

## "Exploring the Role of Traditional Indian Medicine in the Green Synthesis of Biomedical Nanoparticles"

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### Abstract

In recent years, nanoparticles have gained significant importance due to their application through green synthesis, which has become one of the most specific methods. Green synthesis of nanoparticles is a new branch of nanotechnology. Traditionally, Indians have used herbal drugs because of their efficacy and minimal side effects, making them safe for the human body. For centuries, herbal medicines have been manufactured on a large scale, contributing to India's wealth of well-documented traditional knowledge systems, such as Ayurveda, Yoga, Unani, Siddha, Homeopathy, and Naturopathy. In Ayurveda, medicinal plants have played a significant role since ancient times. Parts of medicinal plants and their products are inexpensive sources for Indian Ayurvedic medicines. Various plants and their derivatives are vital subjects of research in contemporary nanobiotechnology, particularly in nanoparticle synthesis. This green synthesis method serves as an alternative to chemical methods, as it is cost-effective, non-polluting, and eco-friendly. Nanoparticles (NPs), typically less than 100 nm in size, are integral to nanotechnology, the study of objects on this scale. Notable nanoparticles include those made of silver, platinum, and gold, which have significant applications in fields like optoelectronics, electronics, magnetism, and information storage. Gold-Silver Nanoparticles are of particular interest in research due to their impact on chemical, electronic, energy, space, and pharmaceutical industries. Nanotechnology encompasses the characterization, manufacture, and manipulative uses of nanoparticles, offering a new frontier for material science. The small size and unique chemical, physical, and biological properties of nanoparticles make them crucial in various scientific domains. Recently, metal nanoparticles have garnered attention for their diverse applications, especially in biomedical areas such as targeted drug delivery, imaging, sensing, and antimicrobial activity.

**Keywords:** Nanobiotechnology, Biomedical areas, Gold-Silver Nanoparticles, Homeopathy, Naturopathy, Ayurveda.

### Introduction

The study of science can't get away from this development and stay significant and critical to mankind. Science applies a colossal impact on human activity and is subsequently inseparably interwoven with the powers that guide human activity particularly morals and certain types of energy (Azam, A., 2019). Nowadays, nanoparticles are synthesized using various techniques, among which chemical methods, lithography, and laser ablation are quite expensive, time-consuming, and environmentally harmful. Green chemistry to be a component of societal practice, we'd like to make a knowledgeable green chemistry community comprised of pros, teachers, students, and therefore the public (Azam, A. Pandey A., 2021). Different plants have shown potential for agglutination of nanoparticles, prompting scientists and technologists to explore the use of plants and their products in nanoparticle synthesis. The presence of enzymes, phytochemicals, proteins, and other components in plants is commonly utilized in synthesizing silver nanoparticles using plant extracts (Kulkarni et al., 2011). Nanoparticles exhibit a high surface area to volume ratio, which significantly enhances their chemical reactivity, catalytic activity, and other functional properties. As particle size decreases, a larger proportion of atoms are present on the surface rather than in the bulk, making them highly effective in applications ranging from medicine to electronics. For example, cadmium sulfide (CdS) and zinc sulfide (ZnS) nanoparticles are widely used in optoelectronic devices such as solar cells and light-emitting diodes due to their superior luminescence properties. Gold nanoparticles (AuNPs) play a crucial role in biomedical applications, particularly in targeted drug delivery and imaging, due to their biocompatibility and ease of functionalization. Zinc oxide (ZnO) nanoparticles exhibit strong antibacterial and UV-blocking properties, making them valuable in sunscreen formulations and antimicrobial coatings. Similarly, silver nanoparticles (AgNPs) have potent antimicrobial activity and are extensively used in wound dressings, textiles, and water purification systems. According to Malarkodi et al. (2014), these nanoparticles have revolutionized multiple fields, including medicine, energy, and environmental science. Their ability to interact efficiently at the molecular level due to their high surface area makes them indispensable in modern technology, offering enhanced performance in various industrial and scientific applications.

