Available online on 15.04.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Review Article

Herbal mediated silver nanoparticles: A new horizon of antineoplastic drug delivery system

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ABSTRACT

Cancer is a disease characterized by the uncontrolled growth and spread of abnormal cells, and is still the second most common cause of death worldwide. Several classes of drugs are available to treat different types of cancer. Currently, researchers are paying significant attention to the development of drugs at the nanoscale level to increase their target specificity and to reduce their side effects. Silver nanoparticles are the topics of researchers because of their distinctive properties (*e.g.*, size and shape and electrical properties). Synthesis of herbal mediated silver nanoparticles targeting biological pathways has become tremendously prominent due to the higher efficacy and fewer side effects as compared to other commercial cancer drugs. A variety of preparation techniques have been reported for the synthesis of silver nanoparticles such as physical, chemical and biological methods. In this review, different medicinal plants and their active compounds, as well as synthesized silver nanoparticles from medicinal plants, are discussed in relation to their anticancer activities.

Keywords: Silver nanoparticles, Medicinal plants and Anti-cancer activities.

Article Info: Received 24 Feb 2019; Review Completed 31 March 2019; Accepted 07 April 2019; Available online 15 April 2019

Cite this article as:

Venkateswara Rao S, Naserunnisa S, Padmalatha K, Herbal mediated silver nanoparticles: A new horizon of antineoplastic drug delivery system, Journal of Drug Delivery and Therapeutics. 2019; 9(2-s):640-648

http://dx.doi.org/10.22270/jddt.v9i2-s.2516

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INTRODUCTION

Cancer is a generic term for a large group of diseases characterized by the growth of abnormal cells beyond their usual boundaries that can then invade adjoining parts of the body and spread to other organs. Normally, human cells grow and divide to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. When cancer develops, however, this orderly process breaks down. The actual process becomes imbalanced and the cells start dividing without stopping and may form growths called tumors (Fig. 1). Cancerous tumors are malignant, which means they can spread into, or invade, nearby tissues and even travel to distant places in the body through the blood and lymph. Unlike malignant tumors, benign tumors do not spread into, or invade, nearby tissues. Benign tumors can sometimes be quite large, however. Nearly every family in the world is touched by cancer, which is now responsible for almost one in six deaths globally (WHO, 2018). According to the recent report from ICMR, 1300 people die every day in India because of cancer. There are variety of cancer exist, more than 100 types of cancer have been recognized and Cancer has become second leading cause of death globally and accounted for 8.8 million deaths in 2015. Lung, prostate, colorectal, stomach and liver cancer are the most common types of cancer in men, while breast, thyroid, colorectal, lung, cervix and stomach cancer are the most common among women. The number of new cancer cases per year is expected to rise to 23.6 million by 2030 (National Cancer Institute). As there are many types of cancers, target drug delivery system has become an emerging phase in treatment of cancer.

The most common cancer treatments are restricted to chemotherapy, radiation and surgery. Due to lack of target drug delivery system these conventional methods are damaging cancer cells and even normal cells. This has been become a main cause for developing several side effects in chemotherapy treatment[1]. According to the National Cancer Institute (NCI), individuals undergoing chemo frequently report experiencing such symptoms as nausea, vomiting, loss of appetite, constipation or diarrhoea, fever and fatigue,hair fall, develop painful mouth sores, heart or kidney problems, lung tissue damage or nerve damage, infertility etc. Though chemotherapy has been proven effective in the resolution of several types of cancer, there is always a risk that the cancer may re-emerge after treatment has ended. To overcome these limitations herbal mediated silver nanoparticles are used to target the herbal medicines to individual organs by using Silver Nanoparticles which improve the targeted drug delivery, effectiveness and safety of the medicine. National cancer institute screened over 35,000 of herbal plants worldwide to validate their use in cancer[2], whichcan be made advantage in synthesis of herbal mediated silver nanoparticles in cancer.

