A COMPREHENSIVE REVIEW: GREEN SYNTHESIS OF NANOPARTICLES FROM AZADIRACHTA INDICA PLANT

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Abstract

Green synthesis of neem plant nanoparticles is a sustainable and environmentally beneficial method. Neem plant extracts are employed as reducing and capping agents because they are high in bioactive components. Neem components are extracted and combined with solutions of metal precursors in the process. Metal ions are reduced and nanoparticles are created under carefully controlled circumstances. These neem-synthesized nanoparticles have special features and are used for environmental cleanup, agriculture, catalysis, and medicine. The use of hazardous chemicals is decreased thanks to the green synthesis approach's affordability, environmental friendliness, and scalability. Green nanotechnology could advance as a result.

Keywords: green synthesis, nanoparticles, neem plant, ecofriendly, sustainability

1. INTRODUCTION

Nanoparticles will play a significant role in the creation of future devices that are both human and environmentally friendly. Synthesis of nanoparticles by plants is a method of green chemistry that connects plant biotechnology and nanotechnology. Plant extracts are utilized to bio-reduce metal ions and create nanoparticles. Since then, showed the critical role that plant metabolites such as proteins, sugars, terpenoids, polyphenols, alkaloids, phenolic acids, and polyphenols play in the reduction of metal ions into nanoparticles and in promoting their ensuing stability. Atoms in nonmetric materials have very distinct characteristics from those in bulk materials. Because of the general toxicity of chemicals used in conventional chemical methods to create nanoparticles, the requirement for ecologically friendly processes is very great [1].

The basic building elements of nanotechnology are thought to be nanoparticles (NPs). The field of nanotechnology is multidisciplinary and encompasses physics, biology, chemistry, health, and material science. Metal nanoparticle production has been described using a variety of physical and chemical techniques at this time. These options are unsuitable for use in biology, medicine, or the clinical field due to all reported chemical processes and energy-intensive routes, which render them environmentally hazardous. Therefore, creating environmentally friendly procedures is essential for synthesizing nanomaterials today. Nanotechnology has given rise to biotechnology, a concentrated fusion of biological and Nano technological methods for the biosynthesis of nanoparticles [2].

Special characteristics, colloidal silver nanoparticles are used extensively in pharmaceuticals, chemical sensing, bio sensing, photonics, and electronics. The variety and significance of these uses have sparked a lot of interest in creating adaptable processes to create silver nanoparticles with clearly defined and controlled properties [3].

Bimetallic Au Core-Ag shell nanoparticles with clearly specified composition and form have been effectively created using neem (Azadirachta Indica) leaf broth. Recently, it was revealed that silver nanoparticles could be produced at room temperature from an extract of parthenium hysterophorous L leaves. However, there was insufficient investigation into the photoluminescence property and the variation in particle size with reaction temperature and reaction time [3].

Magnetic nanoparticles and silicon nanoparticles are two examples of inorganic nanoparticles. Gold, Ag, alloy, zinc, and other metals are included in the groups of metallic nanoparticles. The chemical Ag is magnetic. Nano silver offers key biological properties for consumer goods, food technology, textile/fabric applications, and medical usage. Aside from that, Nano silver has unique optical and physical properties that are expected to have a big future in medicine [4] [5].

In the rapidly expanding area of nanotechnology, matter is manipulated at the atomic, molecular, and supra molecular levels. Nobel laureate Richard Feynman first used the word "nanotechnology" in his 1959 lecture, "There's Plenty of Room at the Bottom," in which he discussed the potential for rearranging and manipulating specific atoms and molecules [6] [7].

1.1 Types of Nanoparticles

Nanoparticles are very small objects with sizes ranging from 1 to 100 nanometers (nm). They can be made from a variety of substances, including metals, electronics, polymers, and ceramics. Nanoparticles are promising candidates for numerous uses in industries like medicine, electronics, energy, and environmental science because they possess distinctive physical and chemical properties that set them apart from their bulk counterparts [8].

1.2 APPLICATIONS OF NANOPARTICLES

1.2.1 Applications of Nanoparticles in Medicine

The unique characteristics of nanoparticles, such as their small size, huge surface area, and high reactivity, have made them attractive instruments for the diagnosis and treatment of diseases. They are easily transportable through biological barriers like the blood-brain barrier and can be functionalized with a variety of chemicals, including medicines, antibodies, and nucleic acids, to target particular cells or tissues. Additionally, controlled release features of nanoparticles can be created, enabling continuous drug administration throughout time-consuming periods of time. The following list includes some of the most important applications for nanoparticles in medicine [9, 10].

- **Drug Delivery:** Nanoparticles have been employed as drug delivery methods for a variety of medications, including antibiotics, vaccinations, and anticancer medications. Targeting them to particular cells or tissues can increase their therapeutic efficacy and shield the medications from immune system breakdown and clearance. For instance, liposomal nanoparticles have been employed to carry anticancer medications to tumour cells, improving the effectiveness of treatment and minimizing adverse effects [9, 10].
- **Imaging:** Nanoparticles can be utilized as contrast agents in a variety of imaging procedures, including computed tomography (CT), magnetic resonance imaging (MRI), and fluorescence imaging. They can increase the sensitivity and specificity of imaging and make it possible to find small lesions that are hard to find with traditional imaging methods.

