International Journal of Nanomedicine

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REVIEW

Revisiting the Green Synthesis of Nanoparticles: Uncovering Influences of Plant Extracts as Reducing Agents for Enhanced Synthesis Efficiency and Its Biomedical Applications

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Background: Conventional nanoparticle synthesis methods involve harsh conditions, high costs, and environmental pollution. In this context, researchers are actively searching for sustainable, eco-friendly alternatives to conventional chemical synthesis methods. This has led to the development of green synthesis procedures among which the exploration of the plant-mediated synthesis of nanoparticles experienced a great development. Especially, because plant extracts can work as reducing and stabilizing agents. This opens up new possibilities for cost-effective, environmentally-friendly nanoparticle synthesis with enhanced size uniformity and stability. Moreover, bio-inspired nanoparticles derived from plants exhibit intriguing pharmacological properties, making them highly promising for use in medical applications due to their biocompatibility and nano-dimension.

Objective: This study investigates the role of specific phytochemicals, such as phenolic compounds, terpenoids, and proteins, in plant-mediated nanoparticle synthesis together with their influence on particle size, stability, and properties. Additionally, we highlight the potential applications of these bio-derived nanoparticles, particularly with regard to drug delivery, disease management, agriculture, bioremediation, and application in other industries.

Methodology: Extensive research on scientific databases identified green synthesis methods, specifically plant-mediated synthesis, with a focus on understanding the contributions of phytochemicals like phenolic compounds, terpenoids, and proteins. The database search covered the field's development over the past 15 years.

Results: Insights gained from this exploration highlight plant-mediated green synthesis for cost-effective nanoparticle production with significant pharmacological properties. Utilizing renewable biological resources and controlling nanoparticle characteristics through biomolecule interactions offer promising avenues for future research and applications.

Conclusion: This review delves into the scientific intricacies of plant-mediated synthesis of nanoparticles, highlighting the advantages of this approach over the traditional chemical synthesis methods. The study showcases the immense potential of green synthesis for medical and other applications, aiming to inspire further research in this exciting area and promote a more sustainable future.

Keywords: nanomaterials, biocompatibility, medicinal plants, surface functionalization, green synthesis, biomedical application

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Introduction

The recent era emerged as a period of development for nanomaterials in diverse areas of research, since they possess exceptional physical, chemical and electronic properties.[1] These properties are essential in various scientific disciplines, such

Received: 2 May 2023
Accepted: 3 August 2023
Published: 18 August 2023

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as catalysis, electronics, targeted drug delivery, water sensing and treatment, corrosion inhibition, oil recovery, and many more.[2–4] Generally, the term 'nanoparticles' is used to describe particles that range in size from 1–100 nanometers although, in the field of biotechnology, this is usually extended to include particles up to 500 nanometers in size.[5] "Size" is the parameter which makes 'nanoparticles' unique from other materials, usually called "bulk materials", and able to generate certain profound physicochemical properties.[5,6] Usually, fabricated nanoparticles are metallic in nature and display an effect commonly known as "Surface Plasmon Resonance", which plays an important role in the quantum mechanical effects of light in UV-Visible regions, leading to unique optronics/optoelectronic properties.[7] Prominently, any type of change in the size or shape of a nanoparticle is reflected on its inter-particle interactions as well as absorption properties.[8] Due to their exceptional properties, nanoparticles are extensively utilized in various biomedical applications.[9–11]

The numerous developments associated with nanoscale science have produced plentiful nano-dimensioned materials to enhance the related research and hence, a variety of valuable nano-sized materials are being produced on a commercial scale.[12] It has been assumed that, in the future, nano-sized materials and their related products will become an aid in day-to-day life. It is equally important that these nano-sized materials possess a strong ability to establish an interaction with different biological molecules, both inside as well as on the surface of cells. Their ability to reach inside cells enables these molecules to guide different cellular physicochemical and biochemical processes.[13] Nanoparticles can be quickly and easily absorbed into cellular compartments/organelles, due to their small dimensions. Furthermore, nano-sized particles can easily cross the placenta and the barriers of the blood-brain.[12,14] This explains the availability of nano-sized materials in various drug formulations (approximately 45), which Weissig et al discussed in detail.[15] For instance, TiO_2 and ZnO nanoparticles are able to resist UV-radiation, and thus have been incorporated into various cosmetic products (specifically sunscreen). On application to the skin surface, these nanoparticles remain transparent to visible light and provide better protection against UV-rays compared to ordinary sunscreen.[16] Furthermore, a collection of NPs based on the single-walled carbon-nanotubes (SWCNT) was introduced to the Russian market recently.[17] In the food market, nano-sized materials are already being used to increase the storage time of edible products and so control the spoilage rate.[18]

Vance et al, extensively evaluated the nanotechnology-based-products in the market and reported that approximately 1814 products containing nano-sized materials, introduced by around 622 companies, are being used by about 32 countries globally. It was claimed that about 435 silver-based, nano-sized materials are readily available in the market, including veils, toothpaste, detergent, humidifiers and shampoo. Currently, there exists a high demand for nanomaterials, which was calculated to be from 300,000 to 1.6 million tonnes worldwide. The market share of the Asia-Pacific area is the greatest, (34%), followed by North America and Europe (at 31% and 30%, respectively).[19]

The method of nano-sized materials synthesis is an important chemical process. At present, both chemical and physical methods are applied when preparing nano-sized materials, but these may not be the optimum choice, due to their high cost and potential pollution of the environment. Consequently, alternatives to these existing methods, which are environmentally-friendly (green synthesis) during the whole production procedure, must be developed for the synthesis of nano-sized materials, which has attracted the interest of researchers worldwide.[19,20] The traditional synthesis procedures (both physical and chemical) are usually carried out under extremely harsh conditions. In contrast, the biological procedures are generally conducted under an ambient temperature and pressure, which indicates simplicity, energy saving and reduced toxicity or harm to both humans and the environment.

Bearing these advantages in mind, various biological resources, including bacteria, fungi, yeast, plants and algae, are being exploited to synthesize both intracellular and extracellular materials possessing nano-size.[21] Even though nanoparticles are synthesized following biological methods (biosynthesis), the mechanism of their synthesis remains challenging.[22] However, these methods are well established and commonly used to synthesize nano-sized materials, as they are more cost-effective and environmental-friendly compared to conventional methods. Biological methods harness the power of renewable sources such as plants and microorganisms, acting as reducing agents to stabilize and cap nanomaterials, eliminating the need for chemical additives.[23,24] A standardized method for the synthesis of nanoparticles utilizing plant extracts involves a systematic approach, where a specific plant material is carefully selected and taxonomically identified, and the desired plant extract obtained. Subsequently to the selection of plant parts, an extraction process using an appropriate solvent/s, followed by filtration/chromatography to eliminate any impurities, is carried out.

Simultaneously, a metal salt solution of choice is prepared as the nanoparticle precursor and the previously prepared plant extract is added to the metal salt solution, maintaining the appropriate temperature and pH for the reaction, and initiating a reaction that leads to the formation of nanoparticles.[25] In the several methods reported in earlier studies, the continuous stirring of the reaction mixture offers better results in the form of uniform-sized nanoparticles, as is visually indicated by a noticeable change in colour. Furthermore, to ensure uniform dispersion, ultrasonic treatment may be applied. Subsequently, the nanoparticles are separated from the solution by employing centrifugation before being washed to remove any remaining impurities. Optionally, the nanoparticle precipitate can be dried to eliminate any additional impurities.[26] Finally, the synthesized nanoparticles are thoroughly characterized using diverse analytical techniques to confirm their composition and physicochemical properties. Following synthesis, different spectroscopic and microscopic methods play a crucial role in characterizing synthesized nanoparticles. For instance, UV-Vis spectrophotometry is used to assess their optical characteristics, while FTIR spectroscopy assists the identification of the functional groups present on the nanoparticle surface. For a detailed analysis of their size, shape, and structure, Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are employed. Additionally, Dynamic Light Scattering (DLS) and Zeta potential measurements are utilized to determine the size and surface charge of the nanoparticles. These methods provide valuable insights into the properties and behaviour of the synthesized nanoparticles.[27–29]

Nanotechnology and Green Synthesis

As discussed in Introduction, the synthesis of nano-sized materials employing "green" processes is relatively cost-effective and does not harm the surrounding environment, as non-toxic chemicals are employed throughout the entire process. Therefore, the usage of stabilizers and reducing agents that possess a biological origin, such as microbial entities, fauna and various other resources, is a sustainable way to produce nano-sized materials.[30,31] Although being cost-effective and environment-friendly are key factors motivating the green synthesis of nano-sized materials, the "stability" of the produced material has attracted the attention of researchers across the globe.[14] Although the methods involved in green synthesis are relatively diverse, the living entities that are involved in the synthesis usually simply react with different salts (metallic) and reduce them to nano-sized materials, which can be utilized for different purposes only following appropriate characterization.[32,33] Both microbe- and plant-mediated approaches are employed to synthesize nano-sized materials. Microbe-mediated construction products involve their inherently sophisticated biochemical machinery, which leads to well-defined nanoparticles of different chemical compositions, shapes and sizes.[34] Scaling-up may, however, sometimes prove challenging with regard to microbial preparations. This drawback can be easily overcome by using plant-based extracts, and the production rates can be amplified as a consequence. Plant extracts are more efficient than microbes with regard to the production rate. They reduce metal-ions faster than microbial entities and produce nano-sized materials, which are also very stable.[18,19] Plants contain various compounds (ie, alkaloids, flavonoids, phenol, tannin, alcohol) with the capability to reduce metallic ions to nanoparticles with decent stability.[17,21] Currently, there is evidence that the benefits of plant-based synthesis arise from the synergy of those compounds. A very-general scheme of "green-synthesis of nano-sized material" is shown in Figure 1.

