



Factors Influencing the Green Synthesis of Metallic Nanoparticles Using Plant Extracts: A Comprehensive Review

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Abstract

Methods for nanoparticle (NP) synthesis of the past were costly, generating toxic compounds, which necessitates a reduction in toxic contamination associated with chemical and physical syntheses. Green nano synthesis using plant extracts has emerged as a sustainable alternative in nanotechnology with applications in various fields. Factors such as pH, extract and salt concentrations, temperature, solvent, biomolecules in plants, and reaction time significantly influence the quality and quantity of metallic NPs synthesized via green nanotechnology. This review highlights crucial factors affecting the size and shape of metallic NPs as the overall properties of the NPs are size- and shape-dependent. Current and future research in green nano synthesis holds promise for expanding our understanding of the parameters that control the synthesis, size, and shape of NPs. Further investigation is necessary to comprehend the impact of these parameters on the synthesis of metallic NPs using plant extracts, which is considered the most sustainable approach for large-scale production.

Keywords

- ▶ green synthesis
- ▶ green nano synthesis
- ▶ metallic nanoparticles
- ▶ plant extracts
- ▶ impact factors

Introduction

Nanotechnology and nano-engineering have emerged as transformative fields of scientific development. The pressing issues of climate change, global warming, and environmental disasters necessitate immediate attention to sustainability in energy and the environment. Just as water, food, and shelter are basic human needs, the pillars of scientific development in today's global landscape encompass environmental preservation, energy resources, and socio-economic sustainabil-

ity. Green chemistry, green engineering, and green nanotechnology have become imperative for human civilization.¹ The advances in nanotechnology have increased drastically in the past decade. Numerous studies have confirmed the advantage of metallic nanoparticles (NPs) in medicine. Recently, approaches are gaining interest for metallic NPs via green synthesis.² Nanomaterials have gained enormous popularity due to their distinctive properties. Consequently, the development of advanced technologies for synthesizing nanomaterials has become crucial. The synthesis pathways of nanomaterials require the use of reagents and solvents, making it imperative to address the

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environmental and biological hazards associated with their toxicity.³

Currently, researchers are increasingly focusing on green alternatives. The rationale behind choosing these alternatives stems from the significant socio-economical changes experienced by humanity in recent years, which have disrupted organic and natural living patterns and resulted in a substantial increase in industrial production and the release of toxic substances into the environment. These harmful pollutants have caused disruptions in ecosystems, leading to irreversible impacts on the planet. Green chemistry emerges as a design philosophy for sustainable process development, emphasizing the use of environmentally friendly and nontoxic technologies for the benefit of the environment and living organisms.⁴ Green synthesis is dedicated to the synthesis of NPs using environmentally friendly techniques. Common green chemistry approaches are presented in ►Fig. 1. These approaches involve the use of green solvents and reagents, as well as low-energy synthesis methods utilizing natural products.⁵ Green synthesis methods rely on green routes for NP production, yielding nanomaterials possessing commercial benefits such as reduced energy and production costs compared with conventional routes. The plant extracts used in green synthesis contain phytochemicals and biomolecules that serve as natural reducing and stabilizing agents. This has led to increased interest in using plant-based extracts for the green synthesis of metallic NPs and metal-based hybrid NPs.⁶

The utilization of plant extracts for the green synthesis of NPs offers a simple, environmentally friendly, and nontoxic alternative to chemical and physical methods of synthesis. Optimization of the reaction conditions is necessary to

obtain NPs with controlled sizes and shapes via plant extracts. To publish comprehensive and significant findings, thorough investigations of various factors influencing metallic NP synthesis using plant extracts are required. Here, this review aims to elucidate and highlight the critical impact factors affecting the synthesis of metallic NPs via green nanotechnology and to provide a better understanding of NP synthesis with controlled sizes and shapes.

Green Chemistry and Green Nano Synthesis

The concept of green chemistry for sustainable development has been proposed for a couple of years. Green nano synthesis refers to an approach to minimize the adverse environmental effects due to toxic chemicals and to reduce the risk of contamination. Green approaches are economically friendly and simple.⁷ The primary conditions to synthesize green NPs include the use of green solvents. Often, the synthesis of NPs can be achieved via various routes, and the most commonly used routes include physical, chemical, or biosynthetic pathways. However, the chemical synthesis of NPs involves the use of toxic chemicals and solvents that are less environmentally friendly.⁸

As an alternative, green nano synthesis refers to the development of protocols and standard operating procedures for the synthesis of environmentally benign nanomaterials. The primary goal is to minimize the toxicity associated with NP synthesis. Green nanoproducts are synthesized by adhering to the principles of green chemistry which directly or indirectly contribute to environmental preservation.⁹ Green chemistry encourages application of green principles in the synthesis of nanomaterials.¹⁰ In green

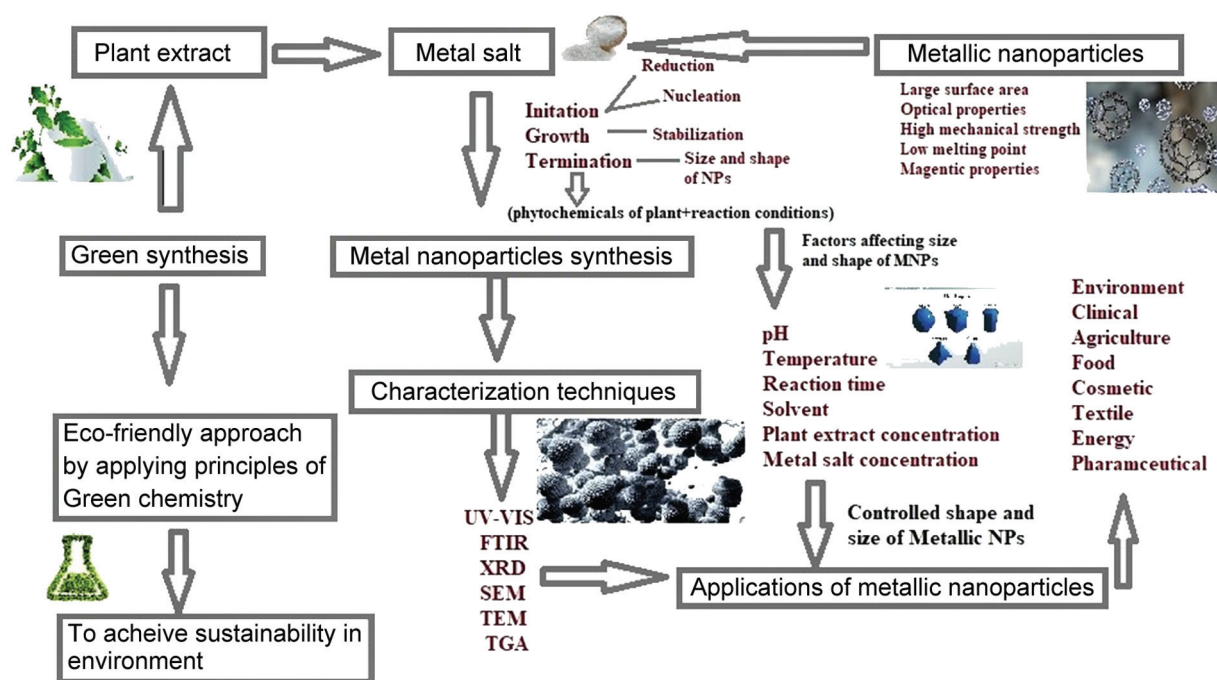


Fig. 1 Green synthesis of metallic NPs using plant extracts including initiation, growth, and termination phases. The size of synthesized metallic NPs depends on various factors. Different characterization techniques and applications of metallic NPs are presented. NPs, nanoparticles.

nano synthesis, emphasis is placed on synthesizing nanomaterials using nontoxic compounds under mild conditions, thereby enhancing environmental sustainability. Green nano synthesis offers advantages such as eco-friendliness, simplicity, and energy efficiency. Consequently, green synthesis approaches contribute to the sustainable and environmentally friendly production of nanomaterials.¹¹

Phyto-green Synthesis of Metallic NPs

Photo-green synthesis utilizes plants for the synthesis of NPs. Green nano synthesis has gained attention due to its use of medicinal plants, which are readily available and contain a wide range of phytochemicals essential for NP synthesis.¹² Various parts of plants including fruit, leaves, bark, stem, and root have been used for NP green synthesis due to their high phytochemical contents. The synthesis process involves washing and boiling the selected plant part, followed by extraction, filtration, and the addition of a metal salt solution. The formation of yellow color indicates the NP formation through the bio-reduction of metal ions present in the solution. Plant extracts rich in phytochemicals selectively reduce metal ions, acting as reducing and capping agents, facilitating eco-friendly NP synthesis.^{8,13}

Crude plant extracts obtained from green synthesis contain enriched secondary metabolites or phytochemicals such as phenolics, flavonoids, terpenoids, and alkaloids, playing a vital role in the reduction of metal ions and stabilization of NPs. Plant extracts comprise various phytochemicals, including phenolics, flavonoids, alkaloids, terpenes, amino acids, polysaccharides, sugars, and organic acids, e.g., ascorbic acid, oxalic acid, malic acid, and tartaric acid. These phytochemicals are involved in the reduction of metal ions and contribute to the stabilization of NPs. Flavonoids, in particular, are frequently reported for their role in the green synthesis of silver NPs using plant extracts.¹⁴ The diverse range of phytoconstituents present in plant extracts act as reducing, capping, and stabilizing agents, eliminating the need for external agents in the green approach of NP synthesis.¹⁵ In the green synthesis of silver NPs, compounds found in plant extracts interact with silver nitrate causing its reduction into silver metal. When silver nitrate dissolves in water, it dissociates into ions, the hydroxyl and carboxyl groups of phytoconstituents with their acidic nature, release H⁺ ions and acquire a negative charge.