The term "nanotechnology" was first introduced by Taniguchi in 1974, who defined it as a technology involving the processes of separation, consolidation, and deformation of materials at the level of individual atoms or molecules (Iqbal et al., 2012 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). "Nanotechnology is the application of science to control matter at the molecular level". Tremendous growth in nanotechnology has opened up novel fundamental and applied frontiers in materials science and engineering, such as nano biotechnology, quantum dots, surface-enhanced Raman scattering (SERS) and applied microbiology. Nanotechnology also focuses on the study of nanomaterials, which exhibit remarkable properties, functionalities, and phenomena due to their nanoscale dimensions (Khan et al., 2017 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Developments in the organization of nanoscale structures into predefined superstructures ensure that nanotechnology will play a critical role in many key technologies. It is gaining importance in areas such as mechanics, optics, biomedical sciences, chemical industry, electronics, space industries, drug-gene delivery, energy science, catalysis, optoelectronic devices, photoelectrochemical applications, and nonlinear optical devices. For instance, nanometre-scale germanium quantum dots (less than 10 nm) could be controllably formed for novel optoelectronic device applications such as single electron transistors (SETs) and light emitters. The ability to tune the optical absorption/emission properties of quantum dots (semiconductor nanoparticles) by simple variation in nanoparticle size is particularly attractive in the facile band-gap engineering of materials and the growth of quantum dot lasers.

### Origin and Properties of Nanoparticles

The term "nano" originates from the Greek word "Nanos," which refers to small animals or plants. A nanometer is equivalent to  $10^{-9}$  meters. Nanotechnology aims to measure and manipulate matter at the nanoscale, with dimensions ranging from 1 to 100 nanometers (Mansoori and Soelaiman, 2005 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). At the nanoscale, materials exhibit unique chemical, physical, and biological properties due to a higher surface-to-volume ratio. This phenomenon occurs because the surface area of nanoparticles is inversely proportional to their size, resulting from an increasing number of surface atoms as particle size decreases (El Saliby et al., 2008 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Consequently, the significantly larger surface area and high surface energy of nanoparticles give them distinct optical, electrical, and magnetic properties compared to their bulk counterparts (Ichinose et al., 1992 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024).

Moreover, advances in nanotechnology are creating a novel class of magnetic resonance image contrast-enhancing agents such as small particles of iron oxide, fullerenes encapsulating  $Gd^{3+}$  ions (gadofullerenes), and single-walled carbon nanotube nanocapsules encapsulating  $Gd^{3+}$  ion clusters (gadonanotubes). Nanoparticles are of great interest due to their extremely small size and large surface to volume ratio, which lead to both chemical and physical differences in their properties (e.g. mechanical properties, biological and sterical properties, catalytic activity, thermal and electrical conductivity, optical absorption and melting point) compared to bulk of the same chemical composition. Therefore, design and production of materials with novel applications can be achieved by controlling shape and size at nanometre scale. Nanoparticles exhibit size and shape-dependent properties which are of interest for applications ranging from biosensing and catalysts to optics, antimicrobial activity, computer transistors, electrometers, chemical sensors, and wireless electronic logic and memory schemes. These particles also have many applications in different fields such as medical imaging, nanocomposites, filters, drug delivery, and hyperthermia of tumors.

