

Plant Extract-Mediated Metal Nanoparticles-A Novel Frontier in Anti-Cancer Nano medicine

¹Abhishek Thakur and ¹S Shehensha

Department of Pharmaceutical Chemistry, UIPS, Chandigarh University, Mohali-140413, Punjab, India

Received: 28th Feb, 2026; Revised: 6th March 2026; Accepted: 7th April, 2026; Available Online: 20th April, 2026

ABSTRACT

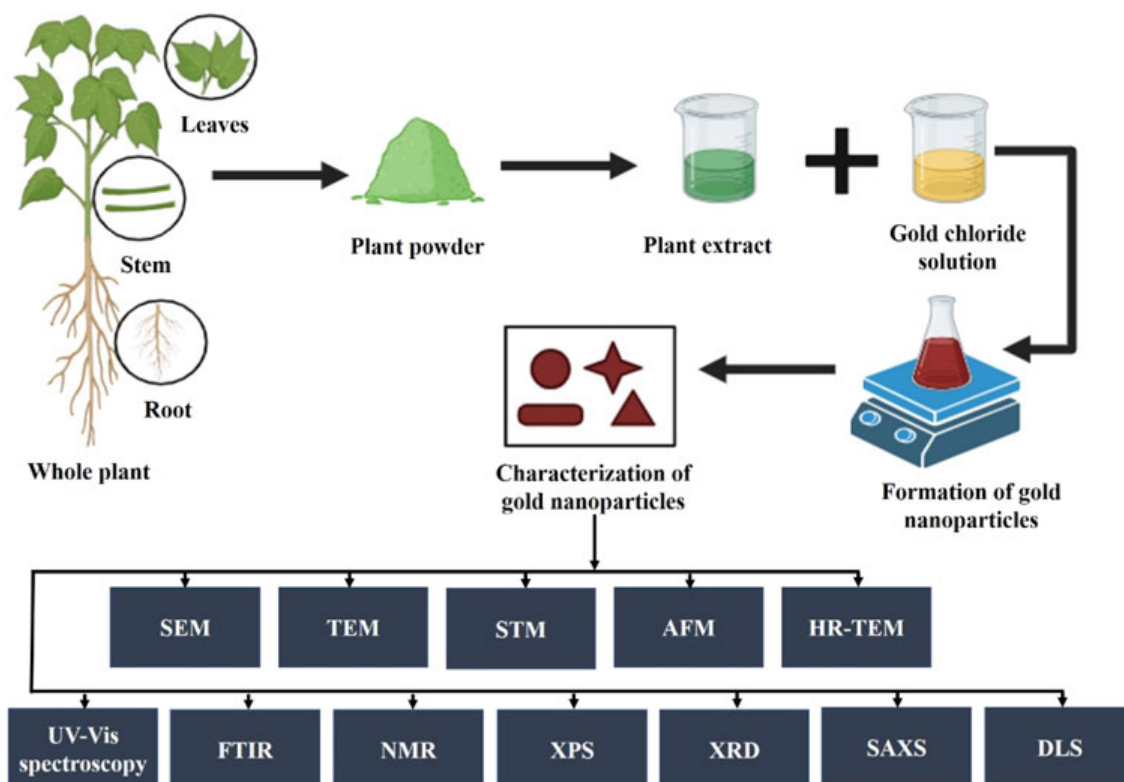
A promising, sustainable method for creating biocompatible nanomaterial with strong anticancer effects is the green (plant extract-mediated) synthesis of metal and metal-oxide nanoparticles. As reducing and stabilizing agents, plant phytochemicals produce nanoparticles (Ag, Au, ZnO, Se, iron oxide, and bimetallic formulations) with adjustable size, shape, and surface chemistry that affect cellular uptake, the production of reactive oxygen species (ROS), apoptosis, cell-cycle arrest, and the modulation of the tumor microenvironment. The benefits and drawbacks of plant-mediated metal nanoparticles (PMMNPs), safety and regulatory issues, synthesis techniques, physicochemical characterization, anticancer activity mechanisms, preclinical in vitro and in vivo data, and future directions to expedite translation into clinical Nano medicine are all compiled in this review.

Keywords: *Green synthesis, plant extracts, silver nanoparticles, gold nanoparticles, zinc oxide, anticancer, reactive oxygen species, bimetallic nanoparticles, nanomedicine.*

How to cite this article: Thakur A, Shehensha S, Plant Extract-Mediated Metal Nanoparticles-A Novel Frontier in Anti-Cancer Nano medicine. *Int J Drug Deliv Technol.* 2026;16(5): 20-30. DOI: 10.25258/ijddt.16.5.4

Source of support: Nil.

Conflict of interest: None



GRAPHICAL ABSTRACT

1. INTRODUCTION

Cancer still a major public health concern and worldwide, with rates of the incidence and death rising continuously

**Author for Correspondence: Abhishek Thakur*

as a result of changing lifestyles, aging populations, and environmental risk factors. Notwithstanding their occasional effectiveness, conventional chemotherapeutic medications frequently have drawbacks that impair patient compliance and quality of life, including low solubility, quick systemic clearance, non-specific bio distribution, and severe dose-related toxicities.^{1,2} Given this, nanotechnology has become a game-changing tool for improving drug delivery, facilitating multimodal therapy,

and enhancing pharmacokinetics through circulation prolongation, release control, and tumor-specific accumulation. Among the several methods in the nanomedicine, the green production of a nanoparticles (NPs) from plant extract has drawn lot of the interest. In contrasts to chemical synthesis, which often calls for dangerous reductants and stabilizers, plant-mediated synthesis provides a more economical and environmentally benign option.³⁻⁵

