academicJournals

Vol. 13(4), pp. 546-554, 22 January, 2014
DOI: 10.5897/AJB2013.13147
ISSN 1684-5315 ©2014 Academic Journals
http://www.academicjournals.org/AJB

African Journal of Biotechnology

Review

Nanosilver: Potent antimicrobial agent and its biosynthesis

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Accepted 16 January, 2014

Silver ions and its salts are well known for their potent antimicrobial agent. These days, the nanosilver are widely used in a growing number of applications ranging from home disinfectants and medical devices to water purifier due to properties of silver at the nano level. Nanosilver has a large ratio of surface which dramatically increases the potential for silver ions to be accessed anywhere in body where larger silver particles cannot. The synthesis of silver nanoparticles has been reported using chemical and physical methods. This review describes a cost effective and ecofriendly approach for the synthesis of silver nanoparticles. Thus, in this review we focus on the role of microorganisms and plants in the synthesis of nanosilver and their potent application as antimicrobial agent.

Key words: Nanosilver, antimicrobial, disinfectant, nanoparticles.

INTRODUCTION

Nanoscale science is the discipline that examine the unique behaviors and properties of materials that emerge at the size range of 1 to 100 nanometers (a billionth of a meter). Nanobiotechnology is a sub-discipline of nano-science that has arisen more recently. It manipulates unique behaviors and properties at the nanoscale to manipulate materials for various applications in biology. Nanobiotechnology already impact in medicine as therapeutic agent.

Nanobiotechnology promises to be critical in advances in other related fields. Silver has been valued for many of its properties that are useful for mankind. It is used in precious goods such as currencies, ornaments, jewelry, electrical contacts and photography, among others. The one of the most potent uses of silver as antimicrobial agent that is toxic to bacteria, fungi, and viruses. Due to their size, nanosilver have a very large surface area which typically results in greater biological activity, chemical reactivity and catalytic behavior compared to larger particles of the same chemical composition (Garnett and Kallinteri, 2006; Limbach et al., 2007). Nanotechnology is being utilized in offering many new developments in the fields of biosensors, biomedicine, bio nanotechnology diagnosis, therapeutic drug delivery and the development of treatments for many diseases and disorders. Nanosilver have novel or enhanced properties based on specific characteristics such as size, distribution and morphology. Nanosilver show potential of applications in various fields such as catalysts in chemical reactions, electrical batteries and in selective coatings for absorption of solar energy, as optical elements, pharmaceutical components and in chemical sensing and biosensing (Kamat, 2002), plasmonics (Maier et al., 2001), optoelectronics (Gracias et al., 2002), biological sensor (Mirkin et al., 1996; Han et al., 2001) and pharmaceutical applications like their potential in drug delivery formulations and routes.

The synthesis of nanosilver has been remarkable developments in the field of nanotechnology from the decade. A large numbers of methods have been reported for the synthesis of nanosilver of particular shape and size depending on specific requirements (Figure 1). Nanosilver was produced by physical and chemical methods. Some of the commonly used physical and chemical

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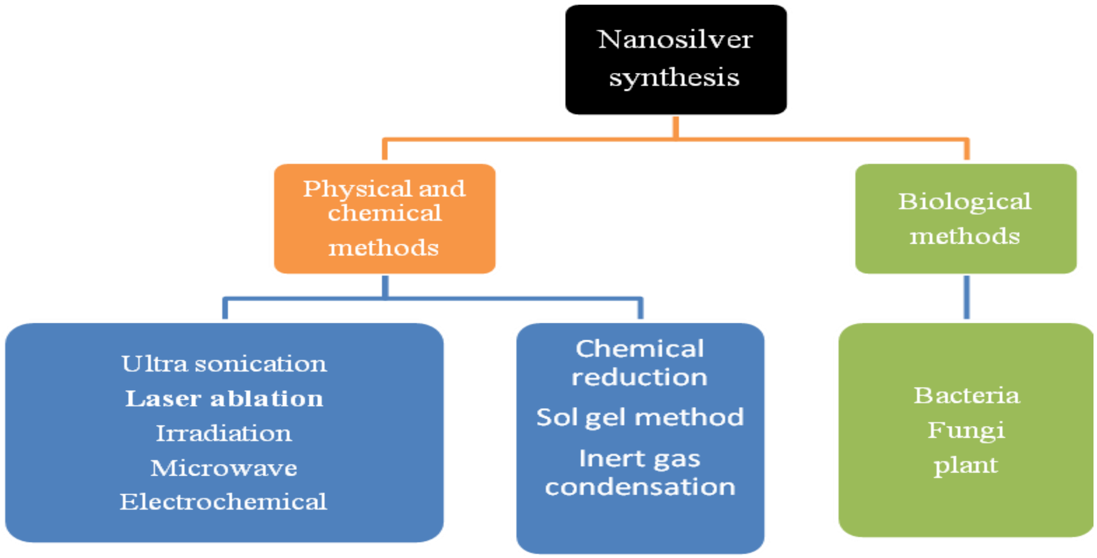

