



A REVIEW ON THE GREEN SYNTHESIS OF SILVER NANOPARTICLE AND ITS THERAPEUTIC APPLICATIONS

Rahul Prakash P¹, Sudha S*

1. Department of biotechnology Sathyabama institute of science and technology, Jeppiaar
Nagar, Chennai-119

ABSTRACT

The nanotechnology is one of the enthusiastic fields in modern materials science. Nanotechnology is based on synthesizing of nanomaterials (1-100 nm) and its applications in various fields especially for industrial revolution. Nanotechnology has been emerging as a cutting-edge technology convergence with physics, chemistry, biology, material science and medicine. The metal nanoparticles like copper, zinc, titanium, gold & silver have potential activity towards medicinal implementations. In recent advancement silver nanoparticles have gained more importance due to their properties and other applications. They are excellent anti-bacterial, anti-microbial & anti-fungal agents. Green synthesis using plants has emerged as a successive method for synthesis of nanoparticles and its less harmful and environmentally friendly. Further, silver nanoparticles have great therapeutic and diagnostic applications. The therapeutic applications of silver nanoparticles (AgNPs) are enormous ranging from anticancer, antibacterial, antidiabetic agents, bioimaging and biosensing properties. These applications could help researchers explore the green synthesis of silver nanoparticles that are still being unknown.

Keywords: Silver nanoparticle, medicinal plants, green synthesis, therapeutic applications.

1. INTRODUCTION

In the time of contemporaneous research, nanotechnology plays a vital role which manages the designing, synthesis and exploitation of particle structures that comprises of nanoscale dimensions (1-100nm) (V. R. Remya *et al.*, 2017). In the fields of fitness care, food and feed, environmental health, biomedical sciences, drug-gene delivery, chemical industries, cosmetics, opto-electronics, optics, catalysis, mechanics, electronics, energy science, single electron transistors, light emitters, nonlinear optical devices, and photoelectrochemical the nanoparticles (NPs) have a multiplicity of choices in their consumption and utilizations (V. R. Remya *et al.*, 2017). In the area of recent developing studies, the implementation of these plants for many biological & biomedical applications have been significantly increased due to the presence of unique elements and their applications (Banerjee *et al.*, 2014). Medicinal plants have a deep history towards India owing to extortion of broad variations of useful and affordable plant species and products. These various medicinal plant species have been employed in Ayurvedha for a very long time dating back to centuries. These plant species can be used as a biological precursor in the green synthesis of nanoparticle. These nanoparticles have significant resistance towards microbial diseases and are majorly used as antimicrobial, antidiabetic, antiangiogenic, anti-inflammatory, anticancer agents in a diverse range of products.

Various scientists have been interested in studying these metal nanoparticles solely due to their unique nature of optical, electrical and catalytic properties. In order to make use of these nano-sized metal particles or metal nanoparticles, a broad spectrum of research and development has been undertaken to facilitate control over size and shape of these particles which is the driving force for their physical, chemical and optical properties (Bar *et al.*, 2009). There have been a number of various kinds of nanoparticles identified such as copper, zinc, titanium (Retchkiman-Schabes *et al.*, 2006), magnesium, gold (Gu *et al.*, 2003), alginate (Ahmad *et al.*, 2005) and silver. Among these different types of nanoparticles, the silver is considered to be better than the others solely due to its antimicrobial activity against bacteria, virus and other micro-organisms (Gong *et al.*, 2007).

The approach of utilizing biopolymer can also facilitate green synthesis of nanoparticles for applications in medical and biomedical therapies. For example, a biopolymer processed from seafood waste known as chitosan (glucosamine and N-acetyl glucosamine residues) is non-toxic, biodegradable, environmentally safe and has large capabilities in agricultural applications and enhancing crop production. A huge part of these benefits of chitosan comes from its biological activities towards plants such as stimulating growth of plant and seed germination, increasing in chlorophyll content, photosynthetic and chloroplast enlargement in the leaves

of plants (Van *et al.*, 2013; Limpanavech *et al.*, 2008), increasing in nitrogen fixing nod of species of Leguminous family, increasing in nutrient uptake of plants and reducing stress of plants and enhancing crop production (Van *et al.*, 2013; Dzung, Nguyen Anh *et al.*, 2011; de Castro *et al.*, 2018). But the implementation of these biopolymer-based nanoparticles into human consumption such as cosmetics and medical treatments haven't emerged due to the fact that the major part of their ability is focused towards development and improvement of the plants and crop production.

