SYNTHESIS OF SILVER NANOPARTICLES FROM MEDICINAL PLANTS AND ITS BIOLOGICAL ACTIVITIES

D. T. Sakhare

U.G., P.G. & Research Centre, Department of Chemistry, Shivaji, Art's, Comm. & Science College Kannad. Dist.Aurangabad.431103, Maharashtra, India.

E-mail- sakharedhondiram@yahoo.com

ABSTRACT

Nanobiotechnology holds a great potential in various field of Life Science. Nanotechnology involves the use of material with components that have dimension less than 100nm. The demand of green synthesis of nanoparticle increased day by day due to drawbacks of Chemical synthesis. Application of nanosize material is an emerging area of Nanotechnology, among various metal nanoparticles silver nanoparticles gain special interest due to its remarkable properties silver nanoparticles are usually ranging from 1 to 100 nm size. They have unique electrical, optical and thermal properties and which can be incorporated into industrial application of Electronics catalyst and photonics. Silver nanoparticle exhibit a broad spectrum of antibacterial and antifungal activity is making them extremely popular in a diverse range of of consumer products including plastic, soaps, paste, foods and textile, thus increasing the market value. The presence of soluble Organics in the plant extracts was mainly responsible for the Silver ions reduction to nanosized Silver particles. The present work provides information of silver nanoparticle synthesis from various medicinal plants various methods of characterization and its biological applications

KEYWORDS: Nano-biotechnology, Spectrophotometer, Nanoparticles, Physico-chemical properties.

INTRODUCTION

Nano-technology is a rapidly growing field in which research deals with the synthesis, design, and particle structures manipulation which are ranging from 1-100 nm. Nanoparticles show various applications such as environmental, food, health care, optics, healthcare, chemical industries, etc. Nanobiotechnology is a part of nanotechnology and multidisciplinary in nature which investigates the use of nanoparticles in the biological systems. Nanobiotechnology provides a crucial technique for the development of a clean, nontoxic, and environment-friendly process for metal nanoparticles synthesis which has the ability to reduce metals by specific metabolic pathways. Nanoparticles show specific characteristics as compared to large particles such as their morphology, size, and distribution. Chemical and physical methods for synthesis of nanoparticles are costly and releases toxic byproducts in nature. Due to these problems, there is a requirement of an alternative for synthesis of nanoparticles. It has also seen that silver nanoparticles synthesized from chemical methods show less antibacterial activity as compared to the nanoparticles synthesized from biological approach. This is may be due to the presence of protein coating of nanoparticles obtained from plant extract [1-5].

Various nanoparticles have been synthesized by using plant extracts which includes silver, gold, and copper oxide. Use of plant extracts for nanoparticles synthesis is favorable over the other biological material as it removes the long process of maintenance of cell culture. Among various metal nanoparticles, silver nanoparticles obtain more attention due to its good conductivity, stability and antimicrobial activity. The biological activity of silver nanoparticles depends on various factors such as size, shape, size, surface chemistry, distribution, particle composition, particle morphology, capping, agglomeration, etc. [3]. Nanoparticles physicochemical properties increase the bioavailability of therapeutic agents [6-26]. Therefore, development of silver nanoparticles with controlled structures that are uniform in morphology, size, and functionality is important for its various applications [27-40].

SYNTHESES OF SILVER NANOPARTICLES USING DIFFERENT MEDICINAL PLANT EXTRACTS

Utilization of various plants extracts for silver nanoparticles synthesis has to gain importance due to its various advantages such as eco-friendly, rapid, non-pathogenic and economical. Reduction and stabilization of silver ions are due to the combination of biomolecules such as amino acids, proteins, enzymes, alkaloids, saponins, terpenoids, phenolics, tannin and vitamins present in plant extracts. Plant extracts reduce the AgNO3 which forms Ag3+ ions to AgO ions; this can be monitored by using a UV-Visible spectrophotometer. Large numbers of plants are reported to have the potential of synthesizing the silver nanoparticles are mentioned in Fig. 1 and Table 1.

