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# Role of Green Route Synthesized Silver Nanoparticles in Medicinal Applications with Special Reference to Cancer Therapy

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**Nanotechnology is a blazing field for the researchers in modern branch of science along with engineering have lot of applications. Nanotechnology is an imminent field with new outlet to fight and prevent many diseases using nanoparticles. Among the most promising materials Silver nanoparticles are having antimicrobial properties which are synthesized from medicinal plant and acts against chronic diseases. Silver nanoparticles synthesized from medicinal plants have lot of applications and eco-friendly, cost effective in nature. The present review article mainly focuses on biologically synthesized silver nanoparticles from medicinal plants and its role on cancer cells. Cancer is one of the most difficult health issues on globe. Although number of treatments may include radiation, chemotherapy and surgery, but these procedures not only targets tumor tissue but also normal healthy tissue. In recent years silver nanoparticles are considered as promising tool for cancer therapy. A numerous studies both in-vitro and in-vivo suggested that sliver nanoparticles can be used as cytotoxic and genotoxic agent due to their apoptotic inducing and anti-proliferative properties.However there is need to overlook the mechanism regarding the anti-cancerous activity.A silver nanoparticle deploys in every field of engineering science and medical sciences are still attracting to explore new scope of nanobiotechnology attributed with smaller size particles.**

**Keywords:** Nanotechnology, Green synthesis, Sliver nanoparticles, Medicinal plants, Cancer.

In the entire plant kingdom, medicinal plants are the main richest natural sources of man's prime companions in this globe. Forest contributes major sources of sheltering for many medicinal plants;there are more than one lakh species of medicinal plants. These plants play a vital role by helping life line of all living organisms (animals as well as humans). Medicinal plants have sustained human civilization through the biologically active compounds present in stem, root, leaf and flowering parts of a plant among them roots have richest compounds involved in curing various diseases[1].

According to current scenario of medicinal plants in India,there are over ten thousand plants species being used by the people of India, among these 60% are found in high altitude regions. Medicinal plants have vide number of applications in curing many diseases by applying various technological methods. Among them nanotechnology holds a great potential by using the components ranging from 1-100nm dimensions. The demand of nanoparticles is increasing day by day[2]. Nanoparticles can be synthesized either using chemical methods or physical methods

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which releases toxic by-products in nature. To overcome from this problems alternative method was synthesized by biological approach that is nanoparticles synthesized by using plant extracts which shows antibacterial activity, less toxicity in nature[3].Various nanoparticles can be synthesised from plant extracts namely Silver nanoparticles,Gold nanoparticles, Zinc nanoparticles and Copper oxide nanoparticles. Among theseSilver nanoparticles have many advantages due to their stability, good conductivity, antimicrobial activity, eco-friendliness, non-pathogenicnature and cost-effectiveness.

The activity of silver nanoparticles depends on various factors such as size and shape, surface chemistry, distribution, particle composition and morphology, capping, agglomeration, etc.The physico-chemical properties of silver nanoparticles increase the bioavailability of therapeutic agents. Therefore, development of silver nanoparticles with controlled structures that are uniform in morphology, size, and functionality is important for its various applications[4].Use of plant extracts for nanoparticles synthesis is favourable over the other biological material as it removes the long process of maintenance of cell culture[5].

Presence of various metabolites and biomolecules such as amino acids, proteins, enzymes, alkaloids, saponins, terpenoids, etc. present in plant extracts help in the reduction of precursor into metal ions. For silver nanoparticles the most commonly used precursor is $AgNO_3$ and after its reduction with plant extract forms $Ag^{3+}$ ions and thenAgO ions[6].

**Synthesizing Route Of Nanoparticles**

Over the years, a number of approaches are available for the synthesis of nanoparticles, such as physical, chemical and biological (green route) methods and some of these methods are listed in Table.1.