The purpose of green synthesis of silver nanoparticle is to design a precise and safer way for utilizing these nanoparticles, control over their vast majority of untapped potential and to devise a more infallible protocol for harnessing their overflowing capabilities in medicine, biomedical applications, electronics, material science and environmental science that can be made accessible for human consumption.

2. NANOPARTICLE SYNTHESIS METHODS

The metal nanoparticles which are mentioned above is synthesized using various methods such as hard-template method, bio-reduction method (Canizal, G., *et al.*, 2001; Mouxing, F. U., *et al.*, 2006) and solution phase synthesis method (Sun, Yugang *et al.*, 2003). In correspondence to the synthesis and construction procedure of nanoparticles and nanomaterials, precursors of various elemental origin are used such as liquids, solids or gases enlisting physical, chemical and biological approaches. The construction techniques fall under two approaches: 'Bottom-up' and 'Top-down' methods. (Leela, Arangasamy *et al.*, 2008)

2.1 BOTTOM-UP APPROACH

In case of Bottom-up approach the most preferred route of silver nanoparticle synthesis is by using chemical methods (Elghanian R *et al.*, 1997; Hurst *et al.*, 2006). Here, reducing agents such as sodium-borohydride, Tollen's reagent, sodium citrate, elemental hydrogen, ascorbate, N, N-dimethyl formamide (DMF) and polyethylene glycol copolymers were used in the silver ions (Ag⁺) reduction in both aqueous and non-aqueous solution (Tran QH *et al.*, 2013; Iravani, Siavach, *et al.*, 2014). To maintain control over the overall size and shape, capping agents were been administered.

In this method large number of nanoparticles (NPs) can be synthesized in a short time period. The use of chemicals in the nanoparticle synthesis has high levels of harmful and toxic effects which leads to various side-effects and non-eco-friendly by-products. This demands for better and safer nanoparticle synthesis led to the method of employing green route of production via Biosynthesis which doesn't produce any toxins and their by-products are environmentally safer to use. This property of biosynthesis has peaked the interests of scientists to undergo research towards gaining a better understanding of them (Reddy, G. A. K *et al.*, 2012).