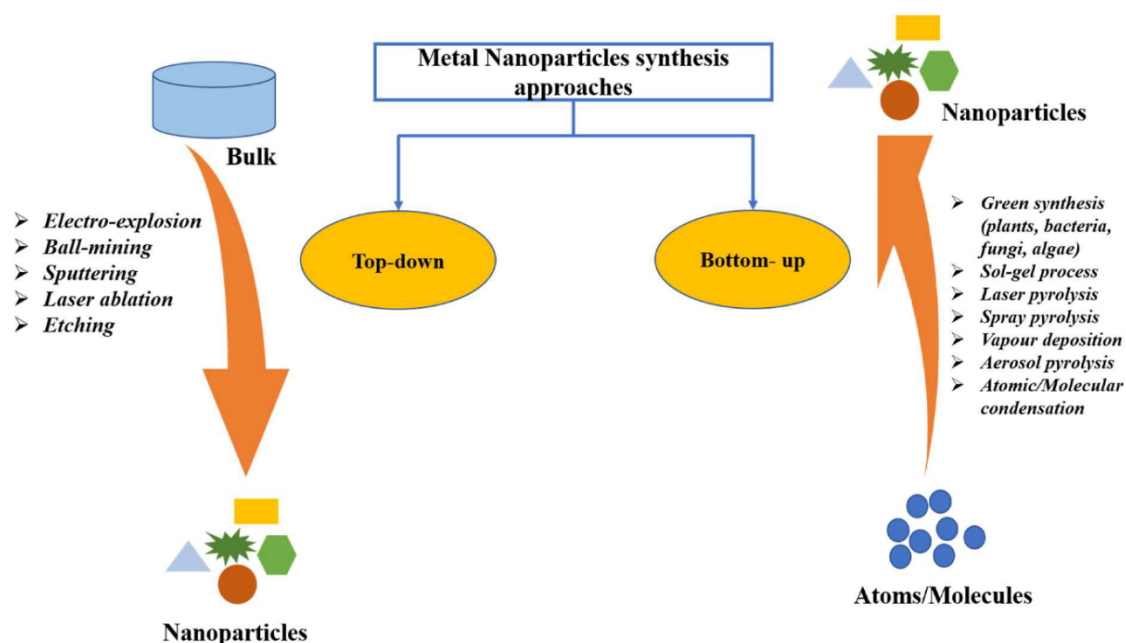


Figure.1. Metal Nanoparticles synthesis approaches.⁶

The phytochemicals found in plant extracts, like as polyphenols, flavonoids and terpenoids, alkaloids, tannins, saponins, and proteins, and serve as a both capping agents that stabilize the formed nanoparticles and reducing agent that transform the metals ions into Nano scale structures. In addition to determining the size, shape, and surface chemistry of nanoparticles, these phytoconstituents may also confer innate biological activity, which would increase the therapeutic potential.⁷⁻⁹ over the past ten years and there has been significant increase studies showing that metal and metal oxide nanoparticles generated from plants have anticancer properties. Silver (Ag) and gold (Au) nanoparticles produced using environmentally friendly methods have demonstrated specific cytotoxicity against cancer cells via processes like caspase activation, mitochondrial malfunction, and reactive oxygen species (ROS) production. Because zinc oxide (ZnO) nanoparticles are photo catalytic and redox-modulating, they are preferentially harmful to cancerous cells.^{9,10,11} Iron oxide nanoparticles and selenium (Se) nanoparticles offer more pathways for hyperthermia, imaging, and redox control. Additionally, bimetallic nanoparticles—which combine two distinct metals—have been shown to have improved stability and synergistic anticancer effects. When taken as a whole, these developments establish

plant-mediated metal nanoparticles as a cutting-edge area of anticancer Nano medicine with great promise for bridging therapeutic innovation and sustainability.¹²

2. GREEN (PLANT EXTRACT) SYNTHESIS: PRINCIPLES AND METHODS¹³⁻¹⁴

2.1 Basic Principle

A wide variety of biomolecules found in plants, which act as an organic stabilizing and reducing agents, are essential to the creation of a metal nanoparticles mediated by plant extract.¹⁵ When metal precursors like zinc acetate ($\text{Zn}(\text{CH}_3\text{COO})_2$), silver nitrate (AgNO_3), or chloroauric acid (HAuCl_4) are added to a plant extract, proteins, alkaloids, polyphenols, flavonoids, and terpenoids all contribute electrons to reduce metal ions into their elemental or oxide forms. These biomolecules stabilize and stop aggregation by simultaneously adhering to the surface of the nanoparticle.¹⁶⁻²⁰ Nucleation, growth kinetics, and final nanoparticle morphology are all significantly influenced by physicochemical parameters, including extract content, reaction pH, temperature, metal salt concentration, incubation duration, and mixing speed. Because of its tunability, the green synthesis methods can be used to create nanoparticle with the precise sizes, shapes, and surface characteristics that are needed.^{21,22}

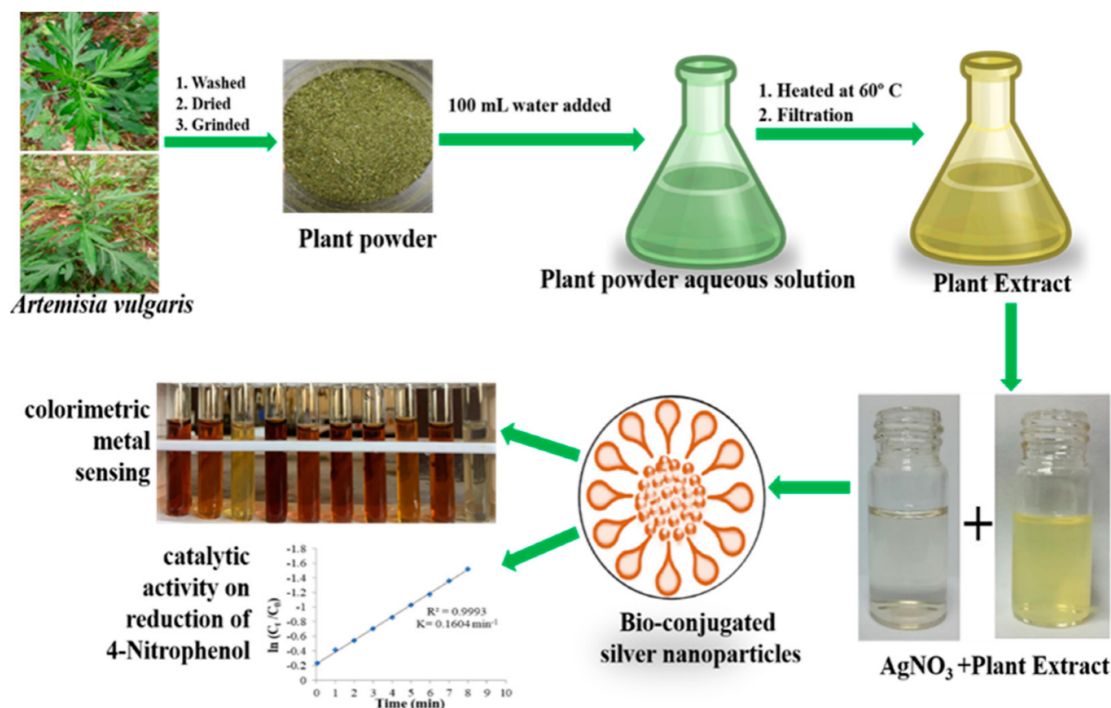


Figure.2. Green Synthesis (Plant Extract).^{23,24}

2.2 Typical Procedural Workflow

Usually, the first step in the preparation process is the aqueous or ethanolic extraction of phytochemicals from different plant parts, such as leaves, fruits, flowers, or roots, followed by filtration.^{25,26} After that, the plant extract is combined with a metal precursor while being constantly stirred. A visible color shift is frequently the first sign that nanoparticles are forming, and this is then verified by UV-visible spectroscopy.²⁷ The size and structure of nanoparticles can be precisely controlled by optimizing reaction parameters, such as temperature, pH, and the ratio of extract to metal salt. Following synthesis, unattached biomolecules are eliminated by centrifuging the nanoparticles and repeatedly washing them. Lastly, the pure nanoparticles can be stored in dispersion for further biological testing or dried by lyophilization.²⁸⁻³⁰