Figure 1. Different methods for nanosilver synthesis.

methods are ion sputtering, thermal synthesis, Inert gas condensation, reduction and sol gel technique.

Unfortu-nately, nanosilver synthesis involves the use of hazardous chemicals, low material conversions, high energy requirements, difficult and wasteful purifications. Further, the synthesis of nanosilver including physical and chemical processes is costly. Therefore, there is a growing need to develop environmentally friendly processes for nanoparticle synthesis without using toxic chemicals. Biosynthetic methods employing either microorganisms or plant extracts have emerged as a simple and viable alternative to chemical synthetic procedures and physical methods.

The development of cheaper reliable, eco-friendly processes for the synthesis of nanosilver is an important aspect of nanotechnology today. Many biological synthesis protocols have been reported using bacteria (Kalimuthu et al., 2008; Fu et al., 1999) fungi (Bhainsa and D'Souza, 2006; Vigenshwaran et al., 2006; Basavaraja et al., 2008; Kathiresan et al., 2009) and plants (Selwal et al., 2013; Singh et al., 2010; Dubey et al., 2009). In this review, we focus on the biological synthesis of silver nanoparticles, potential and the possible mechanism of antimicrobial actions.

NANOSILVER SYNTHESIS- AN OVERVIEW

Nano silver are one of the promising products in the nanotechnology industry. The development of consistent processes for the synthesis of silver nanoparticles is an important aspect of current nanotechnology research. One of such promising process is green synthesis. Silver nanoparticles can be synthesized by several physical, chemical and biological methods. However for the past few years, various rapid chemical methods have been replaced by greens synthesis because of avoiding toxicity of the process and increased quality.

Approaches for nanosilver synthesis

Basically there are two approaches for nanoparticle synthesis namely the Bottom up approach and the Top down approach (Figure 2).

Top down approach

In the Top down approach involve production of nanosilver involve mechanical grinding of a bulk piece of the material.

Bottom up approach

The Bottom up approach involves chemical and biological methods to make nanostructures and nanoparticles. These processes involve controlled condensation of solute molecules that are formed during a chemical reaction. The restriction of the condensation or growth leads to the formation of particles of desired size and shape.

Biosynthesis of nanoparticles is a kind of scale down or bottom up approach where the main reaction occurring is reduction/oxidation. The microbial enzymes or the phytochemicals with anti oxidant or reducing properties are usually responsible for reduction of metal compounds into their respective nanoparticles.

Figure 2. The top-down approach versus the bottom-up approach.

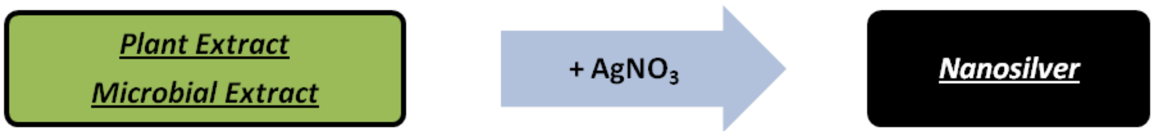

Figure 3. Plant and microbial mediated synthesis of nanosilver.

Physical and chemical methods of nanosilver synthesis

Some of the very successful physical methods for the synthesis of nanoparticles include radiolysis, ultrasonic-cation, laser abalation, microwave and electrochemical methods. However, physical methods have had limited success and therefore chemical methods for the synthesis of inorganic nanoparticles are widely accepted and commonly practiced. Nanosilver can be synthesized chemically by reduction or oxidation of metal ions, inert gas condensation, or by the sol gel methods.