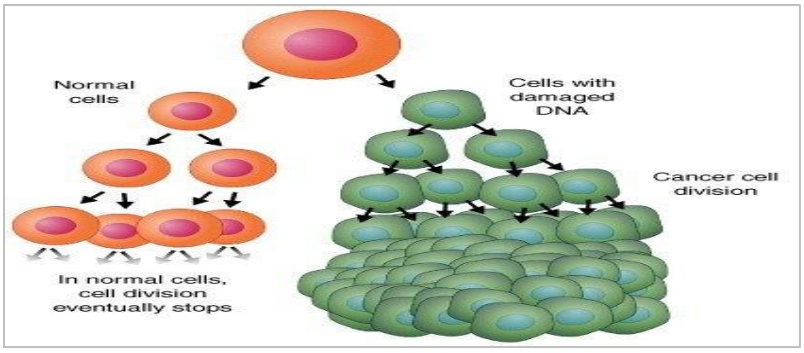

Figure 1: Cell multiplication in cancer cells and normal cells

HERBAL PLANTS TOWARDS THE TREATMENT OF CANCER

Zingiber officinal: *Over the past decades* Ginger perennial herb belonging to the family Zingiberaceae have been widely used as spices, used in traditional medicine as a cure for some diseases including inflammatory diseases.Gingerol, Paradol and Shogoal are the active phenolic compounds of Ginger that have antioxidant, anti-cancer, anti-bacterial[3], anti-angiogenesisand anti-artherosclerotic properties. It has been shown that Ginger exhibited promising cytotoxic activity against CL-6 human cholangiocarcinoma cell line[4]. Ginger leaves are used to induce apoptosis and reduce viability, followed by the increases ATF3 expression via activating ATF3 promoter in human colorectal cancer cells[5].

Paramignya trimera: P.trimera (Xao tam phan) belongs to family Rutaceae. It has been used as a medicinal plant for cancer prevention and treatment in recent years. It contains interesting secondary metabolites like coumarins, triterpenes, alkaloids, and their glycoside derivatives[6]. *Paramignya* species has been employing as ayurvedic medicine against hepatitis, diabetes, cancer, nose infections. P.trimera leafis a rich source of phytochemicals that possess promising antioxidant and anti-proliferative activities in prostate cancer, and its powdered leaf extract is useful in ovarian cancer, therefore it can be used as lead compounds for application in the nutraceutical, medicinal and pharmaceutical industries[7].

Salvia miltiorrhiza: It is Chinese medicinal plant belonging to Lamiacea.It has been widely used in traditional Chinese medicine for the treatment of cardiovascular disease, hemorrhage, hepatitis, miscarriage, edema, menstrual disorders, and insomnia[8]. Along with *Panax* Ginseng which selectively effects lung cancer cells, induces cell apoptosis and inhibits cell migration and invasion but it does not have any cytotoxic effects on normal lung cell[9].

Aloe Vera: A. Vera or Aloe barbadensis (Miller), belongs to Liliaceae family, which has highly healing effects anticancer, antioxidant, immunoprotective, hypoglycemic, hypo-lipidemic and antifungal are special properties of A.vera. Aloe emodin, an anthraquinone found in the gel of Aloe Vera leaves, has been shown to have antineoplastic properties in Cervical cancer derived HeLa cells without generalized cytotoxic effects on healthy tissue[10]. It exhibits antineoplastic effects by inducing apoptosis and modulating the expression of effector molecules such as down-regulating cyclin D1, CYP 1A1, and CYP 1A2, and up-regulating Bax and p21 expression, in breast cancer cells[11].

Curcuma longa: *C. longa* is a well-known traditional and important medicinal herb mainly produced in India. For the last few decades, extensive works have been done to establish the pharmacological actions of Turmeric and its extracts. It has been demonstrating to possess vital biological activities such as anti-oxidation, anti-inflammation, anti-diabetes and anti-cancer activities) where it inhibits colon cancer cell HT-29[12]. The anticancer activity of *C.longa* is presence of curcuminoids including curcumin, demethoxycurcumin (DMC) and bisdemethoxycurcumin (BDMC). Due to its low solubility and instability, curcuminoids are readily metabolizing to other products after *in vivo* administration and this results in low bioavailability and biological activity[13]. Thus, New Drug Delivery System can enhance curcuminoid bioavailability and improve therapeutic efficiency of curcuminoids in various deadly diseases like cancer.