For instance, liver tumour have been found using super paramagnetic iron oxide nanoparticles as MRI contrast agents [9].

- **Bio sensing:** The detection of numerous biomolecules, including proteins, nucleic acids, and carbohydrates, can be done using nanoparticles as biosensors. The ability to identify biomolecules at low concentrations is made possible by their great sensitivity and specificity. Prostate-specific antigen (PSA), a biomarker for prostate cancer, has been detected using gold nanoparticles as biosensors, for instance [9].
- **Gene Therapy:** The delivery of therapeutic genes to cells or tissues in order to treat genetic abnormalities can be accomplished using nanoparticles as vectors. They can help the genes get absorbed by cells and prevent nucleases from destroying them. For instance, lung cancer cells were given therapeutic genes using cationic liposomal nanoparticles, which reduced tumour growth and increased survival rates [9, 10].

1.2.2 Applications of Nanoparticles in Electronics

Solar cells, sensors, and memory devices are just a few of the electronic gadgets that incorporate nanoparticles. By enhancing their conductivity, optical qualities, and mechanical strength, they can improve the performance of electrical devices. Furthermore, nanoparticles are appealing for commercial applications due to their easy, affordable, and scalable synthesis. Nanoparticles are used in electronics for a variety of purposes, some of which are listed below [11].

- **Memory Devices:** Nanoparticles have been utilized to enhance performance and lower power consumption in memory devices like flash memory and phase-change memory. To improve the data retention and durability of flash memory systems, for instance, gold nanoparticles have been utilized [11].
- **Sensors:** Nanoparticles have been employed in the creation of sensors for a variety of uses, including the monitoring of the environment, medical treatment, and food safety. The ability to detect analyte at low concentrations is made possible by their great sensitivity and selectivity. Silver nanoparticles, for instance, have been utilized in the creation of sensors for the detection of heavy metal ions in water [11].
- **Solar cell:** Nanoparticles have been utilized in the creation of solar cells to increase their effectiveness and lower their price. In addition to facilitating charge movement in the cells,

they can improve sunlight absorption. For instance, semiconductor nanoparticles called quantum dots have been utilized in the creation of third-generation solar cells [11].

- **Flexible electronics:** Nanoparticles have been employed in the creation of flexible electronics, which are able to be twisted or stretched without breaking. They may be able to improve the devices' mechanical qualities and make it possible for them to be integrated with flexible substrates. Silver nanoparticles, for instance, have been employed to create flexible, transparent electrodes for touch screens and wearable technology [11].

1.2.3 Applications of Nanoparticles in Energy

Applications for nanoparticles in the realm of energy include fuel cells, energy storage, and energy conversion. By increasing the effectiveness, resilience, and safety of energy devices, they can boost their performance. In addition, the availability of numerous and inexpensive resources for the production of nanoparticles makes them appealing for use in large-scale energy applications. The following are some of the most important applications for nanoparticles in the energy sector [12].

- **Catalysis:** Fuel cells, carbon dioxide reduction, hydrogen production, and other energy-related activities have all utilized nanoparticles as catalysts. They can decrease the quantity of catalyst required while improving the reaction rate and selectivity of the reactions. For instance, oxygen reduction reactions in fuel cells have been catalyzed by platinum nanoparticles [12].
- **Energy Storage:** In order to increase the efficiency and lower the price of energy storage technologies like batteries and super capacitors, nanoparticles have been utilized in their development. They can increase the electrode surface area and make it easier for charge to move around the device. As an illustration, silicon nanoparticles have been utilized to create lithium-ion batteries with increased energy density [12].
- **Solar Energy:** To increase their efficiency and lower their cost, nanoparticles have been utilized in the creation of solar energy technologies such photovoltaic cells and solar fuels. In addition to facilitating charge transport in the devices, they can improve solar absorption. For instance, the development of dye-sensitized solar cells has made use of titanium dioxide nanoparticles [12].

1.2.4 Applications of Nanoparticles in Environmental Science

For a variety of purposes, including soil remediation, air purification, and water treatment, nanoparticles have been used in environmental science. They can clean the air of contaminants and raise the standard of our natural resources. Additionally, because nanoparticles may be created using eco-friendly and sustainable techniques, they are appealing for use in ecologically acceptable applications. In environmental research, the following are some of the most noteworthy applications of nanoparticles [13].

- **Water treatment:** The removal of pathogens, organic pollutants, and heavy metals from water has been accomplished using nanoparticles. They can enhance the quality of the water by adsorbing, oxidizing, or photo catalyzing the impurities out. For instance, arsenic from contaminated groundwater has been removed using iron nanoparticles [13].
- **Air Purification:** Nanoparticles have been employed to clean the air of several contaminants, including particulate matter, nitrogen oxides, and volatile organic compounds. By adsorption, photo catalysis, or electrostatic attraction, they can remove the contaminants and enhance the air quality. For instance, nitrogen oxides have been removed from car exhaust using titanium dioxide nanoparticles [13].
- **Soil Remediation:** Nanoparticles have been used to treat soil for a variety of contaminants, including pathogens, organic pollutants, and heavy metals. In addition to enhancing soil quality, they can remove pollutants by adsorption, oxidation, or microbial decomposition. For instance, the immobilization of heavy metals in contaminated soils has been accomplished using carbon nanoparticles [13].
- **Environmental Monitoring:** Nanoparticles have been employed to track several environmental variables, including soil, water, and air quality. High spatial and temporal resolution can be provided, and they can enable real-time and remote monitoring of the parameters. One application of gold nanoparticles is the creation of colorimetric sensors for the detection of mercury ions in water [13].