Plant extracts contain functional groups, such as phenols and acids, that interact with silver ions, resulting in their reduction. Nitric acid, formed through the capture of H⁺ from plant extract compounds, remains in the aqueous phase while silver is converted to the metallic state, forming silver NPs.¹⁶ The concentration and composition of plant extracts significantly affect NP synthesis. Amino acids present in plants also contribute to silver NP production. The pH of the medium can impact the production rate of silver NPs by altering the total charge of amino acids in the solution.¹⁷

The process for NP synthesis consists of four stages, the reduction of metal ions, clustering or nucleation, growth of the nuclei through an Ostwald ripening process, and stabilization. Polyphenols, flavonoids, tannins, ascorbic acids, and

sugars in plant extracts can reduce metal ions. Plant extracts then act as stabilizing agents, while biomolecules are responsible for the formation of NPs. In the formation of metal NPs, flavonoids containing hydroxyl groups reduce metal ions through enol-to-keto tautomerization to release the reactive hydrogen atom.⁶ After the metallic salts dissolve, the formation of hydroxyl complexes occurs, and subsequent crystallite development of metals with oxygen species begins. This results in the formation of crystalline planes with different energy levels. The reaction system gains energy through heat, and the process continues until the capping agent derived from plant extracts is activated. The capping agent then inhibits the growth of high-energy atomic planes, leading to the synthesis of specific NPs.

The reducing agents give electrons to the metal ions, turning them into NPs, which are now in a condition of high surface energy and have a tendency to collide and transition into a state of low surface energy. To avoid NP aggregation, high concentrations of reducing and stabilizing agents are used. Proteins may also transform metal ions that they come into contact with into their corresponding nuclei, which then assemble into NPs. Amino groups in proteins, hydroxyl groups in polyphenols, hydroxyl groups in polysaccharides, and carboxyl groups in organic acids facilitate the formation of metallic NPs, which inhibit the production of reactive oxygen species.¹⁸

A well-organized study revealed the phytochemical framework and the process of *H. perforatum* L. extract-mediated synthesis of silver NPs. Phenolic acids and flavonoids in the extracts reduce silver ions, whereas xanthenes, phloroglucinols, and naphthodianthrones help cap them. The size of the particles can be controlled by adjusting the concentration of these substances at which the NPs are stabilized. Thus, a significant barrier to the green synthesis of NPs was removed by controlling the size and by altering the ratio between the reducing and capping agents.¹⁸ Literature further showed that silver NPs of small sizes were synthesized by utilizing a high concentration of plant extracts.¹⁹

Moringa oleifera flower extracts were used for green synthesis and characterization of silver NPs. The Fourier-transform infrared spectroscopy (FTIR) spectrum shows stretching vibrations from 1,397 to 1,653 cm⁻¹ indicating functional groups -C=C- and -C-O in the proteins that stabilize the silver NPs.²⁰ The study emphasizes the importance of plant-based phytochemicals or secondary metabolites in the stabilization of metallic NPs produced from bark extracts and in the reduction of metal ions. As reducing and capping agents, the phytochemicals in the bark extracts stabilize and mitigate the aggregation of NPs. An extract of the stem bark from *Terminalia arjuna* wight revealed the presence of phytoconstituents such as phenolics, flavonoids, terpenoids, and reducing sugars. The presence of both reducing sugars and phenolic components increases the reducing capacity of plant extracts. The rapid production of silver NPs and gold NPs took place in a mixed solution containing pure glucose, fructose, gallic and ellagic acids, and isorhamnetin.²¹ Flavonoids have several functional groups that can generate NPs. The metal ion reduction that results in the formation of NPs occurs when

flavonoids undergo tautomeric conversion from enol to the keto form. *Ocimum basilicum* extracts accomplish the conversion of flavonoids such as luteolin and rosmarinic acid. Silver NPs with enol-to-keto transformation are the main driving force of NP synthesis from silver ions.²²

FTIR spectrum revealed that biomolecules containing carbonyl and hydroxyl groups were present in the synthesis of green palladium NPs from *Solanum nigrum* leaf extracts. The decrease of palladium ions may be caused by *S. nigrum* constituents kaempferol, luteolin, and gentisic acid. Phytochemicals failed to cap the palladium NPs, which were spherical with small sizes.²³ Ismail revealed that the method resulted in copper NPs with a size range of 7 to 10 nm, and the capping procedure utilized the hydroxyl and carbonyl groups from the fruit of the *Rhus coriaria*. This structure has been shown particularly in glucosides of anthocyanins and flavanols detected by FTIR.²⁴ Additionally, during a plant-mediated synthesis, several polyphenols contributed to the reduction of gold NPs. Polyphenolic substances including ascorbic, gallic, and caffeic acids are present in *Sansevieria roxburghiana* leaf extracts. Following the reduction of the gold ions, high-performance liquid chromatography analysis revealed that the amount of ascorbic and gallic acids dramatically dropped, and the caffeic acid was consumed to a great extent. Transmission electron microscopy (TEM) showed the morphology of the generated gold NPs with near-spherical shapes.²⁵ ►Table 1 summarizes the impact of phytochemicals (secondary metabolites) on the green synthesis of metallic NPs. Das et al confirmed that the hydroxyl groups of polyphenols in green tea were involved in the reduction of silver ions.²⁶ Overall, the phytochemicals are important in the reduction and stabilization of metallic NPs acting as a capping agent. The structure of important phytochemicals is presented in ►Fig. 2.

Metallic NPs

Metals such as gold, copper, silver, platinum, iron, and palladium are of great interest due to their competence in the synthesis of metallic NPs. Their optoelectronic and

dimensional characteristics are noted to be greater as compared with metal precursors used in synthesis. Their specific properties are an increased surface-to-volume ratio, high reactivity, efficiency, and surface modifications which enable their use in diverse areas.²⁷

Metallic NPs usually have large surface areas, and it is important to understand the thermodynamics of NPs. The increase in the surface-to-volume ratio causes an increase in the dominance of the atoms on the surface of NPs as compared with their interior part. Consequently, this causes an increase in the overall surface energy of metallic NPs. The surface energy of NPs can be calculated by using various thermodynamic approaches. More reactive sites are produced due to high surface area of metallic NPs, which makes them ideal for various clinical applications such as drug delivery.²⁸ Metallic NPs are nano-sized particles in the size range of 1 to 100 nm. The physicochemical properties of metallic NPs depend on their shape, size, composition, and crystallinity. The optical properties of metallic NPs such as silver and gold are size-dependent and vary significantly. Metallic NPs including gold, silver, palladium, and platinum, along with their different combinations have gained vast popularity (►Fig. 3). This is due to their unique properties such as high ionization energy, reduction potential, non-reactivity, high melting point, resistance to corrosion, and oxidation properties. Nobel metal nanomaterials are extensively used in drug delivery, environmental sensing tools, antimicrobials, water purification, and catalysis.²⁹ Scientists are currently focusing on modifications of metal nanomaterials to increase their stability and safety. The doped metals and metal oxide NPs have been used in the biomedical and clinical fields with excellent results.

Metal-based sulfides also called chalcogenides emerge as a semiconductor due to their properties such as high fluorescence, suitable optical band gap, and exceptional magnetic, thermal, mechanical, and structural stability. As a result, they are extensively used in biosensing, drug delivery, bio-labeling, bioimaging, and diagnostics. Currently, metallic sulfides are gaining increasing attention in the biomedical field. Commonly used metal sulfides include AgS, CuS, FeS,

Table 1 Effect of phytochemicals and their functional groups on metallic NP synthesis

Sr. No.	Plant extract	NPs	Phytochemicals	Functional group	Structure	Ref.
1.	<i>H. perforatum L</i>	Ag	Flavonoids, phenolic acids	-OH	►Fig. 2A	19
2.	<i>Moringa oleifera</i>	Ag	Proteins	-NH ₂	-	20
3.	<i>Terminalia arjuna</i>	Ag, Au	Phenolic acids, reducing sugars	-COOH -OH	►Fig. 2A ►Fig. 2D	21
4.	<i>Ocimum basilicum</i>	Ag	Flavonoids	-OH	►Fig. 2A	22
5.	<i>Solanum nigrum</i>	Pd	Luteolin	-OH	►Fig. 2C	23
6.	<i>Rhus coriaria</i>	Cu	Flavonoids	-OH	►Fig. 2A	24
7.	<i>Sansevieria roxburghiana</i>	Au	Phenolic acids, polyphenols	-OH	►Fig. 2B	25
8.	Green tea	Ag	Phenolics	-OH	►Fig. 2C	26

Abbreviation: NP, nanoparticle.