Table-1: Different plants extracts with anti-cancer activity

Plant	Plant part	Cell lines	Type of cancer	Ref
Zingiber officinal	Rhizomes	CL-6 human cholangio-carcinoma cell line	cholangio-carcinoma	4
	Leaves	HCT116, SW480 and LoVo cells	colorectal cancer	5
Paramignya trimera	Leaves	Du145 (prostate)	Prostate cancer	7
	Dried leaves powder	A2780(ovarian)	Ovarian cancer	7
Salvia miltiorrhiza	Rhizomes	lung cancer cell A549 and normal lung epithelial cell BEAS-2B	Lung cancer	9
Aloe Vera	Leaf extract	Cervical cancer derived HeLa cells (CCL-2™, ATCC, Manassas, VA)	Cervical cancer and breast cancer	11
Curcuma longa	Rhizomes	colon cancer cell HT-29	Colon cancer	12

NANOTECHNOLOGY

Nanotechnology is defined as the intentional design, characterization and production of materials, structures and systems by controlling their size and shape in the Nano scale range 1 to 100 nm. The nanoparticles are similar in scale to biological molecules and systems yet can be engineered to have various functions and thus nanotechnology is potentially useful for medical applications. With the use of nanotechnology, various pharmaceutical Nanotechnologies based systems which can be termed as Nano pharmaceuticals like polymeric nanoparticles, magnetic nanoparticles, liposomes, carbon nanotubes, quantum dots, dendrimers, metallic nanoparticles, polymeric nanoparticles, etc. (Fig. 2) have brought about revolutionary changes in drug delivery as well as the total medical service system[14]. From past few years the field of Nano medicine aims to use the properties and physical characteristics of Nanotechnology for the treatment of cancer at the molecular level. It has become clearer that the development of new drugs alone is not enough for better drug therapy. It has become very important to achieve high intra tumor drug concentration along with minimum exposure of healthy tissue to drug. These limitations can overcome by using nanoparticles as drug delivery system. It enhances the permeability and retention of drug onto the tumor cells and not onto normal cells. This has become main reason for enormous attention towards metallic nanoparticles amongst various diversified nano vehicles.

