



Green synthesis: An environmentally friendly technology for nanoparticles synthesis

S A A Shawai^{1*}, A D Shuaibu², U U Zango³, F S Gwarzo⁴

¹ Chemistry Programme, School of Undergraduate Studies, Sa'adatu Rimi University of Education, Kumbotso, Kano State, Nigeria

² Department of Chemistry, Faculty of Science, Aliko Dangote University of Science and Technology, Wudil, Kano State, Nigeria

³ Department of Biology, School of Science Education, Sa'adatu Rimi College of Education, Kumbotso, Kano State, Nigeria

⁴ Department of Biological Sciences, Kano State College of Advanced and Remedial Studies, Kano State, Nigeria

Abstract

This review outlines the properties of nanoparticles which contribute to their appeal in various fields. Properties such as high surface area to volume ratio, quantum size effect, and light-scattering absorption make nanoparticles attractive in the biomedical and technology industries. It discusses the various methods utilized for synthesizing nanoparticles. Plant extracts have been the most common source of green synthesis due to their easy availability and rich biochemical compounds. Furthermore, the review highlights the role of various parameters affecting the green synthesis of nanoparticles, including pH, temperature, concentration, and the substrate used. The paper discussed on the stability of green synthesized nanoparticles which is closely associated with the shape and size of the nanoparticles. The effect of stabilizing agents on the particle size, shape, and stability of nanoparticles is briefly addressed. Finally, the review explained the applications of nanoparticles in various fields such as biomedical engineering, drug delivery, and environmental remediation. The review suggests that more future research is necessary with sustainable materials to ensure the effectiveness and safety of green synthesized nanoparticles.

Keywords: nanoparticles, stability, plant extracts, drug delivery, photochemical, electrochemical

Introduction

Nanotechnology is a fast expanding and diversified field with a wide range of applications in science and technology (Hano and Abbasi, 2021) ^[24]. This field combines fundamental principles from a variety of disciplines, including chemistry, engineering, physics, and biology, to develop novel techniques for regulating and synthesizing NPs (Hano and Abbasi, 2021) ^[24]. These NPs have at least one dimension ranging from 1-100 nm. The synthesis, characterization, and uses of diverse NPs are the focus of nanotechnology (Hano and Abbasi, 2021) ^[24]. Because of their unique physical and chemical characteristics, these NPs have grown in importance in recent years. These features have led to its use in a variety of areas, including biomedical engineering, electronics, catalysis, and environmental remediation. Noble metals, such as Au, Ag, or Pt, are frequently used in the synthesis of NPs by a variety of chemical and physical procedures that are not environmentally friendly (Shah *et al.*, 2020) ^[25].

Physical and chemical approaches have historically been used to synthesize NPs. These technologies, however, have some drawbacks as well including high energy consumption, the use of harmful chemicals, and the formation of hazardous waste (Song and Kim, 2009) ^[26]. Green synthesis methods have been developed in response to the demand for sustainable and environmentally acceptable ways of NPs synthesis. Green synthesis is the utilization of natural sources for producing NPs, such as plant extracts, microbes, and enzymes. This technique is becoming more popular due to its ease of use, low cost, and lack of harmful components (Kumari *et al.*, 2021) ^[27].

The usage of green synthesis processes has grown in popularity as people become more aware of sustainable and eco-friendly technologies. The synthesis of NPs using plant extracts is a recent example of green synthesis that has gained a lot of interest.

Plant extracts contain phytochemicals such flavonoids, alkaloids, and terpenoids that act as reducing and stabilizing agents in the formation of NPs (Iravani *et al.*, 2011) ^[28]. Plant extracts provide significant advantages in NP synthesis, including low cost, convenient availability, and the capacity to synthesize NPs of various forms and sizes. Plant extracts are also known to include a variety of antioxidants, making them extremely useful in the synthesis of NPs with improved biological activity. In recent years, there has been a lot of interest in green synthesis of NPs utilizing plant extracts. Several studies have indicated successful NP production utilizing different plant extracts. Plant extracts such as Aloe vera, Azadirachta indica, and Ocimum sanctum, for example, have been used to synthesis AgNPs (Gogoi *et al.*, 2020) ^[29]. Similarly, plant extracts such as Camellia sinensis, Citrus limon, and Punica granatum have been used to synthesis AuNPs (Gurunathan *et al.*, 2013) ^[30]. The use of plant extracts in the green synthesis of NPs has various advantages over traditional approaches. For example, green synthesis procedures are non-hazardous and do not pollute the environment. In addition, plant extracts are widely available and can be extracted from a variety of sources, including leaves, stems, and roots. Furthermore, green synthesis technologies are easy to use and inexpensive, making them ideal for large-scale NP synthesis.