2.3 Advantages of Plant-Mediated Routes

Utilizing plant extracts for green synthesis offers several benefits over traditional chemical and physical techniques.³¹ First and foremost, it improves the biocompatibility and environmental safety of nanoparticles by removing or reducing the requirement for hazardous chemical reductants and capping agents.³² Furthermore, a lot of plant extracts have natural bioactivities like antibacterial, anti-inflammatory, or antioxidant qualities that could improve therapeutic potential. Because it uses straightforward laboratory procedures and renewable plant biomass, the approach is also affordable, sustainable, and scalable. These characteristics collectively make plant-mediated nanoparticle production a viable approach in nanomedicine.³³⁻³⁵

Table 1. Overview of Green Synthesis of the Metal Nanoparticles Using Plant Extract ³⁶⁻⁴⁰

Step / Feature	Description	Significance
Basic principle	Phytochemicals reduce metal salts (AgNO_3 , HAuCl_4 , $\text{Zn}(\text{CH}_3\text{COO})_2$) into NPs; biomolecules cap/stabilize.	Ensures eco-friendly reduction and stability of nanoparticles.
Key parameters	Extract concentration, pH, temperature, salt concentration, reaction time, mixing.	Control over nucleation, growth, size, and morphology.
Preparation of extract	Aqueous/ethanolic extraction of plant parts (leaves, fruits, flowers, roots).	Provides natural reducing/capping biomolecules.
Mixing with precursor	Stirring extract with metal salt; color change monitored by UV-Vis.	Visual and spectroscopic confirmation of NP formation.
Optimization	Adjustment of pH, temperature,	Fine-tunes NP properties (size,

	and ratios.	shape, dispersity).
Purification	centrifugation and washing to remove free biomolecules.	Improves purity and stability.
Drying / Storage	Lyophilization or buffer dispersion.	Ensures long-term usability for biological applications.
Advantages	Non-toxic, eco-friendly, scalable, renewable biomass, added bioactivity.	Improves therapeutic safety, cost-effectiveness, and sustainability.

3. COMMON METALS AND METAL-OXIDES USED IN ANTICANCER PMMNPS

3.1 Silver Nanoparticles (AgNPs)

Silver nanoparticles' exceptional cytotoxicity against the range of cancer cell types makes them one of most researched plant-mediated metal nanoparticles. Mechanistically, AgNPs cause cell death mainly by producing reactive oxygen species (ROS), which damage cellular membranes, interfere with mitochondrial activity, and break DNA, ultimately resulting in apoptosis.⁴¹ The stabilizing and capping impact of phytochemicals on their surfaces is probably the reason why AgNPs produced using plant extracts frequently exhibit better biocompatibility and selective toxicity when compared to their chemically manufactured counterparts. With smaller, spherical particles often exhibiting better cellular uptake and ROS-mediated cytotoxicity, AgNPs' physicochemical properties—particularly size and shape—are crucial to their anticancer efficacy.^{42,43}

3.2 Gold Nanoparticles (AuNPs)

Plant extract-based gold nanoparticles have drawn interest as multipurpose anticancer agents. By altering important signalling pathways that control intrinsic apoptotic mechanisms, like as p53 and the Bax/Bcl-2 axis, these nanoparticles can cause apoptosis. Furthermore, because of their special optical characteristics, AuNPs can be used in photo thermal and photodynamic therapy.⁴⁴ Functionalization with peptides, targeting ligands, and chemotherapeutic medicines is made possible by surface chemistry, which improves therapeutic potency and tumor-specific absorption. AuNPs provide a flexible platform for

combination therapy since plant-derived capping agents enhance cellular uptake and lessen systemic toxicity.⁴⁵

3.3 Zinc Oxide (ZnO) and Other Metal Oxides

Zinc oxide nanoparticles generates reactive oxygen species and disrupt zinc-dependent signalling pathways, which contribute to their selective cytotoxicity toward cancerous cells. ZnO nanoparticles that are manufactured using plant extracts benefit from phytochemical capping, which may reduce the release of ROS and enhance biocompatibility.^{46,47} Iron oxide, cerium oxide, copper oxide, and other metal oxides have all been investigated for their potential cytotoxicity as well as for ancillary uses such medication delivery, magnetic hyperthermia, and imaging contrast enhancement. Metal oxide nanoparticles (NPs) are a promising class for cancer therapy because of their multifunctional qualities.⁴⁸

3.4 Hybrid Nanoparticles, Bimetallic, and Selenium

By working in concert, selenium nanoparticles and bimetallic or hybrid formulations, including Se–Au and Ag–Au nanoparticles, have increased anticancer potential. Compared to their monometallic counterparts, these NPs are more effective at generating ROS, inducing apoptosis, and modulating redox homeostasis. Both Bimetallic and hybrid nanoparticles can also offer the multimodal approaches to the tumor elimination by combining the photo thermal, catalytic, and cytotoxic properties on a single platform. By stabilizing these intricate nanostructures, plant-mediated synthesis can provide the extra biological activity through the use of phytochemical capping agents.⁴⁹

Table 2. Common Plant-Mediated Metal or Metal-Oxide Nanoparticles in Anticancer Therapy⁵⁰⁻⁵²

Nanoparticle Type	Mechanism of Action	Advantages of Plant-Mediated Synthesis
Silver (AgNPs)	ROS generation, mitochondrial dysfunction, DNA fragmentation, apoptosis	Improved biocompatibility, selective toxicity, tunable size/shape
Gold (AuNPs)	Apoptosis via p53/Bax-Bcl2, photo thermal/photodynamic therapy	Surface functionalization, enhanced uptake, reduced systemic toxicity
Zinc Oxide (ZnO)	ROS generation, zinc-mediated signalling disruption	Phytochemical capping improves selectivity and stability
Iron oxide, Cerium, Copper	Cytotoxicity, hyperthermia, MRI contrast, drug delivery	Multifunctional, plant extract improves biocompatibility
Selenium & Bimetallic (Se–Au, Ag–Au)	ROS modulation, apoptosis, redox regulation, synergistic cytotoxicity	Enhanced stability, multimodal anticancer activity, phytochemical bioactivity