1.3 SYNTHETHIC METHODS OF NANOPARTICLES

Many different techniques can be used to create nanoparticles, and each has benefits and drawbacks. Here are a few techniques of synthesis that are frequently used:

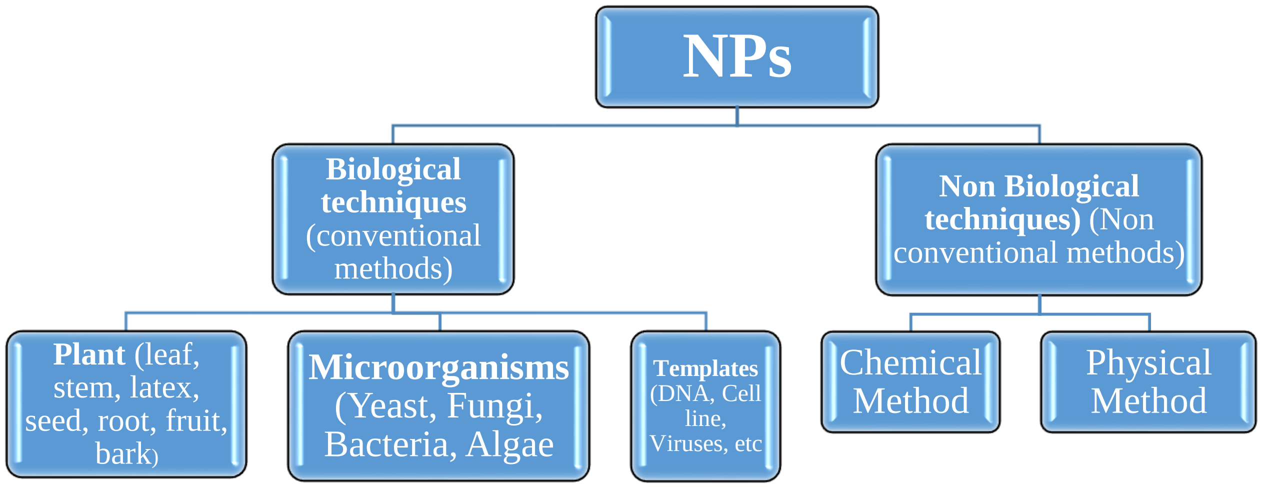

Figure 1: Synthesis Methods of Nanoparticles

1.3.1 Biological techniques

In order to decrease metal ions and stabilize nanoparticles, biological methods of nanoparticle synthesis employ microorganisms, plants, and their extracts. The method is frequently referred to as biosynthesis or bio fabrication of nanoparticles. This approach to nanoparticle synthesis is economical, scalable, and ecologically friendly.

- **Microbial synthesis:** This technique employs yeast, fungi, and bacteria to decrease metal ions and stabilize nanoparticles. The exterior proteins of the microbiological cells serve as a reducing environment and stabilize the synthesized nanoparticles. Examples of microbes that have been used to create metal nanoparticles include Escherichia coli, Bacillus subtilize, and Pseudomonas aeruginosa [7].
- **Plant extract-based synthesis:** In this technique, plant extracts are used as a reducing and stabilizing substance to create nanoparticles. Flavonoids, terpenoids, and alkaloids, among other compounds found in plant extracts, have the ability to lower metal ions and stabilize nanoparticles. Several plant products, including green tea extract, Azadirachta indica, and aloe Vera, have been used to create nanoparticles.
- **Enzyme-mediated synthesis:** The production of nanoparticles has been carried out using enzymes like lysozyme, lactate dehydrogenase, and alkaline phosphatase. Enzymes offer

a particular environment for the synthesis of nanoparticles, and the produced particles are typically uniform in size and structure [7].

- **Cell-free extract-based synthesis:** For the creation of nanoparticles, this technique uses cell-free extracts taken from plants or microbes. The essential reducing agents and enzymes for nanoparticle synthesis are present in the cell-free extracts. For the production of nanoparticles, this technique is both easy and effective.

1.3.2 Non-Biological techniques

Physical and chemical processes are used to create nanoparticles in non-biological ways of nanoparticle synthesis. These processes are usually high-energy ones that produce nanoparticles using thermal, electrical, or mechanical energy.

- The most widely used non-biological technique for synthesizing nanoparticles is chemical reduction. Using chemicals like citrate, sodium borohydride, and hydrazine, metal ions are decreased using this technique. Different kinds of nanoparticles, including gold, silver, and copper, can be created using the chemical reduction technique [14].
- **Sol-gel technique:** Using a precursor solution that is transformed into a gel and then dried, the sol-gel method creates nanoparticles. To produce nanoparticles, the desiccated gel is heated next. Metal oxide nanoparticle production using this technique is possible for materials like titanium dioxide, zinc oxide, and iron oxide [15].
- **Electrochemical method:** Application of an electrical current to a solution containing metal ions causes the formation of nanoparticles using the electrochemical technique. Several kinds of nanoparticles, including gold, silver, and copper, can be created using the electrochemical technique [16].
- **Technique of laser ablation:** The laser ablation technique involves ablating a metal target with a laser beam to produce nanoparticles. The creation of numerous kinds of nanoparticles, such as gold, silver, and titanium dioxide, can be accomplished using the laser ablation technique [17].