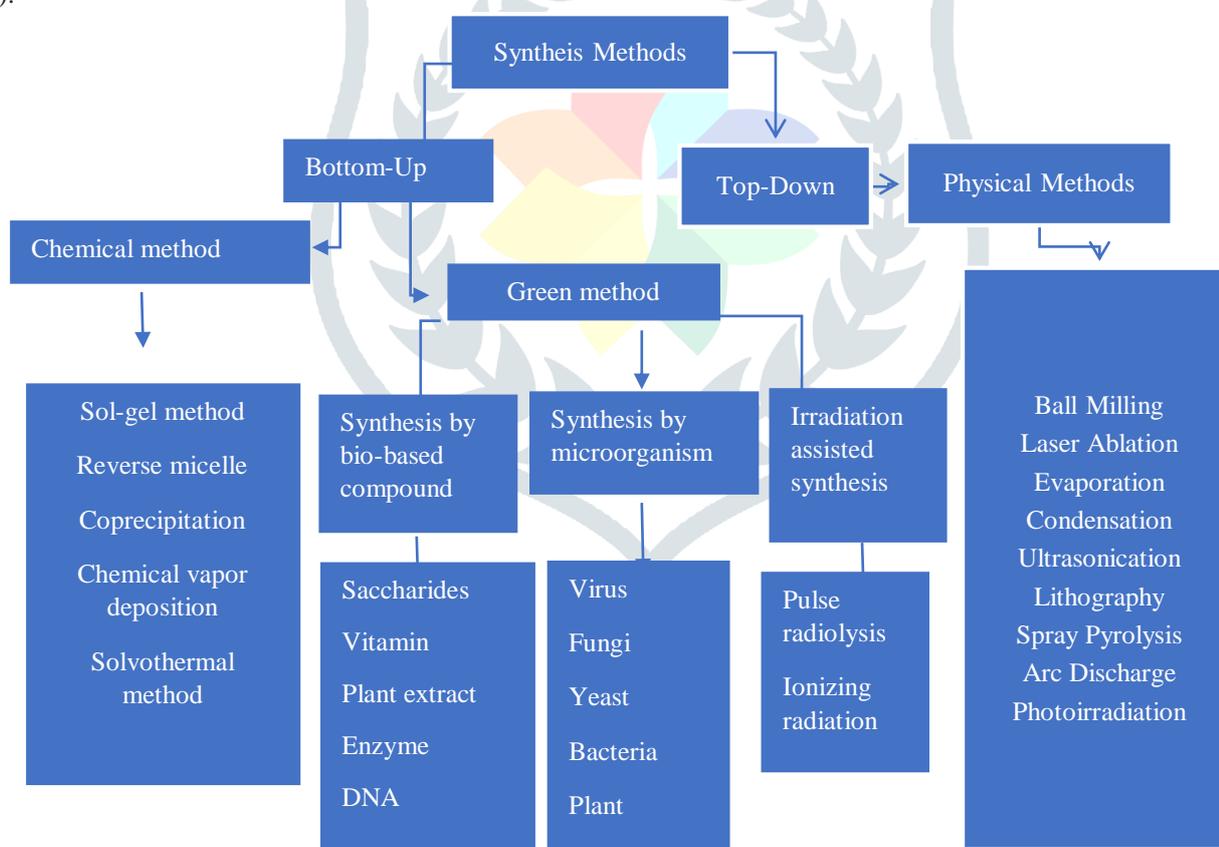


Fig 1: Bottom-up and top-down approaches and its types.

The bottom-up approach can provide greater possibilities for obtaining nanostructures with less defects, superior homogenous chemical composition and improvised range ordering. Even though there is a plethora of useful methods available for nanostructure synthesis like sol-process, micelle, sol-gel process, chemical precipitation, hydrothermal method, pyrolysis, chemical vapour

deposition, Bio-based protocol etc., they are only inferior to the environmentally safer properties and eco-friendly by-products of Biobased method (Leela, Arangasamy *et al.*, 2008).

2.2 TOP-DOWN APPROACH

In this approach, the nanoparticles are synthesised generally by using evaporation and condensation methods with the help of a tube furnace at atmospheric pressure. The synthesis of silver nanoparticles (AgNPs) using a tube furnace is not very effective as it contains numerous flaws like it occupies a great deal of space, uses large amount of energy in return greatly increases the environmental temperature around the source and also required more amount of time to attain thermal stability (Sintubin, Liesje, *et al.*, 2011). The top-down approach is mainly a destructive method (Ealia, S. Anu Mary *et al.*, 2017). It's incapable of producing irregular shapes and minute particles. In this method it's also very difficult to acquire the respective particle size and shape of interest (N. Abid *et al.*, 2010).

2.3 GREEN SYNTHESIS

Green synthesis is one of the bottom-up methods where natural materials like leaves of trees/crops or fruits or microorganisms are used to replace harmful, expensive chemical reducing agents during the synthesis of metals or metal oxide nanoparticles. Biological life-forms hold enormous possibilities in the synthesis of nanoparticles. Biogenic mechanism of reducing metal precursors to their respective nanoparticles holds greater potential such as eco-friendly (Jayaseelan *et al.*, 2012), sustainable (Gopinath, Kasi *et al.*, 2014), free of chemical contamination (Chandran, S. Prathap *et al.*, 2006; Huang, Jiale *et al.*, 2007), less expensive (Mittal, Amit Kumar *et al.*, 2013) and can be used for mass production (Iravani *et al.*, 2011). The customary approach for the synthesis of NPs is costly, harmful and not eco-friendly. Hence to counter this problem, experts have opted for green methods of synthesis of NPs (Kharissova, Oxana V *et al.*, 2013).