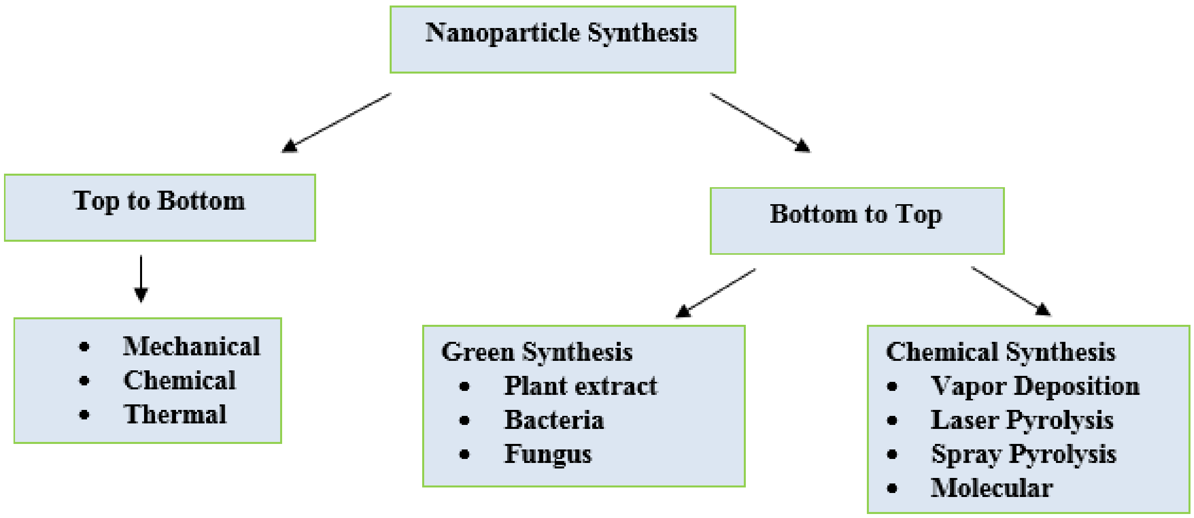

Fig. 1. Nanoparticle synthesis using different screening methods

Table 1. Synthesis of silver nanoparticles from different medicinal plants.

Sr.No.	Plants	Size in nm	Plant part	References
1	*Alternanthera dentate*	50–100	Leaves	Nakkala et al. [33]
2	*Abutilon indicum*	7–17	Leaves	Sadeghi and Gholamhoseinpoor [48]
3	*Acorus calamus*	31.83	Rhizome	Nakkala et al. [34]
4	*Argyreia nervosa*	20–50	Seeds	Thombre et al. [55]
5	*Acalypha indica*	20–30	Leaves	Krishnaraj et al. [21]
6	*Brassica rapa*	16.4	Leaves	Narayanan et al. [35]
7	*Carica papaya*	25–50	Leaves	Jain et al. [15]
8	*Cymbopogan citratus*	32	Leaves	Masurkar et al. [30]
9	*Centella asiatica*	30–50	Leaves	Rout et al. [38], Roy and Bharadvaja [40]
10	*Coccinia indica*	10–20	Leaves	Kumar et al. [23]
11	*Citrus sinensis*	10–35	Peel	Kaviya et al. [25]
12	*Calotropis procera*	19–45	Plant	Gondwal et al. [12]
13	*Datura metel*	16–40	Leaves	Kesharwani et al. [26]
14	*Eucalyptus hybrid*	50–150	Peel	Dubey et al. [4]
15	*Eclipta prostrate*	35–60	Leaves	Rajakumar and Abdul Rahuman [45]
16	*Ficus carica*	13	Leaves	Ulug et al. [57]
17	*Musa paradisiacal*	20	Peel	Bankar et al. [2]

18	*Moringa oleifera*	57	Leaves	Prasad and Elumalai [37]
19	*Melia dubia*	35	Leaves	Kathiravan et al. [16]
20	*Memecylon edule*	20–50	Leaves	Elavazhagan and Arunachalam [6]
21	*Nelumbo nucifera*	25–80	Leaves	Santhoshkumar et al. [45]
22	*Plumbago zeylanica*	60	Leaves	Salunke et al. [46], Roy and Bharadvaja [39]
23	*Premna herbacea*	10–30	Leaves	Kumar et al. [24]
24	*Psoralea corylifolia*	100–110	Seeds	Sunita et al. [49]
25	*Thevetia peruviana*	10–30	Latex	Rupiasih et al. [44]
26	*Vitex negundo*	5 and 10–30	Leaves	Zargar et al. [64]
27	*Vitis vinifera*	30–40	Fruit	Gnanajobitha et al. [11]
28	*Ziziphora tenuior*	8–40	Leaves	Sadeghi and Gholamhoseinpoor [51]

CHARACTERIZATION OF SILVER NANOPARTICLES

Physico-chemical properties are significant for behavior, safety, bio-distribution, and efficacy of nanoparticles. Therefore silver nanoparticles characterization is necessary to evaluate the functional aspects of synthesized silver nanoparticles. Characterization of synthesized silver nanoparticles can be done by using various methods (Fig. 2) [41-60].