1.3.3 Green synthesis

Using natural resources like plants, microbes, and fungi, green synthesis is a technique for creating nanoparticles. Eco-friendly and yielding nanoparticles with distinctive qualities, this technique. Due to its potential to use less harmful chemicals and energy, green synthesis has emerged as an appealing option to traditional techniques for synthesizing nanoparticles [18]. Utilizing plant compounds is one instance of green synthesis. Polyphenols, flavonoids, and alkaloids are just a few of the bioactive substances found in plants that can function in the creation of nanoparticles as reducing and stabilizing agents. Silver, gold, and copper nanoparticles have all been created through the use of various plant products [18]. An extract from Eclipta prostrata leaves was used by Kumar in a 2018 study that examined the green manufacture of silver nanoparticles. According to the study, the plant extract-derived silver nanoparticles were very stable and exhibited strong antibacterial activity against both gram-positive and gram-negative bacteria [18].

Green synthesis is more advantageous than conventional ways of synthesizing nanoparticles than just being environmentally friendly. Due to the use of cheap and easily accessible natural resources, green chemistry is cost-effective. Researchers in developing nations can use green synthesis because it is straightforward and doesn't call for expensive tools [19].

The process of synthesizing different materials, such as nanoparticles, organic compounds, and other materials, using sustainable and ecologically friendly practices is known as "green synthesis." Environmentally friendly synthesis or viable synthesis are other names for this method. By utilizing renewable resources, non-toxic solvents, and lowering the amount of energy and waste produced during the synthesis process, green synthesis hopes to reduce the detrimental effects of chemical synthesis on the environment, human health, and resources [20].There are several green synthesis techniques, including chemical reduction using non-toxic reducing chemicals, microbial synthesis, and synthesis based on plant extracts. Low toxicity, low expense, scalability, and high yield are just a few benefits of green synthesis over traditional chemical synthesis [20].

Natural techniques that have been established for the synthesis of Nano- and micro-scaled inorganic materials have given rise to a relatively new and mostly unknown field of inquiry centered on the biosynthesis of nanomaterials. Bio-organism-based synthesis and green chemistry ideas can coexist [21].

1.4 AZADIRACTA INDICA

Neem, scientifically known as Azadirachta indica, is a multipurpose medicinal shrub that has been used in folk medicine for ages. The Neem tree, which is indigenous to India, is extensively grown throughout the tropics for its numerous benefits, including its capacity to ward off insects and its anti-inflammatory, anti-fungal, anti-cancer, and anti-viral properties. Due to its eco-friendly and sustainable attributes, Neem has recently been used for the ecological synthesis of nanoparticles, which has attracted a lot of attention [22].

The creation of nanoparticles with various uses and characteristics has been done using Neem leaves, bark, seeds, and oil. In this article, we'll examine the different Neem plant components that have been used in the creation of nanoparticles as well as their characteristics [22].

1.4.1 Neem Leaves

Neem leaves are rich in bioactive compounds including Azadirachta, nimbin, and nimbi din, which have potent anti-inflammatory, anti-bacterial, anti-fungal, anti-cancer, and anti-viral properties. In a green synthesis method, Neem leaves were used to create nanoparticles of silver, gold, zinc oxide, and copper oxide [23].

1.4.2 Neem Bark

The bioactive substances found in Neem wood, such as tannins, flavonoids, and triterpenoids, have strong anti-inflammatory, antibacterial, and anti-cancer effects. Silver, gold, and zinc oxide nanoparticles have all been produced environmentally friendly using Neem wood.

1.4.3 Neem Seeds

Neem seeds are rich in bioactive compounds like Azadirachta, nimbin, and nimbi din, which have potent anti-inflammatory, anti-bacterial, anti-fungal, and anti-viral properties. Neem seeds have been used to create environmentally friendly silver, gold, and iron oxide nanoparticles [24].

1.4.4 Neem Oil

Silver, gold, and iron oxide nanoparticles have all been made environmentally friendly through the use of Neem oil. Singh in (2014) looked into the environmentally friendly production of silver nanoparticles using Neem oil in one of their studies. According to the research, the silver nanoparticles made using Neem oil were extremely stable and demonstrated potent anti-bacterial activity against a variety of bacterial strains. The ecologically friendly manufacturing of gold nanoparticles using neem oil was the subject of another experiment by Anitha in (2020). According to the study, the gold nanoparticles made using Neem oil displayed strong anti-inflammatory and anti-cancer characteristics [5].

1.4.5 Applications of Azadirachta indica

Due to their distinctive physical and chemical characteristics, nanoparticles made from Azadirachta indica extract have a variety of uses. The natural chemicals found in Azadirachta indica can be used to create these nanoparticles in a green and eco-friendly manner, making them highly cost- and sustainably-effective. In this piece, we will look at the different uses for these nanoparticles and cite current research that has looked into their potential.