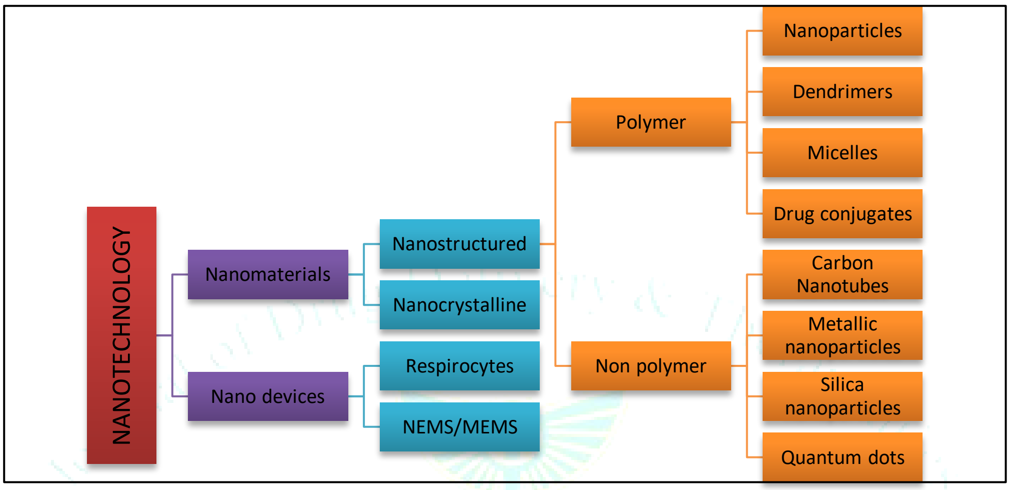

Figure 2: illustration demonstrating various nano pharmaceuticals

Metallic Nanoparticles

Metal nanoparticles (NPs) have the potential to overcome side effects (or) limitations related to conventional chemotherapy. Metal NPs provides better targeting, gene silencing and drug delivery which is very beneficial and powerful role in cancer therapy. Apart from therapeutic benefits, metal NPs are also used as a diagnostic tool for the imaging of cancer cells[15]. Metal NPs based therapeutic systems not only provide simultaneous diagnostic and therapy but also allow controlled and targeted drug release which helps to revolutionise cancer treatment and management[16]. They enhance the therapeutic index of drug molecules by eliminating their toxicity against healthy tissue and achieving controlled therapeutic levels of the drug for a long time to the targeted cells (cancerous cells). It minimizes the concentration of drug intake and maximizes the overall profile of absorption, biodistribution, metabolism, and excretion (ADME) profile. The enhanced permeation and retention of nanoparticles can cross Blood Brain Barrier (BBB) which helps in treatment of brain cancers[17]. Moreover, the major improvements offered by metallic nanoparticles include higher efficacy, lesser side effects, site specificity, efficient delivery, and overcoming multidrug resistance (MDR).

Different metals like Silver, Gold, Alloy, Magnet etc. which are capable of acting as nanoparticles, in treatment of various disease[18]. Gold nanoparticles (AuNPs) are used in immunochemical studies for identification of protein interactions. They are used as lab tracer in DNA fingerprinting to detect presence of DNA in a sample. Gold nanorods are being used to detect cancer stem cells, which is very much beneficial stepin cancer diagnosis[19]. Gold nanoparticles also increase the temperature distribution, making it able to destroy cancer cells[20]. Alloy nanoparticles exhibit different structural properties different from their bulk samples[18]. Magnetic nanoparticles have been used in targeted cancer treatment, stem cell sorting and manipulation, guided drug delivery, gene therapy, DNA analysis, and magnetic resonance imaging (MRI) in early diagnosis of cancer cells[21], other metals like Titanium dioxide ($TiO2$) was used to show cytotoxic effect on HUVEC and A549 cell lines[22], zinc (Zn), copper (Cu) and iron (Fe) are used in several industrial applications such as cosmetics, paint chemicals, food additives, pharmacological coatings, drug delivery systems, biosensor technologies and body implants etc.

Silver Nanoparticles:

Silver has its own importance in the field of medicine right from history. Hippocrates states in his writings about the use of silver in treating wounds. Before antibiotics were started, the colloidal silver was used as disinfectant and germicide in 1940s; sutures were prepared by silver threads in 1920s by surgeons to stitch the surgical wounds/openings. Silver demands will likely to increase by changing the pattern of silver emission as these technologies and products diffuse through the global economy. Silver nanoparticles are undoubtedly the most widely used nanomaterial among all, thereby being used as antimicrobial agents, wound dressing, coating of plastic catheters, bio sensors for water treatment, sunscreen lotions, in textile industry, etc[23]. Due to its cytotoxic properties silver nanoparticles allows us to subject it in Cancer treatment.

The cell toxicity of stored silver nanoparticles increases because of the increased presence of silver ions in the dispersion. Notably, the difference between freshly prepared and stored silver nanoparticles are not able to find out by dynamic light scattering and electron microscopy.

Figure 3: Applications of Silver Nanoparticles

Herbal Mediated Silver Nanoparticles for Treatment of Cancer

According to present research scenario especially the silver nanoparticles have been playing a beneficial and important role in Herbal nanotechnology to prevent chronic diseases like diabetes and cancer etc. Herbal drugs include plants, herbal complexes and herbal products or even a combination of plants which were used thousand years before inventing modern drugs[24]. As they are effective with no side effects now a days herbal plants are used all over the world in different methods both in allopathic and traditional systems. There have been many plants all over the world with anti-cancer activity.

Herbal drugs have been recently getting more attention because of their potential to treat almost all diseases. However, several problems such as poor solubility, poor bioavailability, low oral absorption, instability, slow pharmacological actions and unpredictable toxicity of herbal medicines limit their use. In order to overcome such problems, nanoparticles can play a vital role. Hence, "**Silver nanoparticles"** show potential utilization to deliver herbal medicines with better Cancer therapy (Fig 4).