The fundamental needs for the production of silver nanoparticles (AgNPs) by green synthesis method are silver nitrate and a natural reducing agent (Naidu Krishna *et al.*, 2015; Dong, Xiao-Yun, *et al.*, 2015). In case of using a stabilizing or capping agents, the natural reducing agent or different components present in the cell will act as reducing/capping agents thus eliminating the need for addition of these elements from external sources (Srikar *et al.*, 2016). The AgNPs constructed by Biogenic synthesis exhibits 20 times higher antimicrobial activity compared to chemical synthesis (Gardea-Torresdey, Jorge L., *et al.*, 2003). For the in-vivo method of nanoparticle synthesis bacteria, yeast, fungi, algae and plants are reported to be utilized (Kharissova, Oxana V., *et al.*, 2013).

2.3.1 SYNTHESIS FROM PLANTS

The synthesis of nanomaterial is a simple procedure which involves mixing of plant extract and metal salt at room temperature. The reaction is relatively quicker. A variety of metals could be produced by this method (Kharissova *et al.*, 2013). The use of plant components in the synthesis of silver nanoparticle is highly welcomed due to its rapid, eco-friendly, non-pathogenic, economical protocol which provides a single step technique for the biosynthetic of nanoparticles. In the reduction and stabilization process of silver ions, we use biomolecules like proteins, amino acids, enzymes, polysaccharides, alkaloids, tannins, phenolics, saponins, terpenoids and vitamins which already exists in the plant extract containing medicinal value and environmentally safe to use, yet being chemically complex in structural integrity (Mittal, A. Kumar *et al.*, 2013). Recent research shows that the synthesis of silver nanoparticle from the *Crataegus douglasii* fruit extract by Ghaffari-Moghaddam and Hadi-Dabanlou (Kulkarni *et al.*, 2014). In order to enhance the biosynthesis process, the reaction of experimental variables like extract concentration, mixing ratio of the reactants, time and pH were maintained at their respective levels.

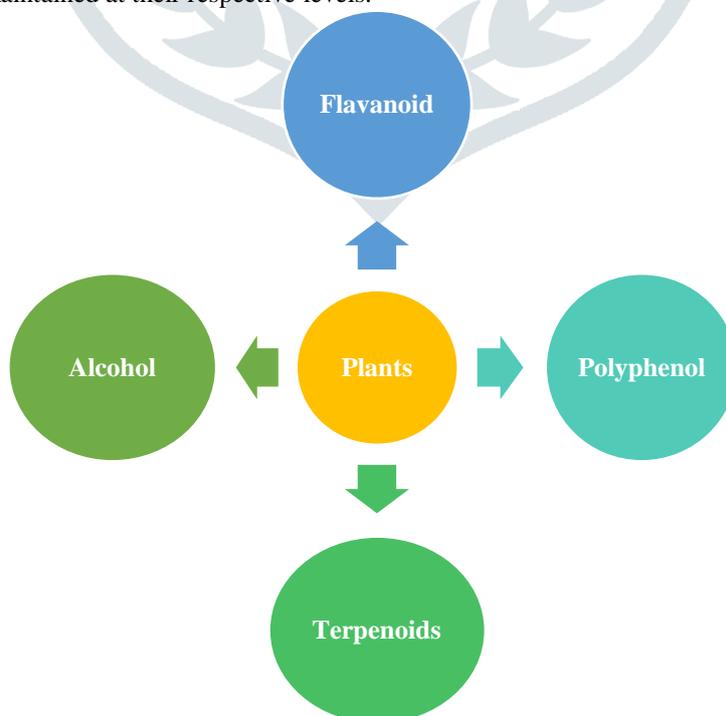


Fig 2: Plant based green synthesis outcomes

2.3.2 SYNTHESIS FROM BACTERIA

The production of nanoparticles from noble metals like silver (Ag) & Gold (Au) is done by utilizing intracellular or extracellular inorganic matter obtained from bacteria. The AgNPs can be synthesized from some bacteria species which are Ag-resistant in nature (Ghaffari-Moghaddam *et al.*, 2014). The silver produced by bacteria is assembled on the cell wall and it can be used to separate silver from its ore in industries (Slawson *et al.*, 1992).