1.4.5.1 Biomedical Applications of Azadirachta indica

Nanoparticles were produced using Azadirachta indica extract and could one day be applied to biomedicine. They are suitable for use as drug delivery devices because to their small size and huge surface area. According to various research, these nanoparticles have been employed to transport antibiotics, painkillers, and anticancer medicines. In a recent study, it was discovered that silver nanoparticles made from Azadirachta indica extract were efficient at delivering the anticancer medication doxorubicin to cancer cells, leading to a significant decrease in tumour growth [25, 26].

1.4.5.2 Environmental Applications of Azadirachta indica

Additionally, discovered to have potential uses in environmental cleanup are nanoparticles made from Azadirachta indica extract. They can be employed as catalysts in a variety of environmental systems, including water and air purification units. These nanoparticles have been used, according to numerous studies, to remove organic contaminants, heavy metals, and colors from water and the air. In a recent study, it was discovered that water chromium may be removed by silver nanoparticles made from Azadirachta indica extract [27, 28].

1.4.5.3 Food and Nutrition Applications of Azadirachta indica

It has also been discovered that nanoparticles created from Azadirachta indica extract may have uses in the food and nutrition sector. They have high antioxidant and antibacterial characteristics, making them suitable for use as food additives and preservatives. Numerous studies have documented the usage of these nanoparticles in food preservation and nutritional value enhancement. In a recent study, it was discovered that silver nanoparticles made from Azadirachta indica extract were efficient at preventing the growth of foodborne bacteria in milk [29].

1.4.5.4 Energy Applications of Azadirachta indica

Azadirachta indica extract-derived nanoparticles have also been discovered to have potential uses in the field of renewable energy. They have outstanding catalytic activity and stability, making them suitable for application as catalysts in fuel cells, solar cells, and other energy conversion devices. These nanoparticles have been used, according to a number of research, to create renewable fuels like methanol and hydrogen. According to a recent study, the electrochemical conversion of carbon dioxide to formic acid using gold nanoparticles made from Azadirachta indica extract was successful [30].

2. LITERATURE REVIEW

2.1 The green synthesis of nanoparticles using Azadirachta indica

Neem trees, sometimes referred to as Azadirachta indica, are indigenous to the Indian subcontinent. It has been discovered to have a variety of pharmacological and biological effects and has been utilized in traditional medicine for millennia. Due to its eco-friendliness, affordability, and lack of toxicity, Neem extract has recently attracted a lot of attention when it comes to the green production of nanoparticles.

Aloufi, A. S. and his coworker reported in (2023) about the Evaluation of Green ($Sn(Fe:Ni)O_2$) Nanoparticles Made from Azadirachta indica Leaf Extract in Terms of Structural, Optical, and Antibacterial Properties. Metal oxide nanoparticles have received substantial recognition due to their fascinating physicochemical properties. Although there are other ways to create these nanoparticles, the biological method using plant extracts is preferred since it provides a simple, basic, environmentally friendly, effective, rapid, and affordable choice for synthesis. In this work, a green method and a leaf extract from Azadirachta indica as a reducing agent were used to create tin (ferrous: nickel) dioxide ($Sn (Fe:Ni)O_2$) nanoparticles. The synthesised nanoparticles were characterized using a number of methods, including dynamic light scattering (DLS), energy-dispersive X-ray (EDX) spectroscopy analysis, Feld emission scanning electron microscopy (FESEM), Fourier transform infrared (FTIR), and photoluminescence (PL) measurement. In addition, the antibacterial effects of ($Sn (Fe: Ni) O_2$) nanoparticles against bacterial strains of

Staphylococcus aureus, Streptococcus pneumoniae, Bacillus subtilis, Klebsiella pneumonia, Escherichia coli, and Pseudomonas aeruginosa were investigated. XRD patterns were used to pinpoint tetragonal Sn (Fe: Ni) O_2 nanoparticles. The hydrodynamic diameter of the nanoparticles, which was 143 nm, was validated by the DLS spectra. The synthesized nanoparticles' spherical shape could be seen in the FESEM image. The EDAX spectrum was used to investigate chemical composites and map data. The Sn-O-Sn stretching band was detected at 615 cm-1 in the FTIR spectra, and the Sn-O stretching band was detected at 550 cm-1. The surface defects on the synthesised (Sn (Fe: Ni) O2) nanoparticles were identified using photoluminescence spectra. According to the inhibition zone, (Sn(Fe:Ni)O_2) nanoparticles demonstrated superior antibacterial activity against all tested pathogens compared to conventional antibiotics like amoxicillin, demonstrating the immense potential of nanoparticles in the healthcare industry [31].