Medicinal Plants Exploited for Nanomaterial Synthesis

Plants are rich sources of medicinal compounds that possess the capacity to produce simple ions by reducing complex metallic ions. The accumulation of metallic-ions in plant cells and tissues inspired the idea of applying metal-reduction to nano-sized materials.[35] For instance, Alfalfa (*Medicago sativa*) and Brown Mustard (*Brassica juncea*), developed in the presence of silver nitrate ($AgNO_3$), accrue 12.4 and 13.6 wt% of Ag, respectively, with Ag-NPs being around 50 nm in size.[21] Similarly, 4 nm sized gold icosahedra were observed in Alfalfa (*Medicago sativa*),[36] and around 2 nm sized semi-spherical Cu-NPs were found in *Iris pseudacorus*, when grown in the salts. Various in-vitro methods, including the utilization of herbal extracts as reducers for synthesizing nano-sized materials, have recently been developed.[35] Extracts of many plant-species, several acids and the salts of different metals (eg, Cu, Au, Ag, Pt, Se and Fe) have been employed in the green synthesis of nano-sized materials.[37,38] Because no bacteria or toxic chemical contaminants are present, plant materials are more favourable when used for NP fabrication compared to methods involving microbes or deleterious chemicals. Furthermore, this approach consumes less energy and has both simple and broad applications.[39,40] For the bio-friendly synthesis of NPs, diverse plant extracts

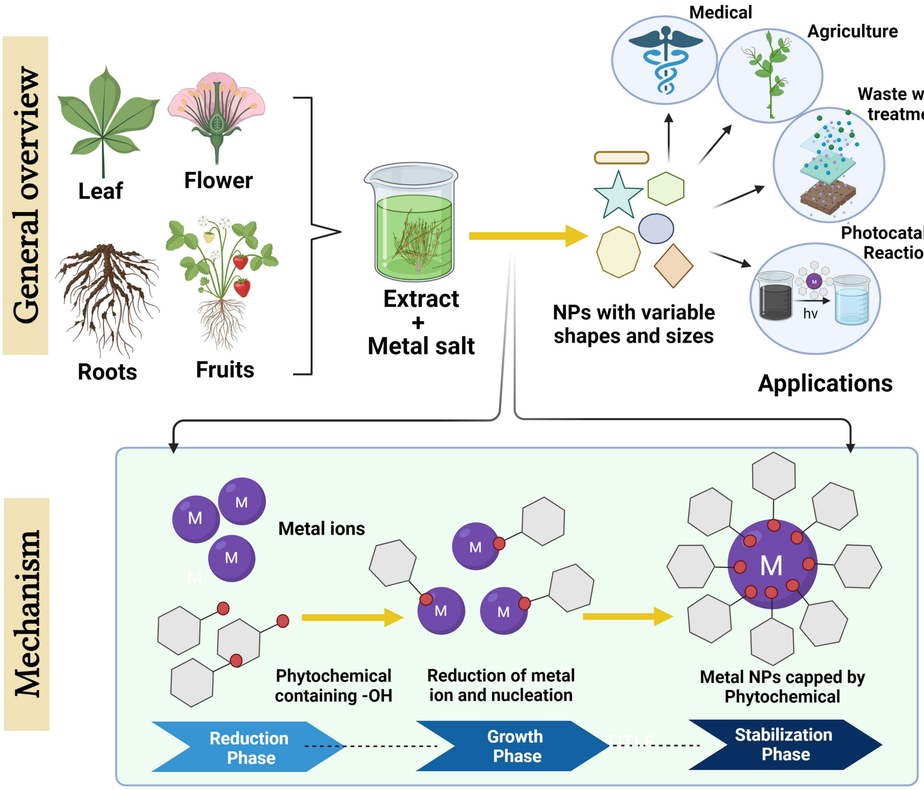


Figure 1 Schematic illustration of the method and mechanism involved in green synthesis of nanoparticles using plants as reducing agents.
Note: Created with BioRender.com.

obtained from various components, including the plant stems, bark, roots, floral parts, leaves, seeds and fruit have been employed.[41–43] In recent years, a range of green synthesized nano-sized materials, obtained from various medicinal plant species, have been described (Table 1). Different features of these synthesized, nano-sized materials, such as their shape, size and quality, are highly dependent on various aspects, such as the concentration of the extract used, and specifically its composition and pH, as well as the temperature at which the reaction occurs.[44–46]

Table 1 Metallic NPs synthesized using plant-extracts

Sr. No.	Plant Species	Utilized Plant-Part	Types of NPs	Size (nm)	Shape/Form	Ref.
1.	*Citrus limon*	Fruit-part	ZnO; TiO_2	20–200	Polymorphous	[47]
2.	*Phyllanthus emblica*	Fruit-part	Ag	20–93	Spherical	[48]
3.	*Rosmarinus officinalis*	Floral-part	MgO	<20	Flower-shaped	[49]
4.	*Matricaria chamomilla*	Floral-part	MgO and MnO_2	9–112	Disc-shaped, Spherical	[50]
5.	*Matricaria chamomilla*	Floral-part	ZnO	50–192	Crystal-form	[51]
6.	*Olea europaea*	Leaf-part	ZnO	41–124	Crystal-form	[51]
7.	*Lycopersicon esculentum*	Fruit-part	ZnO	66–133	Crystal-form	[51]
8.	*Piper nigrum*	Stem-part	Ag	9–30	Crystal-form	[52]
9.	*Citrus maxima*	Fruit-part	Ag	11–13	Sphere-shaped	[53]
10.	*Artemisia absinthium*	Leaf-part	Ag	5–100	Sphere-shaped	[54]

(*Continued*)

Table 1 (Continued).

Sr. No.	Plant Species	Utilized Plant-Part	Types of NPs	Size (nm)	Shape/Form	Ref.
11.	*Trachyspermum ammi*	Leaf-part	Ni	68	Missing	[55]
12.	*Abelmoschus esculentus*	Seed-part	Au	45–75	Sphere-shaped	[56]
13.	*Parthenium hysterophorus*	Leaf-part	ZnO	28–84	Sphere-shaped and Hexagonal	[56]
14.	*Syzygium aromaticum*	Bud-part	Cu	15	Sphere shaped	[57]
15.	*Piper cubeba*	Seed-part	Ag	88	Spherical	[58]
16.	*Nigella sativa*	Leaf-part	Ag	15	Spherical	[59]
17.	*Ixora coccinea*	Leaf-part	CuO	80–110	Spherical	[60]
18.	*Centella asiatica*	–	CeO_2	19	Spherical	[61]
19.	*Curcuma Longa*	–	Ag	5–35	Spherical	[62]
20.	*Acalypha indica*	Leaf-part	Ag, Au	20–30	Spherical	[63]
21.	*Cotyledon orbiculata*	Leaf-part	Ag	100–140	Spherical	[64]
22.	*Cucumis prophetarum*	Leaf-part	Ag	30–50	Ellipsoidal/irregular	[65]
23.	*Senegalia senegal*	–	Ag	1–30	Spherical	[66]
24.	*Ocimum tenuiflorum*	Leaf	Se	15–20	Spherical and monodispersed	[67]
25.	*Asparagus racemosus*	Root	Pt	1–6	Spherical	[68]
26.	*Rosmarinus officinalis*	Leaves	Pd	15–90	Semi-spherical	[69]
27.	*Moringa oleifera*	*Seeds*	Fe	2.6–6.2	Spherical	[70]
28.	*Anogeissus latifolia*	Commercial Powder	Pd	4.8	Spherical	[71]
29.	*Cissus quadrangularis*	Stem	Ag	24	Spherical	[72]
30.	*Ziziphus Mauritiana*	–	Ag	10–45	–	[73]

Mechanistic Investigation of Green Synthesis

Both microbe- and plant-mediated approaches are being employed to synthesize nano-sized materials. Microbes are less efficient than plant extracts in terms of their production rate. In contrast to microorganisms, which contain important enzymes that can serve as a reductant as well as a stabilizer for nano synthesis, plants often possess a phytochemical composition, including “alcohols, phenols, terpenes, alkaloids and proteins”.[74] The mechanistic investigation of the green synthesis of nanoparticles is described in detail in the following subsections.