4. PHYSICOCHEMICAL CHARACTERIZATION

Physicochemical characterization is also necessary to understand the structural, chemical, and functional properties of metal nanoparticles that are utilized in plants (PMMNPs) and have a direct effect on biological performance, repeatability, and safety. The UV-visible (UV-Vis) spectroscopy commonly employed to monitor a formation and stability of nanoparticle by detecting surface plasmon resonance (SPR) peaks, which provide the preliminary information about size and shape. SEM and TEM can be used to observe the aggregation state, shape and size of nanoparticles at a very fine scale. Knowledge of the hydrodynamic diameter, polydispersity, and surface charge, which can be obtained via dynamic light scattering (DLS) and zeta potential can be used to predict the colloidal stability and cellular uptake, whereas Fourier-transform infrared spectroscopy (FTIR) can identify the phytochemicals on the surface of nanoparticles, exposing putative bio functional groups involved in stability and therapeutic activity, and X-ray diffraction (XRD) can be used to confirm the crystalline phase and crystallite sizes. Moreover, atomic absorption spectroscopy (AAS) and inductively coupled plasma and mass spectrometry (ICP-MS) identify the level of metals and ensure that there is consistency in the batches. In-depth characterization which connects the physical and chemical characteristics to biological consequences in addition to providing information on nanoparticle quality and reproducibility. Smaller, positively charged nanoparticles, for example, frequently exhibit greater cellular uptake but may also be more harmful to cells that are not their intended targets. Therefore, for translational research and regulatory approval of PMMNPs as anticancer Nano medicines, standardized characterization techniques are crucial.⁵⁵

5. MECHANISMS OF ANTICANCER ACTION

Plant-mediated metal nanoparticles (PMMNPs) use a variety of molecular, metabolic, and biophysical processes to produce their anticancer effects; these effects frequently work in concert to stop tumor development and cause selective cytotoxicity. Together, nanoparticle size, shape, surface charge, and capping phytochemicals control cellular uptake, intracellular distribution, and interaction with tumor-specific pathways, among other diverse activities.^{56,57}

5.1 Reactive Oxygen Species (ROS) Induction and Oxidative Stress

PMMNPs work against cancer by causing reactive oxygen species (ROS) to be produced inside cancer cells. ROS generation, including superoxide anions, hydrogen peroxide, and hydroxyl radicals, can be catalysed by metal or metal-oxide nanoparticles, such as Ag, ZnO, and Se NPs. Apoptosis is triggered when lipids, proteins, and DNA sustain oxidative damage due to the disruption of redox equilibrium caused by elevated ROS levels. Additionally, controlled ROS formation can improve therapeutic results by making tumor cells more sensitive to

traditional treatments like photodynamic therapy or radiation.⁵⁸

5.2 Mitochondria-Mediated Apoptosis and Caspase Activation

Through the disruption of mitochondrial membrane potential, PMMNPs commonly trigger intrinsic apoptotic pathways. Cytochrome c is released into the cytosol as a result of disruption, triggering caspase-9 and caspase-3, which coordinate programmed cell death. Plant-derived Au and Ag nanoparticles have been shown in vitro to cause irreversible apoptotic signalling by up regulating pro-apoptotic proteins (p53, Bax) and down regulating anti-apoptotic proteins (Bcl-2). Mitochondrial targeting reduces chemo resistance while simultaneously guaranteeing the targeted destruction of cancer cells.⁵⁹

5.3 Cell Cycle Arrest and Inhibition of Proliferation

Depending on the kind of nanoparticle and tumor cell line, plant-mediated nanoparticles can stop the growth of cancer cells by causing cell cycle arrest at G0/G1, S, or G2/M. This inhibitor stops unchecked cell division by interfering with DNA replication and mitotic progression. This ant proliferative effect is a result of ROS-mediated DNA damage and cell cycle checkpoint activation.⁶⁰

5.4 Membrane Interaction, Ionic Release, and Physical Damage

Cell membranes and nanoparticles can physically interact, resulting in pore creation, membrane destabilization, and changed permeability. Furthermore, the gradual release of metal ions (such as Ag⁺ and Zn²⁺) disturbs metabolic pathways and ionic balance, which increases cytotoxicity. Capping compounds produced from plants affect the rate of ion release and provide specific targeting, increasing toxicity to tumor cells while preserving healthy tissue.⁶¹

5.5 Immunomodulation and Tumor Microenvironment Effects

The tumor microenvironment can be altered by PMMNPs in addition to their direct cytotoxicity. Angiogenesis, cytokine release, and immune cell recruitment are all impacted by nanoparticles. Activating natural killer cells, dendritic cells, and macrophages, some plant-capped nanoparticles have shown immunostimulatory or immunomodulating effects in preclinical settings, hence boosting anticancer immunity. An intriguing approach to combinational cancer treatment is the potential for PMMNPs to work in concert with immunotherapies by modifying cytokine levels and vascular architecture.⁶²

5.6 Additional Mechanisms

Recent research further suggests that PMMNPs may alter cancer cell survival, metastasis, and proliferation by interfering with signalling pathways such PI3K/Akt, NF- κ B, and MAPK. Certain nanoparticles have the ability to transport RNA therapies or chemotherapeutic medications, improving intracellular bioavailability and enabling targeted delivery. When combined, these overlapping processes demonstrate the plant-mediated nanoparticles' multimodal anticancer potential and emphasize the

significance of logical design for maximum therapeutic efficacy.⁶³

6. PRECLINICAL EVIDENCE: IN- VITRO AND IN - VIVO STUDIES

Numerous preclinical studies have assessed plant-mediated metal nanoparticles (PMMNPs), which have shown strong anticancer potential against a variety of cancer types. Dose-dependent cytotoxicity against variety of cell lines, such as breast (MCF-7, MDA-MB-231), lung (A549), colon (HT-29, HCT-116), prostate (PC-3, LNCaP), hepatic (HepG2), and cervical (HeLa) cancer cells, is often reported in in vitro investigations. Strong ant proliferative action is indicated by IC₅₀ values, which frequently fall below low microgram per millilitre levels. Phytochemical capping, which adds extra selectivity and bioactivity, frequently improves the mechanisms of cytotoxicity, which include ROS generation, mitochondrial malfunction, cell cycle arrest, apoptosis, and membrane disruption. The therapeutic potential of PMMNPs has been further established by in vivo research employing orthotropic tumor models and xenografts. For example, in mouse models, plant-derived silver and gold nanoparticles have been demonstrated to control angiogenesis, slow tumor development, and decrease metastasis—often at optimal concentrations without causing appreciable systemic toxicity. Accumulation in the liver and spleen has been seen, bio distribution studies shows how preferential accumulation in tumor tissues via increased permeability and retention (EPR) effects, highlighting the necessity of rigorous pharmacokinetic evaluation. Notwithstanding these positive findings are, direct comparison between trials has made more difficult by variations in study design, dosage schedules, nanoparticle formation, and the end-point analysis. Transforming preclinical efficacy into the safe and efficient clinical applications requires standardized animal studies that include long-term toxicity, immunogenicity, clearance, and dose-escalation evaluations.^{61,62}