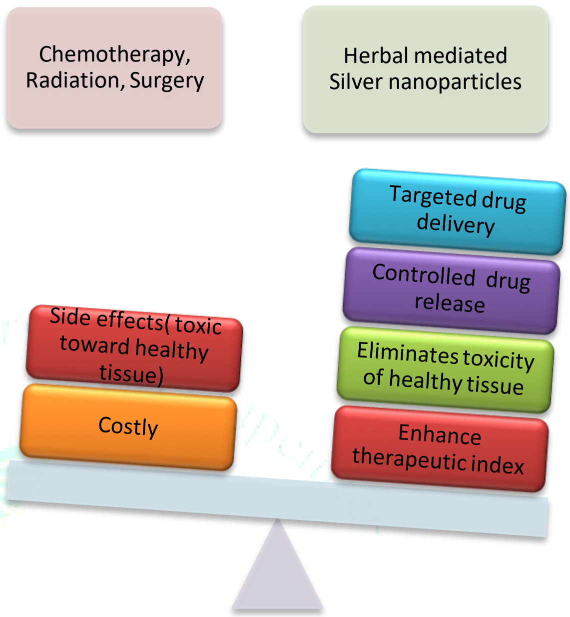

Fig 4: Herbal Mediated Silver Nanoparticles versus Conventional Therapy

Table 2: Herbal mediated Silver Nanoparticles with anti-cancer activity

S.No	Herbal mediated Silver Nanoparticles	Cell lines	Type of cancer	Ref
1	*Origanumvulgare* (Oregano) Silver Nanoparticles	Human lung cancer A549 cell line (LD_{50} – 100 µg/ml).	Lung cancer	25
2	*Taraxacumofficinale* silver nanoparticles (TOL-AgNPs)	Human liver cancer cells (HepG2).	liver cancer	26
3	Silver nanoparticles (AgNPs) using a *Punicagranatum* leaf extract (PGE).	human liver cancer cells (HepG2)	Liver cancer	26
4	*Matricariachamomilla mediated Silver Nanoparticles*	A549 lung cancer cells	lung cancer.	27
5	Silver Nanoparticles of pollen extract of *Phoenix dactylifera* (Date Palm)	MCF-7 breast cancer cells	Breast cancer	28

SYNTHESIS OF SILVER NANOPARTICLES

There are varieties of methods like chemical, physical, photochemical, and biological methods which have been applied for the synthesis of Ag-NPs (Fig 5). Each method has its own merits and demerits.

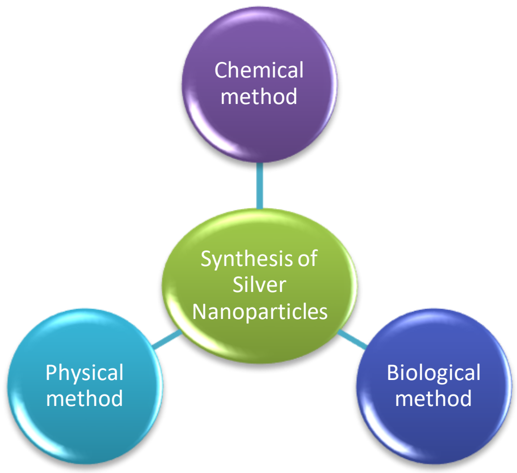

Figure 5: Different methods of synthesis of Silver Nanoparticles

Chemical Methods

The most used chemical approach is **chemical reduction**, which allows synthesis of Silver Nanoparticles in solutions like water or organic solvents. This type of approach mainly depends on **(i) metal precursors**, like Silver Nitrate etc.**(ii) Reducing agents**, like sodium citrate, ascorbate, sodium borohydride ($NaBH_4$), elemental hydrogen, polyol process, Tollens reagent, *N*,*N*-dimethylformamide (DMF), polyethylene glycol (PEG), poly-ethylene glycol block copolymers etc.**(iii) Stabilizingor Capping agents** like, polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), polymethacrylic acid (PMAA), polymethyl methacrylate (PMMA) etc.

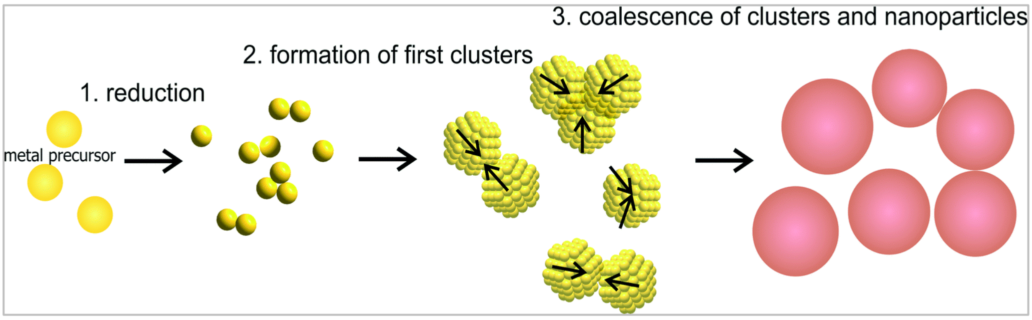

Figure 6: Formation of Silver Nanoparticles[29]