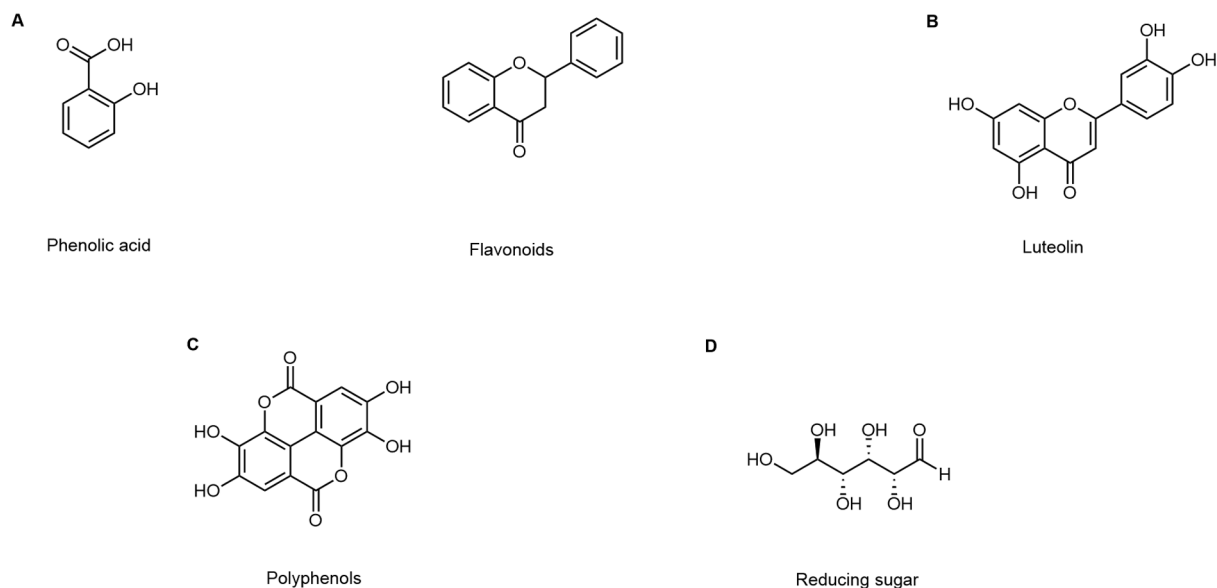


Fig. 2 Chemical structure of (A) phenolics: these phytochemicals include phenolic acids and flavonoids which play important roles in the reduction, stabilization, and capping of metallic NPs; (B) luteolin: this secondary metabolite is a type of flavonoid responsible for reduction of metallic NPs; (C) polyphenols: these phytochemicals belong to phenols responsible for reduction, stabilization, and capping of metallic NPs; (D) reducing sugars: monosaccharides, which play important role in the reduction of metallic NPs. NPs, nanoparticles.

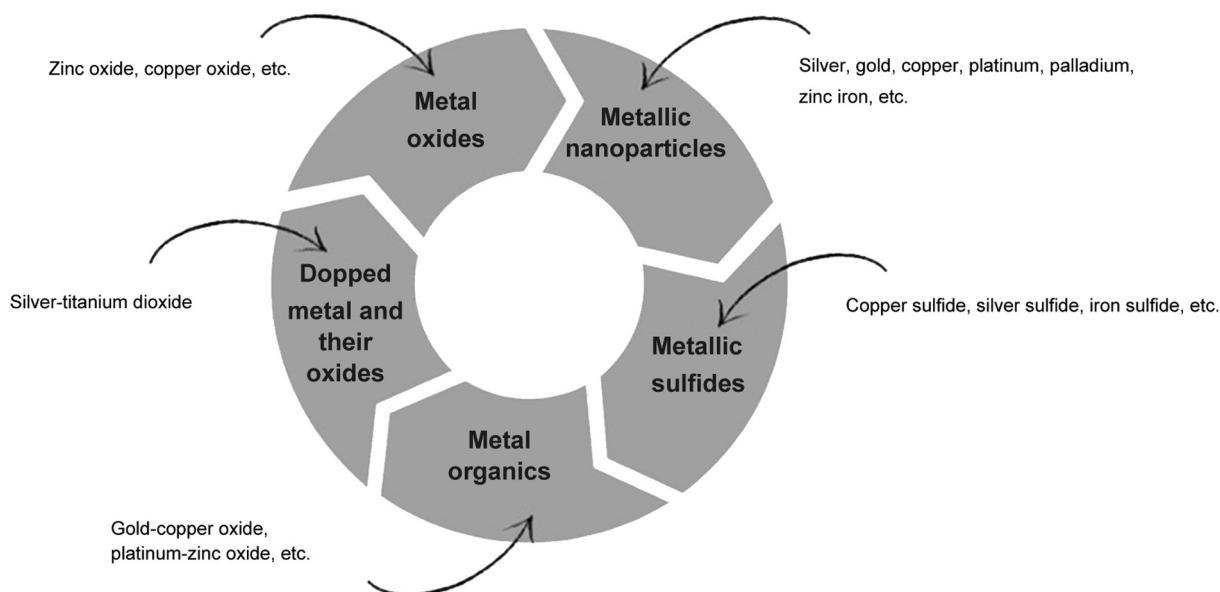


Fig. 3 Metallic NPs: their oxides and sulfides, dopped metals and their oxides, metal organics. All these types are synthesized using plant extracts. NPs, nanoparticles.

and ZnS, which have been used in biomedical applications. Metal oxide nanomaterials such as Ag_2O , FeO , MnO_2 , CuO , ZnO , MgO , and TiO_2 have demonstrated antibacterial activity.³⁰

Advantage of the Green Method Over Physical Chemical and Microbial Methods

The most commonly used methods for the synthesis of NPs are top-down or bottom-up approaches as presented in ► Fig. 4.

The green synthesis method is the best approach for the synthesis of NPs due to its simplicity, nontoxicity, and cost-effectiveness. The use of hazardous and extremely toxic chemicals in chemical and physical synthesis makes them unfavorable for the environment. Moreover, the reducing and capping agents used in the synthesis of NPs are expensive. Thus, green synthesis is preferred over chemical and physical methods.^{31,32}

Depending on plant-type biomolecules and the concentration of plant extracts, it takes less time to complete the synthesis of NPs. On the other hand, a considerable time

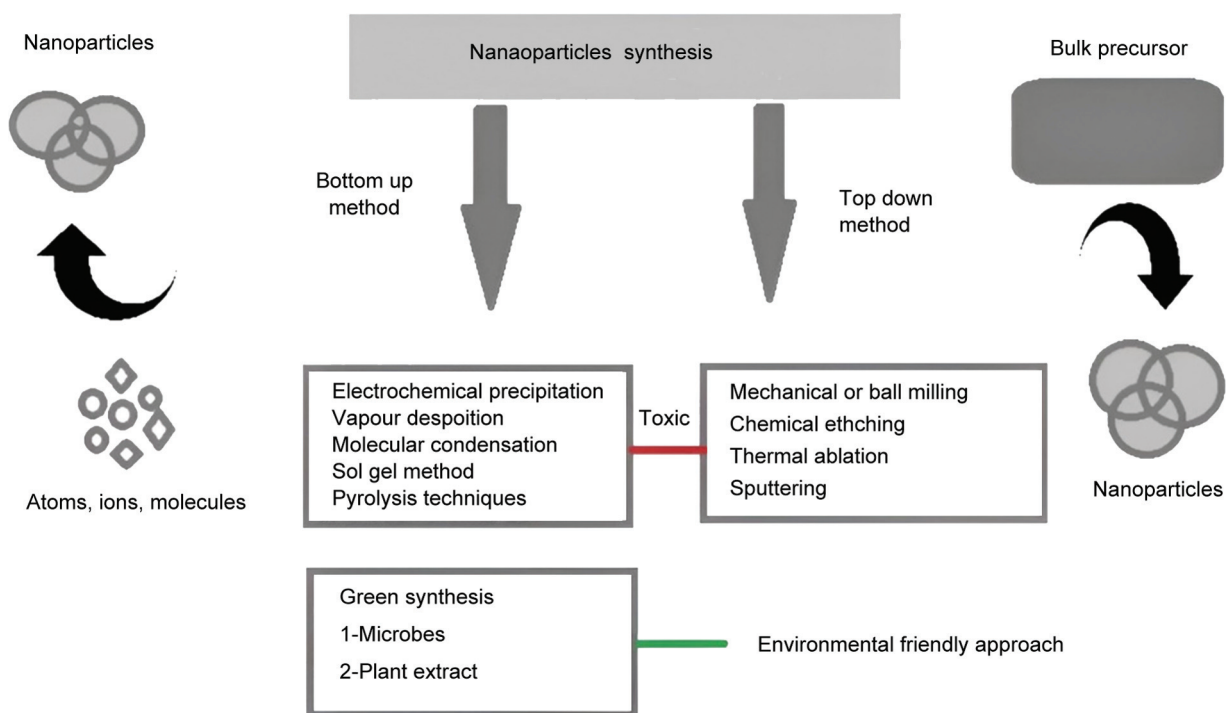


Fig. 4 Methods of NP synthesis, including Top-down or bottom-up approaches. Green synthesis is proven as an environmentally friendly approach. NP, nanoparticle.

