

**GREEN SYNTHESIS OF METAL NANOPARTICLES AND THEIR THERAPEUTIC APPLICATIONS - A REVIEW****Maryam Suhail Khan* and Bharati Gawade**

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This work is licensed under Creative Commons Attribution 4.0 International license.**ABSTRACT**

Green synthesis of metal and metal oxide nanoparticles has emerged as a sustainable and effective approach in nanomedicine, leveraging the bioactive compounds present in plants to produce nanoparticles loaded with plant extracts with enhanced therapeutic potential. This review aims to summarize recent research from publication year 2021-2025 (till date) on the reaction conditions of green synthesis of various metal and metal oxide phyto-nanoparticles to get a concise idea on their formulation. Relevant literature was retrieved from PubMed, ScienceDirect, Google Scholar, and other databases using keywords such as green synthesis, metal nanoparticles, metal oxide nanoparticles, antibacterial, anticancer, cardioprotective, wound healing, and antiviral activity. Investigations encompassing research articles and experimental studies were analyzed to highlight the multifaceted therapeutic applications of plant-mediated nanoparticles. The evidence on the phyto-nanoparticles demonstrates the efficacy in antibacterial, anticancer, cardioprotective, wound healing, and antiviral contexts, largely attributed to mechanisms such as microbial membrane disruption, apoptosis induction, tissue regeneration, oxidative stress modulation, and inhibition of viral polymerases and proteases respectively. This review emphasizes the role of green nanotechnology in combining eco-friendly synthesis with broad-spectrum biological activity and underscores the potential of plant-derived nanoparticles as emerging, effective and safe therapeutic interventions.

KEYWORDS: Green synthesis, Metal nanoparticles, Plant-mediated nanoparticles, Therapeutic applications, Anticancer activity, Antiviral activity.**INTRODUCTION**

Nanotechnology has emerged as a transformative field with profound implications across medicine, pharmaceuticals and environmental sciences. Nanoparticles, owing to their nanoscale dimensions (1–100 nm), have attracted significant scientific attention for their unique structural, physicochemical, and biological properties that differ substantially from bulk materials. Their high surface area-to-volume ratio, tunable morphology, and ability to be functionalized with diverse biomolecules make them highly versatile platforms in modern medicine and drug delivery.^[1] In recent years, particular emphasis has been placed on nanoparticle systems loaded with phytoconstituents derived from medicinal plants. Such phyto-loaded nanoparticles combine the therapeutic potential of natural bioactive

compounds with the favorable pharmacokinetic and delivery properties of nanocarriers.^[2] They offer distinct advantages including enhanced solubility of poorly water-soluble plant metabolites, improved stability against environmental degradation, prolonged circulation time, targeted delivery to specific tissues, and reduced systemic toxicity compared to conventional formulations. This synergistic approach not only addresses limitations associated with traditional phytotherapy but also opens new avenues for developing safer and more effective therapeutic agents. For the synthesis of nanoparticles themselves, multiple methodologies are available, spanning physical, chemical, and biological domains. Among these, the use of metal-based systems has gained prominence as an innovative route, enabling the design of functional

nanoparticles with tailored properties suitable for biomedical and pharmaceutical applications.^{[3][4]} Metal-based nanoparticles (MNPs) such as silver, gold, zinc oxide, iron oxide, copper, titanium dioxide, and palladium have been extensively investigated owing to

their diverse physicochemical and biomedical properties. Each of these nanoparticles demonstrate unique surface plasmon resonance, catalytic potential, antimicrobial activity, or magnetic properties, making them suitable for a wide range of therapeutic and diagnostic applications.