Plant-Mediated Green Synthesis

The utilization of plant extracts has become one of the main biosynthesis techniques being addressed, since the majority of plants are often affordable, accessible and safe to use. Additionally, a variety of phytochemicals, mentioned above, are found in abundance in plant extracts, which function as a reductant as well as a stabilizer in the synthesis of plant derived NPs.[74] The precise mechanisms of phytosynthesis for biogenic NPs are not yet fully known, and several plausible pathways have been postulated for its synthesis.[75–77] Since numerous phytochemicals are present, it is challenging to identify any specific bio-reductant and stabilizer mediators that are responsible for the production and stabilization of metallic nanoparticles (MNPs).[78] The potential influence of various phytochemicals on NP synthesis will be discussed in the following sub-sections.

Influence of Phenolic Compounds in Nano-Synthesis

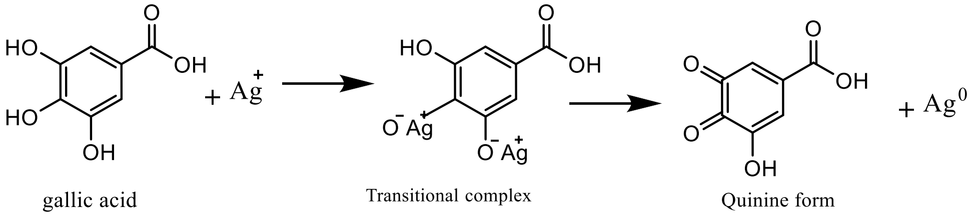
In the polyphenol family, phenolic acid plays a significant role in nano-synthesis. Its structure consists of a "phenolic ring and a functional carboxylic acid group". The nucleophilic aromatic rings of such compounds offer potent support for antioxidant activity and metal chelation.[74,79] Several known phenolic acids function as reductants in the biosynthesis of MNPs, including "caffeic acid, gallic acid and ellagic acid".[80,81] According to Raja et al, the development of a transitional complex between silver ions (Ag^+) and gallic acid's phenolic hydroxyl groups may enable the synthesis of silver nanoparticles (AgNPs). Thereafter, it transforms into quinine via the oxidation process, producing silver nanoparticles (Scheme 1).[82–84]

Wang et al, used *Melaleuca nesophila, Rosmarinus officinalis* and *Eucalyptus tereticornis* leaf extracts to create "iron-polyphenol" NPs, which were then FTIR-characterized. They demonstrated that charged iron combines with polyphenol to create complex nanoparticles, ranging in size from 50–90 nm, with an organic-looking surface.[85] The glycosidic water-soluble tannin in *Gloriosa superba* leaf extract aid the reduction of gold and silver ions into spherical nanoscale particles of gold and silver.[86] Jha et al, reported that the occurrence of "protocatechuic acid, catechol and ascorbic acid" accounts for silver bio-reduction, caused by the production of "H^+" by *Hydrilla* species of the hydrophyte genera. In a similar manner, in *Cyperus* sp., the ability of tautomerization of benzoquinone derivatives has been reported, leading to reduction of silver metal along with formation of coalescent cluster.[87]

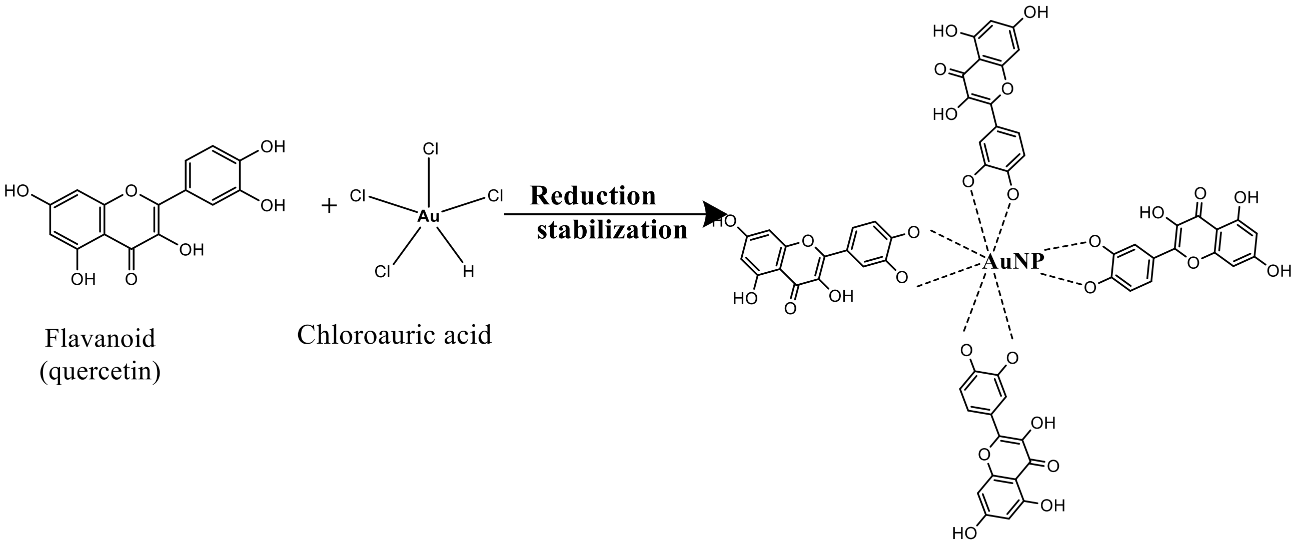
A family of secondary metabolites, known as flavonoids, are indeed the components of plant pigments. There exist numerous types of flavonoids that may be discovered in plants. The capacity of flavonoids to donate "H" atoms or electrons is associated with their reducing capability, which is regarded as the primary bio-reducing component of plant extracts.[88,89] Ahmad et al, suggested the H^+, created in the course of the keto-enol transformation of the flavonoids "luteolin and rosmarinic acid", could be employed to reduce silver metal ions and create silver nanoparticles.[90,91] Sahu et al, employed the poly-hydroxylated secondary metabolites of plants to bio-reduce Ag^+ ions to silver nanoparticles. Moreover, these flavonoids serve as capping agents, which impact on the antibacterial properties of silver nanoparticles.[92,93] Zhou et al, found that bio-compounds interacted with "tetrachloroaurate ion" via an ionic bond or electrostatic force. It was discovered that flavonoids and reducing sugars were the bio-reductants responsible for converting gold ion to gold nanoparticles (AuNP). Proteins were not found to be reductants in this study but were shown to be capping mediators in Au nanoparticles synthesis.[89] Raki et al, explained the mechanism for the formation and stabilization of AuNPs by the flavonoids present in plant extract. The neighboring hydroxyl groups of the polyphenolic molecules first bind with gold to create a chelate ring containing five members. The chelated "ortho-dihydroxyl" moieties are converted into quinones while simultaneously reducing the Au, due to the extremely high oxidation-reduction potential of Au. In order to create AuNPs, neighboring Au atoms collide, and the quinones and polyphenolic molecules work together to stabilize the resulting AuNPs (Scheme 2).[94] In a surfactant-free condition, Nasrollahzadeh et al, synthesized copper nanoparticles through the bio-reduction of copper ions using "quercetin" from the leaf extract of *G. biloba*.[95,96] A redox process caused the -OH in the reduced form of polyphenolics to change into a -C=O, which then caused the metal ions to undergo reduction. The metal nanoparticles are electrostatically stabilized by these carbonyl groups on the oxidized polyphenol.[95]

Influence of Terpenoids During Nano-Synthesis

Terpenoids are obtained from the essential oils of plants, which are intricate blends of volatile organic molecules that are produced by plants as secondary metabolites. Terpenoids are the oxygenated version of terpenes. They may operate as



Scheme 1 A plausible mechanism for AgNP synthesis using plant extract containing gallic acid.

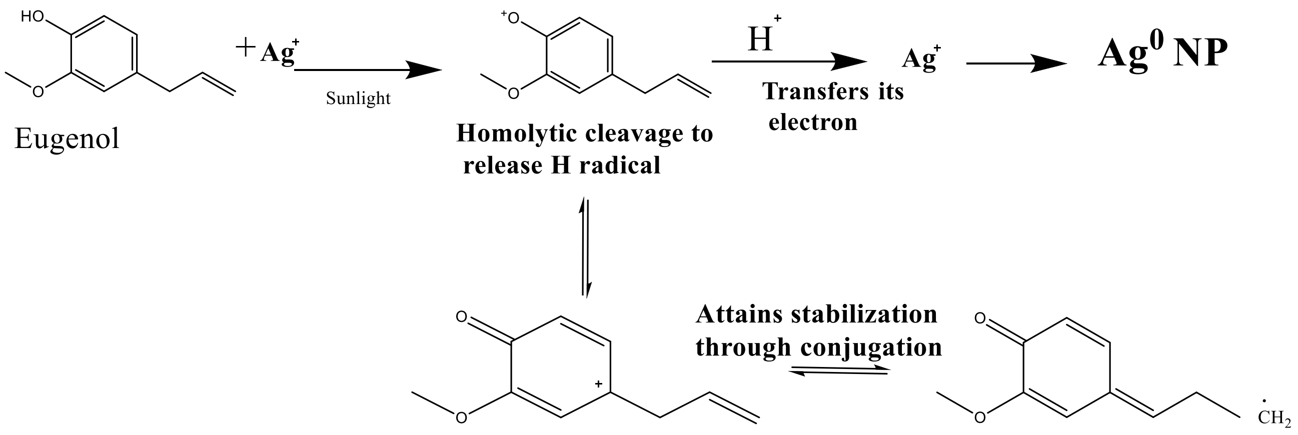


Scheme 2 Mechanism underlying the formation and stabilization of gold nanoparticles (AuNPs) using flavonoids present in plant extracts.