### From Atomic to Molecular: The Science Behind Nanotechnology

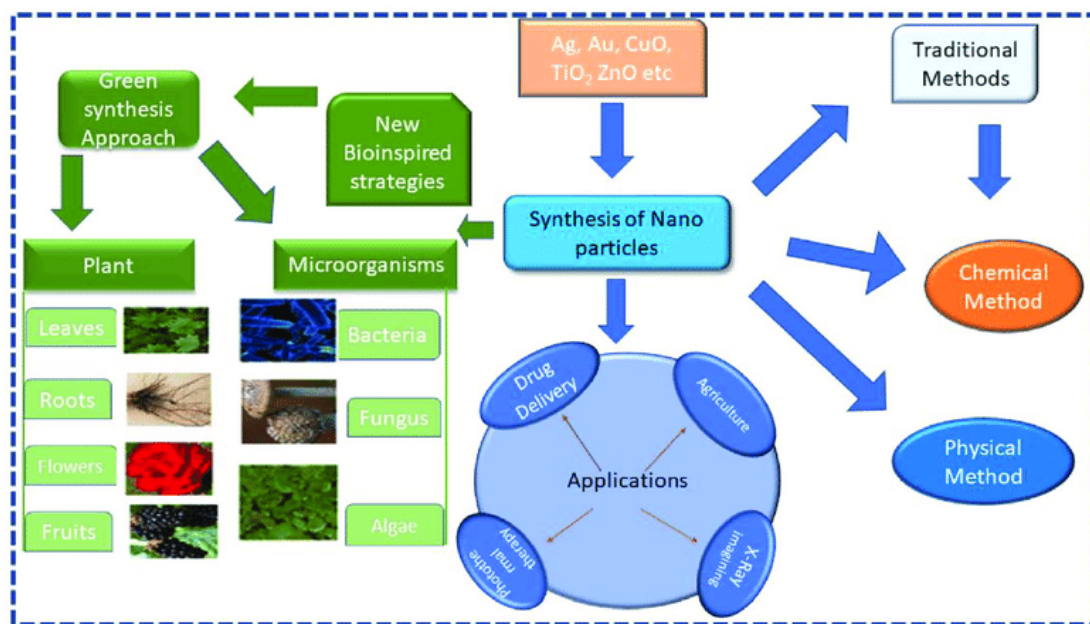
Nanotechnology, the science and technology related to various nanostructures, has emerged as a significant area of research aimed at the sustainable development of human society. This technology is advancing rapidly and is expected to have a substantial impact on future commercialization. The term "nanotechnology" was first introduced by Taniguchi in 1974, defining it as the technology involving the processes of separation, consolidation, and deformation of materials at the atomic or molecular level (Iqbal et al., 2012 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Essentially, nanotechnology also encompasses the study of nanomaterials, which display extraordinary properties, functionalities, and phenomena due to their nanoscale dimensions (Khan et al., 2017). It involves the capability to understand, fabricate, and manipulate materials at the nanoscale (Roco, 2004).

### Plant-Based Synthesis of Therapeutic Nanoparticles

Plant-derived biological synthesis of nanoparticles is gaining importance due to its eco-friendly nature (Azam, A. Pandey A. K. 2021). The biosynthesis of gold nanoparticles using plants like *Tamarindus indica* (Kantak and Gogate, 1992), *Cinnamomum camphora* (Singh et al., 1996), lemongrass (Sharma et al., 2003), alfalfa (Shetty et al., 2006), *Embllica officinalis* (Sood et al., 2006), *Aloe vera* (Gupta et al., 2006), and *Azadirachta indica* (Samjon et al., 2007) has been documented, utilizing plants and plant products as biological agents for nanoparticle synthesis.

Plant-based drugs or medicines are commonly used in the treatment of Parkinsonism, cardiovascular diseases, pulmonary diseases, Alzheimer's disease, cancer therapy, diabetes, and osteoporosis. The development, design, and synthesis of herbal nanoparticles have become a significant focus in the field of nano formulation research. Currently, nanoparticles are extensively developed to enhance bioavailability and to treat various cancers, including lung, breast, and pancreatic cancers. Common nano formulated herbal drugs are derived from *Curcuma longa*, *Panax ginseng*, *Withania somnifera*,

*Silybum marianum*, *Salvia miltiorrhiza*, and *Gymnema sylvestre* (Jadhav et al., 2014 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024) **Fig. 1.**