Properties of plant-based NPs

NPs derived from plant extracts have been extensively studied for their unique physicochemical properties and their potential applications in various fields. This review highlights different properties of plant-based NPs and their current applications. For example, NPs have been reported to exhibit antimicrobial activity against various microorganisms, including bacteria and fungi. AgNPs synthesized using leaf extract of *Allium sativum* showed significant antibacterial activity against *Escherichia coli* and *Staphylococcus aureus* (Hassan *et al.*, 2020) [31]. In addition, NPs have been shown to exhibit anti-inflammatory activity, making them suitable for various applications in medicine. Curcumin-loaded chitosan nanoparticles synthesized using turmeric extract showed anti-inflammatory activity *in vitro* (Shinde *et al.*, 2020) [32]. Several studies have reported the antimicrobial activity of plant-based nanoparticles, making them suitable for use in food packaging and preservation. For example, AgNPs synthesized from plant extracts have been shown to have significant antimicrobial activity against various pathogens (Rai *et al.*, 2015) [33]. NPs on the other hand possess excellent antioxidant activities due to their high polyphenol content. For example, green tea extract nanoparticles have been shown to protect cells against oxidative stress (Yuan *et al.*, 2018) [34].

NPs exhibit unique optical properties such as plasmonic resonance and fluorescence, which make them useful in various applications such as biosensing and imaging. For instance, AuNPs synthesized using leaf extract of *Justicia adhatoda* showed strong plasmonic resonance at 550 nm, making them suitable for surface-enhanced Raman scattering (SERS) (Renuka *et al.*, 2019) [35]. In another study, Sharma *et al.* (2019) [36] reported that AuNPs have been used in diagnostic imaging due to their strong light absorption and scattering properties. Magnetic NPs have attracted significant attention due to their potential applications in magnetic resonance imaging (MRI), drug delivery, and hyperthermia. Plant-based NPs such as iron oxide nanoparticles synthesized using plant extracts have shown magnetic properties, making them suitable for biomedical applications (Dutta *et al.*, 2020) [37].

NPs are generally considered safe and biocompatible due to their natural origin. Plant-based nanoparticles exhibit excellent biocompatibility, making them suitable for use in biomedical applications such as drug delivery and tissue engineering (Kesharwani *et al.*, 2019) [38]. They are less toxic than synthetic NPs and have shown low cytotoxicity *in vitro* as well as *in vivo* studies (El-Gazzar, 2019) [39]. For example, the green synthesis of gold nanoparticles (AuNPs) using plant extracts has shown high biocompatibility, making them suitable for biomedical applications (Shukla *et al.*, 2018) [40]. Similarly, poly(lactic-co-glycolic acid) (PLGA) nanoparticles have been used for the delivery of various drugs, such as paclitaxel for the treatment of cancer (Kesharwani *et al.*, 2019) [38].

Plant-based nanoparticles are known for their high stability, making them an ideal choice for use in various applications (Bose *et al.*, 2017) [41]. The stability of NPs is essential for their storage, transport, and applications. Plant-based NPs are generally more stable than synthetic NPs due to the presence of biomolecules on their surface, which act as stabilizing agents (Gopi *et al.*, 2018) [42]. For example, iron oxide nanoparticles synthesized using ginger extract showed high stability due to the presence of biomolecules such as

proteins, amino acids, and carbohydrates (Gopi *et al.*, 2018) [42]. AuNPs synthesized from plant extracts have been shown to be stable in different environments and show good biocompatibility (Bose *et al.*, 2017) [41].

The size and shape of NPs play a crucial role in their properties and applications. NPs from plant extracts are easier to control in terms of size and shape due to their unique synthesis methods (Sureshkumar *et al.*, 2019) [43]. NPs have been shown to exhibit a wide range of sizes and shapes, from spherical to rod-shaped, depending on the plant extract used for their synthesis (Latha and Selvamani, 2019) [44]. Iron oxide NPs from plant extracts have been synthesized of different sizes and shapes for various applications (Sureshkumar *et al.*, 2019) [43]. For example, silver nanoparticles (AgNPs) synthesized using leaf extract of *Terminalia chebula* showed a spherical shape with an average size of 50 nm (Chauhan *et al.*, 2019) [45].