The physical methods of nanoparticles synthesis takes place at high temperature and pressure by consuming energy and time whereas chemical methodsare very simple and operates at low temperature, uses toxic chemicals as reducing and stabilizing agents, results in least stable and harmful nanoparticles not suitable for medical applications.The limitations of these two methods have made researchers to look for an alternative technique which is an eco-friendly process without involving harmful chemicals and high radiation. Nowadays biological method or green route synthesis is gaining importance because of its advantages compared to physical and chemical methods. Green synthesis involves the use of plant extract from different parts like steam, leaves, roots and fruits, micro organisms (bacteria, yeast and fungi), enzymes and agricultural waste for the synthesis of nanoparticles[2]. The plant extractshas drawn attention for the fabrication of nanoparticles, because of its rapid, economical, eco-friendly protocol, and provideshighly stable and well characterised nanoparticles. Green synthesis using microorganisms and plants for metal nanoparticles synthesis have been suggested as valuable alternatives to chemical methods[7]. Generally various plants materials are used as capping agents for the stabilization of nanoparticles.Previously, plant extracts were used to fabricate Au, Ag, Pd, Pt and many other nanoparticles.Among these, Ag and Au had many medicinal applications especially in cancer treatment.Schematic diagram representing the green route synthesis of nanoparticles is presented in Figure 1.

The experimental procedure for the synthesis of sliver nanoparticles is shown in Figure 2.

**Table 1.** Different Methods of Nanoparticles Synthesis

| Physical Methods | Chemical methods | Biological methods |
|---|---|---|
| Ion beam technique | Sol gel method | |
| Electric arc deposition | Co precipitation | Using plant extracts |
| Mechanical methods | Micro emulsions | Using microorganisms |
| Vapour deposition | Hydrothermal synthesis | Using enzymes |
| Sputter deposition | Sonochemical synthesis | Using agricultural waste |
| Molecular beam epitaxy | Microwave synthesis | |

Silver nanoparticles have found many applications in various fields because of its disinfectantnature, non-toxic to humans and areantiviral, antifungal, anti bacterial, anti inflammatory in nature at low concentrations. Silver nanoparticles are commercially manufactured as antimicrobial agents. Minimum concentrations of Silver nanoparticles are safe for human cells but lethal for microorganisms[2]. For past few years extensive work is going on silver nanoparticles to develop bioactive compounds for production of new drugs isolated from many medicinal plant extracts. Silver nanoparticles are considered as the most promising because of antimicrobial properties and large surface area to volume ratioand thus gained considerable interest in the field of medical science because of their prominent role in the treatment and diagnosis of cancer. Generally, silver nanoparticles are synthesised either from "Bottom to top" or "Top to bottom" approaches[8].

In "Bottom to top" approach atoms and molecules are assembled to form nanoparticlesand in "Top to bottom" approach bulk materials fragmented into fine particles by reducing size