surface active chemicals that can stabilize and decrease nanoparticles, but the mechanism through which they participate in nanoparticle formation is not yet thoroughly understood.[97] Shankar et al, utilized *C. zeylanicum* extracts to reduce chloroauric acid and silver nitrate to gold and silver nanoparticles, respectively, due to the significant concentration of the fundamental terpenoid "eugenol".[98] According to Singh et al, the "eugenol" in *S. aromaticum* extract acts as a bio-reductant to yield gold and silver nanoparticles.[90,99] A clear, concise, effective and useful approach to the fabrication of silver nanoparticles was devised by Brahmachari et al, which entailed employing an *O. sanctum* leaf extract in water under the impact of direct sunlight.[100] The researchers postulated that, upon exposure to sunlight, the "phenolic O-H bond" of eugenol experiences a homolytic breakage to produce a H^+ radical, which then donates its electron to Ag^+ and converts to Ag^0 NP. With prolonged conjugation, the oxygen radical component is stabilized in the solution (Scheme 3).[95,100]

Influence of Proteins During Nano-Synthesis

Proteins may contribute to the biosynthesis and stability of metallic nanoparticles. The -C=O of amino acid sequences often serve as capping ligands for NPs, and FTIR spectra amply illustrate the involvement of diverse C=O groups on the surface of NPs, thus avoiding their aggregation and maintaining their stability during the aqueous phase.[95,101] Proteins and amino acids bearing exposed disulfide bonds and thiols function throughout biosynthesis as non-enzymatic reducers

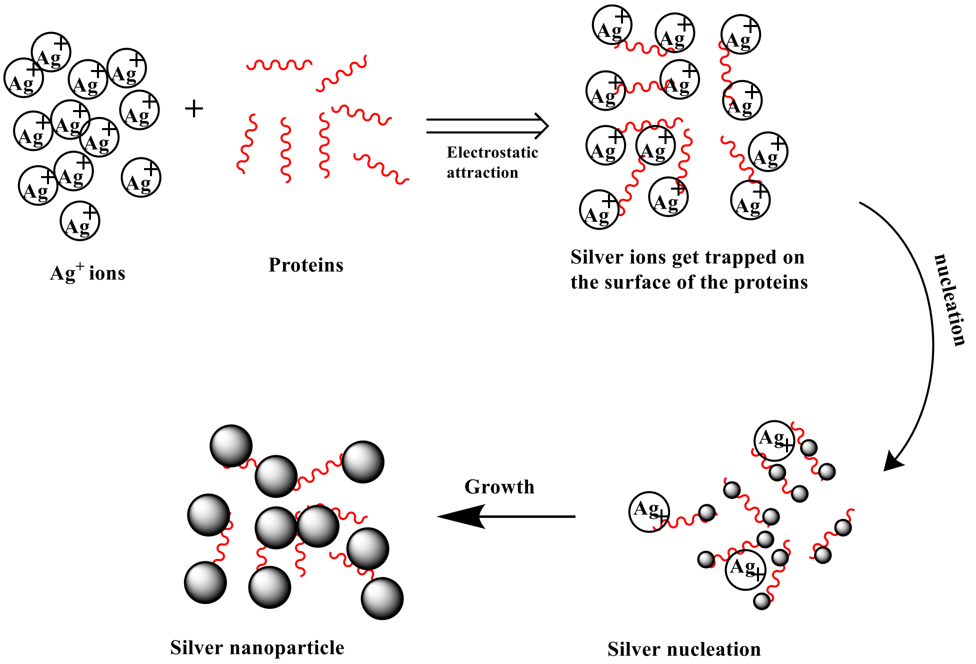


Scheme 3 Photo-induced bio reduction of Ag^+ to Ag^0 nanoparticles using biological agents.

and stabilisers.[95,102] A tripeptide sequence that contains a "C-terminus with tyrosine remnants" that acts as a reductant was used by Bhattacharjee et al, to create gold nanoparticles. This sequence contains an open "N terminal" that may be linked to the developing nanoparticles and generate permanent gold nanoparticles.[103] Li et al, postulated that, during the biosynthesis of AgNPs using *Capsicum annuum* extract, the electrostatic interactions cause the silver ions to become trapped on the surface of the peptides. These silver ions are reduced by the protein, which leads to changes in the 2° structure and the formation of silver nuclei. These nuclei grow further through the accumulation of ions. The versatile protein-biomolecule interaction that was found in the reaction conditions may have contributed to the formation of the sturdy silver nanoparticles (Scheme 4).[104] Stabilizer proteins offer advantages over polymers and surfactants, such as being lower cost, more environmentally friendly and not needing complicated processes. They can also serve as an anchorage layer for medications or genes that need to be introduced into living cells.[95,105]

Physicochemical factors affecting Green Synthesis

A number of factors are associated with the synthesis of NPs utilizing different plant extracts, that influence the nanoparticle's shape and dimension. Even these factors have a straight relation with the characterization procedures of nanoparticles as well as their application. The "adsorbate" type and catalyst activity have a huge impact on the synthesized nanoparticles, as reported by various researchers.[106,107] Also, the time and environment of the reaction have a huge impact on the synthesized nano-material.[107] In addition, the temperature, pH, extract concentrations, raw materials size and methodology employed to synthesize the nanomaterials also influence the resulting products.[108] Indeed, as the temperature of the reaction rises, the particle size also increases, suggesting that the Ostwald ripening, from which the larger sized particles grow, is due to the dissolution of the smaller ones.[109] The phytochemicals present in plant extracts are of chief importance in boosting dispersion and eventually decreasing agglomeration.[110] Moreover, it was believed and later confirmed that these phytochemicals are the deciding factors regarding the origin of novel properties of synthesized materials and play a major role in green synthesis.[111,112] Furthermore, the effect of salt's concentration on the morphology of different metallic particles has been reported by several researchers.[113,114] Some of the major factors that influence the preparation of nanomaterials are summarized below in Table 2 and Figure 2.



Scheme 4 The green synthesis of AgNPs utilizing plant extract-derived proteins as efficient reducing agents.

Table 2 Major factors influencing the synthesis of nano-material

Sr. No.	Factor(s)	Description
1.	**Method or Technique**	Nanoparticles can be shaped in a number of ways, viz. physical, chemical and biological methods. Biological methods have advantages over traditional methods, being non-toxic and eco-friendly.[48,49]
2.	**pH**	At pH ranging from 3 to 6, nanosized materials are less stable due to aggregation of nanoparticles. At pH lower than 3, protonated forces of all molecules work against electrostatic interactions, making them more stable Similarly, pH above 7 causes repulsion of aggregated molecules due to deprotonation.
3.	**Temperature**	In physical approaches, the temperature range should be more than 350°C while it should be lower than 350°C for chemical synthesis. In contrast to these methods, green synthesis requires temperature below 100°C. Synthesized nano-sized materials and their nature can be determined by the reaction temperature.[108]
4.	**Pressure**	Pressure is an important parameter for constructing nanoparticles. At ambient pressure, metal ions reduce significantly faster using biological agents.[50]
5.	**Time**	The time is another significant parameter having an impact on the rate of construction of nanoparticles employing biological agents.[51,52] Synthesis process and storage conditions have great influence on the aggregation of nanoparticles; constructed nanoparticles may shrink or get enlarged if stored for a prolonged time, leading to a change in their functioning.[52,53,106,115]
6.	**Particle Shape and Size**	One of the most important parameters influencing the synthesis as well as functionality of nanoparticles is its size and also its shape. Generally, if the size of nanoparticles is reduced, there is a decline in the melting point of constructed particles is observed.[106]
7.	**Pore Size**	The porosity of formed nanosized material has a huge impact on its quality as well as its applications. Exploiting this parameter, different molecules of biological origin could be bound onto the surface of nanomaterials and could be utilized for applications such as drug delivery.[107]

Synthesized Nano-Sized Materials and Their Characterization

When synthesizing nanoparticles, a number of challenges emerge with regard to characterizing and describing them, so it becomes important to choose an appropriate method for characterizing nanoparticles from among the existing techniques for determining their size, shape, aggregation, chemistry, crystallinity, orientation, fractal dimensions, dispersion and other parameters.[107] In this sense, various analytical methods have been employed to characterize in detail the properties (both chemical as well as physical) of green synthesized nanoparticles. Recently, Catalano et al, highlighted the necessity to develop validated procedures for the characterization of nanomaterials that have been synthesized following green practices to achieve their sustainable, safe application.[33] In this sense, techniques that are frequently employed in this field are "Scanning Electron Microscopy", "Transmission Electron Microscopy", "Fourier Transform Infrared Spectroscopy", and "X-ray Diffraction", among others. A list of techniques is presented in Table 3 below, providing some insight into the methods.

