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REVIEW PAPER OPEN ACCESS

# Review on antimicrobial applications of silver nanoparticles and use of plant extracts for its synthesis

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## Abstract

Metallic nanoparticles are mostly used in medical fields as it has small size and can easily be used in different applications. In this review, silver nanoparticles and its antimicrobial activities are elaborated for ease of study from different research papers. It has been proven by researchers that nanoparticles have antimicrobial properties. In all metallic nanoparticles, silver nanoparticles have much attention towards antimicrobial properties. Chemicals are used as reducing agents to synthesize nanoparticles, hence it can be used in various biological risks and activities because of its toxic nature also having environmental friendly nature. Biological molecules screened out from plant extracts are used in green synthesis as they are prominent over chemical methods. Plants have vital role in synthesis of metal nanoparticles because plants have biological molecules. This review describes plant diversity which mostly meets with silver nanoparticles having antimicrobial activities.

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**Introduction**

This review is about silver nanoparticles and its synthesis from plant extracts and it antimicrobial properties, different research papers was reviewed in which only those were selected for this review which had silver nanoparticles and related stuff. Modern research has an important side that is termed as nanotechnology. It deals with the synthesis and manipulation of small size nanoparticles approximately in range of 1 to 100nm in size. Although it has small size, but it meets with all properties that are biological, physical, chemical and plays their role. Nanomaterials and nanoparticles applications are rapidly emerging because of its tremendous properties that are usually size, morphology and its distribution. Nanotechnology rapidly surrounding different fields including food and feed, health, chemical industries, biomedical, photo electrochemical, rapid diagnostic and photo sensor applications. Novel findings and ease in research has been supported by nanotechnology. Nanoscale materials production mainly investigates its optoelectronic and physiochemical properties (Korbekandi and Iravani *et al.,* 2012; Kaviya and Viswanathan, 2011). Silver has strong bactericidal and inhibitory effects with specific antimicrobic action for virus, fungi and bacteria (Silver, 2003; Cho *et al.*, 2005; Lok *et al.*, 2006). Silver owns high toxicity to microorganisms compared to other metals but lower for the cells of mammal (Zhao and Stevens 1998). Silver nanoparticles are familiar for ages but got minor observation (Lok *et al.*, 2006).

SNPs and its way of working on bacteria are yet unknown, structural and morphological alteration of bacterial cells is the possible mechanism of action studied previously (Rao *et al.*, 2009). SNPs has well organized antimicrobial effects as compare to other salts because its surface area is large, hence provide better platform of adhesion with microorganism (Rai *et al.*, 2009). For short time, *E. coli* cells exposure to antimicrobial SNPs result to accumulate envelope protein precursors. It shows us that SNPs may target cell membrane of bacteria which leads to the excess of proton motive force (Lok *et al.*, 2006). When a bacterial cell has silver nanoparticles inside it, it makes low molecular mass section in the bacteria. Hence bacteria consolidate to keep safe its genome from SNPs. Nanoparticles prefers to strike at respiratory chain, cell which is dividing up and at last lead to death of the cells (Rai *et al.*, 2009). Later on, approaches in research on metal nanoparticles seem to resuscitate use of AgNPs mainly for antimicrobial applications. SNPs which are prepared with different production process have operative antimicrobial applications (Aymonier *et al.*, 2002; Alt *et al.,* 2004; Sondi and Salopek-Sondi., 2004; Baker *et al.*, 2005; Melaiye *et al.*, 2005; Lok *et al.*, 2006; Kim *et al.*,2008a, b; Lee *et al.*,2008). SNPs can be used in wide scope of products inclusive of scaffold, medical devices and water cleaning system (Kim and Kim., 2006; Thomas *et al.*, 2007).

Metallic nanoparticles have most favorable antibacterial properties because of its huge surface area to volume ratio, and it's the foremost interest of researchers because of microbial resistance which is growing against of metal ion, resistant strains development and antibiotics (Khalil *et al.*, 2013). Amongst all noble metal nanoparticles, silver nanoparticles attained a lot of interests because of its best conductivity, chemical stability, anti-viral, antifungal and antibacterial activities which can be consolidate in the form of complex fibres, super conducting materials, electronic components and cosmetic products. (Klaus-Joerger *et al.*, 2001; Ahmad *et al.*, 2003). Scientific community has much interest in synthesis of silver nanoparticles because of multiple types of its applications. Silver nanoparticles are efficiently used in cancer diagnostics and treatment (Popescu *et al.*, 2010; Baruwati *et al.*, 2009). It is best way to synthesize nanoparticles as it avoid hazardous chemicals and give natural agents for capping of silver nanoparticles reduces cost of microorganisms. Hence, this review compiled literature about production of silver nanoparticles having best antimicrobial and bactericidal activities.