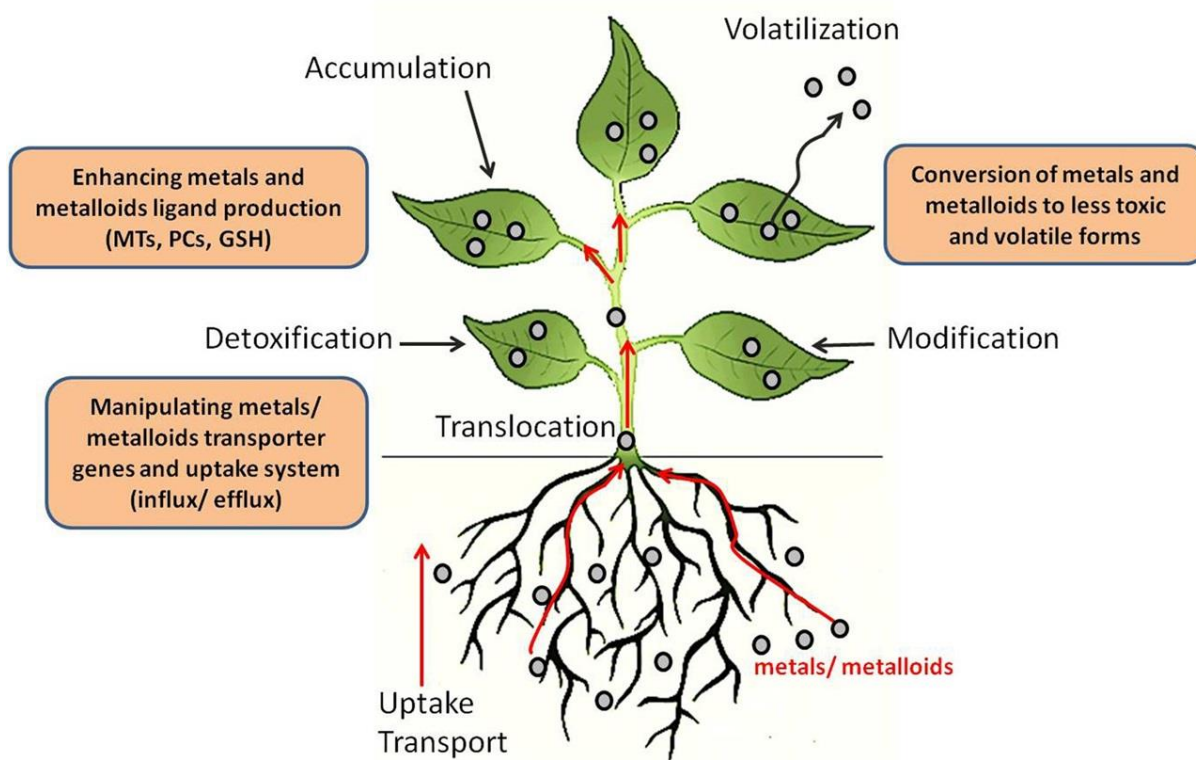


**Fig. 1. Plant-derived biological synthesis of nanoparticles**

The emergence of microbial resistance to various antibiotics and treatments poses a major challenge in healthcare. Researchers are working on developing new, effective antimicrobial drugs that are cost-efficient and do not provoke resistance. The use of herbal nanoparticle-based medicines shows potential in countering microbial resistance more effectively than traditional antibiotics (Nagarajan and Rajagopalan, 2008, Azam, A. Pandey A. K., 2021 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Herbal nanoparticles have demonstrated antibacterial efficacy and cytotoxicity against human cells, which is crucial before considering their therapeutic applications (Bhattacharya and Rajinder, 2005).

### Biological Synthesis of Nanoparticles in Green Chemistry

Green chemistry involves the biological synthesis of nanoparticles, bridging nanotechnology and biotechnology. The biosynthesis of nanoparticles like silver, gold, gold-silver alloys, tellurium, selenium, platinum, silica, palladium, titania, zirconia, quantum dots, magnetite, and uraninite by phototrophic eukaryotes, such as plants and plant derivatives, has been documented (Gardea et al., 1999). These biologically produced nanoparticles are not monodispersed, and their synthesis is typically slow and stable. Various phytochemicals in plants and their parts are already utilized in multiple applications. These phytochemicals play a crucial role in nanoparticle synthesis (Shankar et al., 2003). For instance, certain phytochemical compounds involved in the synthesis of silver nanoparticles function as metabolic fluxes, while others are oxido reductively labile metabolites like ascorbates or catechol/photo-catecholic acids (Jha et al., 2009 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Some are stable polyhydroxy components, such as alkaloids, flavonoids, and polysaccharides (Lin et al., 2010). Metabolites like organic acids, quinones, verbascoside, isoverbascoside, luteolin, and chrysoeriol-7-O-diglucuronide are also involved (Cruz et al., 2010). Additionally, proteins, enzymes, and secondary metabolites like terpenoids, quercetin, and other phenolic compounds contribute to this process (Lukman et al., 2011). Microorganisms play a significant role in the biological synthesis of nanoparticles using enzymes, fungi, plants, or plant extracts. These methods are reported as eco-friendly alternatives to traditional physical and chemical synthesis techniques (Azam, A. Pandey A. K., 2021). The use of plants or their parts in nanoparticle synthesis offers advantages by eliminating the need for complex microbial culture maintenance (Klaus et al., 1999 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). Plant biomass and living plants have demonstrated remarkable potential in the accumulation and detoxification of heavy metals. Numerous studies have highlighted the detoxification and hyper-accumulation capabilities of plants such as *Arabidopsis halleri* and *Thlaspi caerulescens*. Various other plants, including *Acanthopanax sciadophylloides*, *Maytenus founieri*, *Brassica juncea*, *Ilex crenata*, *Sesbania drummondii*, and *Clethra barbinervis*, have shown significant potential for the phytoremediation of heavy metals. **Fig. 2.**