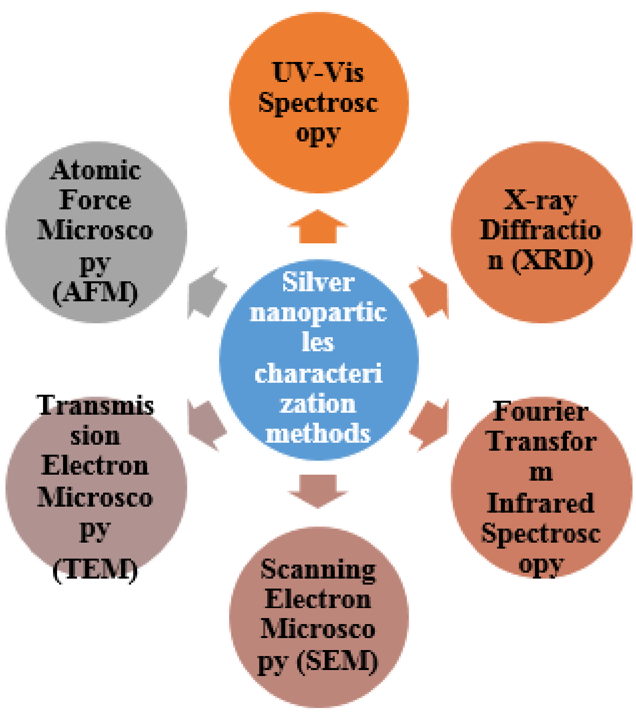

Fig. 2. Various methods for silver nanoparticles characterization.

UV-VIS SPECTROSCOPY

UV-VIS spectroscopy is an exceptionally valuable and essential for characterization of nanoparticles. AgNPs have unique optical properties which make them firmly cooperate with particular wavelengths of light (UV/VIS/IR Spectroscopy Analysis of Nanoparticles in 2012) [50-61]. UV-VIS spectroscopy is quick, simple, basic, and specific for various sorts of NPs, needs just a brief period of time for estimation [62-64]. In AgNPs, the conduction band and valence band lie near each other in which electrons move openly. These free electrons offer ascent to a surface plasmon reverberation (SPR) assimilation band, this is occurring because of the aggregate swaying of electrons of silver nanoparticles in reverberation with the light wave [53]. The assimilation of AgNPs relies upon the molecule estimate, dielectric medium, and synthetic surroundings [53]. Observation of this peak assigned to a surface plasmon is very much recorded for different metal nanoparticles with sizes running from 2 nm to 100 nm [51].

FOURIER TRANSFORM INFRARED (FTIR) SPECTROSCOPY

FTIR can give exactness, reproducibility, and furthermore an ideal signal to noise ratio. By utilizing FTIR spectroscopy, it become possible to identify little absorbance changes on the order of 10^{-3}, which performs distinction spectroscopy, where one could recognize the little assimilation groups of practically dynamic deposits from the extensive foundation ingestion of the whole protein [20].

FTIR spectroscopy is often used to see if biomolecules are associated with amalgamation of nanoparticles, which is more articulated in scholarly and modern research [29]. Besides, FTIR has additionally been stretched out to the investigation of nano-scaled materials, for example, affirmation of useful atoms covalently united onto silver, carbon nanotubes, graphene and gold nanoparticles, or co-operations happening amongst catalyst and substrate amid the reactant procedure [8]. FTIR is an appropriate, important, non-invasive, cost effective, and basic strategy to recognize the role of biological molecules in the reduction of silver nitrate.