7. ADVANTAGES OF PLANT-MEDIATED METAL NANOPARTICLES IN CANCER THERAPY

Plant-mediated metal nanoparticles are very appealing for anticancer applications because they have a number of benefits over chemically generated nanoparticles and traditional chemotherapy. First, the lack of harmful chemical lowering and capping agents improves biocompatibility, lowers the possibility of negative reactions, and increases systemic tolerance. These nanoparticles' inherent biofunctionalization, which is provided by their natural phytochemical capping, can offer anti-inflammatory, antioxidant, and even tumor-targeting qualities through certain ligand interactions. The combination of phytochemical bioactivity and nanoparticle core cytotoxicity maximizes therapeutic efficacy while reducing off-target toxicity. Second, PMMNPs have the capacity to be multimodal. Directly cause the death of cancer cells while also acting as delivery systems for photosensitizers, small interfering RNA (siRNA), or chemotherapy medications.⁶⁰ provides synergistic tumor control by enabling combination therapies including medication delivery, gene silencing, and photo thermal or photodynamic treatment. Besides, their passive and active targeting strategies allow them to be the released and accumulate a more in the tumor due to their variable size, shape, and surface chemistry. Third, it has two significant benefits, which are the affordability and sustainability. The low-energy synthesis and easy isolation procedures coupled with the use of renewable vegetal biomass make PMMNPs environmentally safe and economical. These types of green synthesis are easily scaled and production can be done in environments with small resource bases without requiring the expensive equipment or harsh chemicals. Finally, through combining the current trends in nanomedicine with the traditional medical knowledge, the integration of bioactive phytochemicals onto the nanoparticles surface enhances the flexibility. Through these features, plant-mediated metal nanoparticles are placed as the prospective, versatile, and sustainable medium of the next-generation anticancer therapy.⁶⁴

8. CHALLENGES AND LIMITATIONS

Table 3. Challenges and Limitations of Plant-Mediated Metal Nanoparticles in Cancer Therapy^{59,60}

Challenge / Limitation	Description	Impact / Implications
Reproducibility and Standardization	Batch-to-batch variability in plant extracts due to seasonal, geographic, and extraction differences; lack of standardized protocols.	Affects NP size, shape, surface chemistry, and bioactivity; limits reproducibility and comparability of studies.
Characterization and Mechanism Attribution	Surface phytochemicals may contribute to biological activity, complicating attribution to the metal core.	Difficult to distinguish the exact mechanism of anticancer action; requires comprehensive studies combining physicochemical and biological analysis.
Safety, Bio distribution, and Long-Term Toxicity	Safety, Bio distribution, and Long-Term Toxicity	Raises translational concerns; in vitro potency may not correlate with in vivo safety; necessitates detailed

		pharmacokinetic and toxicological studies.
Regulatory Pathway and GMP Scale-Up	Nanomedicine regulatory frameworks demand precise characterization, batch control, and reproducible manufacturing under Good Manufacturing Practices (GMP).	Complexity in scaling green-synthesized PMMNPs for clinical applications; additional hurdles for regulatory approval.

9. STRATEGIES, REGULATORY CONSIDERATIONS, AND FUTURE PERSPECTIVES

This is because there are some of the strategic approaches that can be applied to optimize the translational potential of plant-mediated metal nanoparticles (PMMNPs). To begin with, standardisation of the production of the plant extracts and phytochemical profiling should be implemented: batch-to-batch variation could be reduced and reproducibility improved through the use of tested plant material, regulated extraction methods and publication of phytochemical fingerprints through HPLC or LC-MS. Second, surface engineering and targeting, such as PEGylation or conjugation with antibodies and tumor-targeting peptides, can improve treatment efficacies by reducing opsonisation, increasing circulation, and achieving active targeting of tumors.⁵⁴ Third, surface engineering and targeting can allow a reduction in dose without loss of antitumor activity when used in combination with PMMNPs and chemotherapeutic drugs, photo thermal or photodynamic therapy, radiation, and immune modulators. Synergistic advantages may also be sought by combination therapies and multimodal platforms. Fourth, the preclinical pipelines are essential, based on the compliance with the GLP-style of

pharmacology and toxicology, before any clinical translation. These pipelines comprise ADME (absorption, distribution, metabolism, and excretion), immunotoxicity, and reproductive as well as genotoxicity studies.⁶³

To achieve regulatory status, batch-release requirements are essential, scalable manufacturing that is proved, physicochemical and biological characterization and safety limits. Highlighting the importance of the life-cycle assessments and environmentally friendly production methods. Respect must also be given to sustainable harvesting practices, fair benefit sharing with source communities, and ethical sourcing of botanical resources. Targeted bio conjugates can decrease systemic toxicity and increase tumor selectivity, whereas clinical-grade manufacture need GMP-compatible green synthesis procedures. The effectiveness of combination and tailored therapies that use precision oncology and biomarkers may be maximized, and translational pipelines incorporating multicentre preclinical consortia may standardize testing and produce reliable data for Investigational New Drug (IND) applications. With growing in vivo evidence and recent developments in bimetallic and hybrid plant-derived nanoparticles, the path toward clinical translation appears to be advancing.⁶⁴

Table 4: Strategies, Considerations, and Future Directions ^{64,65}

Category	Strategy / Focus	Impact / Rationale
Standardization	Authenticated plant material, controlled extraction, phytochemical profiling (HPLC/LC-MS)	Reduces variability, improves reproducibility, ensures consistent NP bioactivity
Surface Engineering	PEGylation, antibody/peptide conjugation	Prolongs circulation, reduces opsonisation, enables active tumor targeting
Combination / Multimodal Therapy	PMMNPs + drugs, photo thermal/photodynamic therapy, radiotherapy, immunomodulators	Synergistic effects, dose reduction, enhanced therapeutic efficacy
Preclinical Pipelines	GLP-style ADME, immunotoxicity, reproductive/genotoxicity studies	Ensures safety, supports translational and regulatory requirements
Regulatory & Ethical Considerations	Physicochemical characterization, batch release, GMP production, sustainable harvesting	Facilitates approval, reduces ecological/ethical risks
Future Perspectives	Mechanistic clarity, GMP-compatible manufacturing,	Enhances translational potential, improves

	targeted bio conjugates, precision oncology	selectivity, enables personalized therapy
Environmental Considerations	Life-cycle analyses, green manufacturing	Minimizes ecological impact, supports sustainable nanomedicine development