*Silver nanoparticles*

*Microbial activities*

Silver nanoparticles can stick to bacterial cell wall and can pierce into it, and thus causes constitutional changes in bacterial cell wall/membrane and cell death occurs.

Thus a large hole is formed at exterior of cell where nanoparticles accumulate (Sondi *et al.*, 2004). Cells also die when silver nanoparticles form free radicals and it is considered another mechanism so far, it has been studied in electron spin resonance spectroscopy which shows that free radicals are formed when bacteria combines to nanoparticle, these free radicals are fine enough to destroy bacterial cell membrane as it make it porous and thus lead the cell to death (Danilcauk., 2006; Kim., 2007).

Nanoparticles can emit silver ions which has been proposed (Feng *et al.*, 2008), which inactivate a lot of vital enzymes by interacting with their thiol group (Matsumura., 2003). When silver and bacterial cells come in contact, silver ions are taken by cells and which stop necessary cell functions and damage the cell. Acid will react with base, silver is soft acid so it will react with soft base (Morones., 2005). Cells have sulphur and phosphorus components which meet with the nature of soft bases. Thus, when action of nanoparticles takes place in reaction cell death occurs. One more fact is that phosphorus and sulphur are the major components of DNA, hence nanoparticles can destroy these soft bases and damage the DNA which will cause (Hatchett., 1996). The interaction of phosphorus and sulphur of the DNA with silver nanoparticles causes problems in bacterial DNA replication and hence put an end to the microbes.

*Biotic production*

Silver nanoparticles produced through physical and chemical methods are much costly and use dangerous harmful chemicals which might initiate probable biotic and climate risks. We cannot avoid this fact that silver nanoparticles which are produced have to be handled and managed by humans and it must have low cost, hence we need to synthesize these nanoparticles in an economically and environmentally feasible way. Biological methods are used for the production of nanoparticles, while growing need of material synthesis which is economically feasible and environmental friendly led to hunt for bio mimetic production (Kalishwaralal *et al.*, 2008). Chemically toxic substances are absorbed on the surface on the method of chemical synthesis which prevent their use in medical applications (Parashar *et al.*, 2009). Synthesis of silver nanoparticles includes three major sources that is fungi, plant extracts and bacteria. Oxidation reduction reactions are involved in bottom up approach of biosynthesis of silver nanoparticles. Plant phytochemicals with reducing properties or microbial enzymes, give the desired nanoparticles by acting their respective compounds. Biological method involves three crucial constituents in the production of nanoparticles, these are reducing agents which are eco-friendly, solvent medium for production and stabilizing agents which are nontoxic.

There is vital role of silver nanoparticles in medical field because of its distinctive properties and also the use in daily life by human, some examples are fabrics cleaning, house cleaning chemical, best electronic appliances, to improve the heat transfer to fuel tanks from collectors of solar energy and numerous other approaches which are prime for silver nanoparticles but we should use it in medical field thoroughly. The effect of nanoparticles is increased when large surface area is accommodated by small size of nanoparticles. Potential silver particles penetration is also increased using nanosized of the particles, which add best resort to metal properties. Nanoparticles can penetrate to circulatory system and shift blood brain barrier.

Medical field uses silver nanoparticles because of its prominent antimicrobial nature. Recent researches show that metal proteinase (MMP) activity is reduced and thus wound healing is boost up in presence of nanoparticles. However non healing wounds are caused when MMP induce inflammation (Kirsner *et al.*, 2001). A burn wounded mouse model was studied when silver nanoparticles were inaugurated, it resulted in reduction in the level of pro-inflammatory cytokines (Tian *et al.*, 2007). Interferon gamma actions can be resisted by silver nanoparticles and also inflammation which is caused by tumor necrosis factor alpha (Shin *et al.*, 2007). Hence proved, silver nanoparticles have role in anti-inflammation, although its exact mechanism is still need to be explored. Nanosilver which induces anti-inflammatory effects is outstanding applicant and is used in lot of therapies.