2.2 Biosynthesis of nanoparticles using leaf extract of *neem*

Asimuddin, and his coworker reported in (2020) about the Azadirachta Indica Base Silver Nanoparticle Biosynthesis and Assessment of Cytotoxic and Antibacterial Effects Given the increasing threat that climate change poses to the environment, it is highly important to develop ecologically friendly and sustainable procedures for the manufacture of metallic nanoparticles (NPs). Here, we provide a simple and eco-friendly method for creating silver nanoparticles (AgNPs) using Azadirachta indica leaf extract and an aqueous solution of silver nitrate (AgNO3) [32]. It is examined how the generation of AgNPs is impacted by temperature and leaf extract concentration. A concentration of 60 mg/mL leaf extract, 1 mM of AgNO3, 30 minutes of reaction time, and 85 °C were discovered to be the ideal conditions for the production of high-quality AgNPs. The surface Plasmon Resonance (SPR) of the AgNPs was used to corroborate the creation of the nanoparticles by utilizing UV-Vis analysis, which revealed the UV spectrum's greatest absorption peak at 410 nm. Inhibitory values of 0.5 g/ml for Escherichia coli and 1.0 g/ml for Staphylococcus aureus were found, according to further investigation into the antibacterial characteristics of biosynthesized AgNPs. In vitro cytotoxicity studies of biosynthesized AgNPs against human acute lymphoblastic leukemia cells using the MTT assay also showed that a minimum inhibitory dosage of 15.6 g/mL was necessary. AgNPs can thus be produced on a wide scale using this approach, which is also economically and environmentally favourable, and has the potential to be used in biological applications. Azadirachta indica leaf extract was used as a reducing agent in the current investigation to establish a safe, non-toxic, environmentally acceptable technique for the production of AgNPs [32]. Using this technique, spherical-shaped AgNPs with a high degree of crystallinity were produced in natural lighting. The quality and quantity of the produced AgNPs were clearly influenced by a number of physicochemical factors, including temperature, duration, the content of leaves extract, and $AgNO_3$. A. Indica plant's geographic location also has a crucial impact in the characteristics of the resulting AgNPs, the light of recent findings and evaluation of earlier research. To study this further, however, natural product chemists and material scientists must cooperate. The biosynthesized AgNPs have further demonstrated their antibacterial activity against harmful bacteria, demonstrating that they have bactericidal properties; nevertheless, the research can be expanded to include resistant strains, and exciting results may be gained [32]. Additionally, this work is the first to evaluate the in vitro effects of biosynthesized AgNPs on PBMCs from ALL patients. The findings show that biosynthesized AgNPs have the ability to prevent leukemic cells from proliferating, and this capability can be investigated further against a variety of additional cell lines to determine whether it is a feasible treatment alternative. The suggested studies are currently being conducted, and the extension of the work that has been provided will be published as a distinct research later [32].

2.3 Others Synthetic Methods

Saravanan, and his coworker in (2020) has been synthesized ZnO nanoparticles from Azadirachta indica leaf extract using a biocompatible and effective home microwave technique. In order to successfully synthesise ZnO nanoparticles using a green synthesis methodology, Azadirachta indica leaf extract and a microwave-assisted solvothermal process were hand-me-down. The structure of greenly synthesised ZnO NPs and the lattice parameters were confirmed by powder X-ray diffraction. Scanning electron microscopy and energy dispersive X-ray analysis allow the morphology and elemental composition of the greenly synthesised ZnO NPs to be seen. ZnO nanoparticles' positive photoconductive nature is revealed by the photoconductivity investigation [33]. Azadirachta indica leaf extract was used to successfully synthesis ZnO NPs utilizing a straightforward solvothermal technique. PXRD patterns demonstrated the ZnO nanoparticles' well-documented crystallization. To establish the typical particle size, Scherer's equation was employed. The morphology and chemical composition of the samples were identified using SEM and EDAX images. The ZnO NP's positive photo-conducting characteristics are established via photoconductivity measurement [33].

3. METHODOLOGY

Due to its eco-friendly and long-lasting characteristics, green nanoparticle synthesis has attracted a lot of attention lately. A prospective source for the manufacture of nanoparticles is the widely accessible medicinal plant neem (Azadirachta indica). Using neem plant extracts as a reducing and stabilizing agent, this process offers a step-by-step tutorial for the environmentally friendly synthesis of nanoparticles.

3.1 Material and Equipment's Required:

Neem leaves or neem extract: The main source of the bioactive chemicals employed in green synthesis is the neem (Azadirachta indica) leaf. Neem leaf extract or fresh neem leaves can both be used throughout the production process.

Solvent: In order to extract the bioactive components from neem leaves, a suitable solvent is required. For this purpose, water, ethanol, methanol, or a mixture of these solvents are frequently utilized.

Reducing agent: In order to aid the reduction of metal ions and the creation of nanoparticles, a reducing agent is necessary. Numerous bioactive substances included in neem extract, including phenolic, flavonoids, and terpenoids, have been shown to have lowering effects.

Metal precursor: If you wish to synthesise metal nanoparticles, you will need a metal precursor or a salt that contains those metal ions. Silver nitrate (AgNO3), gold chloride (AuCl3), or copper sulphate (CuSO4) are examples of common metal precursors.

Reaction vessel: To complete the synthesis process, an appropriate reaction vessel is required. Any container that is appropriate for the reaction conditions, such as a glass flask or beaker, can be used.

Stirrer or magnetic stirring bar: During the synthesis process, a stirrer or a magnetic stir bar is useful to ensure uniform mixing of the reaction components.

Heating device: Depending on the synthesis process, you could need a heating device to speed up the reaction and regulate the temperature, like a hot plate or microwave.

Filtration system: To separate the nanoparticles from the reaction mixture after the synthesis, you will require a filtration setup, such as filter paper or a membrane filter.