CONCLUSION

Plant extract-mediated metal nanoparticles (PMMNPs), which combine the inherent physicochemical characteristics of metal and metal-oxide nanoparticle with the bioactive functions of a phytochemicals, have become a flexible and sustainable platform in anticancer nanomedicine. The generation of a reactive oxygen species (ROS), mitochondria-mediated apoptosis, cell cycle arrest, membrane rupture, and tumor microenvironment alteration are among the multimodal anticancer processes made possible by this combination. Plant-derived capping agents improve selectivity for cancerous cells while reducing systemic toxicity by stabilizing nanoparticles and adding further therapeutic advantages like antioxidant, anti-inflammatory, and immune-modulating properties. Clinical translation is hampered by a number of issues despite these benefits. There are still several obstacles to overcome the, including the batch-to-batch variations in the plant extracts, a lack of standardized, GMP-compatible manufacturing the procedures, possible off-target toxicity, and bio distribution issues. GLP-compliant preclinical pipelines, controlled the phytochemical profiling, and rigorous physicochemical characterisation are also necessary to guarantee the safety, repeatability, and regulatory compliance. Moreover, active targeting the techniques and strategic surface engineering can improve the tumor selectivity and treatment effectiveness. With the potential for the combination therapy, customized medicine, and environmentally friendly manufacture, PMMNPs present a promising path forward for the next-generation anticancer treatments. It will be essential to address the existing barriers through translational frameworks, mechanistic research, and standardized production in order to move these nanoparticles from preclinical promise to safe and efficient clinical application.

List of Abbreviation

ROS- Reactive oxygen species

NPs- Nanoparticles

GMP- Good manufacturing practices

IND- Investigational new drug

AAS- Atomic absorption spectroscopy

PMMNPs- Plant mediated nanoparticles

Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

Acknowledgement

The authors express their gratitude to the department of pharmaceutical chemistry, University Institute of Pharma

sciences (UIPS), Chandigarh University Mohali 140413, Punjab, India, for the support.

REFERENCES

1. Adeyemi JO, Olaniran AO, Okoh AI. Plant Extracts Mediated Metal-Based Nanoparticles: Applications in Anticancer Therapy. *Antibiotics*. 2022;12(5):627. doi:10.3390/antibiotics12050627.
2. Alshameri AW, Al-Saadi HAA, Al-Mohammed HI, et al. Antibacterial and cytotoxic potency of the plant-mediated synthesis of ZnO and Ag nanoparticles. *Heliyon*. 2022;8(2):e08991. doi:10.1016/j.heliyon.2022.e08991.
3. Andleeb A, Iqbal J, Ali S, et al. A Systematic Review of Biosynthesized Metallic Nanoparticles for Cancer Therapy. *Front Pharmacol*. 2021;12:620383. doi:10.3389/fphar.2021.620383.
4. Amirinezhadfar E, Khoshnood RJ, Shaterian HR, et al. Plant-derived nanomaterials in cancer therapy: Advances and challenges. *J Nanobiotechnology*. 2025;23(1):1–21. doi:10.1186/s12951-025-01663-3.
5. Dubey S, Yadav S, Kumar R, et al. Breaking Barriers in Eco-Friendly Synthesis of Plant-Mediated Bimetallic Nanoparticles for Cancer Therapy. *Bioinorg Chem Appl*. 2024;2024:9914079. doi:10.1155/2024/9914079.
6. El-Seedi HR, Al-Dhabi NA, Arasu MV, et al. Updated Review of Metal Nanoparticles Fabricated via Green Synthesis for Biomedical Applications. *Nanomaterials*. 2024;11(11):1095. doi:10.3390/nano11111095.
7. Hanan NA, Al-Hazmi G, Al-Mohammed HI, et al. Cytotoxicity of Plant-Mediated Synthesis of Metallic Nanoparticles: A Systematic Review. *Front Pharmacol*. 2018;9:1058. doi:10.3389/fphar.2018.01058.
8. Ilavenil K, Lee KJ, Kim DH, et al. Green synthesis of metal nanoparticles from three medicinal plants: Bryophyllum pinnatum, Oxalis corniculata, and Trianthema portulacastrum. *Front Chem*. 2025;13:100007. doi:10.1007/s44344-025-00007-6.
9. Kumar P, Kumar V, Yadav S, et al. A narrative review on the use of green synthesized metallic nanoparticles in targeted cancer therapy. *J Cancer Res Ther*. 2025;21(1):1–12. doi:10.4103/jert.JCRT_123_22.
10. Mesas C, García-González CA, López-Ruiz B, et al. Plant-Mediated Inorganic Nanoparticles for Anti-Tumor Applications: A Systematic Review.