In 1995 Dr. Robert Burrell succeed in healing the wound by nanosilver first time in the history, by synthesizing Acticoat which speeds up healing and softens the scars (Burrell *et al.,* 1995). Nanosilver has good consequences on bacteria, which is likely to infect the wound because it easily penetrates the wound via fluids of the body. Artificial joint replacement uses bone cements which uses silver nanoparticles. Nanosilver with Polymethyl methacrylate is considered as bone cement in which the nanosilver produce antimicrobial activity (Alt *et al.*, 2004). High weighted polyethylene is the better option for the replacements of joint, but it is vulnerable to deterioration or decomposition which is a prominent demerit hence silver nanoparticle were introduced to it to decrease the polymers detorioration (Morley *et al.,* 2007). Antiseptics and antibiotics are used to prevent surgical infections.

For tissue repair surgical meshes are used to dress considerable injuries because it is vulnerable to the diseases caused by microbes. Polypropylene mesh coated mesh coated silver nanoparticles have prominent antimicrobial activities which are considered ideal for surgical meshes (Cohen *et al.*, 2007). Silver nanoparticle is reported with antimicrobial activities which is used in disinfectants (Brady *et al.*, 2003). It is accepted that medical treatments just like wound dressings, dental fillings and bone cements can use nanosilver which prevent microbial infections.

Nanosilver has plasmonic properties make it best for bio-imaging which uses fluorescent dyes, which prevent photo bleaching and through which dynamic phenomenon can be checked for long time interval (Lee *et al.*, 2007). Unwanted cells can be destroyed by nanosilver because it has plasmonic nature. Cells with nanoparticles can be conjugated, which can be used to absorb light and convert it to thermal energy which lead to thermal removal of cells which are specifically targeted (Loo *et al.*, 2005).

*Applications*

Textile coatings, food and health industries are using silver nanoparticles while it has number of other environmental related applications.

Products which are prepared with silver nanoparticles have been accepted by US EPA, US FDA, SIAA of Japan and also by FITI testing and research institute (Veeraputhiran., 2013). Antimicrobial property of silver nanoparticles are benefited in home and medicine, to inhibit the inflammation at burn site silver sulfadiazine cream is used and some appliance companies have adjusted silver into their washing machines. Silver is used in many consumer products which elaborate the field of nanotechnology that includes acne creams, baby pacifiers, athletic wear, and socks which protect them from body odour in addition to deodorizing sprays.

Silver nanoparticles show best catalytic activities like dye reduction. Kundu *et al.* stated that methylene blue is reduce in the existence of silver nanoparticles by arsine (Kundu *et al.*, 2002). Phenosafranine dye is reduced by silver nanoparticles studied by Mallick *et al* (Mallick *et al.*, 2006). Antimicrobial activities of silver nanoparticles are also studied by growing E-coli on agar plate and in liquid broth medium which were supplemented with silver nanoparticles (Sondi and Salopek-Sondi., 2004). For membrane transport investigation single nanoparticles are used in living microbial cells (Nancy *et al.*, 2004). Nanosphere lithography with triangular silver nanoparticles functions are sensor. These nanosensors have all interested features that is of Surface Plasmon Resonance (SPR) spectroscopy which is the basic concept at the back of a lot of colour based biosensor applications and also by altering shape and size of nanoparticles, the distinctive features of these nanosensors are two in which one is modest refractive sensitivity and other is a short-range sensing length scale. These two features merge to produce an area of mass sensitivity of 100 to 1000Pg/mm, which is only a feature of 100 poorer than the excellent propagating SPR sensitivities (Larguinho and Baptista., 2012).

Green methods which yield to silver nanoparticles have described to have pathogenic control and biomedical applications. Aqueous piper longum fruit extract were used in a study to synthesize nanoparticles, green synthesized silver nanoparticles and aqueous piper longum fruit extracts have

reported with powerful antioxidant properties studied *in vitro* antioxidant assays (Haes and Van Duyne., 2002). Silver nanoparticles which were coated with starch were studied in normal human glioblastoma cells and lung fibroblast cells. Evaluation of the toxicity level is judged from changes in the morphology of cells, metabolic activity, oxidative stress and cell viability. These nanoparticles can damage mitochondria by production of ATP damage which is measured by cytokinesis blocked micronucleus assay and single cell gel electrophoresis was also dose dependant and more eminent in the cells of cancer (Reddy *et al.*, 2014). Nanosilver based conductors have high electrical frequency which is measured up to 220 GHz. (AshaRani *et al.*, 2009).

Silver nanoparticle has demonstrated antiviral activity against of HIV-1 at non cytotoxic concentrations, but its contraption is yet not fully explained. The way of antiviral action of silver nanoparticles was evaluated against of HIV-1 using multiple in vitro assays (Lara *et al.*, 2010). Bimolecular diagnostic got special interest including biomarker characterization and Single Nucleotide Polymorphism (SNP) detection. For this development of nanoscale devices is encouraged to characterize nucleic acid that is RNA or DNA and protein at increased rate that is less time consuming and cost effective as compare to conventional techniques (Goyal *et al.*, 2009).