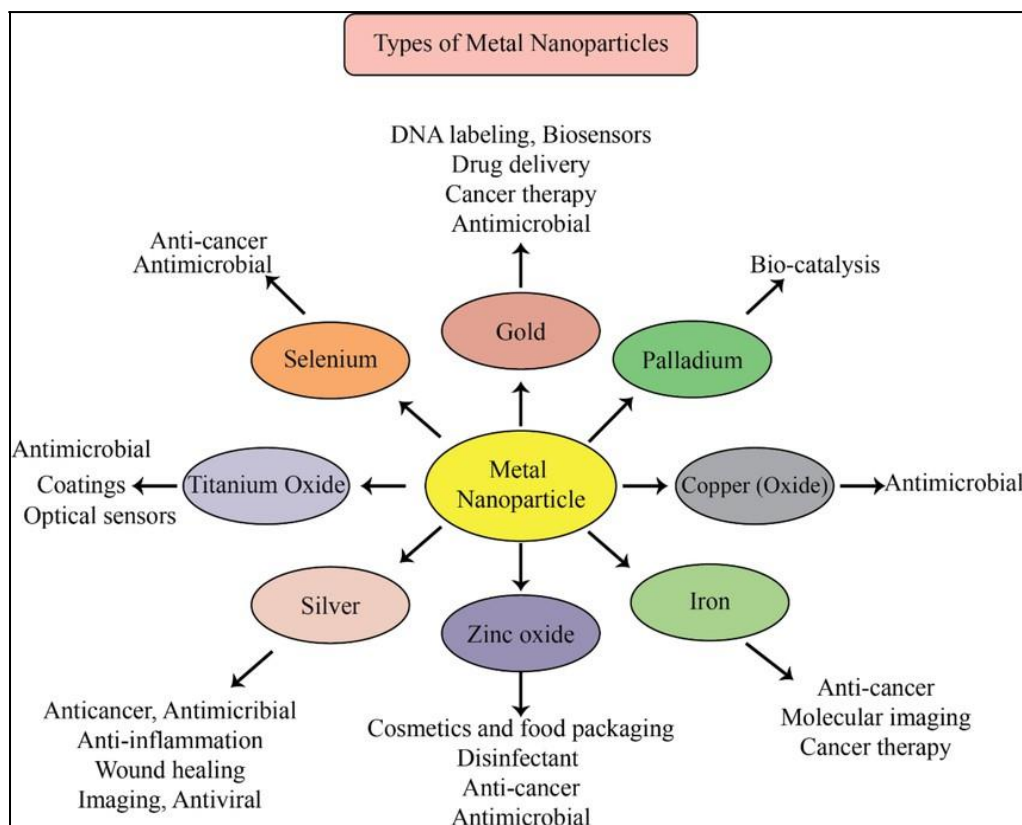


Fig. 1: Types of metallic nanoparticles and their probable applications.^[5]

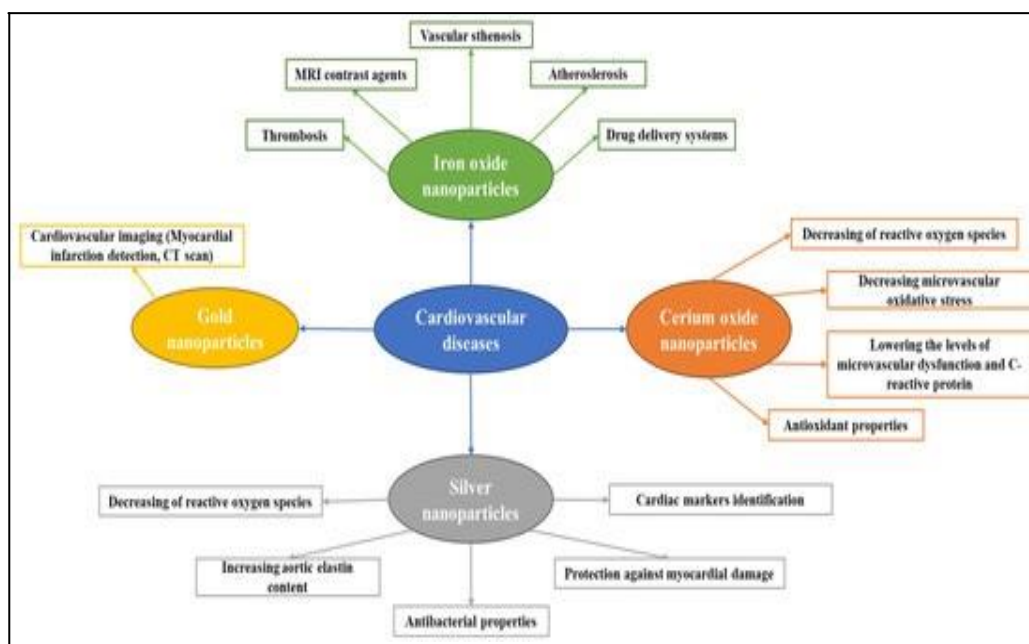


Fig. 2: Metal-based nanoparticles usage in CVDs.^[6]

Green synthesis of these MNPs using medicinal plant extracts has emerged as a sustainable alternative to

conventional physical and chemical methods. Plant-derived phytochemicals (alkaloids, flavonoids,

terpenoids, phenolics, and reducing sugars) act both as reducing agents to convert metal ions into metal nanoparticles and as capping agents that provide stability. However, the preparation parameters significantly affect nanoparticle yield, morphology, and stability. Critical factors include the ratio of plant extract to metal salt, pH of the reaction medium, temperature, stirring speed, reaction time, and purification steps.^{[7][8]} For example, higher plant extract-to-metal ratios often promote smaller particle sizes, while alkaline pH facilitates faster nucleation and growth.^[9] Elevated temperatures accelerate synthesis but may alter phytoconstituent integrity, whereas extended stirring improves homogeneity. Reported percent yields vary widely across studies, ranging from 40% to over 85%, depending on the plant system and synthesis conditions.^{[10][11]}