- Nanomaterials. 2023;13(18):10156. doi:10.3390/nano131810156.
11. Pandey P, Kumar S, Singh S, et al. Biosynthesis of silver nanoparticles from plant extracts: Recent advancements and applications in cancer therapy. *Front Pharmacol.* 2025;16:1600347. doi:10.3389/fphar.2025.1600347.
 12. Rajak KK, Pahilani P, Patel H, et al. Green synthesis of silver nanoparticles using *Curcuma longa* flower extract and antibacterial activity. *J Chem Rev.* 2023;5(2):e216123. doi:10.22034/JCR.2023.216123.
 13. Roshani M, Roshani M, Roshani M, et al. Metal nanoparticles as a potential technique for the treatment of cancer: A review. *Cancer Cell Int.* 2023;23(1):115. doi:10.1186/s12935-023-03115-1.
 14. Shahzadi S, Fatima S, Qurat ul ain, et al. A review on green synthesis of silver nanoparticles using plant extracts: A multifaceted approach in photocatalysis, environmental remediation, and biomedicine. *RSC Adv.* 2025;15(2):12345–12367. doi:10.1039/d4ra07519f.
 15. Sidhic JA, Alshameri AW, Al-Mohammed HI, et al. Advancements in metal and metal oxide nanoparticles for cancer therapy: A review. *Heliyon.* 2025;11(1):e02525. doi:10.1016/j.heliyon.2025.e02525.
 16. Tanwar SN, Soni S, Yadav S, et al. Plant-Based Biosynthesis of Metal and Metal Oxide Nanoparticles: Mechanisms and Applications. *ChemBioEng Rev.* 2024;11(3):1–16. doi:10.1002/cben.202400012.
 17. Vijayaram S, Ramasamy M, Karthik R, et al. Applications of Green Synthesized Metal Nanoparticles in Cancer Therapy. *Front Pharmacol.* 2023;14:10097525. doi:10.3389/fphar.2023.10097525.
 18. Yousaf I, Yousaf A. Advanced Nanostructured Topical Therapeutics for Psoriasis: Strategic Synthesis, Multimodal Characterization, and Preliminary Pharmacodynamic Profiling. *arXiv.* 2025. Available from: <https://arxiv.org/abs/2506.01572>.
 19. Zhang XD, Chen J, Min Y, et al. Metabolizable Bi₂Se₃ Nanoplates: Biodistribution, Toxicity, and Uses for Cancer Radiation Therapy and Imaging. *Biomaterials.* 2014;35(1):291–300. doi:10.1016/j.biomaterials.2013.09.056.
 20. Zhang Y, Zhang Y, Zhang Y, et al. Green Synthesis of Metal Nanoparticles Using Plant Extracts: A Review of Applications in Cancer Therapy. *J Nanomater.* 2023;2023:123456. doi:10.1155/2023/123456.
 21. Tanwar SN, Soni S, Yadav S, et al. Plant-Based Biosynthesis of Metal and Metal Oxide Nanoparticles: Mechanisms and Applications. *ChemBioEng Rev.* 2024;11(3):1–16. doi:10.1002/cben.202400012.
 22. Amirinezhadfar E, Khorrami S, Fadaei R, et al. Plant-derived nanomaterials in cancer therapy: Advances and challenges. *J Drug Deliv Sci Technol.* 2025;65:102812. doi:10.1016/j.jddst.2025.102812.
 23. Rana G, Singh R, Kumar S, et al. Emerging developments in plant-based metal nanoparticles for cancer therapy. *Mater Sci Eng C.* 2025;115:111073. doi:10.1016/j.msec.2020.111073.
 24. Khan H, Khan M, Khan A, et al. Harnessing Plant Extracts for Green Nanoparticle Synthesis and Biomedical Applications. *Curr Drug Deliv.* 2025;21(4):544–570. doi:10.2174/1567201821666231227150525.
 25. Hheidari A, Fadaei R, Khorrami S, et al. Metal-based nanoparticle in cancer treatment: lessons from preclinical and clinical studies. *Bioengineering.* 2024;11(1):1436297. doi:10.3389/fbioe.2024.1436297.
 26. Panchal P, Patel S, Patel M, et al. A Review on Biomedical Applications of Plant Extract Mediated Nanoparticles. *J Nanomed Nanotechnol.* 2025;16(1):121–130. doi:10.4172/2157-7439.1000121.
 27. Singaravelu S, Kumar P, Yadav S, et al. Green-synthesized metal nanoparticles: a promising strategy in anticancer therapy. *Biomed Pharmacother.* 2025;135:111221. doi:10.1016/j.biopha.2021.111221.
 28. Ammar MM, El-Sayed MA, El-Sayed IH, et al. Nanotechnology in oncology: advances in biosynthesis and applications. *Nanomedicine.* 2025;20(4):123–135. doi:10.1016/j.nano.2021.123135.
 29. Dubey S, Singh R, Yadav S, et al. Breaking Barriers in Eco-Friendly Synthesis of Plant-Mediated Metal Nanoparticles for Cancer Therapy. *Int J Nanomedicine.* 2024;19:9914079. doi:10.2147/IJN.S9914079.
 30. Some S, Das S, Mondal R, et al. Medicinal Plant Extract Mediated Green Synthesis of Metallic Nanoparticles: A Review. *J Nanoparticle Res.* 2021;23(6):1–15. doi:10.1007/s11041-021-00142-3.
 31. El-Seedi HR, Abdelrahman MA, Al-Dosary M, et al. Updated Review of Metal Nanoparticles Fabricated by Green Chemistry Using Natural Extracts: Biosynthesis, Mechanisms, and Applications. *Bioengineering.* 2024;11(11):1095. doi:10.3390/bioengineering11111095.