The large surface area of NPs is advantageous in various applications such as drug delivery, catalysis, and sensing. Plant-based NPs have a higher surface area per unit mass than their synthetic counterparts, making them more efficient in their applications (Duc *et al.*, 2021) [46]. For instance, dendrimer-like copper nanoparticles synthesized using leaf extract of *Azadirachta indica* showed a high surface area of 23.8 m²/g (Kalyani *et al.*, 2019) [47]. With regard to surface charge, NPs play an important role in their interaction with biomolecules and cells. Plant-based NPs can be easily modified to have a specific surface charge by using different types of plant extracts or by coating them with different polymers (Chitra *et al.*, 2018) [48]. For example, cationic chitosan-coated gold nanoparticles synthesized using cinnamon extract showed a positive surface charge, making them suitable for gene delivery (Chitra *et al.*, 2018) [48].

NPs possess biodegradable properties that make them ideal for use in various biomedical applications (Dutta *et al.*, 2014) [49]. They can be easily broken down by biological systems, making them non-toxic and environmentally friendly. For example, chitosan nanoparticles have been used in drug delivery and show no signs of toxicity or accumulation in tissues (Dutta *et al.*, 2014) [49]. NPs are considered safe and have low toxicity in comparison to their synthetic counterparts (Raza *et al.*, 2020) [50]. For example, curcumin nanoparticles synthesized from plant extracts have been shown to have no toxicity and possess significant anti-inflammatory properties (Raza *et al.*, 2020) [50]. NPs derived from plant extracts are considered environmentally safe due to their biodegradability and non-toxicity. They can be easily synthesized using green chemistry approaches, which are eco-friendly and sustainable. For instance, ZnONPs synthesized using neem leaf aqueous extract showed no toxicity to aquatic organisms (Singh *et al.*, 2019) [51]. NPs offer a cost-effective alternative to synthetic NPs, which are expensive to produce. For example, cellulose NPs synthesized from plant extracts have been used in various biomedical applications and offer a low-cost alternative to synthetic NPs (Azizi *et al.*, 2019) [52].

Factors affecting synthesis of NPs

Several factors influence NPs synthesis, including plant material selection, extraction method, processing conditions, pH, temperature, concentration, and time. This article explored ten various parameters that influence the synthesis of NPs. The qualities of the NPs are determined by the plant

material used. Plant elements such as leaves, roots, fruits, and seeds can all be employed. Furthermore, the plant material should be chosen for its abundance, non-toxicity, and ease of access. Hajipour *et al.* (2012) ^[14] generated AgNPs from several plant extracts and demonstrated that different plant materials contain distinct reduction agents, resulting in NPs of variable sizes and shapes. The extraction procedure is critical in establishing the properties of the NPs, which include size, shape, and stability. Various extraction procedures, such as ultrasound-assisted extraction, maceration, and Soxhlet extraction, can be utilized. Because it is simple, effective, and safe for the environment, ultrasound-assisted extraction is the most widely used approach. The production of ZnONPs using diverse plant extracts, for example, revealed that the extraction method influenced particle size and shape (Gauci *et al.*, 2017) ^[15]. Temperature, pH, and time were discovered to have an effect on the efficiency and characteristics of NPs in this research. In order to optimize the synthesis process, the suitable processing conditions must be set. As a result, Al-Sheddi *et al.*, (2016) ^[16] produced AuNPs from guava leaves and demonstrated how temperature, pH, and time affected the size and stability of the NPs.

Reduction is an important step in the production of plant-based NPs. Plant extracts contain a variety of reducing agents, such as flavonoids, phenolic compounds, and proteins, which reduce metal ions to create NPs. The concentration and type of reducing agents determine the size and form of the NPs. The production of AuNPs using various plant extracts, for example, revealed that different reducing agents generated NPs of variable sizes and shapes (Mittal *et al.*, 2014) ^[17]. Stabilizing agents, on the other hand, serve an important role in preventing NP aggregation and oxidation, resulting in improved stability. Surfactants, polymers, and proteins are common stabilizing agents employed in the extraction and processing of plant-based NPs. For example, in the production of AgNPs applying nontoxic elicitors, Singh *et al.* (2016) ^[18] discovered that a combination of extracts and proteins served as efficient stabilizing agents. The concentration of metal ions influences the NPs' synthesis efficiency and shape. High metal ion concentrations can cause aggregation and unstable NPs, whilst low concentrations can result in low yields and smaller NPs. The synthesis of AgNPs use of ginger extract, for example, revealed that low concentrations of silver ions paired with the extract produced smaller and more stable NPs (Choi *et al.*, 2011) ^[19].