The present review aims to collate and critically analyze the different green synthesis procedures for metal-based nanoparticles utilizing medicinal plant extracts. By systematically documenting preparation parameters such as extract-to-metal ratios, pH, temperature, stirring speed, reaction time, and percent yield, this work seeks to provide researchers with a comparative framework to identify qualitative optimum conditions for nanoparticle synthesis. Furthermore, the review will highlight the therapeutic applications of various phyto-fabricated MNPs including antimicrobial, anticancer, anti-inflammatory, antioxidant, and cardioprotective effects, while also identifying promising therapeutic domains that remain underexplored. Ultimately, this synthesis of data is intended to serve as a practical guide for researchers in designing reproducible, efficient, and application-driven nanoparticle formulations.

LITERATURE REVIEW

Studies highlighting the advancement of green synthesis and its biomedical potential were identified through a structured search of scientific databases such as PubMed, ScienceDirect, Google Scholar, DOAJ, and Web of Science. The search focused on the scientific literature published between 2021 and 2025 using a combination of terms including green synthesis, plant-mediated synthesis, metal nanoparticles, therapeutic applications, anticancer, cardioprotective, anti-inflammatory, and antimicrobial. A total of recent peer-reviewed publications, including original research articles, systematic reviews, and meta-analyses, were retrieved and evaluated in line with the objective of this review. After screening for relevance and methodological rigor, the most pertinent studies were included to provide a comprehensive understanding of current developments.

This review emphasizes the biogenic methods employed for the synthesis of metal nanoparticles, wherein plant extracts serve as environmentally benign alternatives to conventional chemical routes. The selected literature underscores how these phytochemicals act as reducing,

stabilizing, and capping agents, enabling nanoparticle synthesis under mild conditions without toxic byproducts. In addition to detailing synthetic approaches, this review brings forward their therapeutic applications reported in the past three years. Plant-mediated silver, gold, and iron oxide nanoparticles have demonstrated cytotoxicity against diverse cancer cell lines, often through mechanisms involving reactive oxygen species generation, apoptosis induction, and targeted delivery.

Beyond anticancer activity, evidence from recent studies also suggests significant cardioprotective potential, where nanoparticles synthesized via green methods modulate oxidative stress, improve lipid profiles, and mitigate ischemic injury in experimental models. Anti-inflammatory effects have also been consistently reported, with green-synthesized metal nanoparticles attenuating pro-inflammatory cytokines and oxidative mediators, thereby offering potential in chronic inflammatory disorders. Parallel investigations highlight antimicrobial, wound-healing, and antioxidant properties, further broadening the scope of these nanomaterials.

Overall, this review highlights the progress made in green synthesis methods for metal nanoparticles while also outlining their growing importance in therapeutic applications. By focusing on the literature published between 2021 and 2025, it provides an updated perspective on the translational promise of these eco-friendly nanomaterials across diverse biomedical domains.

ADVENT OF GREEN SYNTHESIS

The synthesis of metal nanoparticles has traditionally relied on physical and chemical methods involving high energy input, toxic solvents, hazardous reducing agents, and stabilizers. While effective in producing nanoparticles of defined size and shape, these methods raised significant concerns regarding environmental pollution, high cost, and potential biological toxicity. With the increasing demand for sustainable and eco-friendly nanotechnology, researchers began exploring alternatives that align with the principles of green chemistry.^[11]

The advent of green synthesis emerged as a response to these limitations. It utilizes natural resources such as plant extracts, microorganisms, enzymes, and biodegradable polymers as reducing and stabilizing agents. Among these, plant-mediated synthesis became particularly remarkable due to its simplicity, scalability, cost-effectiveness, and the presence of diverse phytochemicals (e.g., flavonoids, terpenoids, polyphenols, alkaloids) that serve as both reducing and capping agents.^[11]

The plant extracts act as reducing agents in the synthesis of nanoparticles because they contain various biomolecules with functional groups like polyphenols, flavonoids, proteins, and carbohydrates. These

biomolecules can donate electrons to the metal ions, thereby reducing them and resulting in the formation of nanoparticles. These biomolecules, possessing groups like hydroxyl (-OH) and carbonyl (C=O), undergo oxidation themselves while performing the reduction of the metal ions.^[12]

This approach is considered remarkable because it integrates nanotechnology with biology, producing nanoparticles in a single-step, energy-efficient, and environmentally benign process. Unlike conventional synthesis, green methods avoid the use of toxic chemicals, thereby minimizing harmful byproducts and enabling safer applications in medicine, agriculture, food, and environmental remediation.^[13]