3.2 Collection and Preparation of Neem Plant Extract:

Collect new neem leaves or other neem plant pieces. To remove any dirt or contaminants, thoroughly rinse the harvested plant material in distilled water. To stop active chemicals from degrading, dry the plant material in the shade. Make a fine powder out of the dried neem leaves or plant parts using a mortar and pestle [34].

3.3 Preparation of Neem Extract:

Neem powder in the amount of 10 g should be weighed and then transferred to a clean beaker. In the beaker, mix a suitable solvent (1:10) (w/v), such as distilled water or ethanol. To draw out the bioactive substances from the neem plant, agitate the mixture with a magnetic stirrer at room temperature for a predetermined amount of time (for example, 24 hours) [34].

3.4 Synthesis of Nanoparticles:

Neem extract from step 2 is metered out (for example, 50 mL) and transferred to a clean reaction vessel (for example, an Erlenmeyer flask). To the reaction vessel, add a suitable precursor solution containing metal salts (such as silver nitrate). At a suitable temperature, such as 60°C, stir the mixture using a magnetic stirrer for a predetermined amount of time, such as two hours. Keep an eye on the reaction mixture's colour change, which shows when nanoparticles have formed. Neem plant extract is commonly used to create brownish nanoparticles [34].

3.5 Characterization of Nanoparticles:

To separate the synthesised nanoparticles from the remaining solution, take a tiny sample of the particles and centrifuge the mixture. To get rid of any remaining contaminants or unreacted substances, thoroughly wash the collected nanoparticles with distilled water multiple times. Utilizing several analytical methods, such as UV-Vis spectroscopy, X-ray diffraction, Fourier-transform infrared spectroscopy, scanning electron microscopy, and transmission electron microscopy (TEM), characterize the synthesised nanoparticles. Determine the size, shape, crystallinity, and other pertinent characteristics of the synthesised nanoparticles by analyzing the data that was acquired [34].

3.6 Evaluation of Nanoparticle Applications:

Examine the possible uses of the synthesised nanoparticles, such as their antibacterial, catalytic, or drug transport capabilities. To assess the performance and effectiveness of the nanoparticles in the target application, carry out particular tests or studies.

3.7 Optimization and Further Studies:

Optimize the synthesis procedure and enhance the properties of the nanoparticles by changing the experimental parameters (such as the concentration of neem extract, reaction temperature, and reaction duration). Make more investigations to comprehend the underlying processes and interactions involved in the neem plant extract-based green synthesis of nanoparticles.

Conclusion

In conclusion, the green synthesis of nanoparticles from the neem plant offers a sustainable and environmentally friendly approach to nanoparticle production. Neem extracts contain biologically active compounds that act as reducing and stabilizing agents, eliminating the need for harmful chemicals. The process is cost-effective, easily scalable, and provides nanoparticles with desirable properties for various applications. Additionally, the use of neem-derived nanoparticles offers the potential for enhanced antimicrobial, anticancer, and agricultural activities, making them valuable in diverse fields. Overall, green synthesis from the neem plant represents a promising avenue for nanoparticle synthesis with numerous benefits for both scientific advancements and ecological sustainability.

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CONFLICT OF INTEREST

There is no conflict of interest among the authors.

REFERENCES

1. Parveen, K., V. Banse, and L. Ledwani, *Green synthesis of nanoparticles: Their advantages and disadvantages*. 2016.
2. Salavati-Niasari, M., Z. Fereshteh, and F. Davar, *Synthesis of oleylamine capped copper nanocrystals via thermal reduction of a new precursor.* Polyhedron, 2009. **28**(1): p. 126-130.
3. Ankamwar, B., M. Chaudhary, and M. Sastry, *Gold Nanotriangles Biologically Synthesized using Tamarind Leaf Extract and Potential Application in Vapor Sensing.* Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry, 2007. **35**(1): p. 19-26.
4. Mohanaparameswari, S., M. Balachandramohan, and P. Murugeshwari, *Bio Synthesis and Characterization of Silver Nanoparticles by Leaf Extracts of Moringa Oleifere Leaf, Azardica Indica (Neem) Leaf, Bamboo Leaf, and their Antibacterial Activity.* Materials Today: Proceedings, 2019. **18**: p. 1783-1791.
5. Velusamy, P., et al., *Greener approach for synthesis of antibacterial silver nanoparticles using aqueous solution of neem gum (Azadirachta indica L.).* Industrial Crops and Products, 2015. **66**: p. 103-109.
6. Abdalla, N., et al., *Nanobiotechnology for Plants.* Environment, Biodiversity and Soil Security, 2019. **0**(0): p. 0-0.
7. Li, X., et al., *Biosynthesis of Nanoparticles by Microorganisms and Their Applications.* Journal of Nanomaterials, 2011. **2011**: p. 1-16.
8. Roy, N., et al., *Green synthesis of silver nanoparticles: an approach to overcome toxicity.* Environ Toxicol Pharmacol, 2013. **36**(3): p. 807-12.
9. Gargiullo, L., et al., *Gut Microbiota Modulation for Multidrug-Resistant Organism Decolonization: Present and Future Perspectives.* Front Microbiol, 2019. **10**: p. 1704.
10. Zingg, R. and M. Fischer, *The consolidation of nanomedicine.* Wiley Interdiscip Rev Nanomed Nanobiotechnol, 2019. **11**(6): p. e1569.
11. Košević, M., et al., *A continuous process for the ultrasonic spray pyrolysis synthesis of RuO2/TiO2 particles and their application as a coating of activated titanium anode.* Advanced Powder Technology, 2017. **28**(1): p. 43-49.