**Fig. 2. Phytoremediation Potential of Plants for Heavy Metals**

Trace elements, including heavy metals and metalloids, are significant environmental pollutants, known for their toxicity even at minimal concentrations. The application of plant biomass for the removal of metals from aqueous solutions, a process termed biosorption, has garnered attention due to its promising and eco-friendly potential for eliminating contaminants from effluents. The inherent ability of certain plants to tolerate heavy metals has intrigued researchers, prompting them to explore the biological mechanisms, physiology, and genetics underlying metal tolerance in hyperaccumulator plants.

There is growing interest among researchers in employing plants for phytomining and phytoremediation of heavy metals, aiming to phytosynthesize metallic nanoparticles. A pioneering study by Gardea-Torresdey et al. first documented the formation of gold and silver nanoparticles within living plants. They demonstrated the synthesis of these nanoparticles inside *Medicago sativa* (alfalfa) plants by absorbing gold and silver ions from solid media, with the alfalfa plants being cultivated in an environment rich in  $\text{AuCl}_4^-$  (Boomi P, Poorani GP, Selvam S et al, 2020).

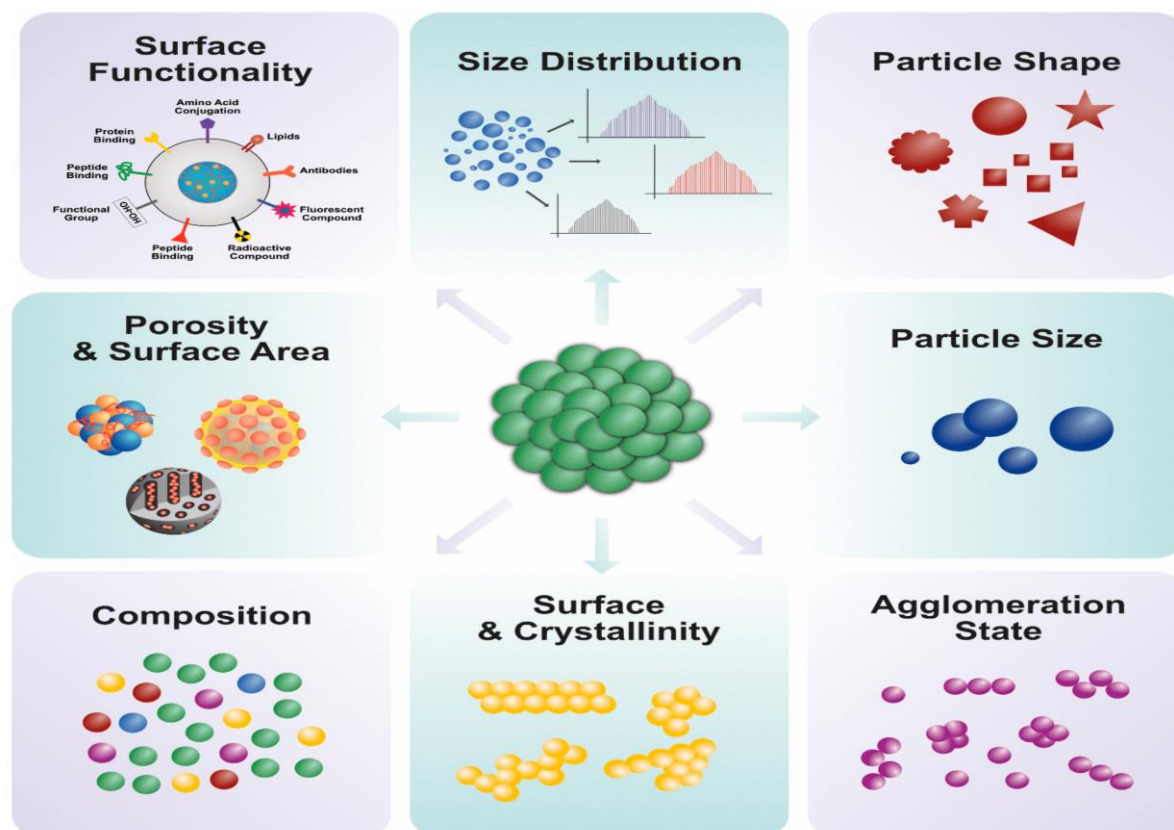
### Biogenic Synthesis and Shape Control of Nanoparticles