Nitrates are the major source of nitrogen for bacteria. Here, nitrates are transformed into nitrites using nitrate reductase also makes use of the reducing power in the form of NADH which is being produced as a byproduct of this reduction. In the bacterial metabolic procedure, the nitrates are utilized with the help of reduction process where they're converted to nitrite and ammonia. This mechanism can be employed in the bio-reduction of Ag⁺ ions by using an intracellular electron donor (Pooley *et al.*, 1982). A principle of invitro enzymatic strategy was demonstrated by Kumar and colleagues on the production of AgNPs using α -NADPH-dependent nitrate reductase and phytochelatin (Lengke *et al.*, 2007). By using natural reducing agents, the AgNPs are synthesized in various shapes in *Bacillus species* (Anil Kumar, S., *et al.*, 2007). A trivial number of bacteria are capable to synthesize AgNPs intracellularly with the help of intracellular components acting as both reducing and stabilizing agents (Vaidyanathan, Ramanathan *et al.*, 2010).

2.3.3 SYNTHESIS FROM YEAST & FUNGI

The biogenic method of metal nanoparticle synthesis which utilizes biological components like microorganisms and plant extract is favored as a valuable alternative to other synthesis procedures. A known fact is that microbes like bacteria and fungi play a major role in refining the toxic materials by means of reduction of metal ions (Patra, Sujata, *et al.*, 2015; Klaus-Joerger, Tanja, *et al.*, 2001). Feasible method of silver nanoparticle production by green synthesis was identified in the biological system of a fungus named *Verticillium species* (Arokiyaraj, Selvaraj, *et al.*, 2017; Gajbhiye, Monali, *et al.*, 2009). It was proposed that AgNPs are accumulated under the cell wall and not in the aqueous solution. The Ag⁺ ions were imprisoned onto the cell surface of the fungal cell due to the electrostatic interaction between Ag⁺ ions and negatively-charged carboxylate groups of the enzyme. Further the intracellular reduction of Ag⁺ ions take place which results in Ag nuclei formation. With the help of transmission electron microscope (TEM) it was studied that AgNPs were assimilated in the cytoplasmic space because of the bio-reduction of Ag⁺ ions (Mukherjee, Priyabrata, *et al.*, 2001) that yields a particle size of 25±12 nm in diameter.

The fungi *Fusarium oxysporum* was used to produce nitrate reductase which is used along with a cofactor α -NADPH in the invitro process. The mechanism of silver nanoparticle production needs the reduction of α -NADPH to α -NADP⁺. The hydroquinoline works as an electron shuttle in the process of nitrate reduction in order to facilitate the conversion of Ag²⁺ ions to Ag. The Ag⁺ ions were reduced using nitrate reductase and subsequently stabilized with help of capping peptide which resulted in the formation of stable silver hydrosol (10-25 nm) (Rauwel, Protima, *et al.*, 2015).

2.3.4 SYNTHESIS FROM BIOPOLYMER

All the biopolymers used for green synthesis of AgNPs perform a dual role of reducing and stabilizing agent in the synthesis process, where starch doesn't confer these roles when used as a capping agent (Durán, Nelson, *et al.*, 2005). The synthesis of AgNPs was carried out using carboxymethylated-curdlan or fucoidan as reducing and stabilizing agents within a time period of 10-15 minutes (Leung TC *et al.*, 2010). According to (Elgorban, Abdallah Mohamed, *et al.*, 2016) the average size of silver nanoparticle ranges from 40-80 nm. The antimicrobial activities of AgNPs are greatly enhanced by utilizing biopolymers. Formation of AgNPs with a small range of below 10 nm, chitosan and ascorbic acid were utilized as the reducing and capping agents (Leung, Thomas Chun-Yiu, 2010). The biogenic silver nanoparticle synthesis of *Nigella sativa* extract (NSE) displayed potential antioxidant activity. The TEM image revealed two phased spherical AgNPs with a particle size of 8 nm (Regiel-Futyra, Anna *et al.*, 2017).