X-RAY DIFFRACTION (XRD)

X-ray diffraction (XRD) is a popular analytical technique which has been utilized for the examination of both atomic and crystal structures, qualitative identification of various compounds, measuring the degree of crystallinity, quantitative resolution of chemical species, particle sizes, isomorphous substitutions, etc. [51]. At the point when X-ray light reflects on any

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crystal, it prompts the development of numerous diffraction designs, and a pattern reflects physico-chemical attributes of crystal structures. In a powder sample, diffracted patterns commonly originate from the specimen and reflect its structural physico-compound features. In this way, XRD can examine the basic features of an extensive variety of materials, for example, inorganic impetuses, superconductors, biomolecules, glasses, polymers, etc. [43-45].

SCANNING ELECTRON MICROSCOPY (SEM)

Field of nanotechnology has given a main thrust in the improvement of different high-determination microscopy procedures with a specific end goal to take in more about nanomaterials utilizing a light emission vigorous electrons to probe object on a fine scale [60]. Among different electron microscopy, SEM is a surface imaging technique, completely equipped for resolving various molecule sizes, size distributions, nanomaterials shapes, and the surface morphology of the particles at the small scale and nanoscales [29]. Utilizing SEM, we can test the morphology of particles and get a histogram from the image by either by measuring and checking the particles physically, or by utilizing particular programming [61].

TRANSMISSION ELECTRON MICROSCOPY (TEM)

TEM is a significant, frequently utilized, and critical system for the characterization of nanomaterials. It is used to get quantitative measures of molecule and additionally grain size, size distribution, and morphology [29]. Magnification of TEM is mainly controlled by the ratio of distance between the objective lens and the sample and the distance between objective lens and its image plane [59].

ATOMIC FORCE MICROSCOPY (AFM)

AFM is used to investigate the aggregation and dispersion of nanomaterials, in addition to their size, shape, sorption, and structure; three different scanning modes are available, including contact mode, non-contact mode, and intermittent sample contact mode [60]. It can also be utilized to characterize the nanomaterials interaction with supported lipid bilayers in real time, which is not achievable with current electron microscopy techniques [53]. AFM does not require oxide-free, electrically conductive surfaces for measurement, does not because appreciable damage too many types of native surfaces and it can measure up to the sub-nanometer scales in aqueous fluids [61-64].

BIOLOGICAL ACTIVITIES OF SILVER NANOPARTICLES

Silver nanoparticles have been extensively used in health care, food, environment and biomedical sectors. Application of silver nanoparticles includes anti-bacterial, anti-viral, anti-fungal and anti-cancer activities.

ANTIFUNGAL ACTIVITY

Fungal infections are more common in patients who are immune-suppressed and overcoming this problem is not an easy process due to the less number of anti-fungal drugs [19]. Therefore there is a requirement to develop antifungal agents which is non-toxic, biocompatible and eco-friendly in nature. Silver nanoparticles play an important role in various fungi. Silver nanoparticles showed potential against clinical isolates and ATCC strains of *Candida* species and *Trichophytonmentagrophytes.* Silver nanoparticles synthesized from biological method showed increased antifungal activity with fluconazole against *Phoma herbarum, Phoma glomerata, Fusarium semitectum, Candida albicans and Trichoderma* sp. [7]. Another study also reported the role of silver nanoparticles against several phyto-pathogenic fungi which include *Alternaria alternata, Macrophomina phaseolina, Sclerotinia sclerotiorum, Botrytis cinerea, Rhizoctonia solani,* and *Curvularia lunata* [22,31] Silver nanoparticles not only inhibits human and plant pathogenic fungi, but also able to inhibit other fungal species such as *Aspergillus fumigates, Penicillium brevicompactum, Chaetomium globosum, Cladosporium cladosporoides, Stachybotrys chartarum*, and *Mortierella alpine* [36].

ANTIVIRAL ACTIVITY

Viral diseases are frequent and becoming more prominent all over the world, therefore, there is a requirement of developing new antiviral agents. Silver nanoparticles show unique interactions with bacteria and viruses due to its certain size and shapes. [5,28]. Anti-viral activity of silver nanoparticles incorporated into the polysulfone ultrafiltration membranes was evaluated against the MS2 bacteriophage and it showed the significant antiviral activity [63]. Lara et al. [27] demonstrated the anti-HIV activity at an early stage of viral replication. Polyvinyl pyrrolidone coated silver nanoparticles blocks the transmission of cell-associated HIV-1 and cell-free HIV-1 isolates [27]. Another study also reported the role of silver nanoparticles against HIV and hepatitis B virus [60].