Microemulsion method is a reproducible technique that permits obtaining of uniform size Silver Nanoparticles and this process involves use of three precursors **(i) polar phase** that commonly is water, **(ii) non-polar phase** as hydrocarbon liquid or oil, and **(iii) surfactant**[30]. The two phases are separated by the presence of surfactant, which forms an interfacial layer, reducing the interfacial tension between the microemulsions, and inhibiting the coalescence of the droplet[31]. Colloidal silver nanoparticles have been synthesized in water-in-oil microemulsion using silver nitrate solubilized in the water core of one microemulsion as source of silver ions, hydrazine hydrate solubilized in the water core of another microemulsion as reducing agent, dodecane as the oil phase, sodium bis (2-ethylhexyl) sulfosuccinate (AOT) as the surfactant[32].

Sol-gel process is a colloidal chemistry technology, which is used to synthesize Silver Nanoparticles at low temperature. In the first phase, the monomers of materials are converted into a colloidal solution (sol), which represents the precursor (metal alkoxides or chlorides) for gel formation, which in turn formed particles or polymers. To obtain colloids, the precursors are hydrolysed and polycondensed[33]. Silver Nanoparticle-loaded strontium titanate ($SrTiO_3$) nanoparticles were attempted to be synthesized by a sol-gel-hydrothermal method by[34].

Recently, **Tollens technique,** which is also called an easy one step method, has been used for the synthesis of silver nanoparticles with a controlled size[35]. Within the changed Tollens procedure, silver ions are reduced by using different types of saccharides within the presence of ammonia[36].

Table 3: Synthesized silver nanoparticle by chemical methods

S. No	Method	Starting Material	Ref
1	Microemulsion method	Silver Nitrate	32
2	Sol-gel method	Silver Nitrate	34
3	Tollens procedure	Silver Nitrate	36
4	Polyol process	Silver nitrate	37

Physical Methods

The common physical methods applied in synthesis if Solver Nanoparticles are Evaporation-condensation, Laser ablation, Thermal decomposition, Ultrasonic spray pyrolysis, Arc discharge method etc. The absence of solvent usage prevents contamination within the ready skinny films and also formation of uniform Nanoparticles measures its benefits as compared with chemical processes[35].

In physical processes, metal nanoparticles are generally synthesized by evaporation–condensation, is carried out by using a tube furnace at atmospheric pressure. The source material within a boat centered at the furnace is vaporized into a carrier gas. Nanoparticles of various materials, such as Ag, Au, PbS and fullerene, have previously been produced using the evaporation/condensation technique. But this technique has its own drawbacks where it occupies more space, consumes more energy and even more time to increase the atmospheric temperature[38].

To overcome these drawbacks Thermal decomposition an eco-friendly technique, laser ablation methods etc, are becoming popular. Single crystalline silver nanoparticles of range 10nm have been synthesized by thermal decomposition of silver oxalate in water and in ethylene glycolby using Polyvinyl alcohol (PVA) as a capping agent. Silver Nanoparticles are also produced by laser ablation method, where uncontalinated colloids are obtained even if the size controlling step is difficult. This method uses a laser beam as the energy source to induce ablation on a solid target material, which vaporizes into atoms and clusters, and successively the Nanoparticles are assembled in ambient media[39] (gas or liquid).