3. CHARACTERIZATION

The conformational details of the synthesized nanoparticles such as shape, size, dispersity, homogeneity as well as surface morphology are directed by using various techniques. The general techniques for characterizing NPs are UV-vis absorption spectroscopy, X-ray diffraction (XRD), Fourier transmission infrared (FTIR) spectroscopy, dynamic light scattering (DLS), energy dispersive X-ray analysis (EDAX), scanning electron microscopy (SEM), transmission electron microscopy (TEM), etc.

The UV-Vis spectroscopy was established to monitor the amount of UV or visible light that has been absorbed by NPs in aqueous suspension (Tarannum, Nazia *et al.*, 2019). The nanoparticles are generally characterized in the wavelength within 300-800 nm for the particle size ranging from 2-100nm (Raut Rajesh, W., *et al.*, 2009). The

The SEM and TEM analysis were done to characterize the morphology of nanoparticles (Sangeetha *et al.*, 2011).

The XRD analysis of nanoparticles shows translational symmetry, size and phase identification (Schaffer, Bernhard, *et al.*, 2009). The X-ray beam is passed through the sample that results in a diffraction pattern and is compared with standard values to get structural information.

The FTIR spectroscopy techniques is employed to identify the nature of functional groups or metabolites present on the surface of nanoparticles that involve in the reduction and stabilization properties (Sun, Shouheng, *et al.*, 2000).

4. DRUG DELIVERY APPLICATION

The process of drug delivery using metal nanoparticles is an effective method in treatment of various diseases (Sankar, Renu, *et al.*, 2015). To obtain higher efficiency in drug delivery, the drugs are released slowly towards their respective target sites (De Jong *et al.*, 2008). This optimization can be obtained by using active or passive drug delivery system (De Jong *et al.*, 2008). The latest literature studies have demonstrated the effectiveness of metal nanoparticles for drug delivery purposes (Torchilin, 2010). The study of silver nanoparticles has provided greater affinity towards cancer therapy and treatment (Kotcherlakota, Rajesh, *et al.*, 2018). There've been only very few reports at present talking about drug delivery potential of silver nanoparticles. A cancer drug delivery

system was devised which consists of silver nanoparticles that are obtained from *Butea monosperma* plant extract. These silver nanoparticles were administered with chemotherapeutic drug *doxorubicin* to develop a drug delivery system (DDS) and identify its anticancer efficacy in various cancer cells (Kotcherlakota, Rajesh, *et al.*, 20187). The DDS system showed higher cytotoxicity than other existing drugs by executing *doxorubicin* into the cancer cells. This study helped to understand that biosynthesized AgNPs can be utilized for drug delivery procedure in cancer therapies. The delivery of antifungal drug into cells was demonstrated by kumar *et al* by using AgNPs obtained from the supernatant of *Delftia sp.* strain KCM-006 culture. The experiment was a success which inhibited ergosterol biosynthesis and biofilm formation of fungus (Patra, Sujata, *et al.*, 2015) and also the antifungal drug miconazole was successfully administered.

4.1 TARGETED DRUG DELIVERY

This provides a secure way of delivery/accumulation of the drug to its target or be released in their respective site-directed region. The targeted drug delivery system works by using site specific drugs that promotes chemical targeting of the localized agent towards the target site. The localized agent uses enzyme/chemical reactive for site-directed delivery and it helps the agent take control over the targeted release action of the carrier. The agent can be made to target its respective target area with help of peptides, antibodies, other compounds, or proteins which are attracted towards their respective organs, biological target or receptor sites in a specific manner (Kumar *et al.*, 2015).

The site specificity is attained by making the drug adhere to the nanoparticle which has affinity towards the targeted area of interest. The administration of the drug-nanoparticle complex is guided towards the region of infection. This method is possible only in localized method of drug delivery. The aim of targeted drug delivery is to provide better therapeutic techniques and treatment with the aid of biosynthesized nanoparticles. The chemotherapeutic agents work as foreign entities in the human body which are interrupted by the immune system finally removing them through excretion. A small change in the dosage can lead to drug resistance by the body and also problems in drug delivery (Dobson *et al.*, 2006). This resulted in the need for using biosynthesized agents for drug delivery practices. These agents are non-toxic in nature and promotes better drug target delivery and also helps to improve the potency of the drug.