Disadvantages of using physical and chemical methods

The synthesis of nanoparticles including physical and chemical processes is costly. The use of these synthesis methods requires both strong and weak chemical reducing agents and protective agents like sodium borohydride, sodium citrate and alcohols. These agents are mostly toxic, flammable, cannot be easily disposed off due to environmental issues and also show a low production rate.

There is need to search of cheaper path-ways for nanoparticle synthesis, so used microorganisms and plant extracts for synthesis. The biosynthesis of nanoscale nanosilver may contribute to the development of relatively new and largely unexplored area of research.

Biological synthesis of nanosilver

Green plant and microorganisms have a remarkable ability to form exquisite nanosilver. Biological synthesis using plant and microorganisms is eco-friendly and cheaper. Nowadays a large number of microorganisms and plant extracts are used for nanosilver synthesis (Figure 3).

Bacterial mediated synthesis of nanosilver

The probability of the bacterial mediated synthesis of silver nanoparticles has been successfully reported (Table 1). Bacterial cells are used to produce silver nanoparticles. These particles possess interesting physical and chemical properties (Figure 4).

Fungus mediated synthesis of nanosilver

The probability of the fungal system for the synthesis of silver nanoparticles has been successfully demonstrated (Table 2). The fungal system shows the capability of both intracellular and extracellular synthesis of silver nanoparticles. In the recent past, research work using the fungal system has been carried out using both aspects of intracellular and extracellular methods for synthesis of nanosilver.

Plant mediated synthesis of nanosilver

The probability of the plants extract for the synthesis of silver nanoparticles has been successfully reported (Table 3). Plants extracts can be used in the synthesis of silver nanoparticles. However, the mechanism for the synthesis of silver nanoparticle from plants is not yet fully understood. Phytochemicals are assumed to be responsible for the formation of silver nanoparticles.

APPLICATIONS OF NANOSILVER

Nanosilver as powerful antimicrobial

The potent application of nanosilver is use as antimicrobial agent. Nanosilver shows strong antimicrobial activity is a major reason for the development of nano-

Table 1. List of bacteria synthesizing silver nanoparticles.

Bacteria	Size of the particle (nm)	Reference
Bacillus licheniformis	50	Kalimuthu et al., 2008
Bacillus megaterium	46.9	Fu et al., 2009
Pseudomonas stutzeri	200	Tanja et al., 1999
Corynebacterium sp.	10-15	Zhang et al., 2005
Bacillus licheniformis	50	Kalishwaralal et al., 2008
Geobacter sulfurreducens	200	Law et al., 2008
Morganella sp.	20-25	Parikh et al., 2008
Bacillus subtilis	5-60	Saifuddin et al., 2009
Escherichia coli	1-100	Gurunathan et al., 2009b
Klebsiella pneumonia	50	Ahmad et al., 2007
Proteus mirabilis	10-20	Samadi et al., 2009
Bacillus sp.	5-15	Pugazhenthiran et al., 2009
Staphylococcus aureus	1-100	Nanda and Saravanan, 2009
Lactic acid bacteria	11.2	Sintubin et al., 2009
Brevibacterium casei	50	Kalishwaralal et al., 2010
Cryphonectria sp.	30-70 nm Dar	Dar et al., 2013