ranging from 2 to 10 days is needed for the cultivation of microorganisms. Green synthesis using microbes is a time-consuming process. Some microbes are toxic, and their toxicity affects the properties of synthesized NPs. Plants are easily accessible, whereas the availability of microbes remains an issue. Plant extracts-based metallic nano synthesis is processed at ambient temperatures. On the contrary, microbes-based metallic NP synthesis requires high temperatures. Hence, plant extract green synthesis is used for mass production.³³

Microbes such as fungi, bacteria, and yeast-based nano synthesis are affected by contamination of culture medium, lengthy and time-consuming procedures, and uncontrolled size and shape of metallic NPs.³⁴ NP synthesis using plant extracts has advantages over other biological synthesis by microbes in terms of efficiency. The synthesized NPs are mono-dispersive. The main challenges for using microbial are the toxicity of some bacterial species and the separation methods. The lengthy incubation procedures make microbial NP synthesis not suitable for most researchers. Plant extracts are used for the green synthesis of metal and metal oxide NPs, and different parts of plants are used in the phyto-green synthesis of NPs with high quality.³⁵

Factors Affecting the Synthesis of Metallic NPs

Types of Plants and Biomolecules

A large number of biological compounds in plants are reported for the synthesis of metallic NPs, e.g., plant metabolites, aldehydes, alkaloids, amino acids, aromatic amines, flavonoids, phenolic compounds, ketones, polysaccharides,

proteins, saponins, steroids, sugars, tannins, and terpenoids. These compounds act as either reducing or stabilizing agents. The optimized conditions for synthesizing NPs with desired size and shape can be adjusted in terms of metal salt, temperature, pH, reaction time, the amount of plant extracts, and the types of biological compounds present.³⁶ NP synthesis from plant extracts consists of four phases: (1) initiation phase, the activation phase that includes reduction of metal ions. Nucleation is also included in this phase. (2) Growth phase, in which the tiny adjacent NPs join to form larger sized NPs. (3) Stabilization phase, in which reduction, as well as nucleation phases, continues to cause the growth of stable metal NPs. (4) Termination phase that determines the size and shape of metal NPs. Each stage of NP synthesis has features depending on the biomolecule's nature and concentration.

In the synthesis of silver NPs, the hydroxyl groups of plant biomolecules (amino acids, proteins, alkaloids, flavonoids, polyphenols, tannins, and polysaccharides) are responsible for the reduction and stabilization of silver ions.³⁷ Plant extracts including aloe vera (*Aloe barbadensis* Miller), oat (*Avena sativa*), alfalfa (*Medicago sativa*), tulsi (*Osimum sanctum*), lemon (*Citrus limon*), neem (*Azadirachta indica*), coriander (*Coriandrum sativum*), mustard (*Brassica juncea*), and lemon grass (*Cymbopogon flexuosus*) are used in the synthesis of silver NPs and gold NPs. The synthesis of metallic NPs including zinc, nickel, cobalt, and copper was also observed in mustard (*B. juncea*), alfalfa (*M. sativa*), and sunflower (*Helianthus annuus*). Also, ZnO NPs have been prepared with a great variety of plant leaf extracts such as coriander (*C. sativum*), crown flower (*Calotropis gigantean*), copper leaf (*Acalypha indica*), China rose (*Hibiscus rosa-sinensis*), green

tea (*Camellia sinensis*), and aloe extract (*A. barbadensis* Miller).³⁸

Proteins and carbohydrates are the major elements present in plant extracts. As a reducing agent, they account for the synthesis of metallic NPs through the reduction of metal ions. Functional moieties including amino groups play important roles in the reduction process. The functional groups of alkaloids, flavones, and anthracenes, e.g., C–O–C–, –C–O–, –C<glyph name="dbnd"/>C–, and –C<glyph name="dbnd"/>O–, promote the synthesis of metallic NPs.²² Phytochemicals reduce metal ions in the salt solution, and the degradation of phytochemicals produces oxygen. A report described the proteins in plant extracts responsible for the synthesis of metallic and metallic oxide NPs, which serve the role of reducing and stabilizing agents.²²

The type of phytochemicals and biomolecules present in the plant is an important factor that depends on the type of plant used for the synthesis of metallic NPs. After initiation the next phase is bioreduction in which biomolecules in the form of phytochemicals reduce metal ions present in salt solution and are converted to zero-valent oxidation states from mono or divalent oxidation states, i.e., nucleation (►Fig. 5). The nucleation can be observed visually by a color change of sample solution. In the growth phase, smaller particles merge to form larger, stable particles, while in the termination stage, the shape of the NPs is determined by the bioactive compounds. Different plants have varying mechanisms for NP synthesis due to the presence and structure of bioactive molecules. Interaction between plant extracts and metal ion solutions varies, resulting in NPs of different sizes based on factors such as pH, temperature, and reaction time. These size differences contribute to the unique physical, chemical, and biological properties of the synthesized NPs. Thus, the properties of phytochemicals in plant extracts are

essential for the bioactivities of the NPs, offering potential solutions in the medical field.³⁹

Reaction Conditions

To synthesize metallic NPs from plant extracts, it is crucial to optimize the reaction parameters. This involves carefully monitoring and controlling the concentrations and ratios of plant extracts to metal salts, as well as pH, reaction time, and temperature. By increasing the concentration of plant extract, the size and shape of the NPs can be controlled. Longer reaction times have been shown to increase NP production. Conversely, higher temperatures have been found to decrease both the average size and production of NPs (►Fig. 6). According to studies, the binding of metal ions to the biomolecules of the extracts depends upon pH. At different pH, NPs having tetrahedral, hexagonal, spherical, rod-shaped, and irregular shapes can be synthesized. Generally, higher pH tends to result in small-sized NPs.⁴⁰

pH of the Plant Extract

Changing the shape and size of metallic NPs can greatly improve their efficiency. These morphological parameters can be controlled by adjusting experimental conditions, such as reaction time, reactant concentration, pH, temperature, and the concentration of plant extracts and salts. Proper control of these parameters is crucial for optimizing the synthesis of metallic NPs. pH specifically plays a significant role in determining NP morphology. In an acidic pH environment, larger NPs tend to form. For example, when studying *A. sativa* biomass synthesis, smaller sized gold NPs were observed at pH 3.0 and 4.0 compared with pH 2.0, likely due to the presence of more functional groups favoring nucleation at higher pH levels.⁴¹ At lower pH, silver ions interact with amino and sulfhydryl groups, resulting in the reduction of Ag^+ to Ag

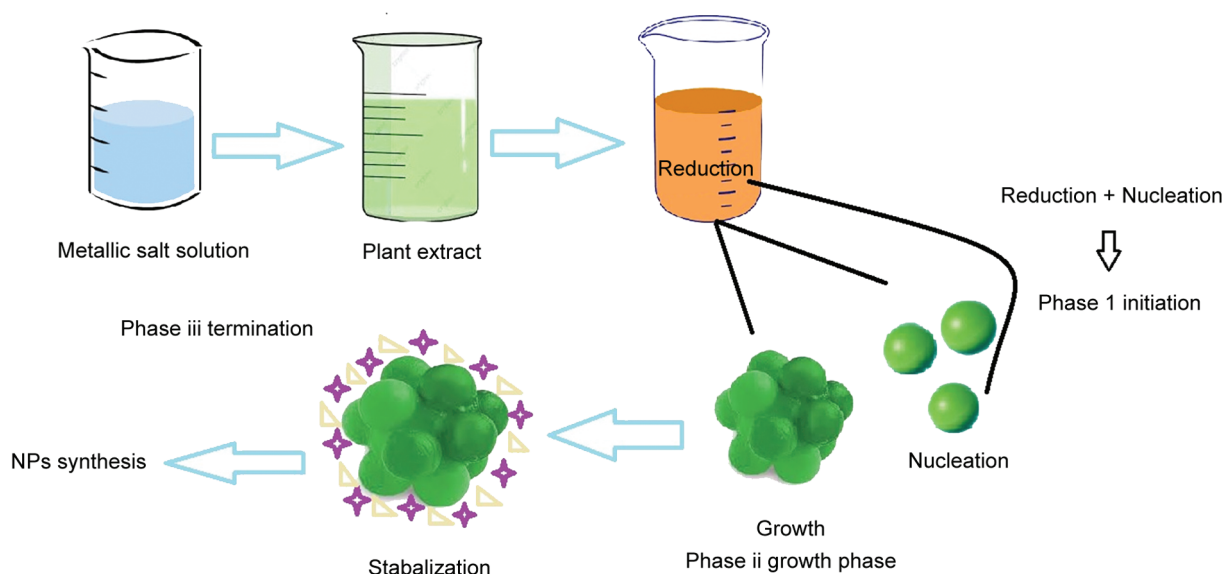


Fig. 5 Metallic NP synthesis using plant extracts. Reduction is visually detected by the color change from yellow to orange. Metallic NPs are synthesized following reduction, nucleation, growth, and stabilization processes. NPs, nanoparticles.