Plant vs Chemical Synthesis: Advantages for Biomedical Applications

Recent studies that have compared the plant-based green synthesis of nanoparticles with chemical methods have consistently demonstrated the advantages of the former. Green synthesis offers a sustainable, environmentally friendly approach to synthesizing nanomaterials, including metal and metal oxide nanoparticles, with wide-ranging applications.[123] Plant-based green synthesis ensures non-toxic, biocompatible nanoparticles, making it a safe, eco-friendly alternative to chemical methods, particularly with regard to biomedical applications.[124,125] In relation to this, Sabeena et al, conducted a comparative study of the green and chemical synthesis of CuO-NPs, evaluating their in vitro and in vivo bioactivity and toxicity in zebrafish (*Danio rerio*) embryos. The green synthesis method utilized a leaf extract from *Salacia reticulata*, which acted as both a reducing and capping agent, enabling the conversion of copper ions to CuO-NPs and ensuring their stability. In contrast, the chemical synthesis method employed sodium hydroxide. The in vitro assessments revealed that the green CuO-NPs exhibited higher antibacterial activity against both Gram-negative

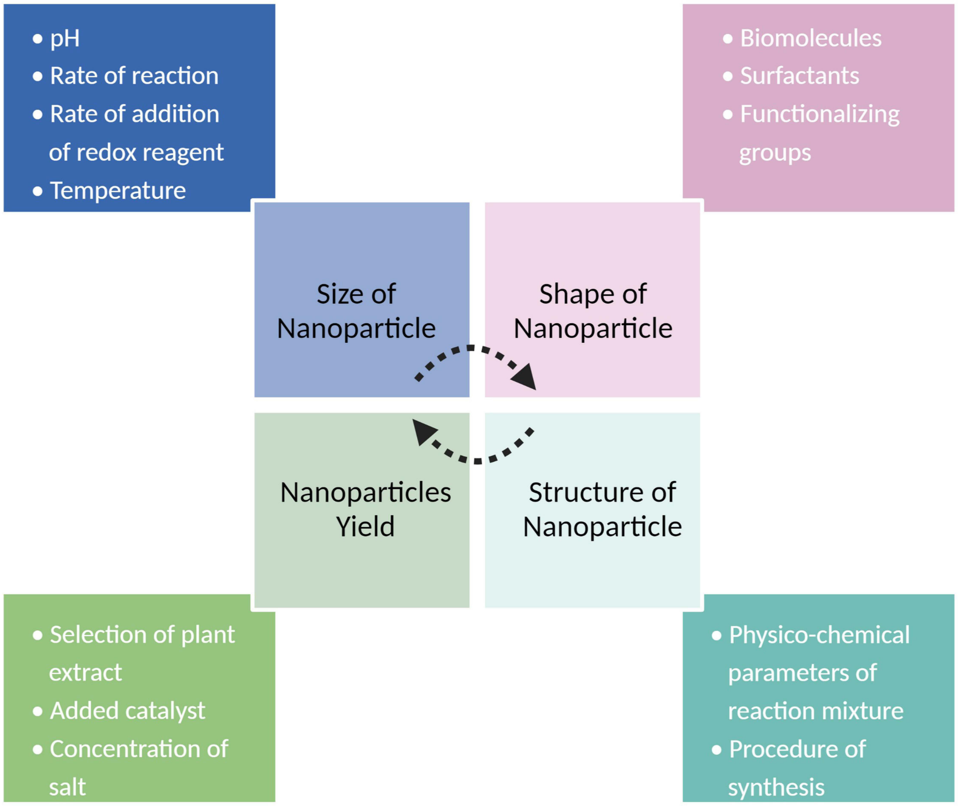


Figure 2 The impact of diverse factors on the morphology and yield of nanoparticles.
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and Gram-positive bacteria, increased cytotoxicity in human breast cancer cells (MCF-7), and greater antidiabetic as well as anti-inflammatory effects compared to the chemically synthesized CuO nanoparticles. Notably, the green CuO-NPs demonstrated reduced toxicity in zebrafish embryos. These findings highlight the significance of environmentally friendly green synthesis for CuO nanoparticles in diverse biomedical applications.[126] In another study, Sudhasree et al, performed a comparative analysis of nickel nanoparticle synthesis via the chemical and green routes to evaluate the biological and toxicological effects of nickel nanoparticles. Chemical synthesis involved the use of polyethylene glycol and hydrazine

Table 3 An assortment of techniques involved in the characterisation nanoparticles with associated rationale(s)

Parameter	Method	Purpose	References
Nanoparticle's formation	UV (Ultraviolet-visible) spectrophotometry	To evaluate structure, size, stability of nanoparticles including their aggregation	[48,54]
NPs morphology and size	TEM (Transmission electron microscopy)	For the determination of morphology (size and shape) as well structural allography of NPs	[55,108]
	High-resolution TEM (Transmission electron microscopy)	For determining atom's arrangement and local microstructures	[51,52]
	SEM (Scanning electron microscopy)	Direct examination of morphology	[53,56,106]
	AFM (Atomic force microscopy)	To determine size, surface texture or morphology	[55,107]
	DLS (Dynamic Light Scattering)	To determine the distribution of particle size	[56,107,108]

(Continued)

Table 3 (Continued).

Parameter	Method	Purpose	References
Charge on surface and surface related study	Zeta potential	To determine the charge on surface and stability of the NPs (colloidal)	[57]
	FT-IR (Fourier-transform infrared-spectroscopy)	Characterization of function groups present over the plane of particles	[48,52,56]
	XPS (X-ray photoelectron spectroscopy)	Used to determine reaction mechanism occurring on nanoparticle's surface and characterization of involved bonding	[52]
	Thermal gravimetric analysis	To confirm the binding efficiency of coating on the nanoparticle's surface	[52]
Crystallinity	XRD (X-ray diffraction)	Used for the determination of crystallinity of nanoparticles	[54,107,108]
Magnetic properties	VSM (Vibrating sample magnetometry)	Used to evaluate magnetic nanoparticle's magnetization	[52]
	Superconducting-quantum-interference device magnetometry	Verify the magnetic nanoparticle's magnetic properties	[52]
Other techniques used in nanotechnology	Chromatography	Affinity (towards mobile phase) based separation of nanoparticles	[108,116]
	X-ray spectra (Energy dispersive)	Used to determine nanoparticle's elemental composition	[48,50]
	Field-flow-flotation	Magnetic nanoparticles are separated on the basis of magnetic susceptibility	[51]
	Centrifugation techniques	Density gradient separation of nanoparticles	[117–119]
	Laser-induced breakdown detection	To examine colloidal concentration and size determination	[120,121]
	Mass spectrometry	Depth profiling, characterization of size and charge state	[122]

hydrate as stabilizing and reducing agents, while green synthesis utilized the aqueous root extract of *Desmodium gangeticum* without any additional agents. The characterization techniques revealed that both methods produced similar nanoparticles, but that green-synthesized Ni-NPs exhibited a smaller size and better uniformity. The green-synthesized Ni-NPs demonstrated significant antioxidant and antibacterial activity. Additionally, the toxicity assessments of the animals and cell lines confirmed the non-toxic nature of the Ni-NPs that had been synthesized through the green route. This study highlighted the comparable biological activity and lower toxicity of green-synthesized nickel nanoparticles compared to those that had been synthesized chemically.[127]

Additionally, plant extracts facilitate the controlled synthesis of nanoparticles, allowing a precise control of their size, shape and composition, along with the presence of natural stabilizers and reducing agents for enhanced biomedical compatibility.[128] A comparative analysis of green synthesis and chemical synthesis of SiO_2 NPs was carried out by Rahimzadeh et al, using *Rhus coriaria* L. extract and sodium metasilicate. Characterization techniques, such as FTIR, UV-Vis, XRD, FESEM, EDX, zeta potential, DLS, TGA and DSC, were employed to analyze the structure, thermal properties, and morphology of both types of nanoparticles. The results demonstrated that the green-synthesized SiO_2 nanoparticles outperformed the chemically synthesized ones. The researchers concluded that the presence of phytochemicals in *Rhus coriaria* L. extract enhanced the stability, improved the thermal properties, and increased the surface area of the nanoparticles.[129]