5.THERAPEUTIC APPLICATION

The therapeutic applications of silver nanoparticles (AgNPs) are enormous ranging from anticancer, antibacterial, antidiabetic agents, bioimaging and biosensing properties. These wide range of applications led to using silver nanoparticle for medicinal purposes.

5.1 ANTI-CANCER ACTIVITY

The implementation of chemotherapeutic agents has various limitations like increasing drug resistance, poor bio-availability and non-specific toxic nature. This resulted in fabrication of alternative treatment methodologies for cancer therapy and cure. The experiment of silver nanoparticle synthesis from *Bacillus funiculus* culture supernatant displayed antiproliferative properties in MDA-MB-231 (human breast cancer) cells through generation of ROS (reactive oxygen species) thereby progressing to apoptosis (Mirza, Salma, *et al.*, 2020). The generation of protein-capped silver nanoparticle from *Penicillium shearii* AJP05 fungus displayed effective anticancer properties in epithelial (hepatoma) and mesenchymal (osteosarcoma) cells. The cytotoxic effectiveness of these biosynthesized silver nanoparticle were viewed due to their production of ROS (reactive oxygen species). These biosynthesized silver nanoparticles modify the cancer cells as cisplatin resistant by sensitizing them (Gurunathan, Sangiliyandi, *et al.*, 2013). Firdhouse *et al* reported that AgNPs produced by using *Alternanthera sessilis* plant extract showed high amount of cytotoxic activity towards prostate cancer cells (PC-3) (Fageria, Leena, *et al.*, 2017).

5.2 ANTI-ANGIOGENIC ACTIVITY

The angiogenesis is the system of formation of new blood vessels from existing old ones (sprouting of vascular network) is an essential method for organ growth and repair which now has become an important topic of research for the scientific community. The angiogenesis basically regulates endothelial cell growth, differentiation, significant importance in the process of embryonic development and etiology of various pathologies including cancer. The ideology of anti-angiogenesis was first postulated by Dr. Judah Folkman in 1970s (Bikfalvi *et al.*, 2002). The anti-angiogenic drug contains several properties like suppressing cell proliferation, tube formation and migration of cells through the down-regulation of different cytokine levels. The suppression of IL-1 β molecules and vascular endothelial growth factor (VEGF) in porcine retinal endothelial cells (PRECs) using silver nanoparticle obtained from the biomass of *Bacillus licheniformis* demonstrated anti-angiogenic property that led to the reduction of vascular permeability (Folkman *et al.*, 1995).

5.3 ANTI-DIABETIC ACTIVITY

Diabetes is the cause of increase in blood sugar level due to irregular production of insulin by the pancreas. The diabetes can be insulin dependent or independent. The green synthesized silver nanoparticles are programmed towards the suppression of secretory levels of enzymes majorly α -glucosidase and α -amylase. The production of silver nanoparticle from aqueous leaf extract of *Lonicera japonica* by various physicochemical techniques (UV-vis, XRD, FTIR, and HR-TEM) was studied (Sheikpranbabu, Sardarpasha, *et al.*, 2010). It was observed that spherical and hexagonal shaped nanoparticles were found stable with size of 53 nm, charge of -35.6 mV, and absorption band at 435 nm in response to their surface plasmon resonance. The nanoparticles were observed to be effective against α -amylase (IC₅₀=54.56 μ g/mL) and α -glucosidase (IC₅₀=37.86 μ g/mL) carbohydrate digestive enzymes for diabetes. The silver nanoparticles experience reversible non-competitive inhibitory activity with Ki values of 24.6, 25.9 for α -glucosidase and α -amylase which explained the activity of anti-diabetes by silver nanoparticles (Sheikpranbabu, Sardarpasha, *et al.*, 2010).