Tabl 4: Synthesized silver nanoparticle by physical methods

S. No	Method	Starting Material	Ref
1	Evaporation-condensation method	Silver material	37
2	Thermal decomposition method	Silver oxalate	38
3	Laser ablation method	Metallic Silver	39

Biological Methods

Although chemical and physical methods are considered to be successful methods to produce well-defined nanoparticles, but they have certain limitations like an increase in the cost of production, the release of hazardous by-products, long time for synthesis and difficulty in purification[40]. Even conventional methods need (a) Ag precursors, (b) reducing agent, and (c) stabilizer/capping agent for preventing agglomeration in order to get perfect Silver Nanoparticles. In biological methods Silver Nanoparticles are synthesized by using algae, bacteria, fungi, yeast, plants etc. They themselves act as reducing agents, stabilising agents etc. Green synthesis of Silver Nanoparticles from *Cleome viscosa* L fruit extract showed reliable anticancer activity on the lung (A549) and ovarian (PA1) cancer cell lines[41]. Now a days fungi is also playing a very significant role in synthesis of Silver Nanoparticles, *Bacillus tequilensis* and *Calocybe indica both used as reducing agents in synthesis of silver nanoparticles, they showed cytotoxic effect against* MDA-MB-231 human breast cancer cells[42]. Silver Nanoparticles can synthesise from various seaweeds and sea grasses (Derek Fawcett *et al.,*). Chitosan Alginate, which is obtained from brown algae (*Sargassum sp*) is used to synthesis Silver Nanoparticles which show cytotoxic effect against the breast cancer cell line MDA-MB–231[43]. Currently Phytochemical synthesis is a mostly used system in synthesis of Silver Nanoparticles, Phyto synthesis of silver nanoparticles using *Alternanthera tenella* leaf extract showed a dose-dependent cell inhibition in Human breast adenocarcinoma (MCF-7) cells[44] and the phytochemical screening showed that flavonoids are responsible for formation of Silver Nanoparticles.

Table 5: Synthesized silver nanoparticle by biological methods

Source	Biological Name	Property	Cell Lines	Ref
Bacteria	*Bacillus* brevis (NCI M 2533)	Antibacterial property against multi-drug resistant pathogens	----	41
Fungi	*Calocybe indica*	Cytotoxic property	MDA-MB-231 human breast cancer cells	42
Algae	Chitosan Alginate from *Sargassum sp.*	cytotoxic effect	breast cancer cell line MDA-MB–231	43
Plants	*Cleome viscosa* L fruit extract	Anticancer activity	lung (A549) and ovarian (PA1) cancer cell lines	41
	Alternanthera tenella leaf extract	Cell inhibition	Human breast adenocarcinoma (MCF-7) cells	44

CHARACTERIZATION OF SILVER NANOPARTICLES

Evaluation or characterization of silver Nanoparticles is study of materials about their physical and chemical properties, composition and structures. Silver Nanoparticles are generally characterized by their size, surface area, dispersity, morphology and surface charge, using advanced microscopic techniques as given below.

UV-Visible Spectroscopy

UV-Visible (UV-Vis) spectrometry is a simple and quite a sensitive technique used to identify, characterize and analyse the silver nanoparticles. Synthesis of AgNPs by reduction of silver ions by the phytoconstituents of the extract were initially observed with the appearance of characteristic yellowish brown color, which is due to excitation of Surface Plasmon Resonance (SPR) phenomena. During formation of Silver Nanoparticles the intensity of color increases, as more and more silver ions got reduced with reaction time and attaines stable dark chocolate brown color. The progress of the silver ion reduction can be monitored by UV–vis spectroscopy analysis in the wavelength range from 300 to 700 nm[45].

Dynamic Light Scattering (DLS)

Currently most popular method which allows a proper characterization of the surface charge, size distribution and quality of Silver Nanoparticles is photon-correlation spectroscopy (PCS) or dynamic light scattering (DLS). Particle size distribution and morphology of the Nanoparticles are most important parameters for characterization of synthesized nanoparticles. The particle size distribution was done by using dynamic light scattering (DLS) measurement by Arun S. Sonker et al.[46]. DLS is also used as quantitative and qualitative tools to monitor adsorption of bovine serum albumin (BSA protein) onto silver nanoparticles[47] (AgNPs).

The Zeta potential of a nanoparticle is commonly used to characterize the surface charge property of nanoparticles. It reflects the electrical potential of particles and is influenced by the composition of the particle and the medium in which it is dispersed. The zeta potential of the biosynthesized AgNPs, from Pedalium murex leaf extract is characterised by DLS[48].