12. Romero, V., et al., *Degradation of Metoprolol by photo-Fenton: Comparison of different photoreactors performance.* Chemical Engineering Journal, 2016. **283**: p. 639-648.
13. Williams, A.N., G.G. Galbreth, and J. Sanders, *Accurate determination of density, surface tension, and vessel depth using a triple bubbler system.* Journal of Industrial and Engineering Chemistry, 2018. **63**: p. 149-156.
14. Song, J.Y., H.-K. Jang, and B.S. Kim, *Biological synthesis of gold nanoparticles using Magnolia kobus and Diopyros kaki leaf extracts.* Process Biochemistry, 2009. **44**(10): p. 1133-1138.
15. Kusiorowski, R. and B. Psiuk, *Fused magnesia-zirconia co-clinker for fired refractories.* Ceramics International, 2017. **43**(16): p. 14263-14270.
16. Zhang, D., et al., *Mechanically strong and electrically stable polypyrrole paper using high molecular weight sulfonated alkaline lignin as a dispersant and dopant.* J Colloid Interface Sci, 2019. **556**: p. 47-53.
17. Siposova, K., et al., *Dual effect of non-ionic detergent Triton X-100 on insulin amyloid formation.* Colloids Surf B Biointerfaces, 2019. **173**: p. 709-718.
18. Behravan, M., et al., *Facile green synthesis of silver nanoparticles using Berberis vulgaris leaf and root aqueous extract and its antibacterial activity.* Int J Biol Macromol, 2019. **124**: p. 148-154.
19. Sargazi, S., et al., *Application of Green Gold Nanoparticles in Cancer Therapy and Diagnosis.* Nanomaterials (Basel), 2022. **12**(7).
20. Shaha, S.K. and H. Jahed, *Characterization of Nanolayer Intermetallics Formed in Cold Sprayed Al Powder on Mg Substrate.* Materials (Basel), 2019. **12**(8).
21. Lomova, T., *Recent progress in organometallic porphyrin-based molecular materials for optical sensing, light conversion, and magnetic cooling.* Applied Organometallic Chemistry, 2021. **35**(8).
22. Sohail, M.F., et al., *Green synthesis of zinc oxide nanoparticles by Neem extract as multi-facet therapeutic agents.* Journal of Drug Delivery Science and Technology, 2020. **59**.
23. Thirumurugan, A., et al., *Green synthesis of platinum nanoparticles using Azadirachta indica – An eco-friendly approach.* Materials Letters, 2016. **170**: p. 175-178.
24. Nagar, N. and V. Devra, *Green synthesis and characterization of copper nanoparticles using Azadirachta indica leaves.* Materials Chemistry and Physics, 2018. **213**: p. 44-51.

25. Sharma, V.K., R.A. Yngard, and Y. Lin, *Silver nanoparticles: green synthesis and their antimicrobial activities.* Adv Colloid Interface Sci, 2009. **145**(1-2): p. 83-96.

26. Beşer, N., Z.Ç. Mutafçılar, and S. Hasançebi, *Diversity analysis of the rice cultivars (Oryza sativa L.) by utilizing SSRs rice diversity by SSRs.* Journal of Food Processing and Preservation, 2021. **45**(2).

27. Zhang, J., et al., *Microwave induced dielectric heating for the on-demand development of indomethacin amorphous solid dispersion tablets.* Journal of Drug Delivery Science and Technology, 2021. **61**.

28. Plutino, M.R., et al., *1,1'-Bis(diphenylphosphino)ferrocene Platinum(II) Complexes as a Route to Functionalized Multiporphyrin Systems.* Nanomaterials (Basel), 2021. **11**(1).

29. Ceja-Medina, L.I., et al., *Microbiological stability and general sensory acceptance of microfiltered skim milk with agave fructans of a high degree of polymerization added.* Journal of Food Safety, 2020. **40**(5).

30. Xia, T., et al., *Ultrabroad-spectrum, multidrug resistant bacteria-killing, and biocompatible quaternized chitin derivative for infected wound healing.* Mater Sci Eng C Mater Biol Appl, 2021. **126**: p. 112177.

31. Aloufi, A.S., *Assessment of Structural, Optical, and Antibacterial Properties of Green Sn(Fe : Ni)O(2) Nanoparticles Synthesized Using Azadirachta indica Leaf Extract.* Bioinorg Chem Appl, 2023. **2023**: p. 5494592.

32. Asimuddin, M., et al., *Azadirachta indica based biosynthesis of silver nanoparticles and evaluation of their antibacterial and cytotoxic effects.* Journal of King Saud University - Science, 2020. **32**(1): p. 648-656.

33. Saravanan, P., et al., *Biofriendly and competent domestic microwave assisted method for the synthesis of ZnO nanoparticles from the extract of Azadirachta indica leaves.* Materials Today: Proceedings, 2020. **33**: p. 3160-3163.

34. Moorthy, S.K., et al., *Synthesis and Characterization of Mgo Nanoparticles by Neem Leaves through Green Method.* Materials Today: Proceedings, 2015. **2**(9): p. 4360-4368.

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