By controlling the shape and size of materials at the nanoscale, scientists can design and produce materials with novel applications. The size- and shape-dependent properties of nanoparticles are valuable for a wide range of uses, including biosensing, catalysis, optics, antimicrobial applications, computer transistors, electrometers, chemical sensors, and wireless electronic logic and memory systems (Azam, A. Pandey J. K., Ahmed R. et. Al., 2024). In another study,  $\text{AuFe}_3\text{O}_4$  composite nanoparticles were prepared with a combined chemical and biological reducing process (semi-biosynthesis method). Magnetic cores were primarily produced using a fabrication method consisting of coprecipitation of  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$ . An ethanol extract of *Eucalyptus camaldulensis* was used for the reduction of  $\text{Au}^{+3}$  on the surface of the magnetite nanoparticles and for the functionalization of the  $\text{Au-Fe}_3\text{O}_4$  nano-composite particles.

Armendariz et al. reported for the first time the formation of rod-shaped nanoparticles by biomaterials. They characterized the gold nanoparticles formed by wheat biomass exposed to a 0.3 mM potassium tetra choloaureate solution at pH values of 2–6 at room temperature. It was concluded that wheat biomass was able to reduce  $\text{Au(III)}$  to  $\text{Au(0)}$  forming fcc tetrahedral, hexagonal, decahedral, icosahedral multi twinned, irregular, and rod-shaped nanoparticles. In another study, pH dependent synthesis of rod-shaped Au nanoparticles using *Avena sativa* (oat) has shown that biomass might carry more positive functional groups such as positive amino groups, sulfhydryl groups and carboxylic groups which allowed the  $\text{Au(III)}$  ions to get more closure to binding sites and approved the reduction of  $\text{Au(III)}$  to  $\text{Au(0)}$ . A 0.1 mM solution of  $\text{Au(III)}$  was reacted with powdered oat biomass at pH values of 2–6 for one hour. As in the case of wheat, oat biomass produced fcc tetrahedral, hexagonal, decahedral, icosahedral multitwinned, irregular, and rod-shaped nanoparticles.

It was reported that most of the nanoparticles synthesized by using alfalfa, wheat, and oat at pH 2 had an irregular shape. However, it seems that pH has a major impact on the size of the produced nanoparticles rather than on the shape of them.

Sterilized geranium leaves (*P. graveolens*) when exposed to chloroaurate ions separately resulted in rapid reduction of the metal ions and formation of stable gold nanoparticles of variable size. **Fig. 3.**



**Fig. 3. Biomaterial-mediated Synthesis and Shape Control of Nanoparticles**

### Biosynthesis of Silver and Gold Nanoparticles via Biomass

The reduction of the  $\text{AuCl}_4^-$  ions was nearly complete after 60 min of reaction and the particles (20–40 nm) were predominantly decahedral and icosahedral in shape. Not only silver nanoparticles (55 to 80 nm) could be produced, but also triangular or spherical gold nanoparticles could be easily formed by reaction of the novel sundried biomass of *Cinnamomum camphora* leaf with aqueous silver or gold precursors at ambient temperature. Size dispersity of quasi spherical silver nanoparticles as well as triangular or spherical shapes of gold nanoparticles could be facily controlled by simple variation of the amount of biomass reacting with aqueous solution of  $\text{AgNO}_3$  or  $\text{HAuCl}_4$ .