ANTI-MICROBIAL ACTIVITY

Anti-microbial effect of silver nanoparticles has been widely investigated, yet their mode of actions is not fully elucidated. This activity was attributed to many factors summarized as small size of the nanoparticles and increased surface area provide opportunities for interactions with bacterial cell because it leads to increased membrane permeability and cell destruction to bacteria and fungi. Silver nanoparticles can cause cell breaking down and changes in the cell membrane permeability. In addition, silver nanoparticles attach the surface of the cell membrane, penetrating in bacteria and disturb the cell function, interactions of silver nanoparticles with amino acids and enzymes: bonding with amino acids (especially to –SH group), generation of ROS. It is also attributed to the fact that cells are majorly made up of sulfur and phosphorus which are soft bases and DNA has sulfur and phosphorus as its major components; silver nanoparticles can act on these soft bases and destroy the DNA which would definitely lead to cell death. In the current review, more than 35 medicinal plants have proven to show significant anti-microbial activities against various Gram-positive and Gram-negative bacteria as well as anti-fungal effects. It is reported that green silver nanoparticles showed more efficient anti-microbial activity than the plant extract alone as in cases of *Azadirachta indica* [65], *Calatropis procera* [66], *Fagonia cretica* [67], *Tinospora cordifolia* [68]. While antimicrobial activity of synthesized silver nanoparticles from *Phyllanthus amarus* was reported to be higher than that of the standard drug used in the study [68]. Silver nanoparticles from *Lawsonia inermis* gel in combination with antibiotics showed a synergistic anti-microbial effect [69]. Whereas Dias et al. stated that a cream incorporated with silver nanoparticles biosynthesized from *Withania somnifera* possessed a significantly higher antimicrobial activity [70]. Some green synthesized silver nanoparticles have exhibited a prominent antifungal activity such as *Calatropis procera* [67], *Lawsonia inermis* [69], *Phyllanthus amarus*, *Tinospora cordifolia* [68] and *Withania somnifera* [7018]. The actual mechanism behind the antifungal activity of silver nanoparticles is not yet fully understood. However, it is assumed that disrupting the structure of the cell membrane by destructing the membrane integrity could be responsible for this biological action [71]. Nanoparticles synthesized from spice medicinal plants e.g. *Allium sativum* (garlic), *Zingiber officinale* (ginger), and *Capsicum frutescens* (cayenne pepper); which are important spices with well-known medicinal uses; were evaluated. These spices were reported to have various biological activities including antimicrobial and antioxidant activities. Silver nanoparticles synthesized from these spices exhibited broad-spectrum antibacterial activities thus, being suggested as valuable potential alternatives [72]. However, it was noted that the antimicrobial activity of silver nanoparticles against Gram-positive bacteria was reported to be less compared to Gram-negative bacteria and this may be attributed to the presence of the peptidoglycan layer which is negatively charged and prevents the free entry of silver ions into the cell wall of the bacteria [73].

ANTICANCER ACTIVITY

Induced cell death in cancer cells was assumed to be mediated by increased oxidative stress leading to apoptosis of these cells. In the present article, it was found that silver nanoparticles synthesized from *Abutilon indicum* showed a dose dependent anti-cancer activity against human colon cancer at a very low concentration. Their anticancer activity was attributed to the enhancement of intracellular ROS generation and depletion of mitochondrial membrane potential that leads to further DNA fragmentation and cell cycle arrest [74]. Whereas silver nanoparticles synthesized using *Pimpinella anisum* seeds has shown cytotoxicity on human neonatal skin stromal cells and colon cancer cells [75]. Biosynthesized silver nanoparticles and *Piper nigrum* extract showed promising anticancer activity against breast cancer cells (MCF-7) and human pharynx cancer cell line (Hep-2) [76]. Other findings revealed that silver nanoparticles from *Nigella sativa* seeds were found to be effective against hepatocellular carcinoma using HepG2 cell lines [77].

ANTI-OXIDANT ACTIVITY AND RADICAL SCAVENGING ACTIVITY

In biological systems, uncontrolled accumulation of H2O2 leads to the formation of oxygen free radicals which causes massive damage to cell membranes. The antioxidant ability of green silver nanoparticles could be attributed to the functional groups adhered to them that came from the medicinal plant extracts. Many studies have investigated the anti-oxidant activity of silver nanoparticles from various medicinal plants, e.g. *Abutilon indicum* [74], *Allium sativum*, *Capsicum frutescens*, *Cassia occidentalis* [78] and *Zingiber officinale* [72].