*Antimicrobial mechanism*

Different purposes have been carried out through silver metal, it can be used for ornamentation as jewellery, cutlery and wares which is considered transmit health benefits to the users. Earlier study show history of silver used as antimicrobial, Milk bottles are coated by silver, it acted as natural biocide developed by Phoenicians. Familiar antimicrobial which is used against of viruses, fungi and bacteria is silver, which is recently used at configuration of silver nanoparticles. Several diseases have been treated through use of silver in old Indian medical system. In 1884, this was believed and practiced to operate aqueous silver nitrate drops in the eyes of newborn to stop the transmission of Neisseria gonorrhoea from infected mothers. Silver is found less toxic to animal cells while having best antimicrobial action amongst all metals. Silver was commonly used in treatment during World War I to inhibit microbial growth in soldiers injuries (Ankanna *et al.*, 2010). For 2000 years silver has been used for medical purposes (Prabhu S, Poulose., 2012). For antimicrobial effect silver is used in the form of nitrate but surface area which is available for microbes is increased when nanoparticles of silver are used. Plants extracts is used in synthesis of silver nanoparticles, these nanoparticles are used to analyze their antimicrobial activities against of several microbes. The antimicrobial characters of silver nanoparticles rely on environmental conditions, size and capping agent.

Silver nanoparticles toxicity and antimicrobial mechanism is still need to be explored and investigated. Silver ion has positive charge which is considered vital for antimicrobial activites. When silver is in the ionized form it owns antimicrobial characteristics. Silver is inert in its ionized form but releases silver ion when come in contact with moisture (Klueh *et al.*, 2000). Silver ion tend to interact with nucleoside instead of nucleic acid phosphate group, silver ions are placed into the substance and releases slowly with sulfadiazine or silver ion can be generated from solid piece of silver as with silver nanoparticles (Yakabe *et al.,* 1980; Sondi and Sondi., 2004) Literature shows electrostatic attraction that is negative charge of bacterial cells and positive of nanoparticles (Cao *et al.,* 2001) and they are proposed to be more satisfactory bactericidal agent (Wright *et al.*, 1999, Matthew *et al.,* 2009). Cell membrane is usually damage by nanoparticles because it accumulates inside and penetrates to cells. Silver form stable bonds with thiol containing compounds which causes inactivation of enzyme in the cell membrane which facilitate ion transport and generation of trans membrane energy. Silver ion inserted between pyrimidine and purine base pairs derange hydrogen bonding and hence denature DNA. When bacterial cell ruptures it could be a reason for antibacterial activities when enters to the cell.

Peptidoglycan molecule is the main component of gram positive bacteria cell wall that's why it is less susceptible to silver ion as compare to gram negative bacteria. Silver ions are positively charged while peptidoglycan molecule is negatively charged so more silver will stuck in gram positive bacteria in comparison to gram negative bacteria. The low accountability of gram positive bacteria can also can also be described by the fact that gram positive bacteria has the thicker cell wall (Ankanna *et al*., 2010).

**Conclusion**

Nature has graceful and innovative ways of creating the most systematic miniaturized serviceable materials. Silver is used as an excellent microbial agent for ages. The efficacy of silver is increased through chemical and physical properties of silver nanoparticles. Eco friendly techniques need to be developed by increasing awareness towards green route for production of metal nanoparticles. The use of plant extracts for the synthesis of silver nanoparticle is that it is cost effective and energy efficient as well as protect human health, provide healthier work places and leading the environment to be clean and safe. Nanoparticles synthesized from plants have advantage over rest of biological entities in response to time consumption, hence in this view in coming decades plants extracts will have great impact on production of silver nanoparticles. Researches have been carried out on silver nanoparticles, its synthesis using plant extracts but still need for commercially feasible and applicable, economic and ecofriendly which reduce constituents to synthesize silver nanoparticles not been studied yet. Plant extracts collected from same species from various parts of the world may have different chemical compositions which lead to different results in the laboratories. This is the major disadvantage in using plant extracts for synthesis of silver nanoparticles as stabilizing and reducing agents which need to be fixed. On recognizing biomolecule which is present in the plant are liable for moderating the nanoparticles synthesis for quick single step protocol to get control over the above said problem which gives a new facelift towards production of silver nanoparticles green synthesis.

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