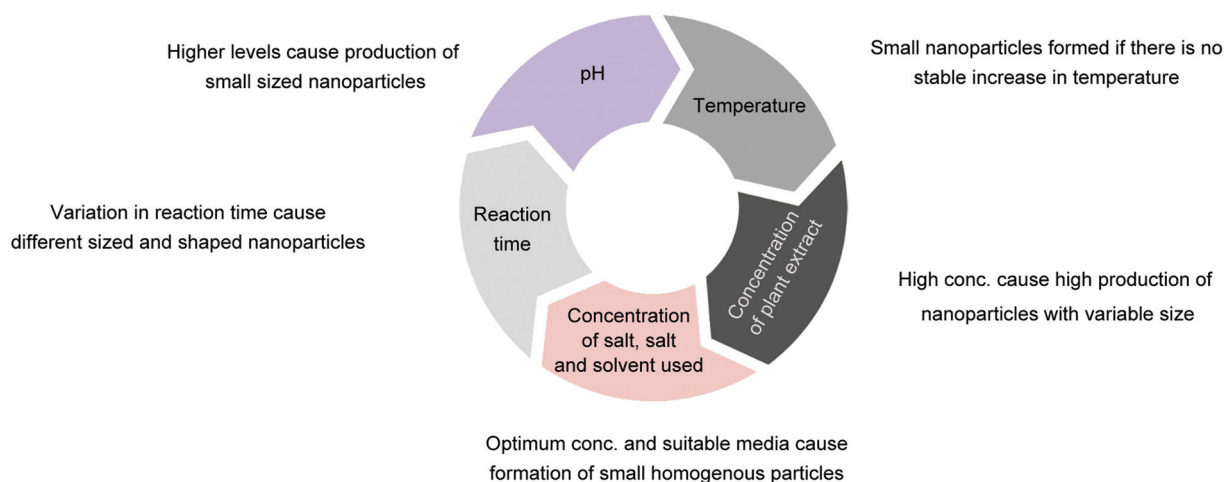


Fig. 6 Factors affecting the green synthesis of metallic NPs. Specifically, pH, temperature, reaction time, the concentration of metallic salt, solvent medium, and concentration of plant extracts need to be optimized. NPs, nanoparticles.

(0). Reduction via ionic bonding is favored at lower pH values, around pH 8, due to positively charged functional groups. At higher pH values, both high bioreduction and dispersion of silver NPs, along with negative zeta potential, lead to the production of larger sized NPs.⁴² Similarly, in the study of fruit rind extract of *Punica granatum* plant on the synthesis of copper NPs, the pH of the solution influences the bioreduction of copper sulfate. A lower pH leads to smaller crystallite sizes due to an increase in the rate of nucleation.⁴³

Kondagogu gum extract, derived from the bark of *Cochlospermum gossypium*, can be modified into carboxymethylated kondagogu gum (CMKG). CMKG is biodegradable, nontoxic, cost-effective, and readily available. The stability of gold NPs was investigated across a pH range of 2 to 10. Particle aggregation occurred at pH 2, while stability was observed between pH 5 and 12 without any spectral shifts in the ultraviolet (UV) spectra.⁴⁴ For the synthesis of gold NPs, *Brassica oleracea* extract, commonly known as red cabbage, was used. The pH affected the colors produced by anthocyanins, the natural pigments in red cabbage. At pH 7 and 4, a purple color was observed when anthocyanins were in their neutral form. In acidic solutions below pH 3, a pink-red color was observed, while blue and green colors appeared at pH 8 and above when anthocyanins were in their basic and negatively charged form. Gold NPs were synthesized at pH 2.5 in the acidic range and at pH 11 in the basic range. The most stable and colloidal gold NPs with sizes ranging from 18 to 30 nm and a spherical shape were obtained at pH 11.⁴⁵ *Amaranthus tricolor* leaf extract was used for the synthesis of MgO NPs. Smaller NPs were formed at lower pH levels due to low electronegativity. Highly acidic pH led to the formation of neutral, stable MgO NPs with smaller sizes.⁴⁶ Cherry fruit extract was utilized for the synthesis of ZnO NPs at various pH levels (4, 6, 7, 8, and 10). The pH had an impact on the reaction, and at strongly alkaline conditions, the formation of ZnO NPs was hindered due to the presence of abundant OH ions reacting with Zn^{2+} cations to form Zn (OH)₂ complexes. The optimal pH for green synthesis of

small-sized hexagonal ZnO NPs using cherry fruit extract was found to be pH 8.⁴⁷

Tragopogon Collinus leaf extract was used for the synthesis of silver NPs. The stability of the NPs was influenced by pH, with the highest absorption observed at pH 10, resulting in smaller and homogeneous NPs.⁴⁸ *Ziziphus joazeiro* leaf extract was utilized for the synthesis of silver NPs. It was found that neutral pH reduced the intensity of the characteristic peak in the surface plasmon resonance (SPR) spectrum.⁴⁹ Bilberry and red currant waste extract were studied for silver NP synthesis. The NPs exhibited a face-centered cubic structure with sizes ranging from 25 to 65 nm. The spectral position of the SPR band was pH- and temperature-dependent, with a blue shift observed as pH increased from 8 to 12.⁵⁰ Hawthorn berries extract was examined for the green synthesis of copper and silver NPs. The pH of the solution played a role in the color and characteristics of the NPs, with small-sized silver NPs observed at pH 7 and dark brownish NPs with wider size distribution at pH 9 and 11.⁵¹ *Annona reticulata* leaf extract was used for silver NP synthesis, with pH affecting the reduction of silver salt to ions. *Annona squamosa* leaf extract, a plant of the same genus, showed a favorable environment for silver NP formation at pH ≥ 9.8 .⁵² Coffee arabica plant extract was employed for the synthesis of gold NPs across a pH range of 5 to 11, resulting in small-sized spherical NPs.⁵³ Stable nanomaterials were formed in both acidic and basic conditions. *Cassia auriculata* flower extract was utilized for the synthesis of silver NPs, and it was observed that the size of the NPs increased with decreasing pH in the green synthesis process.⁵⁴

Ficus hispida Linn. f. leaf extract was used for the synthesis of silver NPs. The optimal pH for the production of small-sized silver NPs with high stability was found to be pH 9, with increased intensity of the SPR peak.⁵⁵ Zulfiqar et al described the stability of the silver NPs at pH 4 obtained from green synthesis of *Fagonia cretica* plant extract.⁵⁶ Gold NPs synthesized from *Nepenthes khasiana* plant extract exhibited pH-dependent colors, with purple NPs formed at neutral pH and fluorescent purple NPs at alkaline pH 10.⁵⁷

Garcinia mangostana plant extract was utilized for the synthesis of silver NPs, with the size decreasing from 32.7 nm at pH 4 to 7.12 nm at pH 7.⁵⁸ The pH of the solution played a significant role in the synthesis and stability of gold NPs using various plant extracts. pH affected the reduction rate, functional group's activity, size, and anisotropy effect of the NPs. The formation of platinum NPs from Saudi dates extract was influenced by the pH of the medium, with smaller and homogenous particles formed at a higher pH.⁵⁹ *Carissa carandas* leaf extract was used for silver NP synthesis, with pH 7 determined as the optimized pH based on UV-visible (UV-vis) spectroscopy.⁶⁰ The intense peak at 410 nm confirmed the synthesis of silver NPs at pH 7, while a wider absorption peak at pH 9 indicated NP agglomeration.