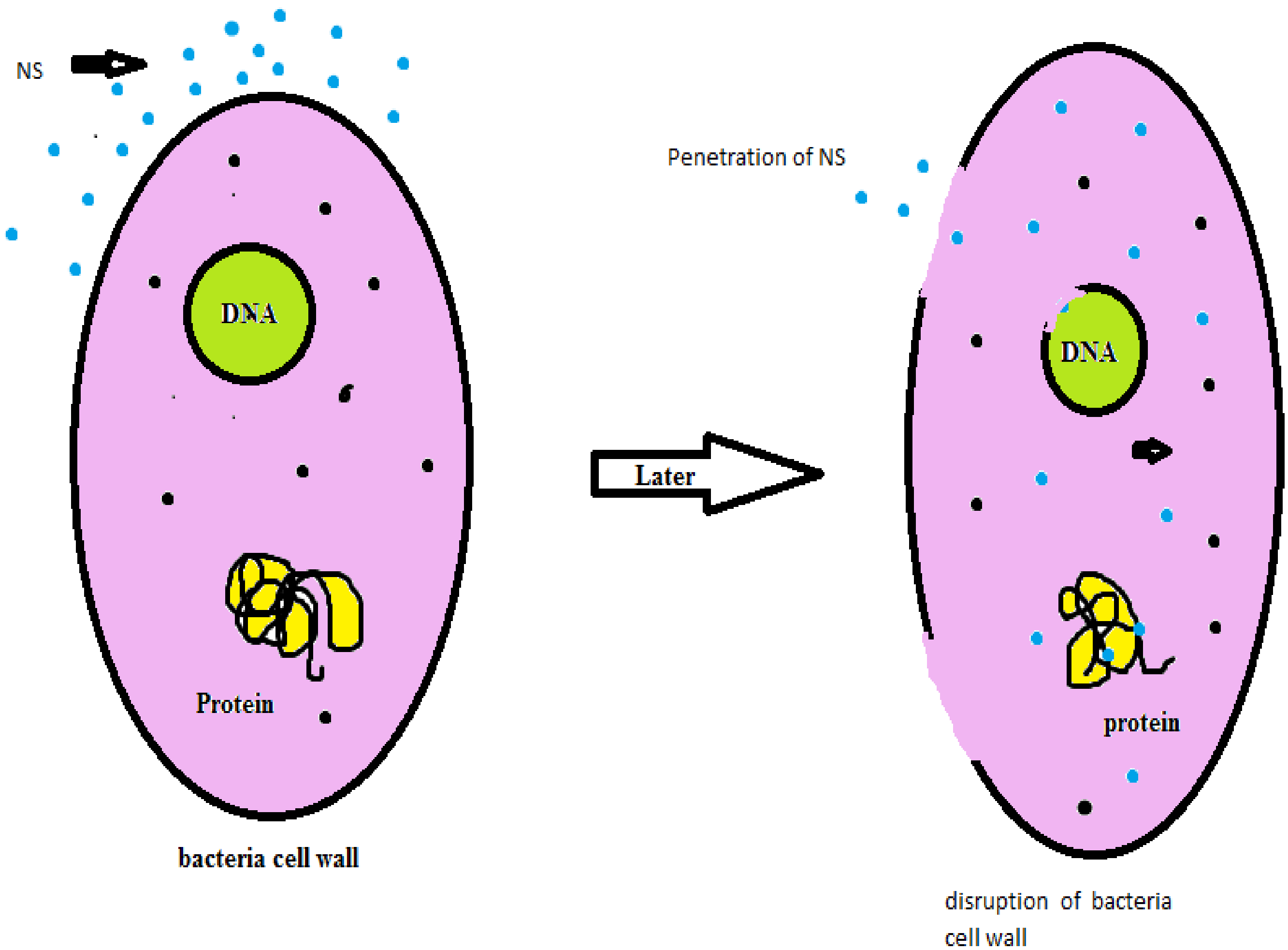

Figure 4. Attachment and penetration of nanosilver with bacterial cell membrane.

Table 2. List of Fungi synthesizing silver nanoparticles.

Fungi	Size of the particle (nm)	Reference
Aspergillus fumigates	5-25	Bhainsa et al., 2006
Phaenerochaete chrysospouirm	100	Vigenshwaran et al., 2006
Fusarium semitectum	10-60	Basavaraja et al. 2008
Pencillium fellutanum	1-100	Kathiresan et al, 2009
Fusarium oxysporum	5-50	Ahmad et al., 2003
Trichoderma viride	5-40	Fayaz et al., 2010
Fusarium oxysporum	5-40	Kumar et al., 2007
Fusarium semitectum	13-18	Basavaraja et al., 2007
Aspergillus niger	20	Gade et al., 2008
Fusarium acuminatum	5-40	Ingle et al., 2008a
Trichoderma asperellum	13-18	Mukherjee et al., 2008
Penicillium	10-100	Sadowski et al., 2008
Phoma glomerata	60-80	Birla et al., 2009
Fusarium solani	5-35	Ingle et al., 2008b
Coriolus versicolor	67.6-74.52	Sanghi and Verma, 2009
Cladosporium cladosporioides	10-100	Balaji et al., 2009

Table 3. List of plant synthesizing silver nanoparticles.