Abdelmigid et al, further suggested the equivalent antimicrobial efficacy of synthesized silver nanoparticles (Ag-NPs) using both chemical and biological methods. In this study, trisodium citrate, pomegranate fruit peel extract and coffee ground waste extract were used as the reductant agents. Ag-NPs that had been synthesized chemically (AgNPs_Chem) exhibited higher stability and negativity of the zeta potential compared to Ag-NPs synthesized using coffee ground waste extract (Ag-NPs_CE) and pomegranate peel extract (Ag-NPs_PPE). All the synthesized Ag-NPs showed antimicrobial activity against *Enterobacter aerogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa* and methicillin resistant *Staphylococcus aureus*. The most effective concentration was found to be 8 mg/mL, with the Ag-NPs demonstrating higher efficacy against *K. pneumoniae*. This study supports the eco-friendly synthesis of Ag-NPs using agro-waste as a viable alternative to chemical methods. The biologically synthesized Ag-NPs exhibited similar antimicrobial properties to their chemically synthesized counterparts, suggesting the potential for sustainable nanoparticle production.[130,131] Correspondingly, Aravind et al, synthesized titanium dioxide nanoparticles (TiO_2 NPs) using both chemical and green synthesis methods. The green synthesis involved using jasmine flower extract as a reducing and stabilizing agent. The TiO_2 NPs exhibited a rutile phase, with a crystalline size of 31–42 nm. UV-Visible spectroscopy confirmed their presence in the visible spectrum. SEM images showed spherical-shaped NPs, arranged randomly. The green-synthesized TiO_2 NPs demonstrated higher photocatalytic degradation efficiency for methylene blue dye compared to chemically synthesized NPs. They also exhibited enhanced antibacterial activity against both gram-positive and gram-negative strains. These findings suggest that the green-synthesized TiO_2 NPs possess the potential for application in environmental and biomedical fields.[132]

In addition to the points noted above, the plant-based, green synthesis of nanoparticles is cost-effective, utilizing readily available plants instead of expensive chemicals or metal precursors. It allows diverse nanoparticles' compositions and surface functionalities, offering a high level of tolerability, reproducibility and biocompatibility. Plant extracts enable precise control over the size, shape, and composition while at the same time acting as natural stabilizers and reducing agents. Notably, combined plant extracts can exhibit synergistic effects, thus enhancing nanoparticle properties. Therefore, plant-based green synthesis provides a cost-effective, versatile and controlled approach for synthesizing nanoparticles with diverse biomedical applications.[128,133,134]

Bio-Derived Nanomaterials and Future Prospects

The ability of living things to produce nanoparticles and nanodevices with a variety of applications is vast (Figure 3). In the reaction mixture, it is possible to produce nanoparticles and nanodevices with a specified form and size, ranging from simple microbes to highly complex organisms. Although nano-biotechnology remains in its infancy, the numerous examples used to demonstrate this science and its implications in this article will draw readers' attention to its potential uses. Various researchers have suggested that diverse reductases from these species fulfil a pivotal function in the construction of nanoparticles of various shapes and sizes, although far more research is needed to determine the optimum method for creating nanoparticles using living things.[108]

Currently, it is vital to create and develop unique drugs due to the numerous limitations imposed on the conventional procedures, such as their escalating cost and perniciousness. The opportunity to use a variety of nanosized materials in a more environmentally responsible manner, that is also economical, readily accessible, and secure without any involvement of harsh substances (chemicals), thus opens up a fresh avenue. Nanotechnology has advanced rapidly over the past decade, fostering healthcare and industrial uses, such as drug administration, imaging, and detection. According to the literature, it appears that in vitro research on bio-derived nanomaterials has taken place, but there have been no reports of in vivo uses. The potential toxicological processes of metallic NPs are also poorly understood. Therefore, before embarking on preclinical research, extensive in vivo experiments should be conducted to produce figures that represent nano-structured medicine's behavior.

The number of applications for biologically driven nano-sized materials will increase, and are anticipated to reveal more about their long-term effects on people, animals and the ecosystem. To fully comprehend the true mechanism of nanomaterials at the molecular level and the associated dynamics contained by bodily tissue, more research is needed. Metallic nanoparticles produced through biosynthesis will significantly impact the nanodrug business and provide other commercial applications in the coming years.

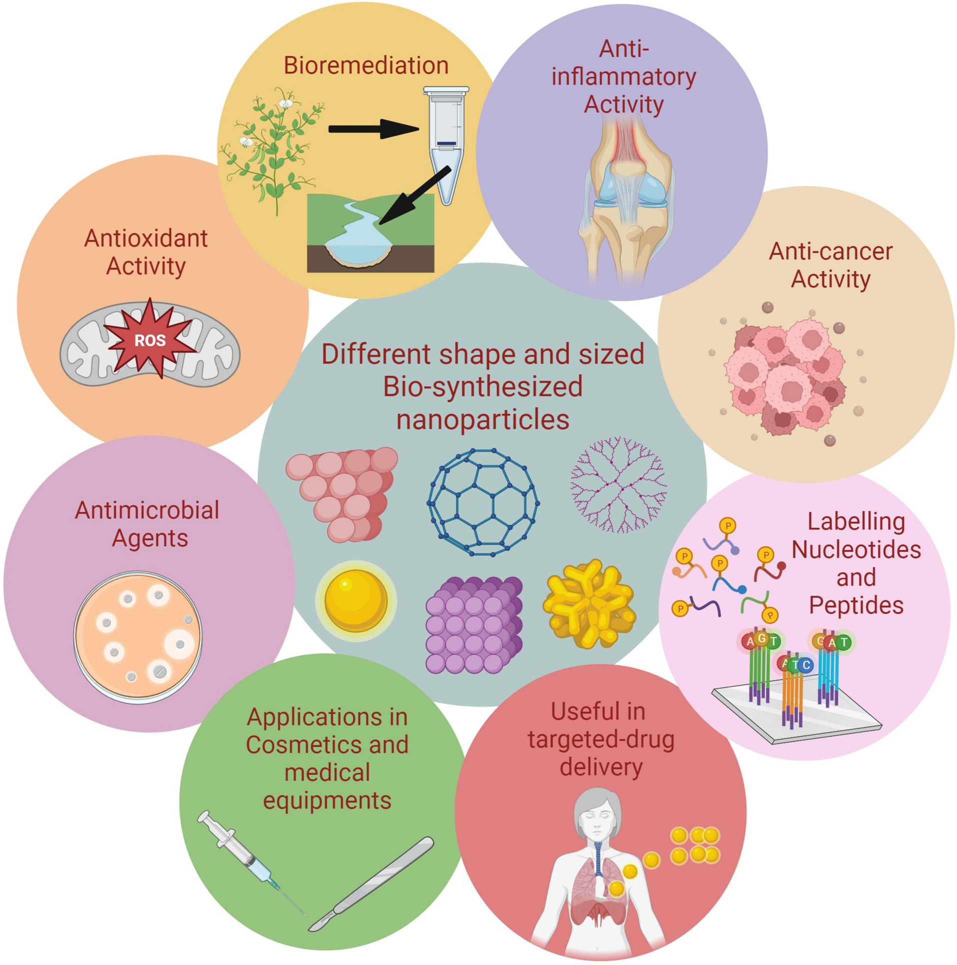

Figure 3 Illustrative representation of different sized and shaped nanoparticles with their potential application.
Note: Created with BioRender.com.

Potential Applications of Synthesized Nanomaterials

Therapeutic Application of Nanoparticles

Anti-Bacterial Activities of Metallic Nanoparticles

Numerous studies are presently being conducted worldwide to explore how metal and metal oxide nanoparticles interact with bacteria. Researchers have demonstrated that unbound metal nanoparticles cause the bacterial surface's outer membrane to dissolve in a hazardous manner, while the main mechanism related to metal oxide nanoparticles is oxidative stress brought on by reactive oxygen species (ROS).[135] According to the literature, Ag NPs cause perforations and openings to appear in the bacterial membranes by releasing ions following interactions with the enzyme's disulphide or sulfhydryl groups, and ultimately break off the metabolically important pathways, causing bacterial cell death.[136] Several researchers have found that ZnO NPs increased the production of ROS on the membrane's surface, which led to membrane malfunction and bacterial cell death.[137] In the case of TiO_2 NPs, a comparable means of oxidative stress, mediated by ROS production, has already been recognized. It has been demonstrated that TiO_2 NPs can generate ROS, which can in turn alter the fluidity and stability of the bacterial cell wall by causing lipid peroxidation. Gold nanoparticles have been found to be effective against several bacterial strains, including *Pseudomonas aeruginosa* and *Staphylococcus aureus*. They can disrupt the bacterial cell membrane and inhibit bacterial growth. In a recent study, gold nanoparticles were found to be effective against multidrug-resistant strains of *Acinetobacter baumannii*.[138] Copper nanoparticles have been shown to exhibit strong antimicrobial activity against a wide range of bacterial strains, including *E. coli* and *Salmonella*. They can disrupt the bacterial cell membrane and interfere with the bacterial DNA replication. In a recent work, copper nanoparticles were found to be effective against drug-resistant strains of *Pseudomonas aeruginosa* (Figure 4).[139]