Plant Extract Concentration

The concentration of plant extract used in the synthesis of metallic NPs has a significant effect on their size, shape, and production rate.⁴¹ Gold NPs were synthesized using *Ginkgo biloba* leaf extract as a reducing and stabilizing agent. Different concentrations of leaf extract (2, 5, and 8 mL) were studied. Increasing the concentration from 2 to 8 mL resulted in a slight blue shift in the SPR peak of the UV-vis spectra, indicating a variation in the size of the gold NPs.⁶¹ *Anogeissus latifolia* gum concentration was found to affect the reduction rate of palladium ions. Increasing the gum concentration from 0.1 to 0.5% favored the synthesis of small-sized palladium NPs. The optimal concentration for the synthesis of small-sized palladium NPs was determined to be 1 mmol/L PdCl₂.⁶²

Increasing the concentration of *T. Collinus* leaf extract led to larger quantities of secondary metabolites, resulting in the synthesis of more stable and smaller NPs. Similarly, the concentration of plant extract affected the size of ZnO NPs synthesized from *Hibiscus sabdariffa* plant extract.⁶³ The quantity of plant extract also influenced the shape of metallic NPs.⁶⁴ Aloe vera leaf extract concentration controlled the shape and size of gold NPs, with lower concentrations leading to triangular-shaped NPs of larger size and higher concentrations resulting in spherical NPs.⁶⁵ Red carrot extract concentration of 5% was optimal for the synthesis of stable ruby-red gold NPs.⁴⁵ The concentration of *F. cretica* plant extract affected the absorption peak of gold NPs, with an increase in concentration resulting in a sharper peak.⁵⁶ *Garcinia mangostana* peel extract concentration influenced the production of silver NPs, with higher concentrations leading to greater NP yield.⁶⁶ Ajwa date extract concentration caused a red shift in the absorption spectra of Pt NPs, indicating a smaller particle size.⁵⁹ Additionally, the concentration of leaf and bark extract of *Croton macrostachyus* affected the rate of reduction of silver ions in the green synthesis of silver NPs.⁶⁷

Temperature

Green synthesis of silver NPs using plant extracts was studied. Plant extracts containing phytochemicals are typically heated below 60°C for a short duration. Prolonged high-temperature heating can lead to the decomposition of phy-

toconstituents present in biomass extract.⁶⁸ Temperature plays a crucial role in the synthesis of silver NPs. Operating at room temperature is important to maintain the stability of plant metabolites. However, some researchers have explored higher temperatures to accelerate the synthesis process and achieve the complete conversion of silver ions to silver NPs.⁶⁹ Raising the temperature leads to the rapid depletion of silver ions and the formation of homogeneous silver nuclei, resulting in the generation of small NPs. The higher temperature promotes a faster reduction rate of silver ions and enhances the intensity of the SPR peak.⁵⁸

Temperature affects the size, shape, and rate of production of metallic NPs. As the temperature increases, the formation of nucleation centers is enhanced leading to increased NP production. The synthesis of gold NPs was investigated using *Piper betle* leaf extracts for temperature variation. TEM analysis confirmed triangular-shaped NPs at 20°C. NPs ranging from 5 to 500 nm were detected at 30 to 40°C. At 50 to 60°C, NPs with consistent size and shape were observed. The reduction processes of Au and Ag ions using *Anacardium occidentale* leaf extracts were examined in relation to the concentration of the extract and temperature. At 100°C, 0.6 mL of leaf extracts was needed for NP synthesis, resulting in the production of large-sized NPs. Conversely, increasing the extract concentration to 2.5 mL at 27°C led to stable NPs. In the case of *Pinus eldarica* bark extracts, higher reaction temperatures ranging from 25 to 150°C resulted in the formation of smaller silver NPs.⁶⁵ *Ginkgo biloba* leaf extracts were examined at different temperatures (25, 50, and 80°C) to assess their effect on the synthesis of gold NPs. At 25°C, the SPR peak was observed at 544.5 nm. Increasing the temperature to 50 and 80°C resulted in a blue shift of the SPR peak to 539 nm. These findings suggest that higher temperatures lead to a decrease in the size of the synthesized gold NPs.⁶¹ *Citrus sinensis* peel extracts were studied for the synthesis of silver NPs, and the size of synthesized NPs decreased from 35 to 10 nm when the temperature increased from 25 to 60°C.⁴¹ The synthesis of copper NPs using *P. granatum* plant extracts was investigated, which showed that higher temperatures resulted in an increased reduction of copper ions, making it difficult to control the size of NPs. Therefore, an optimum temperature of 350°C was determined for the synthesis process.⁴³

Different plant extracts were examined for the synthesis of NPs, and their temperature dependence was studied. Pd NPs synthesized from various plant extracts, including *A. latifolia*, *Catharanthus roseus*, *A. squamosa*, and *Gardenia jasminoides*, showed slower synthesis rates at 60°C, with reduction times ranging from 2 to 24 hours. The size range of the synthesized NPs varied from 38 to 100 nm, and 3 to 5 nm. In contrast, banana peel extracts could synthesize NPs within 3 minutes at the same temperature.⁶² For the synthesis of ZnO NPs using cherry extracts, increasing the temperature from 25 to 90°C led to an increase in NP size from 87.5 to 116 nm. This indicated an accelerated reduction rate of metal ions with higher temperatures. The optimal temperature was determined to be 25°C.⁴⁷ *Tragopogon collinus* leaf extracts were utilized for silver NP synthesis, and it was

observed that the synthesis was not significantly affected when the temperature was increased from 40 to 80°C. However, an increase in temperature from 60 to 80°C resulted in an intensified peak, indicating a higher number of synthesized NPs. The optimized temperature for stable NP synthesis was found to be 40°C.⁴⁸ Silver NPs synthesized from *Eriobotrya japonica* leaf extract exhibited an increase in average diameter with higher temperatures due to enhanced nucleation rates. The sizes of the NPs were 9.26 ± 2.72 nm at 20°C, 13.09 ± 3.66 nm at 50°C, and 17.28 ± 5.78 nm at 80°C.⁷⁰

Hawthorn berries extracts were utilized for the synthesis of copper and silver NPs. At 20°C, a light brownish color was observed, while higher temperatures resulted in a dark reddish-brown color. Increasing the temperature led to a decrease in the size of metallic NPs when a water plant extract solution was used. Conversely, at 60°C, small-sized metallic NPs were obtained regardless of the type of salt used, with the smallest size observed.⁵¹ In general, the size of NPs is inversely proportional to the temperature. Silver NPs synthesized using olive leaf extracts exhibited a quick reduction of Ag⁺ ions and uniform nucleation of silver nuclei at higher temperatures, resulting in the formation of smaller sized NPs. Higher temperatures facilitated a higher reduction rate by utilizing silver ions for nucleus production, while secondary reduction was limited to the surface of preformed nuclei. The temperature's influence on NP formation revealed that high temperatures favored the generation of small and spherical particles, whereas lower temperatures resulted in polydisperse particles ranging in size from 5 to 300 nm.⁵⁸

Garcinia mangostana peel extract was utilized for the synthesis of silver NPs, and the effect of temperature was examined. At 27°C, distorted spherical NPs with a size of 49.91 nm were observed, while at 45°C, uniform silver NPs with spherical shapes and a size of 33.61 nm were synthesized. Increasing the temperature from 27 to 75°C resulted in a blue shift. The synthesis of small NPs was facilitated by the homogeneous nucleation reaction and rapid reduction of silver salt at higher temperatures.⁶⁶ The synthesis of silver NPs using bilberry and red currant waste extracts was also investigated. Increasing the temperature from 20 to 60°C led to an increase in the intensity of the SPR band and the rate of NP formation. Higher temperatures also contributed to a reduction in the size of the silver NPs, indicating a favorable nucleation process at elevated temperatures.⁵⁰

Ficus hispida Linn. f. leaf extracts were examined for their catalytic and antioxidant properties, and the influence of temperature on silver NP formation. Increasing the temperature from 35°C to 90°C resulted in an intensified SPR peak and a blue shift from 426 to 399 nm. However, above 90°C, a decrease in the SPR peak intensity was observed. Thus, the optimum temperature for silver NP synthesis was determined to be 90°C.⁵⁵ The synthesis of Pt NPs using Saudi date extracts was also investigated. In the UV-vis spectra, a broad peak was observed with a temperature exceeding 30°C, indicating the oxidation of phenolics in the dates extracts. As a result, the antioxidant content in the extracts decreased, leading to a reduction in Pt NP synthesis. Specific factors

affecting the size and shape of metallic NPs are summarized in ►Table 2.⁵⁹

Reaction Time

The reaction time is a crucial parameter in NP synthesis. *Azadirachta indica* leaf extract was used, and increasing the reaction time from 30 minutes to 4 hours resulted in a change in the size of silver NPs, ranging from 10 to 35 nm.⁴¹ The appropriate duration of the reaction is essential for the complete nucleation and stability of NPs.⁷¹ *Berberis vulgaris* leaf extracts were also studied, and an increase in reaction time enhanced the reduction of NPs, leading to increased production.⁷² The size of silver NPs can increase with longer reaction times due to the accumulation of colloidal silver NPs.⁴² Synthesis using *C. sativum* seed extracts and *Chenopodium album* leaf extracts showed relatively shorter reaction times compared with microorganisms, with completion within 1 to 2 hours and 15 minutes, respectively.⁶⁵ *Capsicum annum* L. extract resulted in spherical NPs with sizes of 10 ± 2 nm and 25 ± 3 nm to 40 ± 5 nm with reaction times of 5 hours and 9 to 13 hours, respectively.⁶⁵