Electron Microscopy Methods

Scanning electron microscopy (SEM) and Transmission electron microscopy (TEM) are electron microscopy methods which allows surface and morphological characterization at both nanometer and micrometer scale. TEM is more accurate than SEM and is used to determine the exact size and shape of the synthesized AgNPs. TEM has advantages over SEM in providing better spatial resolution and capability for additional analytical measurements[49]. For SEM characterization, nanoparticles solution should be first converted into a dry powder, which is then mounted on a sample holder followed by coating with a conductive metal, such as gold, using a sputter coater. The sample is then scanned with a focused fine beam of electrons. The mean size obtained by SEM is comparable with results obtained by dynamic light scattering.

Fourier Transformed Infrared Spectroscopy (FTIR)

Fourier transformed Infrared spectroscopy (FTIR) allows the identification of all the organic functional groups and determines which of them are attached to AgNPs' surface. The FTIR spectrum of silver nanoparticles synthesized using Celastrus Paniculatus leaf extract by Mohsen Younus, was analysed , and he found the different functional groups like alcohols, amines etc. in synthesised Silver Nanoparticles.

Atomic Force Microscopy (AFM)

AFM offers ultra-high resolution in particle size measurement and is based on a physical scanning of samples at submicron level using a probe tip of atomic scale. Samples are usually scanned in contact or noncontact mode depending on their properties. In contact mode, the topographical map is generated by tapping the probe on to the surface across the sample and probe hovers over the conducting surface in noncontact mode. The prime advantage of AFM is its ability to image non conducting samples without any specific treatment, thus allowing imaging of delicate biological and polymeric nano and microstructures. AFM provides the most accurate description of size and size distribution and requires no mathematical treatment.

Surface Area Analysis

The specific surface area of the particles is the summation of the areas of the exposed surfaces of the particles per unit mass. There is an inverse relationship between particle size and surface area. Nitrogen adsorption can be used to measure the specific surface area of a powder. The method of Brunauer, Emmett, and Teller (BET) is commonly used to determine the total surface area[50].

Drug Entrapment Efficiency

Entrapment efficiency (EE) is determined by analysing the nano particles spectrophotometrically. The amount of drug loaded in Ag NPs is estimated by dispersing a known amount of nanoparticles in 10 ml deionized water and stirring the sample vigorously. The absorbance of the solution is measured spectrophotometrically and amount of drug present was calculated from calibration curve[51]. The entrapment efficiency was calculated using the formula given below

$$\%\ EE = \frac{\text{Amount of drug present in Ag NPs}}{\text{Amount of drug used}} \times 100$$

Other Methods

X-ray diffraction (XRD) examines time dependent particles oxidation state. Energy dispersive spectroscopy (EDS) is used to identify the elemental composition of AgNPs. Auger electron spectroscopy (AES), scanning probe electron microscopy (SPM), X-ray photoelectron spectroscopy (XPS), time of flight secondary ion mass spectrometry (TOF-SIMS) are very important techniques that allow a primary surface analysis of AgNPs. AES and XPS determine the presence, composition and thickness of AgNPs (XPS may be used occasionally to determine the particle size). TOFSIMS gives information regarding surface layers and functional groups attached to the surface. · Low energy ion scattering (LEIS) determines the amount of energy lost by ions during the scattering stage and it is used to identify the elements present on the outmost surface of the AgNPs. · Scanning tunneling microscopy (STM), atomic force microscopy (AFM) allows surface characterization on an atomic scale[52].

CONCLUSION

Herbal mediated silver nanoparticles playing important role to create eco-friendly, cost effective and stable nanoparticles. The researches on synthesis of silver nanoparticles using various plant extracts found that it is safer and better in cancer treatment, but more plants are still not explored for the synthesis of nanoparticles and its applications in pharmaceutical industries. Generally chemotherapy, surgery and radiation treatment are the most prevalent therapeutic option for cancer. Unfortunately, these treatments have various side effects due to lack of targeted delivery. Synthesis of herbal mediated silver nanoparticles provides controlled and targeting action of drug, which can also overcome the problems associated with conventional cancer treatments.

ACKNOWLEDGMENTS

The presenting authors are thankful to principal, Vijaya institute of pharmaceutical sciences for women, Vijayawada for their valuable support in carrying out this work.

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