Plant	Size of the particle (nm)	Reference
Mangifera indica	-	Selwal et al., 2013
Argemone mexicana	10-50	Singh et al.,2009
Eucalyptus hybrid (Safeda)	50-150	Dubey et al., 2009
Brassica juncea	15-25	Lamb et al., 2001
Azadirachta indica	5-100	Shankar et al., 2004
Emblica officinalis	10-20	Ankamwar et al., 2005
Aloe vera	15±4.2	Chandran et al., 2006
Capsicum annum	-	Li et al., 2007
Helianthus annus	-	Leela and Vivekanandan, 2008
Gliricidia sepium	10-50	Raut et al., 2009
Jatropha curcas	10-20	Bar et al., 2009
Carica papaya	60-80	Mude et al., 2009
Coriandrum sativum	26	Sathyavathi et al., 2010
Artemisia nilagirica	70-90	Vijayakumar et al., 2013
Rhinacanthus nasutus	11.5- 22	Pasupuleti et al., 2013

silver containing products. Nano-silver have used for thousands of years without ill effects. Nanosilver is an effective killing for bacteria, fungus, and viruses.

Nanosilver as antibacterial

Nanosilver is an effective killing agent against a broad spectrum of Gram negative and Gram- positive bacteria (Burrell et al., 1999; Wijnhoven et al., 2009; Yin et al., 1999) including antibiotic-resistant strains (Percival et al., 2007; Wright et al., 1998). Silver nanoparticles show potential antimicrobial effects against infectious organisms including *Escherichia coli*, *Bacillus subtilis*, *Vibrio cholera*, *Psuedomonas aeruginosa*, *S.typhus*, *and S*taphylococcus *aureus*. It is important that silver is a natural element that is commonly used throughout the world at low concentrations with no evidence to support a concern for widespread bacterial resistance. Nanosilver has a large surface which increases the potential for silver ions to interact with the bacteria and reduction in size of silver at nanoscale make enable it to be released

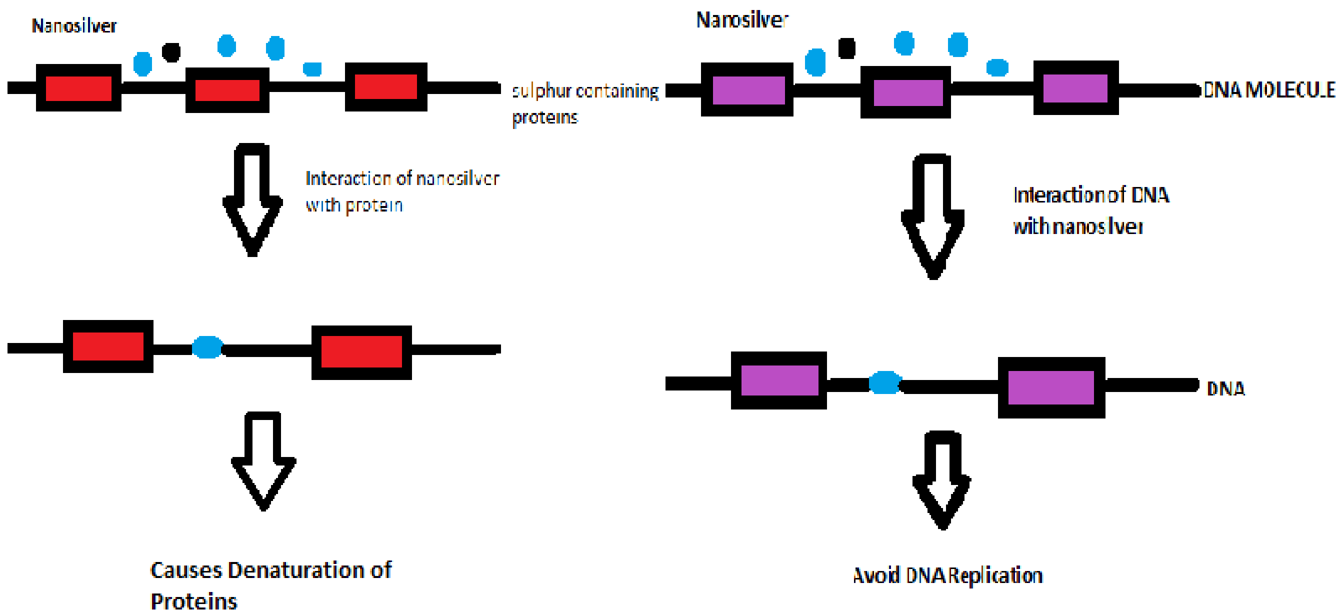

Figure 5. Interaction of nanosilver with proteins and DNA.