Optimum reaction times were determined for specific NP synthesis. For example, *P. granatum* plant extracts showed higher production of copper NPs at 2 hours,⁴³ *F. hispida* Linn. f. leaf extracts exhibited increased SPR peak intensity within 1 hour of reaction time,⁵⁵ and Saudi dates extracts achieved the highest production of Pt NPs within 10 hours.⁵⁹ *Cassia auriculata* L. flower extracts confirmed the formation of silver NPs with an optimized reaction time of 24 hours.⁵⁴ *Gum C. gossypium* resulted in the reduction of gold ions with increasing reaction time.⁴⁴ *Carissa carandas* leaf extracts showed stability in silver NP synthesis within 20 minutes.⁶⁰

Solvent

The choice of solvent has a significant impact on the morphology of NPs. In the case of hawthorn berries extract, the aqueous solution was found to be more optimized for the production of copper and silver NPs compared with ethanol, likely due to the higher ratio of flavonoids present.⁵¹ When investigating the effect of chloroauric acid solvent on gold NP synthesis, increasing the concentration of chloroauric acid solution resulted in a blue shift in the SPR peak, indicating a decrease in particle size.⁶¹ Similarly, in the synthesis of silver NPs using *C. auriculata* flower extracts, increasing the quantity of the aqueous fraction (AS solution) led to an increase in the absorbance peak, confirming the synthesis of silver NPs.⁵⁴

Metal Salt Concentration

The effect of zinc nitrate concentration on ZnO synthesis using cherry extract was investigated. Increasing the concentration from 0.005 to 0.3 mol/L favored the reduction process. At lower concentrations, hexagonal-shaped NPs with an average size of 20.7 to 96.5 nm were formed. This can be attributed to the presence of groups/biomolecules in the cherry extract, such as proteins, vitamins (A, B, C), and sugars, which capped and stabilized the NPs. Scanning electron microscopy analysis revealed that the competition

Table 2 Parameters affecting the size and shape of NPs in green synthesis

Plant name	Metal	pH	T (°C)	PE	RT (min)	ST	SZ (nm)	Shape	Ref.
<i>Punica granatum</i>	Cu	5	37	50%	0–120	1–20 mmol/L	20	S	43
<i>Brassica oleracea</i>	Au	11	25	5% w/w	0–12	100 mmol/L	18–30	S	45
<i>Amaranthus tricolor</i>	MgO	3	60	1:10	–	0.001 mmol/L	45	S	46
<i>Tragopogon collinus</i>	Ag	10	40	40 mL	30, 90, 150	0.0025 mmol/L	7–18	S	48
<i>Ziziphus joazeiro</i>	Ag	11	95–98	4 mL	15, 30, 45, 60	1 mmol/L	5–50	S	49
<i>Bilberry and red currant waste extract</i>	Ag	8–12	20–60	10 mL	15–300	3 mmol/L	25–65	fcc	50
<i>Annona reticulata</i>	Fe/Ni	>9.8	25	3–20 µg/mL	120	1 mmol/L	6–8	fcc	52
<i>Coffee arabica</i>	Au	1–13	–	–	–	2.5–200 mmol/L	5–11	S	53
<i>Cassia auriculata</i>	Ag	3–6	–	0.1–1.0 mL	0, 1, 2, 3, 4, 5, 8, 18, 18,000	1 mmol/L	10–30	Ts	54
<i>Ficus hispida</i> Linn. f.	Ag	9	90	5% w/v	60	1–5 mmol/L	20	S	55
<i>Fagonia cretica</i>	Ag	4	50	10–20 mL	15–120	2.0 mmol/L	16	S	56
<i>Garcinia mangostana</i>	Ag	4	45	0.5 g		1, 2.5, 7.5, 10 mmol/L	32.7	S	58
<i>Saudi dates</i>	Pt	5.5	30	1–5 mL	960	0.0001 mmol/L	2.6	S	59
<i>Ginkgo biloba</i>	Au	–	50–80	2–8 mL	120	2–4 mL	10–40	S	61
<i>Anogeissus latifolia</i>	Pd	–	25	0.50%	30	0.125–1.0%	4.8	S	62
<i>Cherry</i>	ZnO	8	25	10 mL	720	0.005 mol/L	20.18	H	47
<i>Croton macrostachyus</i>	Ag		25	75 mL	150	0.1 mol/L	8.9–13.68	S	67
<i>Eriobotrya japonica</i>	Ag	7	20	1:1, 1:2, 1:10	20	1:1, 1:2, 1:10	9.26	fcc	70
<i>Hawthorn berries</i>	Ag/Cu	7–11	60	–	60	30 mL	60–200	S	51
<i>Berberis vulgaris</i>	Ag	–	25	5 mL	60–18,000	0.5–10 mmol/L	30–70	S	71
<i>Carissa carandas</i>	Ag	7	27	1.25 mL	20	12.5 mmol/L	100	fcc	60
<i>Cochlospermum Gossypium</i>	Au	5–12	27	0.50%	5, 10, 15, 25, 30	0.5–3 mmol/L	11	S	44

Abbreviations: fcc, face-centered cubic; H, hexagonal; NPs, nanoparticles; PE, plant extract concentration; RT, reaction time; S, spherical; ST, salt concentration; T, temperature; Ts, triangular spherical.

between zinc ions and functional groups of the plant extract led to the synthesis of larger NPs, resulting in an increased rate of reduction. The optimum concentration of zinc nitrate for ZnO NP synthesis was determined to be 0.005 mol/L.⁴⁷

The green synthesis of silver NPs using *T. Collinus* leaf extracts was studied. Different concentrations of silver nitrate ranging from 0.001 to 0.02 mol/L were prepared to investigate their effect. Each concentration was mixed with 20 mL of the plant extracts. Among the tested concentrations, 0.0025 mol/L silver nitrate was selected as the optimum concentration, which resulted in increased absorbance.⁴⁸ The synthesis of palladium NPs using *Lentian* (LNT) in plant extracts was also investigated. As the molar ratio of Na₂PdCl₄ salt to LNT increased, the intensity of absorbance was observed to increase, as shown by the UV-vis spectrum.⁷³ The effect of silver nitrate concentration on the synthesis of silver NPs using *B. vulgaris* leaf extracts was studied. Aqueous extract (5 mL) was used, and the UV-vis spectrum revealed that increasing the concentration of silver nitrate led to an increase in the intensity of the peak, indicating the reduction of silver ions into silver. Conse-

quently, the concentration of silver NPs also increased. The resulting solution exhibited a dark brown color, indicating a higher concentration of silver NPs.⁷² Studies found that silver nitrate is commonly used as a precursor in green synthesis methods employing plant extracts. The concentration of silver nitrate significantly influences the size determination of the synthesized NPs.⁴²

Rahuman et al conducted a study on the synthesis of silver NPs using *C. carandas* leaf extracts. They determined that the optimal concentration of silver nitrate was 1.25 mmol/L, which resulted in an intense SPR peak at 410 nm. Additionally, the concentration of silver ions was optimized by varying the metal ion concentrations in the solution, ranging from 0.25 to 2.5 mmol/L, along with an optimized pH value.⁶⁰ In another study, *Cassia auriculata* L. flower extracts were utilized for the synthesis of silver NPs. Various concentrations of metal ions were added to an aqueous extract known as AS. The UV-vis spectra analysis confirmed the presence of an SPR peak at 435 nm, indicating the successful synthesis of silver NPs. The intensity of absorbance increased with higher concentrations of silver ions. At lower volumes of silver ions,

the NPs did not aggregate on the particle surface, while a higher volume of silver ions resulted in a rapid increase in absorbance, potentially leading to particle aggregation on the surface area.⁵⁴

In the study on gold NP synthesis, *Gum C. gossypium* (CMGK) was investigated. The researchers observed that gold NPs remained stable at concentrations below 2 mol/L NaCl. However, when the concentration of NaCl was increased, a red shift in the SPR spectrum was observed, indicating that gold NPs became less stable with higher salt concentrations. These findings indicated the aggregation process initiated above a salt concentration of 2 mol/L.⁴⁴ In another study, *G. mangostana* plant extracts were examined for the synthesis of silver NPs. The UV-vis analysis revealed a red shift in the spectrum, indicating the presence of synthesized silver NPs. The size of the NPs increased as the concentration of silver nitrate increased. Nucleation was favored at lower concentrations of silver nitrate, resulting in the production of smaller sized silver NPs. Conversely, higher concentrations of silver nitrate led to an increased reduction process and the formation of larger sized NPs. A red shift in the spectrum was observed at 433 nm for a concentration of 5 mmol/L and 465 nm for a concentration of 10 mmol/L.⁶⁶