6. DIAGNOSTIC APPLICATION

Researchers round the world are updating their research postulates structuring it towards an immense application in medicine and biology (Balan, Kannan, *et al.*, 2016). In these diagnostic applications, Bioimaging and biosensing are two major subsets. Metal nanoparticles like gold, silver and quantum dots are now vastly used for disease diagnosis and biosensing (Farias, Patricia *et al.*, 2009).

6.1 BIOIMAGING PROPERTY

Recent bioimaging technology implements the visualization of cellular compartments and observation of functional alterations in the cell that helps in improved disease diagnostic accuracy. The bioimaging efficiency of AgNPs were identified from the silver nanoparticle synthesis acquired from leaf extract of *Oxalys scandens* biosynthesized silver nanoparticles (b-AgNPs) (Graham, Duncan *et al.*, 2006). Red colour was exhibited from b-AgNPs in B16F10 cells which can aid in bioimaging process. The B16F10 is a murine melanoma cell line from a C67BL/6J mouse. It's a subclone of the B16 tumor line. The silver nanoparticle produces a red colour when it interacts with cancer cell wherein the fluorescence is absent in normal cells. This shows that b-AgNPs paves a way towards bioimaging applications using plants (Mukherjee, Sudip, *et al.*, 2014).

6.2 BIOSENSING PROPERTY

The silver nanoparticles have wide range of applications towards biosensing due its effective optical and chemical properties (Taton, T. Andrew, 2000). The presence of surface plasmon resonance (SPR) has greater sensitivity towards its surroundings which plays a major role in biosensing. By means of green chemistry methods, the AgNPs synthesized are highly effective and cost efficient and can be modified into biosensors. Recent advances in biosensing applications of silver nanoparticles involve synthesis from aqueous solution of polysaccharide of *guar gum* plant (*Cyamopsis tetragonoloba*) which act as reducing agent (Ahmed, Shakeel, *et al.*, 2016). Guar gum-based silver nanoparticles (GG/AgNPs) exhibited greater optical sensing activity towards ammonia had a very low response time (2-3s) and detection limit (1ppm) at room temperature. It was proven that it can be used for ammonia detection in minute concentrations of biological fluids like plasma, saliva, cerebrospinal liquid, sweat which proposes towards future studies and development of these biosensors.

7. TOXICOLOGY STUDIES

The toxicity studies is the preliminary procedure for newly developed drugs to be transformed into clinically accepted medicinal materials. The toxicity analysis requires several factors like blood and serum biomarkers, histopathological analysis, immune response, genotoxicity, mutagenicity, and effect on organ function.

The silver nanoparticles obtained from *Brassica oleracea* plant extract was used to study the toxicity effect with the help of zebra fish model. A revelation obtained was that nanoparticles caused apoptosis of human epithelial carcinoma cells (HepG-2) and were less toxic to zebra fish embryos (Lathamuthiah *et al.*, 2015). Another toxicity study was undergone using herbal-mediated silver nanoparticles (HMSNP) which were regulated in female albino mice. A dosage of 100-2000mg/kg of HMSNP were administered and histopathology study of all the vital organs were done to identify the toxicity effect for a period of 15 days. The results revealed that there was nontoxicity of HMSNP and no mortality rate (Shanker K, Mohan GK *et al.*, 2017). This proved that biosynthesized silver nanoparticles are safe and can be implemented in various biological & biomedical applications through these studies.

8. CONCLUSION

Silver nanoparticles have gained significant importance due to their properties and applicability in medicine, catalysis, textile engineering, biotechnology, nanobiotechnology, bio-engineering sciences, electronics, optics, and water treatment. The Green synthesis of silver nanoparticles (AgNP) exhibits wide range of advantages over chemical and physical methods like cost effectiveness, environment friendly, easily scaled up for large scale synthesis and no need to use high pressure, energy, temperature and toxic chemicals. It's also non-toxic in nature hence they're safe to be used by humans as skincare, medicine, drug, etc. In the process of green synthesis, microbial precursors has taken more time and loses their nanoparticle synthesis potential when not sub-cultured and maintained regularly. These problems are rectified when plant-based precursors were used for the synthesis process. Thus, as a result the use of plant extract for the green synthesis of AgNPs have proven significantly advantageous over other methods of synthesis and can have large impact in future.

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