Plant-mediated synthesis uses aqueous or alcoholic extracts of leaves, flowers, roots, seeds, bark or fruit peels to reduce metal salts and simultaneously cap the newly formed nanoparticles. Phytochemicals, principally polyphenols, flavonoids, terpenoids, reducing sugars, alkaloids and proteins play dual roles as electron donors (reducing agents) and as steric/electrostatic stabilizers (capping agents) that determine nucleation, growth and ultimate colloidal stability. This approach is widely used for silver, gold, iron oxide, copper and zinc/titanium oxide systems owing to its simplicity, safety and facile scalability compared with classical chemical routes.^{[14][15][16]}

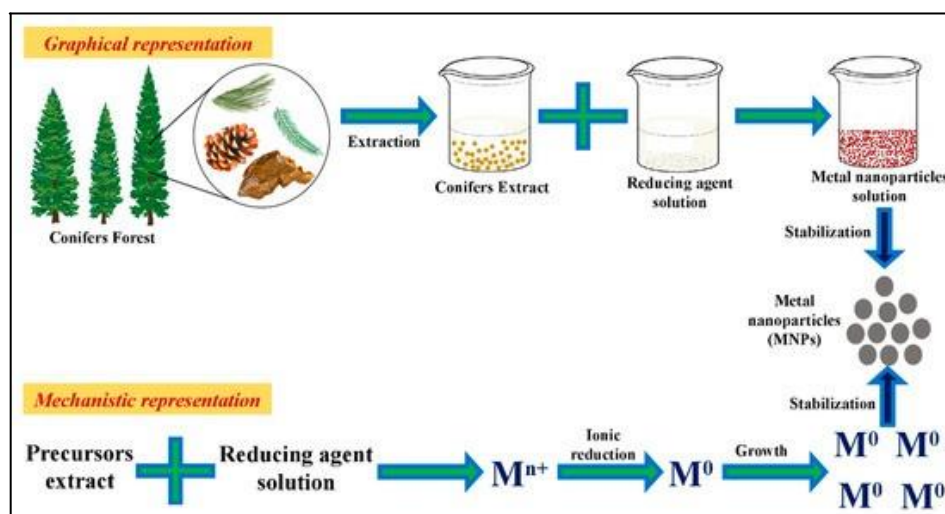


Fig. 3: Graphical overview of the green synthesis protocol using conifer extracts for synthesizing metallic nanoparticles.^[17]

Table 1: Green synthesis parameters of various metal nanoparticles.

Sr. no	Nanoparticle	Plant & part used	Ratio w/w (plant extract:metal)	Reaction Time	Average Particle size
1.	Silver NPs ^{[18][19]}	<i>Moringa oleifera</i> leaf ext ^[20]	0.5:1	60 mins	18 nm
2.	Copper NPs ^{[21][22]}	<i>Aegle marmelos</i> leaf extract ^[23] <i>T. chebula</i> dried fruit extract ^[24]	3.2:1 1.4:1	24 hrs with stirring 24 hrs at 750 rpm	32 nm 12 nm
3.	Iron oxide NPs ^[25]	<i>Vitex leucoxydon</i> leaf extract	16:1	180 mins at RT	45-100 nm
4.	Zinc NPs ^{[26][27]}	<i>Silybum marianum</i> seed extract ^[28]	2:1	120 mins at 80°C	52 nm
5.	Gold NPs ^[29]	<i>Equisetum diffusum</i> ^[30]	1.7:1	60 min at 80°C	68.8 nm

Table 1 compiles the different plant to metal ratios and reaction time involved in the green synthesis of Ag, Cu, Fe, Zn nanoparticles along with the particle size of the nanoparticles achieved in the existing peer-reviewed articles. The plant extract:metal ratios were calculated by finding weight of plant extract used by referring to the water soluble extractive values of the plant extracts acquired from existing literature.

Asif M. et al.,2022^[18] synthesized silver nanoparticles

containing *M. oleifera* leaf extract for its antimicrobial action against *E. coli*. Aqueous extract of *M. oleifera* leaves was used as the reducing agent and silver nitrate ($AgNO_3$) was used as the precursor for the synthesis of silver nanoparticles. For the reduction of Ag^+ ions, the leaf extract was added dropwise into 100 mL of 1 mM aqueous solution of $AgNO_3$ and heated 60-80°C for 60 mins. The color change was observed from dark brown to reddish brown which indicated the formation of silver nanoparticles. They measured the particle size using

Scanning Electron Microscope (SEM) and the particle size was found to be in the range of 10 to 25 nm and their average size was 18 nm.