anywhere in body where larger silver particles cannot. The exact mechanism of silver nanoparticles is not scientifically justified and is a debated topic. There are however various theories are put forwarded on the possible mechanism for the antimicrobial action of nano silver. The possible mechanisms of action are:

1. Nanosilver as nanometer scale silver provides an extremely large surface area for better contact with bacteria. These silver nanoparticles get attached to the cell membrane and easily penetrate inside the bacteria (Rai et al., 2009).
2. Nanosilver attack the respiratory chain in microbial mitochondria which lead in to the death (Sondi and Salopek-Sondi, 2009).
3. Nanosilver interacts with sulphur containing proteins on microbial cell membrane causing disruption (Liau et al., 1997) (Figures 4 and 5).
4. The surface of microbes having phosphorus containing compound like DNA, nanosilver inhibit their functions (Matsumura et al., 2003).
5. Nanosilver release Ag+ ion inside the microbial cell which may create free radicals and induce oxidative stress, thus further enhancing their bactericidal activity (Kim et al., 2007).

Nanosilver as antifungal

Nanosilver is an effective, fast-acting fungicide against a broad spectrum of fungi including genera such as *Aspergillus*, *Candida*, and *Saccharomyces*. The mechanisms similar to that of the antibacterial actions have been proposed for fungi (Wright et al., 1999).

Nanosilver as antiviral

Nanosilver (average diameter ~10 nm) inhibit HIV-1 virus replication (Sun et al., 2005). Size- dependent antiviral activity of silver nanoparticles has been shown with HIV-1 virus (Elechiguerra et al., 2005). It is evident that nanosilver due to its biological and physiochemical properties is potent as antimicrobials and therapeutic agents. They can be used for many challenges in the field of nanomedicine.

Nanosilver in medicine

Nanosilver shows potent antibacterial activities against various pathogens and immensely useful in the medical field (Guzman et al., 2012). Earlier studies have suggested that nanosilver can inhibit the gamma interferon and alpha tumor necrosis factor which are involved in inflammation (Shin et al., 2007). These anti-inflammatory responses induced by nanosilver make it an anti-inflammatory agents. Polymethyl methacrylate along with nanosilver is being considered as bone cement as the nanosilver can encourage antimicrobial activity (Bechert et al., 2004). The antimicrobial property of nanosilver shows enormous potential to be used in disinfectants (Brady et al., 2003).

The plasmonic properties of nanosilver can effectively biosense that makes it ideal biosensors for a large number of proteins that normal biosensors find more difficulty in detections. This unique advantage that nanosilver has, can be utilized for detecting various abnormalities and diseases in the human body including cancer (Moores and Goettmann, 2006; Zhang et al., 2009; Ghodselahi et al., 2011). Due to potent application as antimicrobial agent nanosilver used for development of novel chitin/nanosilver composite scaffolds for wound dressing (Madhumathi et al., 2010), nanosilver are currently being used in many household products such as cloths, washers, water purification systems, tooth paste, shampoo, fabrics, deodorants, filters, paints, kitchen utensils, and toys to impart antimicrobial properties (Baker et al., 2005).

CONCLUSION AND FUTURE PROSPECTS

Silver nanoparticles are conveniently prepared through leaves extract. The biological synthesis of silver nano-particles is fast, ecofriendly and cheaper. The biological method for synthesis of silver nanoparticles with high antimicrobial activity has been developed. Nanosilver is an excellent antimicrobial and has been used for many years. Chemical and physical methods of nanosilver synthesis have been used for decades, but they are found to be expensive and the use of various toxic chemicals for their synthesis therefore, the biological synthesis is the most preferred option. Plant, bacterial, and fungal extract can be used for nanosilver synthesis, the easy availability, the nontoxic nature, the various options available, and the advantage of quicker synthesis make plant extracts the best and an excellent choice for nanosilver synthesis.

Rapid synthesis and excellent reproducibility of silver nanoparticles from the plant extract is a time saving and advantage over microbial synthesis because laborious and lengthy procedures are involve in mantainace of microbial cultures. Nanosilver contributes into potential application as antimicrobial agent. This has been utilized in various processes in the medical field and has hence been exploited well.

ACKNOWLEDGMENT

The first authors are thankful to University Grant Commission (UGC), New Delhi for the award of Junior Research Fellowship.

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