite thin films with different concentrations of silver were tested as a possible photocatalyst. Yeast *Saccharomyces cerevisiae* extract was used to synthesize silver nano particles 80Organic dye methylene blue was used to confirm photocatalytic action of these bio-mediated nanoparticles under solar radiation and caused degradation of dye within few hours of contact.In another study Suárez-Cerda *et al., 94* worked on production of ultra-small silver nanomaterial. Extract of *Rosa Andeli* petals were used to synthesize nano particles. Synthesized silver nanomaterial proved photocatalytic property for decolorization of commercial dye with effectiveness of 95%.

Solanum tuberosum extract was used to formulate silver nanoparticles. Degradation of methyl orange dye showed successful photocatalytic activity of silver nanocrystals under sunlight irradiation (Roy *et al*., 2015). *Cirsium japonicum* mediated silver nano particles were applied for photo-decolorization of bromo phenyl blue and results were efficient 111. Aqueous extract of *Lychee Litchi chinensis* fruit peel were used to synthesize silver nanoparticles. Synthesized nano-product revealed amazing 99.24% degradation of methylene blue 10. Due to strong reductive properties of silver nano-materials proved in literature, their use should be adopted in water purification and degradation of organic hazardous to non-hazardous materials 6.

CYTOTOXICITY OF SILVER NANO PARTICLES

It has been investigated that shape, size, exposure time and environmental conditions of nano particles effect toxicity and genotoxicity. The toxic concentration for silver nano particles is 5-10 lgmL and size ranges from 10-100 nm, which disrupt function of mitochondria 58. In another study toxicity in mitochondria was induced by the silver nano particles through gluthione reduction (GHS), reactive oxidative species responding genes and high lipid peroxidation that leaded to DNA damage, apoptosis and then necrosis 28. These nano particles have adverse effects on different body functions like deformities in reproduction and morphological features along with their malformations 5.

Silver Nano particles are commercially available in markets and are widely used in antimicrobial actions. Their neurotoxic, hepatotoxic, genotoxic, cytotoxic and pulmonary inflammation have been diagnosed with the association of silver nano particles of different sizes. These silver nano particles initiate

production of reactive oxygen species and Oxidative stress which leads to cytotoxicity and genotoxicity. In cytotoxicity, the production of reactive species mechanism enhanced, that triggers cell apoptosis. These studies have been conducted on mammalian cell cultures 59.

Silver nano particles have high toxicity in central nervous system. They can enter into respiratory tract through the olfactory bulb and then to central nervous system 93. These nano particles accumulate in various regions of the brain and induce the strocyte swelling, mitochondrial dysfunction, neural degradation and many others 90; 105. In another study the silver nano particle toxicity was checked on prenatal mice, where the offspring showed behavior of depression and it was estimated that this behavior was result of induced neurotoxic effects during neural development 97.

INTERACTION OF SILVER NANO PARTICLES WITH OTHER METALS IN THE ENVIRONMENT

Nano particles are increasing in environment; currently they are more than 1800 consumer products that contain nano particles. These nano particles are increasing in different sectors of environment and posing serious health effects 15. As their concentration is increasing in the environment, the concern about nano pollution is also increasing 16. In a study silver nano particles were synthesized in the presence of iron species and their effect on silver nano particles was analyzed. Silver nano particle were produced in both oxic and anoxic environment for 1 hour monitored by UV-visible spectrophotometer. The results showed that silver nano particles synthesis is dependent on the type of organic matter present. It also observed that the iron species prevented the small cluster formation of particles and formulizes the larger silver particles 107.

Silver nano particles interaction with other particle, like gold nano particles was also studied. The nano particles can come from medical, catalytic and sensing application and cause them to be bio-available for environment 108. The interaction between silver and gold nano particles was studied under various environmental conditions like different Ph, different fractions of silver salt and organic matter. The stability of silver gold (AgAu) was analyzed by UV-visible spectrophotometer and their characterization was done by using TEM and X-ray spectroscopy techniques 7.

Silver nano particles interact with titanium oxide and reduce the dissolution and toxicity of silver nanoparticles 91. In another study the biotransformation of silver nano particles was also investigated. In the absence of light, aggregation of silver and titanium oxide nanoparticles were formed. Titanium oxide enhanced the release of silver ions by dissolution. As the concentration of Titanium oxide increased the release of silver nano particles were also increased 110.

In other study mitochondria was exposed to the silver and titanium nano particles for the exposure time of 21 days. The targeted and deposition site was mitochondria for silver and titanium oxide nano particles and resulted in more intense damage than single nano particle exposure 73.

CONCLUSION

The awareness of green chemistry and its benefits led the scientists to discover the miniaturized metal particles from nature. Silver nanoparticles have great potential in nano chemistry and environmental aspects to solve issues. Many reports have been published for the synthesis of nano particles and some are discussed above. Their efficient application must be further explored and eco friendly ways need to be evolved in a sustainable way for their beneficial use. Using the plant extracts for nano material production is easy way but as same plant can vary in composition in different parts of the world which is the main drawback of the using plant material. The biomolecules, role as mediator, present in plant material must be identified and well known to make efficient nano particles. These nano particles are being applied in many fields which is being discussed above with their consequences. So, there is a need to adopt the sustainable use of silver nano particles to avoid any nano pollution in future.

CONFLICTS OF INTEREST

NO

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CITATION OF THIS ARTICLE

S Riaz, Mamoona, A Khalid, S Ashfaq , F Bahir. A review on phytogenic synthesis of silver Nano- Particles and their future application with multifaced impacts. Bull. Env. Pharmacol. Life Sci., Vol 8 [11] October 2019: 10-21