Manimegalai S. et al., 2022^[19] synthesized silver nanoparticles using *Solanum trilobatum* leaf extract, for antioxidant and anti-inflammatory activities. The aqueous leaf extract of *S. trilobatum* served as both reducing and stabilizing agent; silver nitrate (AgNO_3) was used as the metal precursor. The extract and AgNO_3 were mixed at ratio 1:1 at ambient (room) temperature, and left to react. The color change indicating nanoparticle formation was from colourless to brown. The reaction time was short, with UV-Vis detection of the plasmon resonance peak (~430 nm) being observed as soon as 20 minutes after mixing. The average particle size (determined via transmission electron microscopy) was found to be 27.6 nm, and particles were spherical in shape.

Ali S.G. et al., 2023^[21] synthesized copper-oxide nanoparticles mediated by *Aegle marmelos* leaf extract for antimicrobial and photocatalytic applications. Aqueous extract of *A. marmelos* leaves was used as the reducing and stabilizing agent, and copper(II) sulfate was used as the metal precursor. For nanoparticle formation, 10 mL of the leaf extract was mixed with 90 mL of a 1 mM Cu(II) sulfate solution and the reaction mixture was stirred at ambient temperature for 24 h, during which a colour change was observed indicating nanoparticle formation. The product was centrifuged (10,000–12,000 rpm), the pellet dried, and characterized; transmission electron microscopy (TEM) showed nanoparticles with an average particle size ~ 32 nm.

Munusamy T. et al., 2023^[22] synthesized copper oxide nanoparticles using *Terminalia chebula* dried fruit extract for its antibacterial action. An aqueous extract of *T. chebula* was used as the reducing/capping agent, and copper(II) sulfate was used as the precursor. For nanoparticle formation, 40 mL of the fruit extract was mixed into 60 mL of 20 mM CuSO_4 solution and stirred at 750 rpm under ambient conditions for 24 h. A colour change from light golden to dark brown indicated nanoparticle formation. After centrifugation and washing, TEM showed particles in the size range ~10–12 nm.

Nahari M.H. et al., 2022^[25] synthesized iron nanoparticles using *Vitex leucoxylon* leaf extract for biomedical applications. An aqueous extract of *V. leucoxylon* leaves (cold extraction, 1:10 ratio of leaf to water) was used as the reducing (and stabilizing) agent, with ferric sulfate (Fe^{3+}) as the metal precursor. In the reduction step, 1 mL of plant extract was mixed with an equimolar 1 mM Fe^{3+} solution and the reaction was allowed to proceed; a colour change (from yellowish to black) occurred within 1 h, indicating nanoparticle formation. SEM imaging revealed spherical particles in the size range ~45 to 100 nm, while XRD-based

crystallite size estimation gave an average diameter of 136.43 nm. This paper also reported the zeta potential value of the synthesized iron nanoparticles. They exhibited a negative zeta potential of -10.6 mV (averaged over three measurements). A negative zeta potential means that the particles have a net negative surface charge, leading to electrostatic repulsion between them which enhances their stability and prevents aggregation.

Jahan N. et al., 2023^[26] synthesized zinc oxide nanoparticles using *Silybum marianum* (milk thistle) seed extract for pesticidal and antimicrobial application. An aqueous seed extract of *S. marianum* (10 g seed powder in 100 mL distilled water, heated at 80 °C for 20 min, left overnight, then filtered) was used as the reducing and stabilizing agent; zinc nitrate hexahydrate was used as the metal precursor (Zn^{2+} source). For nanoparticle synthesis, 10 mL of seed extract was added into 100 mL of 0.06 M $\text{Zn}(\text{NO}_3)_2$ solution, with sodium hydroxide to adjust pH to ~12, under stirring at 60–80 °C for 40–120 min. A milky white suspension formed, indicating nanoparticle formation. After centrifugation and washing, the average particle size measured by Zetasizer was ~51.80 nm, and the particles were monodispersed.

Mohammed Y.H.I. et al., 2023^[27] synthesized zinc oxide (ZnO) nanoparticles using *Cymbopogon citratus* (lemongrass) extract for antibacterial applications. An aqueous extract of *C. citratus* leaves was used as the reducing and stabilizing agent, and zinc nitrate hexahydrate was used as the metal precursor. For nanoparticle synthesis, the leaf extract was added to a 0.06 M aqueous solution of zinc nitrate hexahydrate, and the reaction was carried out at 60–80 °C for 40–120 minutes. The color change from colorless to white indicated the formation of ZnO nanoparticles. Particle size was measured using X-ray diffraction (XRD), and the particles were found to be in the range of 20 to 24 nm.