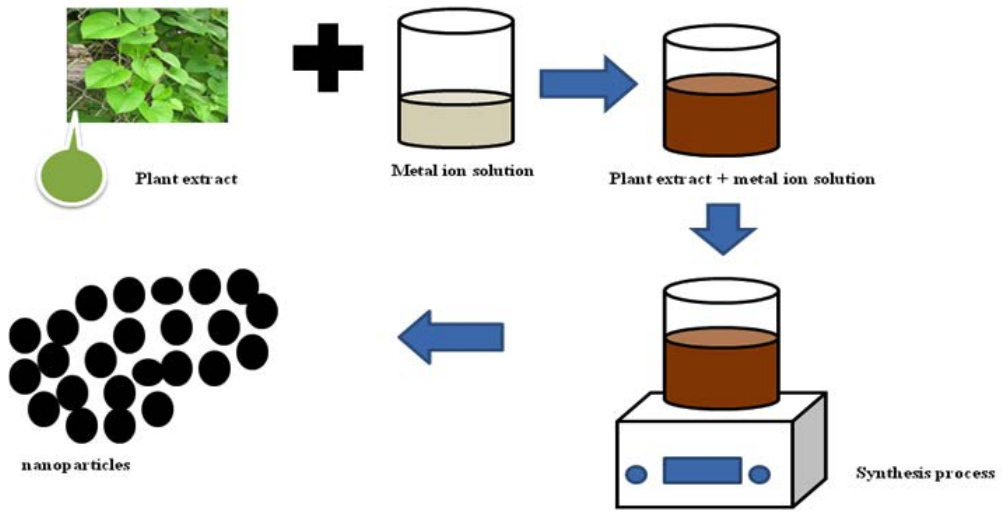


**Fig. 1.** Schematic representation of green synthesis of Nanoparticles

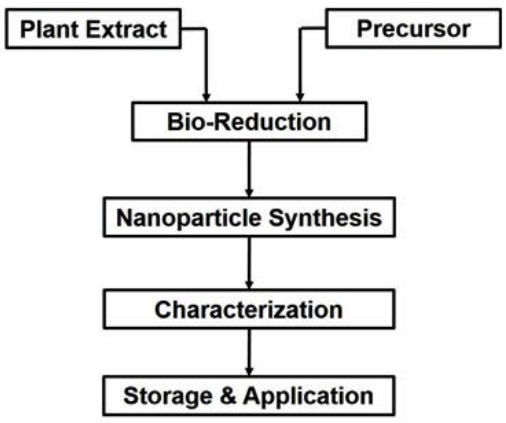


**Fig. 2.** Steps involved in green synthesis of nanoparticles

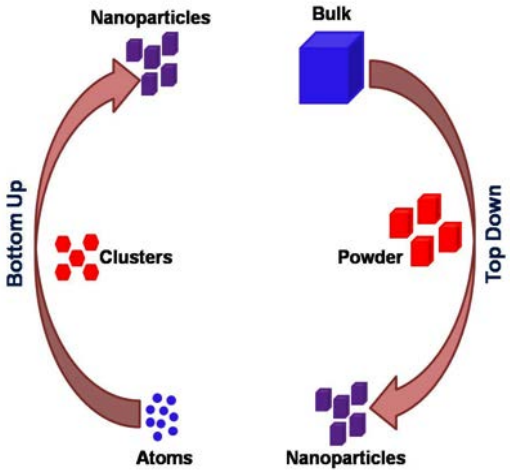


**Fig. 3.** Schematic diagram representing Bottom-Up and Top-Down approaches

with various lithographic techniques as shown in figure 3[9]. Green synthesis using plant extracts has potential advantages over microbes due to the ease of improvement, less biohazard and elaborate process of maintaining cell cultures[5].

**Medicinal Plants**

On the globe, so far about nearly five lakh plant species were discovered. Out of these fifty thousand species of world flora is present in India. Among them twenty thousand are flowering plants and nearly two thousand are medicinal plants[5]. Medicinal plants are still used in many rural areas because of their ready availability and at the same time cheaper than modern medicines. Medicinal plants produce chemical compounds which have many advantages, like defending against herbivores by producing phytochemicals (Alkaloids, Glycosides, Polyphenols, Terpenes) which enhance pharmacological activity. Medicinal plants are divided into various families namely *Ranunculaceae* (Butter-cup family), *Dilleniaceae* (Dillenia family), *Magnoliaceae* (Magnolia family), *Annonaceae* (Cherimola family), *Menispermaceae*(Moonseed family), *Nelumbonaceae* (Nelumbium family), *Nymphaeaceae* (Water-lilly family),*Papaveraceae* (Poppy family), *Brassicaceae* (Musturd family) and many[10].

Most important medicinal family is Menispermaceae also known as Moonseed family applicable in day to day life for curing and protecting from many diseases. *Anamirtacocculus, Cissampelospareira, Cocculushirsutus, Cycleapeltata, Pachygoneovata, Tiliacora*and *Tinosporacordifolia*are some of the medicinal plants thatcome under Menispermaceae. The list of most commonly available medicinal plants in the state of Andhra Pradesh, India along with their extensive medicinal applications is given in Table.2

**Applications Of Silver Nanoparticles**

Silver nanoparticles are applicable in large number of fields such as health care, food and cosmetic industries, biomedical field as drug-gene delivery, environment, optics, chemical industries, spaceand energy science, light emitters, single electron transistors, non-linear optical devices,