In the investigation of silver NP synthesis, the leaf extracts of *F. hispida* Linn. f. were utilized. The absorption peak in the SPR spectrum increased from 424 nm to 437 nm as the concentration of silver nitrate increased from 1 to 3 mmol/L, indicating a red shift. However, a blue shift in the SPR peak from 437 to 433 nm was observed at a concentration of 4 mmol/L of silver nitrate. This suggests that higher concentrations of silver nitrate accelerate the synthesis of silver NPs. The increased interactions between the plant extract and silver ions result in the red shift and an increase in the size of silver NPs.⁵⁵ In another study on the synthesis of silver NPs, *C. carandas* leaf extract was used. Different concentrations of silver nitrate were employed to optimize the synthesis. A silver nitrate concentration of 1.25 mmol/L exhibited an intense peak at 410 nm. Consequently, the reaction mixture turned dark brownish when the optimized leaf extract concentration of 1.25 mL was added at a pH of 7. Silver nitrate concentrations of 2.0, 1.75, and 1.5 mmol/L showed weaker absorbance peaks at 410 nm.⁶⁰ Similarly, the effect of silver nitrate concentration was investigated in the synthesis of silver NPs using *F. cretica*. The concentration of silver nitrate was found to greatly influence the synthesis of silver NPs. A sharp absorption peak was observed at a concentration of 2.0 mmol/L silver nitrate compared with concentrations of 0.5 and 1.0 mmol/L.⁵⁶

Toxicity of Metallic NPs

The cytotoxicity of silver NPs synthesized using *Veronica officinalis* extracts was evaluated, and results indicated these NPs, with a spherical shape and an average size of 40 nm, exhibited minimum toxic profiles.⁷⁴ Another study focused on examining the toxicity of silver NPs synthesized using *Stenocereus queretaroensis* peel extracts. Acute oral and

dermal toxicity tests were conducted, along with an analysis of cytotoxicity, genotoxicity, and mutagenic potential. The results demonstrated that these NPs showed no obvious toxic effects when tested *in vitro* and *in vivo*. Therefore, these NPs can be considered for use as a component in antibacterial or therapeutic products.⁷⁵ Gold NPs possess distinct physicochemical characteristics that make them suitable for surface modification through attachment to amine and thiol groups. This quality has led to their investigation as contrast agents and carriers for cancer treatment and heat therapy. With their inert and nontoxic core, gold NPs are generally considered safe. In one study, the cytotoxicity of various gold NPs with different capping agents was assessed using a leukemia cell line. The results indicated that spherical gold NPs were able to penetrate cells without affecting cellular functions.⁷⁶ Another study aimed to produce silver NPs using *T. arjuna* and *Eucalyptus camaldulensis* extracts as green reducing and capping agents. These sustainably synthesized silver NPs exhibited potent antibacterial properties and minimal cytotoxicity.⁷⁷

In vivo distribution and acute toxicity tests were also conducted to investigate ultrasmall gold NPs with diverse biological activities. Gold NPs with a diameter of less than 10 nm showed significant biological utility. The tests, performed on male albino rats, demonstrated little to no toxicity when low doses of these ultrasmall gold NPs were administered.⁷⁸ A low-cost and simple method utilizing an aqueous extract of mangrove leaves was employed to create titanium dioxide-doped NPs on a large scale. The resulting C-TiO₂ NPs were found to have mild toxicity, with titania having a negligible impact.⁷⁹ The toxicity of copper oxide NPs synthesized from *Olea europaea* leaf extract was evaluated in mice, and the assessment involved measuring the weight of the liver, kidneys, spleen, thymus, and body of mice. Normal dermal fibroblasts showed minimal cytotoxic effects, suggesting that these copper oxide NPs may have potential as anticancer agents.⁸⁰

Conclusion and Future Perspective

Metallic NPs have various applications in fields such as medicine, agriculture, food, cosmetics, and herbal products. The green route, which is environmentally friendly, cost-effective, and simple, shows great potential. It is projected that the market value of metallic NPs will reach \$40.6 billion by 2027. In the health care sector, green synthesis of metallic NPs offers a great alternative that can combat microbes and address the challenges of mutation and antibiotic resistance. ▶ **Fig. 7** illustrates the potential applications of various metallic NPs, and it is crucial for producing controlled-sized NPs, as their effectiveness is size-dependent.

Current and future research in green nano synthesis holds promise for expanding our understanding of the parameters that control the synthesis, size, and shape of NPs. Further investigation is necessary to comprehend the impact of these parameters on the synthesis of metallic NPs using plant extracts, which is considered the most sustainable approach for large-scale production. Research should address challenges

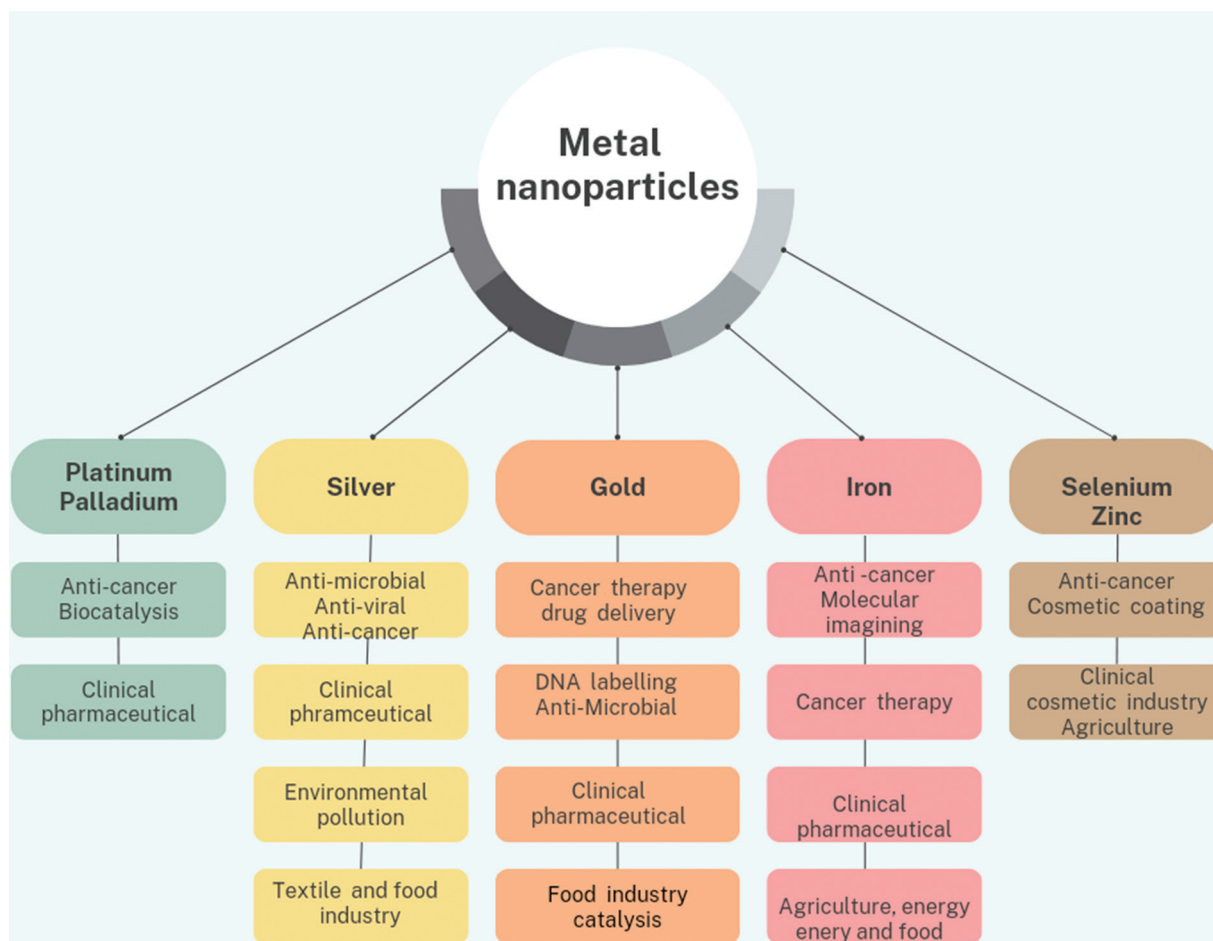


Fig. 7 Applications of commonly used metallic NPs. NPs, nanoparticles.

related to toxicity profiles, develop protocols for green nano synthesis, and uncover mechanisms of NP synthesis. These advancements will contribute to the production of NPs on a larger scale. Researchers should prioritize the exploration of parameters that influence the morphology of metallic NPs, aiming for green synthesis methods that minimize toxicity, enhance clinical applications, and enable precise control over size and shape.

Conflict of Interest

None declared.

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