Assad N. et al., 2025^[29] synthesized gold nanoparticles (AuNPs) using *Equisetum diffusum* D. Don. (horsetail) extract to exhibit a range of activities including their broad-spectrum antibacterial, anticancer, antidiabetic, and antioxidant activities. The aqueous extract of *E. diffusum* served as both the reducing and stabilizing agent, while gold chloride (HAuCl_4) was used as the precursor. The extract was mixed with the gold salt solution and heated at 60–80 °C for 60 minutes. A color change from colorless to ruby red indicated the formation of AuNPs. Characterization using UV-vis spectroscopy, Fourier-transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), scanning electron microscopy (SEM), energy-dispersive X-ray (EDX) analysis, and dynamic light scattering (DLS) confirmed the stability, morphology, and crystalline nature of the nanoparticles. The average particle size was found to be approximately 68.8 nm.

Collectively, these studies highlight the versatility and effectiveness of plant-mediated green synthesis approaches, demonstrating that diverse plant extracts can serve as eco-friendly reducing and stabilizing agents to produce metal and metal-oxide nanoparticles with controllable size, morphology, and promising biological activities, while offering a sustainable alternative to conventional chemical synthesis methods.

THERAPEUTIC APPLICATIONS

In recent years, it has come to light that biogenic nanomaterials are not just benign alternatives; they have biological attributes which can be harnessed for therapeutic use. This is due to the combined effects of small dimensions, large surface area and surface functionalization with plant-derived phytochemicals to facilitate effective interaction between these NPs and biological systems. Therefore, green synthesized NPs have demonstrated promising activities in various biomedical fields, including antimicrobial, anticancer, antioxidant, and anti-inflammatory effects. Understanding these therapeutic potentials not only underscores the value of environmentally conscious synthesis but also highlights the role of nanotechnology in modern medicine.

Antimicrobial application

Ahmad S. et al. 2024^[31] synthesized nanoparticles using *Aconitum violaceum* extract showed promising activity in several therapeutic areas. Both gold and silver nanoparticles were effective against bacterial strains, particularly *Escherichia coli* and *Lactobacillus acidophilus*. Among them, silver nanoparticles demonstrated stronger antibacterial action, which aligns with their established broad-spectrum properties. The study also revealed notable antioxidant effects, with both types of nanoparticles able to scavenge free radicals in a concentration-dependent manner. Interestingly, gold nanoparticles performed better in the DPPH assay, while silver nanoparticles were slightly more effective in the PTIO test, pointing toward their complementary antioxidant potential. Beyond biomedical relevance, these nanoparticles were also capable of breaking down methylene blue dye under UV light, showing excellent photocatalytic activity and stability over repeated cycles. Together, these findings indicate that *A. violaceum*-based nanoparticles are promising as antimicrobial and antioxidant agents, with additional potential for eco-friendly environmental remediation.

Similar to Ahmad S. et al., more than eighty other articles reported antibacterial and antimicrobial activity of silver phyto-nanoparticles in the publishing year 2021-2025 (till date).

In this work, Imade et al. 2022^[32] explored an eco-friendly route to synthesize zinc oxide nanoparticles (ZnO NPs) using waste plantain peel extract as a reducing and stabilizing agent, and then tested their antibacterial properties. The resulting particles were

evaluated for antibacterial activity against *Salmonella enterica*, *Klebsiella pneumoniae*, *Bacillus cereus*, and *Staphylococcus aureus*. All strains were inhibited at 100 µg/mL, with *S. aureus* showing the greatest susceptibility. The antibacterial effect was attributed to reactive oxygen species generation, Zn²⁺ release, and membrane disruption, supported by phytochemicals in the extract. These findings highlight plantain-derived ZnO NPs as a sustainable, low-cost antimicrobial with potential applications in infection control and food safety.

Similar to Imade et al., more than forty other articles reported antibacterial and antimicrobial activity of Zinc oxide phyto-nanoparticles showing activity against various bacterial cell lines in the publishing year 2021-2025 (till date).

Elkhateeb et al. 2024^[33] reported a green synthesis of iron oxide nanoparticles (13–23 nm) using cabbage, turnip, and moringa leaf extracts. The plant phytochemicals not only stabilized the nanoparticles but also influenced their functional groups and mineral phases. The nanoparticles exhibited dose-dependent antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*, with stronger effects on *S. aureus*, likely due to differences in cell wall structure. Moringa-derived nanoparticles, with higher phenolic content, showed the most potent activity. The antibacterial effect is mainly attributed to oxidative stress via reactive oxygen species, potentially involving Fenton-like reactions. These biogenic nanoparticles offer a promising, low-cost, and safe approach for antibacterial applications, particularly in food preservation, though further studies on toxicity, stability, and practical use are needed.

Similar to Elkhateeb et al., four other articles reported antibacterial and antimicrobial activity of iron oxide phyto-nanoparticles in the publishing year 2021-2025 (till date).