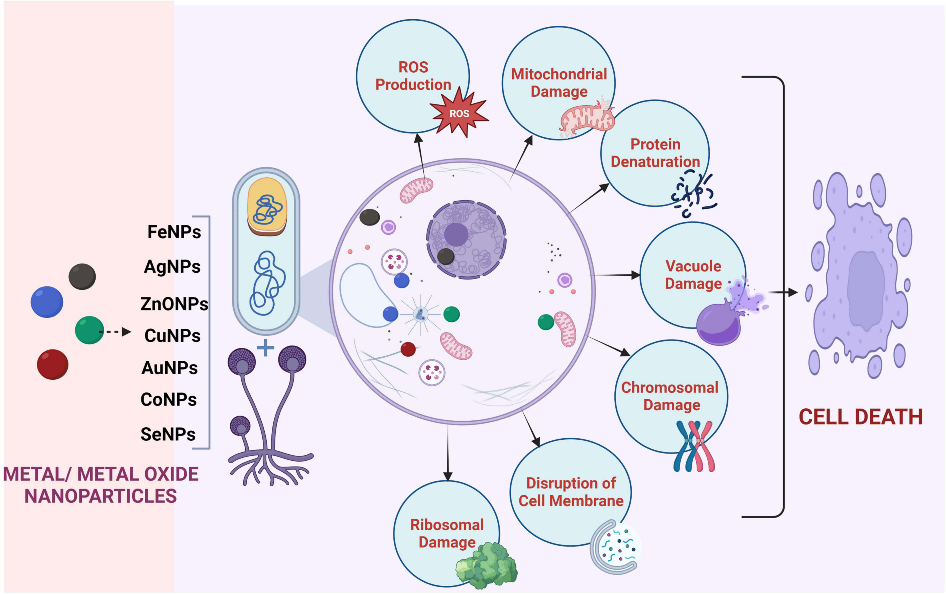

Figure 4 Diverse mechanisms involved in the antimicrobial activities exhibited by metal and metal-oxide nanoparticles.
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Anti-Fungal Activities of Metallic Nanoparticles

The most extensively researched nanoparticles for preventing the growth of fungi that are pathogenic to various plant species are Ag and Cu. Other metal nanoparticles, such as Se,[140–142] Ni,[143,144] Mg,[144] Pd[145] and Fe,[146] have been tested as antifungal agents, and the findings have been encouraging. Se nanoparticles were recently tested in vivo at dosages ranging from 0–1000 ppm against *S. graminicola*. Approximately six strains of species belonging to *Trichoderma* (*T. longibrachiatum, T. atroviride, T. asperellum, T. harzianum, T. brevicompactum* and *T. virens*) were employed to create these nanoparticles, using filtrates of culture and the lysates of the cells as well as the cell wall in a crude form. *T. asperellum* in culture filtrate produced superlative results, revealing the ability of Se-based nano-sized-particles to prevent the germination of fungi.[142] Another study used *T. viride* biologically to create Se nanoparticles, which were then tested in vitro against *A. solani* at various concentrations (50, 100, 200, 300, 400, 500, 600, 700 and 800 ppm). The growth of the fungus was shown to be inhibited by Se nanoparticles at 800 ppm.[140] Finally, the effectiveness of chemically produced Se nanoparticles against certain strains of fungi (*D. longicolla, M. Phaseolina* and *S. sclerotiorum)* was assessed at variable doses (100, 50, 10, 5, 1, 0.5 and 0.1 ppm). The Se NPs restrained the growth of *D. longicolla* at concentrations up to 10 ppm and of *M. phaseolina* at concentrations of 50–100 ppm. For *S. sclerotiorum*, however, the various doses failed to exhibit any kind of inhibition, instead permitting the pathogen to proliferate and develop.[141]

The Ability of Nanoparticles to Reduce Inflammation

An essential component of the wound healing process is "anti-inflammation". This is a cyclic process that results in the production of inter leukines and cytokinins like immuno-responsive substances, usually produced by B and T lymphocytes, and macrophages, among other keratinocytes.[147] The endocrine system secretes a variety of inflammatory mediators, including enzymes and antibodies. The key immune organs also release other cytokines, interleukin-1 and 2, which have a capacity to reduce inflammation. These agents that reduce inflammation promote healing.[148] Inflammatory mediators also regulate the biochemical processes and eventually control the spread of illnesses. Biosynthetic Au nanoparticles improve tissue regeneration and wound healing processes in inflammatory function.[149]

The following are some of the ways in which nanoparticles can reduce inflammation:

1. Targeted drug delivery: Nanoparticles can be engineered to deliver drugs directly to inflamed tissue, thereby reducing inflammation without affecting healthy tissue. For example, in one study, researchers developed chitosan

nanoparticles that were able to deliver curcumin, a potent anti-inflammatory agent, to the colon, where it reduced inflammation in a rat model of inflammatory bowel disease.[150,151]

2. Inhibition of inflammatory cytokines: Nanoparticles can also be used to inhibit the production of pro-inflammatory cytokines, which play a key role in the inflammatory response. For example, a study showed that gold nanoparticles had the ability to inhibit the production of tumour necrosis factor-alpha (TNF-alpha), a pro-inflammatory cytokine, in macrophages.[152]
3. Scavenging of reactive oxygen species (ROS): Nanoparticles can also scavenge ROS, which are highly reactive molecules that contribute to inflammation.[153] For example, a work reported that cerium oxide nanoparticles were able to scavenge ROS and reduce inflammation in a rat model of acute lung injury.[154]

While nanoparticles show promise as anti-inflammatory agents, it is important to note that further research is needed in order fully to understand their potential benefits and risks. It is important to ensure that any nanoparticles used in medical applications are safe and do not cause unintended harm to patients.

Investigations into the Role of Plant-Mediated Nanoparticles in Cancer Prevention

Raghunandan et al, investigated and reported the in vitro anti-cancer effectiveness of biofunctionalized nano-sized-particles of Au and Ag nanoparticles against four distinct cell lines of cancer, including human cancer cells related to the large intestine (colorectal adenocarcinoma), human glomerular cells, leukaemia cells related to human bone marrow, and cells associated with the human cervix.[155] They claimed that clove bud extract in aqueous form, combined with AuNPs functionalized with flavonoids, offered greater anti-cancer potential than guava leaf extract. The irregular shaped, functionalized Au nanoparticles prepared using clove bud extract (aqueous) demonstrated acceptable anti-tumour activity on the tested cell lines, according to the MTT assay and microscopic investigations. The same extracts were used to create silver nanoparticles, but these lacked any anti-cancer properties. The MTT experiment showed that the cell lines of cancer were cytotoxic in a "dose-dependent" manner. Also, the anticancer impact of gold nanoparticles is caused by free radicals.[155]

Several studies have shown that plant-mediated nanoparticles can inhibit cancer cell growth and induce cell death, thereby preventing cancer development and progression. For example, nanoparticles synthesized from green tea leaves have been shown to inhibit the growth of breast cancer cells and induce cell death in colon cancer cells.[156] Similarly, nanoparticles synthesized from turmeric have been shown to inhibit the growth of prostate cancer cells and induce cell death in lung cancer cells. These nanoparticles are thought to work by targeting and damaging cancer cells while leaving healthy cells unharmed. One of the advantages of plant-mediated nanoparticles as a potential cancer prevention strategy is their biocompatibility and low toxicity compared to synthetic nanoparticles.[26] Plant-mediated nanoparticles are also readily available and easy to synthesize, making them a cost-effective, sustainable alternative to synthetic nanoparticles.

Despite the promising results of preclinical studies, more research is needed to understand fully the mechanisms of plant-mediated nanoparticles and their potential applications regarding cancer prevention. Further studies should focus on the safety and efficacy of these nanoparticles in both animal and human studies, as well as their potential interactions with other drugs and therapies.

Green Nanoparticles: Targeting Cancer Cells and Mitochondria for Effective Cancer Treatment

Green nanoparticles have displayed great potential for use as targeted cancer treatments by specifically targeting cells and mitochondria, and offer several advantages regarding cancer therapy. Mitochondria, once considered solely responsible for energy production, have emerged as important drug targets in diseases like cancer. Their dysfunction plays a role in various human conditions. Targeting mitochondria with nanoparticles provides new therapeutic approaches, thereby overcoming the limitations of conventional drugs. In a mini-review, Tabish and Hamblin introduced the concept of "mitoNANO", which refers to the use of nanoparticles for targeting mitochondria. They explore the design and application of mitoNANO as a promising approach to advanced cancer therapies. MitoNANO has the potential to overcome drug resistance and minimize the side effects, making it an exciting avenue for future cancer treatments.[157]

George et al, established the cytotoxic effects of Rubus-conjugated silver nanoparticles (RAgNPs) on MCF-7 cells, with a focus on mitochondrial-mediated intrinsic apoptosis. The RAgNPs exhibit dose-dependent cytotoxicity, decreased proliferation and increased cell death. They induce nuclear damage, intracellular ROS production and apoptotic protein upregulation (caspase 3, Bax, and P53). These findings highlight the potential of RAgNPs to target mitochondria and trigger cell death through the intrinsic apoptosis pathway, making them promising candidates for anticancer drug development.[158]

In another study, the mitochondria-targeted delivery of chemotherapeutic drugs using TPP-Pluronic F127-hyaluronic acid (TPH) nanomicelles showed promise in overcoming multidrug resistance in cancer. PTX-loaded (a natural plant product derived from the bark of *Taxus brevifolia*) TPH (TPH/PTX) nanomicelles efficiently entered acidic lysosomes and underwent lysosomal escape, ultimately localizing to mitochondria in drug-resistant cancer cells. This leads to mitochondrial outer membrane permeabilization, cytochrome C release and caspase enzyme activation, resulting in significant antitumor efficacy in xenograft tumour models. This study highlights the potential of mitochondria-targeted nano-micelles as a nontoxic nanoparticle platform for combating drug-resistant cancers.[159]