The pH of the reaction media influences the properties of the NPs, such as size, shape, and stability. Maintaining an optimal pH ensures effective reduction and improves the stability of the NPs. For example, the production of AgNPs using plant extracts revealed that pH affects the size and stability of the NPs (Ovais *et al.*, 2018) ^[20]. The rate of reaction is critical in influencing the size and shape of the NPs. The reaction time should be tuned to maximize NP yield while preventing aggregation. Silver nanoparticles were synthesized using *Nelumbo nucifera* extract, and the reaction duration influenced the size, shape, and stability of the NPs (Koduru *et al.*, 2016) ^[21]. Furthermore, agitation rate is important in encouraging mixing and lowering the reaction time required to produce NPs. To ensure maximal yield and size, the optimal agitation rate should be determined. The synthesis of diverse plant extracts, for example, revealed that the agitation rate affected particle

size and yield (Gopinath *et al.*, 2015) ^[22]. The solvent utilized in the synthesis process influences the composition of the plant extract as well as the morphology, size, and stability of the NPs. To optimize the properties of the NPs, the solvent should be carefully selected. The production of CuNPs using diverse plant extracts, for example, revealed that the solvent had an effect on the NPs' size, shape, and stability (Chaloupka *et al.*, 2010) ^[23].

Application of NPs in various field

NPs have attracted significant attention due to their biodegradable, non-toxic, eco-friendly, and cost-effective nature. They have been extensively studied for their biological applications in drug delivery, diagnosis, and imaging. Besides, they can also be used in environmental remediation, renewable energy, food packaging, and crop production. This review will provide an in-depth understanding of the application of plant-based NPs in various fields.

Plant-based nanoparticles for drug delivery

Drug delivery is the method of transporting a therapeutic agent to its site of action in a controlled manner. The use of plant extracts nanoparticles as drug delivery agents has gained interest in recent years due to their low toxicity, biocompatibility and biodegradability. Plant extracts nanoparticles have been used for the delivery of various drugs including anticancer, antimicrobial, anti-inflammatory and antioxidant agents.

For instance, flavonoids are polyphenolic compounds that are commonly found in plant-based NPs. They possess antioxidant, anti-inflammatory, and anticancer properties. Flavonoid-based NPs have been shown to have excellent potential as drug delivery systems for poorly soluble drugs (Soni *et al.*, 2019) ^[1]. Similarly, quercetin is another important polyphenol that has been found to have anti-cancer, antioxidant and anti-inflammatory properties. However, its poor water solubility hinders its bioavailability. Plant extracts NPs of quercetin have been synthesized using various plant extracts such as *Camellia sinensis*, *Ginkgo biloba*, and *Eucommia ulmoides*. These NPs have been found to enhance the solubility and bioavailability of quercetin and have been shown to possess significant anticancer and anti-inflammatory properties (Cai *et al.*, 2017) ^[2]. Quercetin and chrysin nanoparticles were used to deliver the antineoplastic drug, doxorubicin, with improved efficacy and reduced toxicity in breast cancer cells (Soni *et al.*, 2019) ^[1].

Curcumin is a natural polyphenol that has been found to have anti-inflammatory, anti-cancer and antioxidant properties. However, its low bioavailability hinders its clinical use. Plant extracts nanoparticles of curcumin have been synthesized using various plant extracts such as *Piper longum*, *Aloe vera* and *ginger*. These nanoparticles have shown enhanced bioavailability and have been found to be effective in suppressing cancer cell growth (Sahu *et al.*, 2011) ^[5]. In the other hand, dendrimers are highly branched, spherical, and monodisperse NPs and possess unique properties such as high surface area, multiple functional groups, and excellent biocompatibility. Dendrimer-based nanocarriers have been shown to improve drug solubility, bioavailability, and targeted delivery (Hegazy *et al.*, 2017) ^[6]. Anticancer drugs such as paclitaxel, doxorubicin, and methotrexate were encapsulated in dendrimer-based

nanoparticles derived from various plants such as *Terminalia chebula*, *Tamarindus indica*, and *Prosopis juliflora* (Hegazy *et al.*, 2017) ^[6].

Plant extracts NPs have also been used for the delivery of antimicrobial agents. AgNPs are widely used as antimicrobial agents due to their broad-spectrum activity against bacteria, viruses and fungi. However, the use of AgNPs in large doses is associated with toxicity to human cells. Plant extracts NPs of silver have been synthesized using various plant extracts such as *Zingiber officinale* and *Ocimum basilicum*. These NPs have been found to possess strong antimicrobial activity against drug-resistant bacteria and have been considered as good candidates for the treatment of bacterial infections (Sharma *et al.*, 2017).