Anticancer application

Rajagopal G. et al. (2021)^[34] synthesized copper nanoparticles using *Wrightia tinctoria* extract and demonstrated their selective anticancer potential. In vitro studies showed significant cytotoxicity against MCF-7 breast cancer cells with an IC₅₀ of ~119.23 µg/mL, while exhibiting much lower toxicity in noncancerous Vero cells (IC₅₀ ~898.75 µg/mL). Molecular docking supported these findings by revealing interactions of phytochemicals with cancer-related targets, and hemolysis assays confirmed low red blood cell damage, indicating good biocompatibility. These results highlight *Wrightia tinctoria* copper nanoparticles as promising candidates for safe and effective anticancer applications.

Similar to Rajagopal G. et al., four other articles reported anticancer activity of copper phyto-nanoparticles in the publishing year 2021-2025 (till

date).

In this article, Mohamad Sukri S. et al. (2023)^[35] developed zinc oxide–silver nanoparticles (ZnO–Ag NPs) using *Punica granatum* peel extract and demonstrated significantly enhanced anticancer effects compared to ZnO alone. The ZnO–Ag NPs inhibited proliferation of colorectal, lung, and cervical cancer lines in a dose-dependent manner, reaching full inhibition at ~31.25 µg/mL, whereas ZnO required > 500 µg/mL. At pH 9, they achieved the lowest IC₅₀ (15.12–16.11 µg/mL) among variants. The authors propose that the improved cytotoxicity is due to ROS generation from released Zn²⁺ and Ag⁺ ions, leading to oxidative stress-mediated apoptosis. Thus, *P. granatum*-mediated ZnO–Ag NPs exhibit strong potential as green-synthesized therapeutic agents against multiple cancer types.

Similar to Mohamad Sukri S. et al., eight other articles reported anticancer activity of zinc oxide phyto-nanoparticles in the publishing year 2021–2025 (till date).

Wound healing

B. R. Sari et al. (2025)^[36] synthesized silver nanoparticles (Nc–AgNPs) using *Nepeta cataria* (catnip) extract and evaluated their wound-healing potential in an excision wound model in rats. The topical application of Nc–AgNPs demonstrated a significant wound closure rate of 94% after 10 days of treatment, comparable to the positive control group treated with silver sulfadiazine cream. Histopathological analysis revealed increased collagen maturation and complete epithelialization in the Nc–AgNPs-treated group, indicating enhanced tissue regeneration. Additionally, Nc–AgNPs exhibited strong antioxidant activity, which likely contributed to reducing oxidative stress and promoting healing. These findings suggest that *N. cataria*-derived silver nanoparticles are promising candidates for wound healing applications.

Similar to B. R. Sari et al., five other articles reported wound healing activity of silver phyto-nanoparticles in the publishing year 2021–2025 (till date).

Adel Moalwi et al. (2024)^[37] synthesized zinc oxide nanoparticles (ZnONPs) using *Wodyetia bifurcata* fruit peel extract and evaluated their wound healing potential. The ZnONPs demonstrated significant wound closure in both in vitro and in vivo models, with accelerated healing observed in treated wounds. Additionally, the ZnONPs exhibited strong antimicrobial activity and antioxidant properties, contributing to enhanced wound repair. Importantly, the extract used for synthesis was found to be non-cytotoxic, indicating the safety of the ZnONPs for therapeutic applications. These findings suggest that *W. bifurcata*-derived ZnONPs hold promise as effective agents for wound healing, combining therapeutic efficacy with biocompatibility.

Similar to Adel Moalwi et al., one other article reported wound healing activity of zinc oxide phyto-nanoparticles in the publishing year 2021–2025 (till date).

Cardioprotection

In this article, Habila Obidah Abert et al. (2022)^[38] synthesized iron oxide nanoparticles (FeONPs) using *Spinacia oleracea* leaf extract and evaluated their anti-atherosclerotic effects in Triton X-100-induced hyperlipidemic rats. The FeONPs normalized lipid profiles, reduced cardiac injury markers, and restored heart tissue architecture while enhancing antioxidant defenses (SOD, CAT). These benefits occurred without organ toxicity, highlighting *S. oleracea*-derived FeONPs as safe and promising agents for managing atherosclerosis through combined lipid-lowering and antioxidant actions.

Similar to Habila Obidah Abert et al., six other articles reported cardioprotective activity of iron oxide phyto-nanoparticles in the publishing year 2021–2025 (till date).

In another article, Arozal et al. (2022)^[39] formulated alginate-stabilized silver nanoparticles (AgNPs) and investigated their cardioprotective role in isoproterenol-induced myocardial infarction in rats. The AgNPs effectively lowered cardiac injury markers and oxidative stress, while enhancing antioxidant enzymes such as SOD. They further promoted mitochondrial biogenesis and suppressed NF-κB-mediated inflammation, resulting in preserved myocardial architecture and reduced tissue damage. Importantly, no significant liver or kidney toxicity was observed, confirming their safety. These findings suggest that alginate-based AgNPs hold promise as cardioprotective agents, offering combined antioxidant, anti-inflammatory, and mitochondrial-supportive benefits.