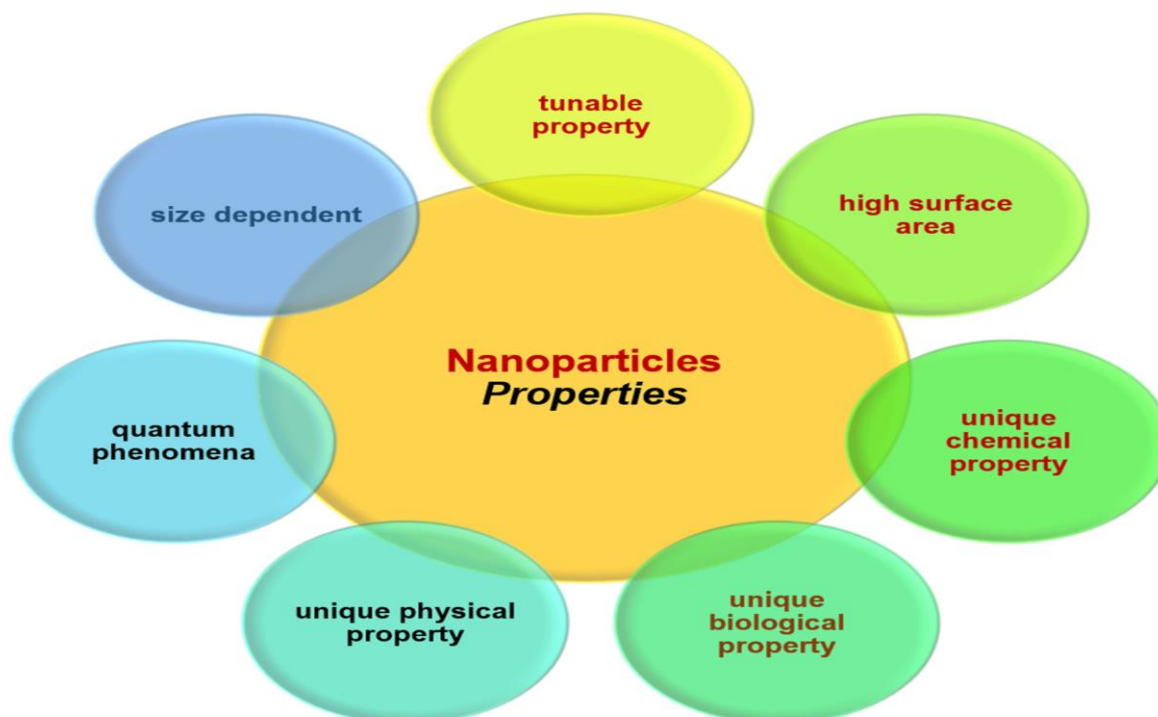
When Huang et al. (2008) switched the amount of the dried biomass from 0.1 to 0.5 g subjected to the same chloroauric acid, the particles shifted from nanotriangles to spherical particles. The utilization of sundried *C. camphora* leaf for biosynthesis of the nanoparticles has some defects. For example, the drying process of the leaf in the sun was time-consuming.

The polyol components and the water soluble heterocyclic components were mainly found to be responsible for the reduction of silver or chloroaurate ions and the stabilization of the nanoparticles, respectively.

Huang et al. (2008) investigated biological production of silver nanoparticles by lixivium of sundried *C. camphora* leaf in continuous-flow tubular microreactors. They introduced polyols in the lixivium as possible reducing agents. Harris et al. have investigated the limits (substrate metal concentration and time exposure) of uptake of metallic silver by two common metallophytes, *Brassica juncea* and *Medicago sativa*. They demonstrated that *B. juncea* and *M. sativa* could be used in phytosynthesis (a broad application of phytoextraction) of metallic silver nanoparticles. *B. juncea*, when exposed to an aqueous substrate containing 1000 ppm silver nitrate for 72 h, accumulated up to 12.4 wt% silver. *M. sativa* accumulated up to 13.6 wt% silver when exposed to an aqueous substrate containing 10 000 ppm silver nitrate for 24 h. In the case of *M. sativa*, an increase in metal uptake was observed with a corresponding increase in the exposure time and substrate concentration. In both cases, TEM analysis showed the presence of roughly spherical silver nanoparticles, with a mean size of 50 nm. In another study, after a 9-week growth in gold, silver, and copper-enriched soil, seeds of *B. juncea* grow into a plant containing Au–Ag–Cu alloy nanoparticles.