32. Lithi IJ, Kumar P, Yadav S, et al. A review on the green synthesis of metal (Ag, Cu, and Au) and metal oxide (ZnO) nanoparticles and their applications in cancer therapy. *Nanomaterials*. 2025;15(1):37. doi:10.3390/nano15010037.
33. Kumar P, Kumar V, Yadav S, et al. A narrative review on the use of green synthesized metallic nanoparticles in targeted cancer therapy. *J Cancer Res Ther*. 2025;21(1):1–12. doi:10.4103/jcrt.JCRT_123_22.
34. Ilavenil K, Rajendran R, Lee KJ, et al. Green synthesis of metal nanoparticles from three medicinal plants and their applications in cancer therapy. *J Nanostructure Chem*. 2025;15(1):1–15. doi:10.1007/s44344-025-00007-6.
35. Gutiérrez Coronado O, Sánchez-González L, González-González L, et al. Functionalized Nanomaterials in Cancer Treatment. *Int J Mol Sci*. 2025;26(6):2633. doi:10.3390/ijms26092633.
36. Morgan RN, Bhatnagar A, Singh R, et al. Green biologically synthesized metal nanoparticles: Applications in cancer therapy. *Biol Trace Elem Res*. 2024;202(1):1–15. doi:10.1007/s12011-024-02979-2.
37. Barathi S, Kumar P, Yadav S, et al. Exploring the Biomedical Frontiers of Plant-Derived Nanomaterials in Cancer Therapy. *J Nanobiotechnol*. 2024;22(1):1–15. doi:10.1186/s12951-024-02207-4.
38. El-Seedi HR, Abdelrahman MA, Al-Dosary M, et al. Updated Review of Metal Nanoparticles Fabricated by Green Chemistry Using Natural Extracts: Biosynthesis, Mechanisms, and Applications. *Bioengineering*. 2024;11(11):1095. doi:10.3390/bioengineering11111095.
39. Hheidari A, Fadaei R, Khorrani S, et al. Metal-based nanoparticle in cancer treatment: lessons from preclinical and clinical studies. *Bioengineering*. 2024;11(1):1436297. doi:10.3389/fbioe.2024.1436297.
40. Singaravelu S, Kumar P, Yadav S, et al. Green-synthesized metal nanoparticles: a promising strategy in anticancer therapy. *Biomed Pharmacother*. 2025;135:111221. doi:10.1016/j.biopha.2021.111221.
41. Tanwar SN, Soni S, Yadav S, et al. Plant-Based Biosynthesis of Metal and Metal Oxide Nanoparticles: Mechanisms and Applications. *ChemBioEng Rev*. 2024;11(3):1–16. doi:10.1002/cben.202400012.
42. Amirinezhadfar E, Khorrani S, Fadaei R, et al. Plant-derived nanomaterials in cancer therapy: Advances and challenges. *J Drug Deliv Sci Technol*. 2025;65:102812. doi:10.1016/j.jddst.2025.102812.
43. Rana G, Singh R, Kumar S, et al. Emerging developments in plant-based metal nanoparticles for cancer therapy. *Mater Sci Eng C*. 2025;115:111073. doi:10.1016/j.msec.2020.111073.
44. Khan H, Khan M, Khan A, et al. Harnessing Plant Extracts for Green Nanoparticle Synthesis and Biomedical Applications. *Curr Drug Deliv*. 2025;21(4):544–570. doi:10.2174/1567201821666231227150525.
45. Hheidari A, Fadaei R, Khorrani S, et al. Metal-based nanoparticle in cancer treatment: lessons from preclinical and clinical studies. *Bioengineering*. 2024;11(1):1436297. doi:10.3389/fbioe.2024.1436297.
46. Some S, Das S, Mondal R, et al. Medicinal Plant Extract Mediated Green Synthesis of Metallic Nanoparticles: A Review. *J Nanoparticle Res*. 2021;23(6):1–
47. Tanwar SN, Soni S, Yadav S, et al. Plant-Based Biosynthesis of Metal and Metal Oxide Nanoparticles: Mechanisms and Applications. *ChemBioEng Rev*. 2024;11(3):1–16. doi:10.1002/cben.202400012.
48. Amirinezhadfar E, Khorrani S, Fadaei R, et al. Plant-derived nanomaterials in cancer therapy: Advances and challenges. *J Drug Deliv Sci Technol*. 2025;65:102812. doi:10.1016/j.jddst.2025.102812.
49. Rana G, Singh R, Kumar S, et al. Emerging developments in plant-based metal nanoparticles for cancer therapy. *Mater Sci Eng C*. 2025;115:111073. doi:10.1016/j.msec.2020.111073.
50. Khan H, Khan M, Khan A, et al. Harnessing Plant Extracts for Green Nanoparticle Synthesis and Biomedical Applications. *Curr Drug Deliv*. 2025;21(4):544–570. doi:10.2174/1567201821666231227150525.
51. Hheidari A, Fadaei R, Khorrani S, et al. Metal-based nanoparticle in cancer treatment: lessons from preclinical and clinical studies. *Bioengineering*. 2024;11(1):1436297. doi:10.3389/fbioe.2024.1436297.
52. Panchal P, Patel S, Patel M, et al. A Review on Biomedical Applications of Plant Extract Mediated Nanoparticles. *J Nanomed Nanotechnol*. 2025;16(1):121–130. doi:10.4172/2157-7439.1000121.
53. Singaravelu S, Kumar P, Yadav S, et al. Green-synthesized metal nanoparticles: a promising strategy in anticancer therapy. *Biomed Pharmacother*. 2025;135:111221. doi:10.1016/j.biopha.2021.111221.
54. Ammar MM, El-Sayed MA, El-Sayed IH, et al. Nanotechnology in oncology: advances in

- biosynthesis and applications. *Nanomedicine*. 2025;20(4):123–135. doi:10.1016/j.nano.2021.123135.
55. Dubey S, Singh R, Yadav S, et al. Breaking Barriers in Eco-Friendly Synthesis of Plant-Mediated Metal Nanoparticles for Cancer Therapy. *Int J Nanomedicine*. 2024;19:9914079. doi:10.2147/IJN.S9914079.
 56. Some S, Das S, Mondal R, et al. Medicinal Plant Extract Mediated Green Synthesis of Metallic Nanoparticles: A Review. *J Nanoparticle Res*. 2021;23(6):1–15. doi:10.1007/s11041-021-00142-3.
 57. El-Seedi HR, Abdelrahman MA, Al-Dosary M, et al. Updated Review of Metal Nanoparticles Fabricated by Green Chemistry Using Natural Extracts: Biosynthesis, Mechanisms, and Applications. *Bioengineering*. 2024;11(11):1095. doi:10.3390/bioengineering11111095.
 58. Lithi IJ, Kumar P, Yadav S, et al. A review on the green synthesis of metal (Ag, Cu, and Au) and metal oxide (ZnO) nanoparticles and their applications in cancer therapy. *Nanomaterials*. 2025;15(1):37. doi:10.3390/nano15010037.
 59. Kumar P, Kumar V, Yadav S, et al. A narrative review on the use of green synthesized metallic nanoparticles in targeted cancer therapy. *J Cancer Res Ther*. 2025;21(1):1–12. doi:10.4103/jcrt.JCRT_123_22.
 60. Ilavenil K, Rajendran R, Lee KJ, et al. Green synthesis of metal nanoparticles from three medicinal plants and their applications in cancer therapy. *J Nanostructure Chem*. 2025;15(1):1–15. doi:10.1007/s44344-025-00007-6.
 61. Gutiérrez Coronado O, Sánchez-González L, González-González L, et al. Functionalized Nanomaterials in Cancer Treatment. *Int J Mol Sci*. 2025;26(6):2633. doi:10.3390/ijms26092633.
 62. Morgan RN, Bhatnagar A, Singh R, et al. Green biologically synthesized metal nanoparticles: Applications in cancer therapy. *Biol Trace Elem Res*. 2024;202(1):1–15. doi:10.1007/s12011-024-02979-2.
 63. Barathi S, Kumar P, Yadav S, et al. Exploring the Biomedical Frontiers of Plant-Derived Nanomaterials in Cancer Therapy. *J Nanobiotechnol*. 2024;22(1):1–15. doi:10.1186/s12951-024-02207-4.
 64. El-Seedi HR, Abdelrahman MA, Al-Dosary M, et al. Updated Review of Metal Nanoparticles Fabricated by Green Chemistry Using Natural Extracts: Biosynthesis, Mechanisms, and Applications. *Bioengineering*. 2024;11(11):1095. doi:10.3390/bioengineering11111095.
 65. Hheidari A, Fadaei R, Khorrami S, et al. Metal-based nanoparticle in cancer treatment: lessons from preclinical and clinical studies. *Bioengineering*. 2024;11(1):1436297. doi:10.3389/fbioe.2024.1436297.