Anti-Diabetic Management Employing Metallic Nanoparticles

The majority of medicines are obtained from nature and are herbal in nature. The care of diabetes and diabetic complications has a long history of the successful use of herbal medications.[160,161] It has been reported that a number of medicinal plants, including *Allium sativum, Asparagus racemosus, Azadirachta indica, Emblica officinalis, Eugenia jambolana, Gymnema sylvestre, Inula racemosa, Momordica charantia, Pterocarpus marsupium, Syzygium cumini, Tinospora cordifolia* and *Trigonella foenum gracecum* exhibited some effectiveness regarding the treatment of diabetes. Diabetes management has been reported to benefit more from the green synthesis of polymeric or metallic nanoparticles made from herbal products than from native crude materials.[162,163] Numerous commercially available, anti-diabetic medications are clinically equal to phyto-nanotherapy, which has greater biopharmaceutical properties. Additionally, a synergistic effect can be used by plant-metal nanoparticles to achieve special medicinal qualities. Green preparations of Ag, Au and zinc oxide (ZnO) nano-formulations have attracted considerable attention due to their ability to enhance the stability, pharmacokinetics and biopharmaceutical outcomes of plant-based chemicals in herbal drug formulations.[164] These advances aim to harness their augmented therapeutic potential regarding diabetes prevention and management.[165]

There has been a growing interest in the use of metallic nanoparticles for antidiabetic management. Metallic nanoparticles, such as gold, silver and platinum, possess unique physicochemical properties that make them promising candidates for drug delivery and therapeutic treatment. One approach is to use AuNPs to deliver insulin to the pancreas. In a study, an AuNPs-based insulin delivery system was able effectively to lower blood glucose levels in diabetic mice.[166] The AuNPs were coated with a polymer that protected the insulin from degradation and allowed it to be released in a controlled manner.

Another approach is to use silver nanoparticles to improve insulin sensitivity. A recent published study reported that AgNPs were able to improve insulin sensitivity in diabetic mice by reducing inflammation and oxidative stress in liver.[167] Platinum nanoparticles (Pt NPs) have also been investigated for their potential regarding antidiabetic management.[168] Alternatively, researchers developed a Pt NP-based glucose biosensor that could detect glucose levels in diabetic rat models. The biosensor was found to be highly sensitive and selective, with potential use as a diagnostic tool for diabetes.[169]

It should be noted, however, that the use of metallic nanoparticles in antidiabetic management remains in its infancy, and further research is needed to understand fully their potential benefits and risks. It is important to ensure that any nanoparticles used in medical applications are safe and do not cause any unintended harm to patients.

Other Applications of Bio-Derived Nanoparticles

Agriculture

The antibacterial action described above may also be useful for crop protection, when agricultural diseases are the focus. In particular, ZnO NPs have shown their potential for broad agricultural application by demonstrating activity against "plant pathogens" (both bacteria and fungi), obtained from *Citrus limon* (L.) Burm (against soft-rot bacteria). It is notable that TiO_2 NPs prepared utilizing lemon fruit exhibited an anti-bacterial action against *D. dadantii* that was comparable to ZnO NPs.[170]

AgNPs created from wheat extract helped to mitigate the detrimental effects of salinity stress considerably on wheat-crop by altering the concentration of "abscisic acid", ion-homeostasis and defense mechanisms embodying both enzymatic and non-enzymatic antioxidants.[171] Strikingly, ZnO NPs displayed less toxicity and an ability to strengthen flax seedlings' antioxidant defense mechanisms.[172]

Antioxidant Action

A range of cell biomolecules, such as DNA, polypeptides and membrane lipids, might experience oxidative injury resulting from high oxidative stress brought on by the deed of "mitochondria" and other internal or external causes. This deterioration can result in neurodegenerative disorders and senescence.[173] Antioxidants have the potential to stop these harmful processes and be utilised to manage ailments associated with ageing. Ag NPs made from leaf extract prepared using *C. carandas*,[174] nanoparticles of silver and gold attained from leaf extract of *C. inerme*[175] or nickel oxide-based nano-sized particles prepared using leaf extract of *Stevia rebaudiana*[42] have been documented for their antioxidant potential. The phytochemicals deposited on the surface of the NPs undoubtedly play a significant role in the reported antioxidant effect. For assaying antioxidant activity, usually, only one in vitro test is performed, such as a "DPPH-assay." However, "antioxidant activity" should not be validated by a solitary technique. The assessment of antioxidant activity, therefore, relies mainly on the associated reaction system, due to the intricate nature of phytochemicals.[176] The reliability of the findings from in vitro cell-free antioxidant testing must be restricted to the evaluation in the context of chemical reactivity, since in vivo substantiation is strongly advised.

Bioremediation

There are also descriptions of additional possible applications, including (i) "photo-catalytic" applications and (ii) "absorption" applications. Silver based nano-sized particles, prepared by the employment of *chamomilla*, exhibits strong activity against "Rhodamine B" when exposed to ultra-violet radiation, making them a potential wastewater treatment material.[177] The capacity to remove diverse both organic and inorganic pollutants has been demonstrated by magnesium oxide-based nano-sized particles generated from leaf extract of "Indian mallow" which also showed excellent photo-catalytic activity and effective absorption related properties against the high-density metallic element *viz*. Cr(VI).[175] Finally, it should be mentioned that reduced forms of graphene oxide, synthesised employing leaf extract of *Stevia rebaudiana*, were coated on "Palladium-silver" bimetallic nano-sized structures to facilitate photocatalytic H_2 synthesis.[178]

Challenges

The synthesis of plant-derived nanoparticles for various applications presents several challenges. Standardizing the extraction methods is crucial to ensure consistent, reproducible synthesis. The contamination and impurities in plant extracts must be effectively removed to maintain the purity and functionality of the nanoparticles. Scaling-up production while maintaining quality and stability is a significant consideration. Advanced characterization techniques specific to plant-derived nanoparticles are needed to understand their complex structures. Their long-term stability and storage, as well as regulatory considerations, must be addressed for their successful translation into clinical use. Batch-to-batch variability in composition also poses a challenge that needs to be minimized. Overall, interdisciplinary collaboration, method optimization and protocol standardization are essential if we are to overcome these challenges and unlock the full potential of plant-derived nanoparticles.

Conclusion

The synthesis of nanoparticles through plant-mediated green synthesis represents a significant advance in the field of nanoscience and green chemistry. This review paper provides an up to date comprehensive overview of the research conducted in this field, highlighting the advantages and potential applications of this eco-friendly approach. The utilization of plant extracts as reducing and stabilizing agents for nanoparticle synthesis offers numerous advantages over the traditional chemical methods, including cost-effectiveness, scalability and the absence of toxic contaminants, thus making plant-mediated synthesis a sustainable alternative to its counterparts. The use of renewable plant-based resources facilitates controlled synthesis processes, resulting in nanoparticles with enhanced size uniformity and stability making them highly suitable for various applications. Furthermore, the bio-inspired nanoparticles derived from plants exhibit intriguing pharmacological properties, such as biocompatibility and nano-dimensions, which make them highly promising for various biomedical applications and the targeting of specific cells in a controlled manner. These applications include drug delivery, disease management, agriculture, bioremediation, and other industrial applications.

While the plant-mediated green synthesis of nanoparticles has demonstrated tremendous potential, several challenges and areas for future research have been identified. The relation between metal salt concentration and nanoparticle yield, as well as the optimization of the parameters to overcome polydispersity, require further investigation. Understanding the chemical components and underlying mechanisms involved in the synthesis, action and stabilization of biological nanoparticles is crucial for their effective utilization. Moreover, addressing issues related to the distribution profile, excretion, clearance, biocompatibility and bioavailability of biological nanoparticles through conducting extensive in vivo trials and research is essential if we are to exploit their biomedical applications to the full. The convergence of green chemistry and nanotechnology has paved the way for the development of environmentally friendly nanomaterial synthesis methods, and plant-mediated nanoparticle production has emerged as a promising field, with further applications related to catalysis, agriculture, water treatment, biotechnology, electronics and other industries. Green plant-based nanoparticles offer potential benefits, related to areas such as phytopathogen treatment in the field of agriculture, and water disinfection for environmental clean-up. It is important to consider the long-term impacts of these nanoparticles on animals, humans, and the environment, however, and further research is required to address concerns regarding the accumulation and influence of green nanoparticles, ensuring their safe, sustainable utilization.

In conclusion, this review paper provides valuable insights into the scientific intricacies of the plant-mediated synthesis of nanoparticles. The adoption of green synthesis approaches using plant extracts as reducing agents has immense potential regarding cost-effective, environmentally friendly nanoparticle production, with significant pharmacological properties. It is hoped that this review will serve as a comprehensive resource for researchers and scientists working in the field, and inspire further exploration and innovation in this rapidly-growing area of nanoscience and green chemistry.

Acknowledgments

The authors extend their appreciation to the Deputyship for Research & Innovation, Ministry of Education in Saudi Arabia for funding this research work through the project number: IFP22UQU4420118DSR061.

Disclosure

The authors report no conflicts of interest in this work.

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