### Advances in Nanoscience Applications

Nanoscience and nanotechnology offer numerous promising applications due to the significantly altered and enhanced properties of materials at the nanoscale. This field encompasses a wide range of technologies based on various physical, chemical, and biological processes at the nano level, not only for creating nanomaterials but also for manipulating or utilizing them according to specific objectives. As materials transition from bulk to nanostructures, their properties and functionalities can change significantly. Ultimately, if the structural arrangement of atoms or molecules and the length scale of the materials are appropriately adjusted, variations in their properties can be achieved (Heath, 1995). Nanotechnology provides promising techniques for wastewater treatment, including (a) photocatalysis, (b) nanofiltration, and (c) nano sorbents (Bora and Dutta, 2014 & Azam, A. Pandey J. K., Ahmed R. et. Al.,2024). **Fig. 1.**



**Fig. 1. Enhanced Material Properties and Applications in Nanotechnology**

### Applications of Gold and Silver Nanoparticles in Medicine

There are many important applications for metal nanoparticles in medicine and pharmacy. Gold and silver nanoparticles are the most common ones used for biomedical applications and in emerging interdisciplinary field of nanobiotechnology. For instance, oligo nucleotide capped gold nanoparticles have been used for polynucleotide or protein detection using various detection/characterization methods, including atomic force microscopy, gel electrophoresis, scanometric assay, surface plasmon resonance imaging, amplified voltametric detection, chronocoulometric, and Raman spectroscopy. Furthermore, gold nanoparticles have been employed in immunoassay, protein assay, cancer nanotechnology (especially detection of cancer cells), and capillary electrophoresis. In the field of medicine, gold nanoparticles are used for different proposes. They can be used as markers for biological screening test. After cellular uptake, they can act as precise and powerful heaters (thermal scalpels) to kill cancer. Moreover, gold nanoparticles are capable of inducing apoptosis in B cell-chronic lymphocytic leukaemia (chronic lymphoid leukaemia).

Silver nanoparticles have drawn the attention of researchers because of their extensive applications in areas such as integrated circuits, sensors, bio labelling, filters, antimicrobial deodorant fibres, cell electrodes, and antimicrobials. Antimicrobial properties of silver nanoparticles caused the use of these nanometals in different fields of medicine, various industries, animal husbandry, packaging, accessories, cosmetics, health and military. Silver nanoparticles show potential antimicrobial effects against infectious organisms such as *Escherichia coli*, *Bacillus subtilis*, *Vibria cholera*, *Pseudomonas aeruginosa*, *Syphilis typhus*, and *Staphylococcus aureus*.

### Conclusion

The green synthesis of metal nanoparticles (NPs) using plant and microorganism sources offers a sustainable, non-toxic, and eco-friendly alternative to conventional physical and chemical synthesis methods. This approach utilizes a variety of plant materials such as leaf extracts, fruit extracts, seeds, bark, and microorganisms including bacteria, fungi, and actinomycetes for the synthesis of diverse metal and metal oxide nanoparticles, such as Au, Ag, Pt, Pd, Ni, Se, Cu, CuO, and TiO<sub>2</sub>.

The size, shape, and reaction rate of the synthesized nanoparticles are influenced by experimental parameters like reaction time, reactant concentration, pH, temperature, aeration, and salt concentration. Traditional methods like chemical synthesis, lithography, and laser ablation are not only costly and time-consuming but also pose environmental hazards. In contrast, green synthesis using plants has shown potential for nanoparticle agglutination, with enzymes, phytochemicals, proteins, and other plant components playing a crucial role in synthesizing silver nanoparticles (Azam, A. Pandey J. K., Ahmed R. et. Al.,2024).

In recent years, the biological synthesis of nanoparticles from plants has gained significant attention due to its simplicity and environmental benefits. Plants such as *Tamarindus indica*, *Cinnamomum camphora*, lemongrass, Alfa alfa, *Embllica officinalis*, Aloe vera, and *Azadirachta indica* have been successfully used for nanoparticle synthesis. Additionally, the rise of antibiotic-resistant microorganisms poses a significant challenge in healthcare, prompting researchers to develop new antimicrobial drugs. Nanoparticle-based herbal medicines have emerged as a promising, cost-effective alternative in the medical field, offering potential solutions to these pressing issues.

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