OTHER BIOLOGICAL ACTIVITIES OF GREEN SILVER NANOPARTICLES

Acacia Seyal silver nanoparticles significantly reduced cellular infiltration and granulamatous inflammation in ankle joints tissues of induced arthritic rats. So, it is concluded that gum arabic- silver nanoparticles worked as nano-cargo for enhanced anti-arthritic hesperidin (standard drug) in induced arthritic rats [79]. Anti-plasmodial effect against *Plasmodium falciparum* was detected using silver nanoparticles from *Catharanthus roseus* extract [8050]. However, no proper mechanism for anti-plasmodial action of silver nanoparticles from this plant was demonstrated. Alternatively, *Magnifera indica* silver nanoparticles enhanced dual dentistry applications and hence can be used for dental restoration [81].

CYTOTOXICITY

The effect of silver nanoparticles synthesized from aqueousleaf- extract of *Mentha piperita* was detected on one of the most important neurological enzymes, i.e. acetylcholinesterase (AChE). It showed that these green synthesis nanoparticles from this plant extract might cause neurotoxicity via inhibiting AChE activity. This activity was confirmed by conduction of enzyme kinetic studies which revealed that silver nanoparticles were capable of binding to both the free AChE enzyme and to the enzyme–substrate (AChE-AChI) complex [82]. Results of this study showed that; due to their small size, nanoparticles may easily cross the blood brain barrier and could interact with various neurological targets, which in turn causes neurotoxic effects. This may draw the attention that even green silver nanoparticles are not safe and could cause some neurotoxicity due to their interaction with AChE. While *Cassia occidentalis* silver nanoparticles showed lower heomolytic activity (1.7%) to human blood i.e. less toxicity [78].

EFFECT OF SIZE AND SHAPE OF THE NANOPARTICLES ON BIOLOGICAL ACTIVITY

It is noted that almost all silver nanoparticles of the present plant extracts included in this review attained a spherical shape. Studies showed that spherical shaped silver nanoparticles have high surface to volume ratio to interact with the cell walls of pathogens which gives better antimicrobial activity [83]. Nanoparticles with a size range of 11–15 nm is highly suitable for biomedical application because the size of synthesized nanoparticles is within the tolerable range and will not cause toxicity within the cell [67]. In the current review, it is stated that small size nanoparticles have more penetration power to cell membranes, however, too small size brings the issue of enhanced toxicity compared to larger size nanoparticles, thus, an appropriate size is highly desirable for specified biological applications. Small particle size proves its higher potential antimicrobial activity as in *Cassia auriculata* [84] and *Adansonia digitata* [83]. Researchers on their future work regarding green synthesis of silver nanoparticles. Wide range of medicinal plants traditionally used in Sudanese folk medicine has been exploited for the green synthesis of silver nanoparticles as simple, cost-effective, ecofriendly and rapid technique. However, this area is still dormant and more researches are required to explore the potentiality of other Sudanese flora. The silver nanoparticles synthesized using reducing and capping plants extracts are reported to have wide variations in shapes and sizes; which showed an impact on their biological activities. However, more studies are required to elucidate the effect of pure secondary metabolites that may control the morphology of the silver nanoparticles and hence their biological activities and other applications. These kinds of studies could provide better understanding of mechanism and efficiency of silver nanoparticles. A thorough research on Sudan flora is in way to exploit green synthesized silver nanoparticles. This would be associated with a possible warranty on their safety and realization of their full potentiality in the era of green nanotechnology.

CONCLUSION

An increasing attention towards green chemistry and utilization of plant extracts for metal nanoparticles synthesis lead to the development of environment-friendly techniques. A benefit of silver nanoparticles synthesis by using plant extracts is that it's economical, energy efficient and cost-effective, provides healthier workplaces, and protects human health and environment. Green synthesized silver nanoparticles play a significant role in the area of nanotechnology. Synthesis of nanoparticles using plants has several advantages over other biological organisms which overcome the time-consuming process of growing microbial cultures and maintenance. Therefore utilization of plant extract for the synthesis of silver nanoparticles has potential impact in coming decades. This review discusses the various approaches to nanoparticles synthesis, a protocol forsilver nanoparticles synthesis, various medicinal plant extracts utilized for the silver nanoparticles synthesis, characterization methods and its biological applications.

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