**Table 2.** List of Medicinal plants available in Andhra Pradesh state

| Botanical name | Common name | Distributed Areas | Medicinal applications |
|---|---|---|---|
| *Anamirtacocculus* | Koditeega, kakichampu, Fish berry, Louse berry | Akasaganga valley in Tirumala hills | Fruit skin disease, Fish poison. Spasmodic diseases |
| *Cissampelospareira* | Adivibankateega, Pateruteega, False paraiara root | Tirumala, Talakona, Kailasakona and Bhimavaram | Root-Antiperiodic, Urinary disorders, Diabetes |
| *Cocculushirsutus* | Katlateega, Broom creeper | Common in all dry regions of Andhra Pradesh | Root-dyspepsia, Demulcent, Eczema, Abdominal disorders, Diabetes |
| *Cycleapelata* | Ballepuakuteega | Tirumala, Talakona and Chelluru reserve forest | Diarrhoea, Ulcers, Worm infestations |
| *Pachygoneovata* | Peddadhusarateega, Godhalidusarateega | Common on bushes and small trees in forests in all regions of Andhra Pradesh | Fish poision, Leaf and dried fruit vermicide |
| *Tiliacoraacuminata* | Kappa teega, Nallateega | Berikonda, Pallampeta, Thondavada regions of chittoor district, Andhra Pradesh | Root snake bite |
| *Tinosporacordifolia* | Tippateega, guduchi | Very common in all forest regions | Leprosy, Fever, Jaundice, Daibetes, Diarrhoea, Urinary disorders |

textilesindustries, storage and also in many medical devices[11]. The most common application of Silver nanoparticles is in wound healing. Wound healing is a multiple step process which involves integration of different tissues and cell lineages. Acticoat is first commercial wound dressing which is made up of two layers of polyamide ester members covered with nano crystalline silver ions. MIC (Minimum Inhibitory Concentration) and MBC (Minimum Bactericidal Concentration) values are observed with Acticoat thechances of developing the resistance to silver bybacteria are less due to sustained release of silver particles from this product[12]. The use of silver nanoparticles as wound dressing is evidenced inthe treatment of various chronic non-healingwounds such as leg ulcers, diabetic foot ulcers andpressure ulcers. Silver nanoparticles also protect the cells of wound from bacterial contamination. Central venues catheters have wide applications in hospital practice these have potential ineffective complications to overcome from this antibiotic impregnated catheters were used to decrease the rate of infection but eventual use of this impregnated catheters leads to eventual bacterial resistance. Latest advancement is silver impregnated catheters by using inorganic silver powder[13]. Now-a-days joint replacement is commonly observed by many. The bone cement which is used in this treatment is made of PMMA (Poly Methyl Meth Acrylate) which is a biomaterial developing high risk of infection in human body to overcome from this a biomaterial filled with silver nano particles have maximum antibacterial activity against methicillin-resistant *S. Aureus*(MRSA) and

**Table 3.** Application of plant extract on different cancer cell lines

| S. No | Botanical name | Source of extract for synthesis of AGNPs | Cancer cell lines | Size of sliver nanoparticles (nm) | IC50 µg/ml |
|---|---|---|---|---|---|
| 1 | *Citrullus colosynthis*[21] | Seeds, leaves, Fruits, roots | Hep-G2,MCF-7, HCT-116, Caco-2 | Seeds-16, leaves-13, Fruits-19, roots-7 | leaves Hep- G2- 10.2 Fruits Hep- G2 - 17.2 & MCF-7- 22.4 roots HCT-116- 21.2 & Hep-G2- 22.4 |
| 2 | *Origanum vulgare*[22] | Leaves | A-549 | 63-85 | 100 |
| 3 | *Cissus quadrangularis*[23] | Steam | Hep-2 | 20-56 | 64 |
| 4 | *Seaweed Ulva lactuca*[15] | micro-algae | MCF-7, HT-29,Hep-2 | 5-30 | MCF-7- 37, HT-29- 49, Hep-G2-12.5 |
| 5 | *Brassica oleracea*[24] | Cauli flower | MCF-7 | 48 | 190.501 |
| 6 | *Seaweed Gelidiella sp*.[25] | Seaweed | Hep-2 | 31.25 | 40-50 |
| 7 | *Quercus*[26] | Fruit | MCF-7 | 40 | 50 |
| 8 | *Rheum emodi*[27] | Roots | MCF-7 | 27.5 | Dose |
| 9 | *Sesbania grandiflora*[15] | Leaf | MCF-7 | 22 | 20 |
| 10 | *Podophyllum hexandrum*[28] | Leaf | Hela | 14 | 20 |
| 11 | *Syzygium cumini*[29] | Flower | Hela | 40 | Dose |
| 12 | *Rosa indica*[30] | Petal | HCT-15 | 23-60 | 30 |
| 13 | *Vitexnegundo L*[31] | Leaf | HCT-15 | 22 | 20 |
| 14 | *Rubusglaucus benth*[32] | Leaf | Hep-G2 | 12-50 | Dose |
| 15 | *Azadirachta indic*[29] | Leaf | MCF-7 | 40 | 4.25 |
| 16 | *Azadirachta indica*[33] | Leaf | SiHa | 2-18 | Dose |
| 17 | *Butea monosperma*[34] | Leaf | MCF-7 | 20-80 | Dose |
| 18 | *Citrullus colocynthis*[35] | Callus | Hep-2 | 31 | 3.42 |
| 19 | *Cucurbita maxima*[36] | Petal | A431 | 76 | 82.39 |
| 20 | *Moringa oleifera*[36] | Leaf | A431 | 94 | 83.53 |
| 21 | *Achillea Biebersteinii*[37] | Flower | MCF-7 | 12 | 20 |
| 22 | *AlternantheraSessilis*[38] | Aerial Parts | MCF-7 | 10-30 | 6.85 |
| 23 | *Alternanthera sessilis*[39] | Leaf | PC3 | 30-50 | 31.5 |