Similar to Arozal et al., four other articles reported cardioprotective activity of silver phyto-nanoparticles in the publishing year 2021–2025 (till date).

In this article, Alshehri M. A. (2022)^[40] synthesized zinc oxide nanoparticles mediated by *Artemisia herba alba* leaf extract (AHAL–ZnONPs) and tested their cardioprotective efficacy in a rat model of isoproterenol-induced myocardial infarction. The nanoparticles normalized cardiac biomarkers, improved lipid profiles, suppressed oxidative stress, enhanced antioxidant defenses, and reduced apoptosis. The histopathological and molecular findings together support that *A. herba alba*-derived ZnO nanoparticles exert cardioprotective effects via synergistic anti-oxidative, anti-lipid peroxidation, anti-apoptotic, and lipid regulatory mechanisms, collectively preserving heart tissue integrity and function without notable toxicity.

Similar to Alshehri M. A., six other articles reported cardioprotective activity of Zinc oxide phyto-

nanoparticles in the publishing year 2021-2025 (till date).

Antiviral application

In their research, Mahsa A. et al. (2023)^[41] synthesized copper nanoparticles (CuNPs) using *Juglans regia* green husk extract and tested them with iron oxide nanoparticles (FeNPs) against HSV-1. While FeNPs alone showed strong antiviral activity, reducing viral titers by about 3.25 log₁₀ TCID₅₀, CuNPs alone were less effective. Notably, combining CuNPs with FeNPs produced a more pronounced effect, lowering viral titers by 4.5 log₁₀ TCID₅₀. These results highlight the therapeutic promise of green-synthesized metal nanoparticles, particularly when used in synergistic combinations, as effective antiviral agents against HSV-1.

Similar to Mahsa A. et al., three other articles reported antiviral activity of copper phyto-nanoparticles in the publishing year 2021-2025 (till date).

Abo-El-Yazid et al. (2022)^[42] reported the green synthesis of silver nanoparticles (AgNPs) using *Cyperus rotundus* aqueous extract and evaluated their antiviral efficacy against infectious laryngotracheitis virus (ILTV) and infectious bronchitis virus (IBV). The biosynthesized AgNPs, measuring 11–19 nm, were non-toxic at therapeutic concentrations and showed strong inhibition of viral replication, particularly in post-infection treatments where significant reductions in viral load were observed. The authors attributed this activity to the ability of AgNPs to interact with viral envelope proteins and disrupt key processes required for viral entry and propagation. These findings highlight the potential of *C. rotundus*-mediated AgNPs as safe and effective antiviral agents, offering a sustainable nanotherapeutic approach against enveloped viruses.

Similar to Abo-El-Yazid et al., one other article reported antiviral activity of silver phyto-nanoparticles in the publishing year 2021-2025 (till date).

CONCLUSION

This review summarizes the recent advances made in the green synthesis of metal and metal oxide nanoparticles over the past five years, with emphasis on the reaction conditions employed and the phytochemicals that guide nanoparticle formation, for easy reference for researchers working on green synthesis of phyto-nanoparticles. The evidence demonstrates that plant-derived nanoparticles exhibit diverse therapeutic properties, ranging from antibacterial and anticancer effects to cardioprotective, wound healing, and antiviral activities. These activities are mediated through multiple mechanisms such as microbial membrane disruption, apoptosis induction, tissue regeneration, oxidative stress modulation, and inhibiting viral enzymes respectively. Overall, the literature suggests that green-synthesized nanoparticles represent a promising

avenue for the development of next-generation therapeutics. Their eco-friendly synthesis not only minimizes environmental impact but also enhances bioactivity through the inherent contribution of phytoconstituents. By combining sustainability with broad-spectrum therapeutic efficacy, green nanotechnology holds significant potential for advancing safe and effective treatments across various disease areas.

FUTURE PROSPECTS

Although most studies on green-synthesized metal and metal oxide nanoparticles remain at the laboratory scale, future research should focus on clinical validation, safety, and optimal dosing. Standardizing synthesis methods and exploring diverse plant sources will improve reproducibility and efficacy. Further investigation into molecular mechanisms and long-term biocompatibility is essential. We hope this review inspires continued research in green nanotechnology, advancing the development of safe, effective, and sustainable nanomedicines for diverse therapeutic applications.

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CONFLICTS OF INTEREST

The authors confirm that they have no conflicts of interest regarding the publication of this review article.

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