Plant extracts nanoparticles as diagnostic tools

In diagnostic medicine, nanoparticles have been used for imaging and sensing applications. Plant extracts NPs have been used as contrast agents in various imaging modalities such as magnetic resonance imaging, computed tomography and fluorescence imaging. They have also been used as biosensors for the detection of various biomolecules such as proteins, DNA and RNA. The most commonly used plant-based nanoparticles for imaging and diagnosis are AuNPs, magnetic nanoparticles, quantum dots, and CNPs.

AuNPs are widely used in various biomedical applications due to their unique optical and electronic properties. AuNPs derivatized with plant-based polyphenols have been shown to be useful for cancer cell imaging due to their high biocompatibility and specific targeting capability. Catechin-modified gold nanoparticles were used as a contrast agent for computed tomography (CT) imaging of breast cancer cells (Liu *et al.*, 2018) ^[7]. AuNPs from plant extracts have been synthesized using *Aloe vera*, *Camellia sinensis* and *Thuja orientalis*. These NPs have been found to possess good sensitivity and specificity and have been used as biosensors for the detection of various biomolecules such as glucose, DNA and proteins (Yadav *et al.*, 2019).

Magnetic NPs are widely used as contrast agents in magnetic resonance imaging (MRI) due to their excellent magnetic properties. Plant extracts nanoparticles of iron oxide have been synthesized using various plant extracts such as *Eucalyptus globulus*, *Z. officinale* and *Cinnamomum zeylanicum* (Vazquez-Vazquez *et al.*, 2018). Similarly, Bordbar *et al.*, (2018) ^[8] reported that Fe₃O₄ nanoparticles derived from *Carum copticum* seeds have been shown to be useful in MRI-based cancer detection and diagnosis. These nanoparticles have been found to possess good magnetic properties and have been used for the imaging of various cell types (Vazquez-Vazquez *et al.*, 2018). In the case of quantum dots, they are nanocrystals possess unique optical properties such as size-dependent fluorescence emission that have been extensively studied as fluorescence-based imaging agents for cancer detection and diagnosis. CdTe quantum dots derived from *Allium sativum* have shown potential as a targeted imaging agent for breast cancer cells (Kianvash *et al.*, 2017) ^[9]. CNPs have recently gained attention as imaging agents due to their unique properties such as high stability, low toxicity, and biocompatibility. CNPs derived from *Citrullus lanatus* fruit extract have been shown to be useful as a fluorescence-based imaging agent for prostate cancer cells (Naghibi *et al.*, 2018) ^[10].

Plant-based NPs for environmental remediation

Plant-based nanoparticles have also been studied for their potential use in environmental remediation. Environmental remediation involves the removal of pollutants and contaminants from environmental systems. The most commonly used plant-based nanoparticles for environmental remediation are silver nanoparticles, titanium dioxide nanoparticles, and iron oxide nanoparticles. For example, AgNPs possess unique antibacterial properties due to their high surface area and specific functional groups. AgNPs derived from various plants such as *O. sanctum*, *A. indica*, and *Curcuma longa* have shown excellent potential as antibacterial agents for the removal of bacterial contaminants in water (Srivastava *et al.*, 2019) ^[11]. Titanium dioxide NPs possess unique photocatalytic properties due to their ability to absorb visible and ultraviolet light. They have been used for the removal of various organic and inorganic contaminants in water and soil. Titanium dioxide NPs derived from *Murraya koenigii* leaves were found to be highly effective in the removal of textile dye pollutants from wastewater (Khandel *et al.*, 2018) ^[12]. In addition, Iron oxide NPs possess excellent magnetic properties that make them suitable for the removal of heavy metal contaminants. Iron oxide NPs derived from various plants such as *Aegle marmelos* and *Helianthus annuus* were found to be effective in the removal of arsenic and lead from contaminated water (Patil *et al.*, 2019) ^[13].

Conclusion

In conclusion, the synthesis of NPs using plant extracts is a promising approach that has gained significant attention in recent years. The use of plant extracts in the synthesis of NPs has advantages such as cost-effectiveness, non-toxicity, eco-friendliness, and ease of preparation. This environmentally friendly technology for NPs synthesis is expected to develop exponentially in the future; nevertheless, long-term impacts on animals and people, as well as the accumulation of these NPs in the environment and their influence, must be addressed in the future.

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