other strains are used in testing.Silvernanowires are an advanced application used to provide conductive coatings fortransparent conductors and flexible electronics.To enhance the plasmonic activity for sensing and imaging applications of metallic nanoparticles attached to silver nanowires function as antennas. Silver nanowires withsingle layers are being used to build arraysfor molecule specific sensing in combinationwith Raman Spectroscopy. Silver nanowires havebeen studied as components of nanocomposites and can show high dielectric constantsin such systems.

Silver nanoparticles in the treatment of cancer: In recent past, the most common chronic disease in human beings is Cancer. Every year around 15 lakh people in India are subjected to cancer. The current methods in treating cancer are surgery, radiation and chemotherapy (In some cases targeted therapy) which lead to organ dysfunction and radiation induced complications[6]. In recent advancements nanotechnology shows potential promise in the management of cancer. Nanoparticles are attached to cancer marker targeted antibodies to detect cancer at earlier phases. Novel designed nanoparticles carries cytotoxic drugs or lethal toxins inside cancer cells and protects normal cells without causing any side effects to normal tissues[14].

Biogenic Silver nanoparticles extracted from *Sesbaniagrandiflora* leaf found their cytotoxicity effect against human breast adenocarcinoma cell lines (MCF-7). This was the fourth generation of nanoparticles research[15]. Sliver nanoparticles extracted from *Alternantheratenella* leaf are rich in flavanoid component. The cytotoxic effect of these 48nm nanoparticles was examined on Human Breast adenocarcinoma cells (MCF-7) and these nanoparticles have shown reduction in the migration of MCF-7 cells with Minimum Inhibitory concentration ($IC_{50}$) value of 42.5 µg/ml[16]. *Saccharina japonica* extract was used to synthesize sliver nanoparticles and their cytotoxicity effect was examined on cervical carcinoma cells (HeLa). The apoptotic feature of HeLa cells was examined by using confocal laser Scanning microscopy and Fluorescence microscopy[17]. The spherical and cubic sliver nanoparticles was synthesised from Alma extract with an average size of 188nm. Amla mediated sliver nanoparticlesand Amla extract was used to examine the cytotoxic effect on Hep2 cell lines. Amla sliver nanoparticles shows more cytotoxic and genotoxic effect on Hep2 cancer cells than Amla extract[18]. The lists of applications of plant extract used in different cancer cell lines[19-39] are shown in Table.3.

## CONCLUSIONS

Biological synthesis of silver nanoparticles has lot of importance and wide number of applications in treatment of many chronic diseases (especially cancer). Silver nanoparticles are eco-friendly, cost effective, stable and have wide number of applications in medicine. This current review mainly focuses on medicinal applications of silver nanoparticles synthesised from medicinal plants. Green synthesized sliver nanoparticles are beginning to a new era in the cancer diagnosis. Sliver nanoparticlesmight become a potential nanomedicine for cancer in the near futurebut still needs a lot of research. Moreover, there is a need to investigate the issues on sliver nanoparticles such as bioavailability, biocompatibility, and toxicity before it develops as potential target for cancer therapy.

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