***Review Article***

**A REVIEW ON GREEN-SYNTHESIZED PHYTOGENIC NANOPARTICLES: BRIDGING TRADITIONAL PLANT WISDOM WITH MODERN BIOMEDICAL APPLICATIONS**

**ABSTRACT**

The combination of nanotechnology and plant-based phytochemicals is transforming drug delivery and therapy. Plant extracts have bioactive compounds that offer numerous promising medical applications, however, the medicinal benefits of the bioactive compounds are limited due to challenges such as poor penetration of the cell membrane and large molecular size. Nanotechnology can improve absorption, bioavailability, targeted delivery of the bioactive compounds, increasing efficacy and reducing adverse side effects. Plant-mediated nanoparticles deliver sustainable environmentally friendly nanoparticles with strong bioavailability, controlled release, and targeted delivery systems, allowing for improved therapeutics to treat infections, cancer, inflammation, etc. Examples of the bioactive compounds from plant extracts are silver and gold nanoparticles, which have good antimicrobial and anticancer properties. This review examines the rapidly evolving field of nanoparticles in nanomedicine by advocating their synergy with Ayurveda and plant extracts in herbal nanomedicine. It discusses green synthesis pathways, practical therapeutic uses, and their current limitations such as toxicity and producing bulk therapeutics. By connecting traditional medicine with modern nanotechnology, the emerging area of nanoparticle use represents an important new frontier in the exploration and development of plant-based therapeutics and drug-delivery systems. The review also provides significant new insights into the role of nanoparticles in producing efficient and defined therapeutic mechanisms, and therefore, will likely help spearhead future clinical applications and improved health care experiences. The field is an exciting time in medicine and is destined to undergo further growth, change and innovation.

**Keywords:** *Nanoparticles, Plant extracts, Green synthesis, Drug delivery, Nanomedicine*

**1. INTRODUCTION**

In traditional healing systems around the world especially in Ayurveda, Traditional Chinese Medicine and Unani systems, plant-based medicine has been a fundamental component. To treat a variety of illnesses Ayurveda makes extensive use of herbal extracts prepared from different parts of medicinal plants-leaves, bark, roots, seeds, flowers, and fruits. These extracts are abundant in bioactive phytochemicals with strong pharmacological properties including anti-inflammatory antimicrobial antioxidant and anticancer effects such as flavonoids alkaloids tannins glycosides terpenoids and polyphenols [**1,2**]. However, a number of phytochemicals have significant limitations in contemporary therapeutic applications because of their limited bioavailability, high metabolic degradation, low gastrointestinal absorption and poor water solubility [**3**]. For example, while resveratrol from grapes, curcumin from turmeric and quercetin from onions and apples are all potent bio-actives, but their therapeutic efficacy is restricted when given in traditional forms because of their poor systemic retention and quick metabolism [**4**].

**2. INTEGRATION OF NANOTECHNOLOGY WITH HERBAL MEDICINE**

Nanotechnology offers a promising solution to these limitations. Nanoparticles—defined as particles with a size range of 1–100 nm—can encapsulate plant extracts or their individual compounds thereby protecting them from degradation enhancing solubility prolonging circulation time in the bloodstream and enabling targeted delivery to specific tissues or cells [**5,6**]. These features lead to improved therapeutic efficacy with lower doses and fewer side effects. The integration of nanotechnology and herbal medicine stems from the urgent need to bridge the gap between traditional healing wisdom and modern therapeutic standards. This fusion not only modernizes phytotherapy but also validates and amplifies the efficacy of Ayurvedic formulations. Modern biomedical innovation and traditional healing systems are connected through the use of nanotechnology in herbal medicine. For example, Bhasma and other metallic preparations used in Ayurveda are already nanosized substances and their special qualities are believed to be part of the reason for their high therapeutic potency. The bioavailability and bioactivity of plant extracts loaded into contemporary nanocarriers are frequently noticeably higher than those of crude plant extracts alone [**7,8**]. This kind of integration is especially crucial for chronic illnesses as prolonged use of synthetic medications can result in resistance or serious adverse effects. Herbal treatments made with nanotechnology provide a longer-lasting safer option. For instance, it has been demonstrated that herbal substances such as resveratrol quercetin and berberine have strong anticancer properties in cancer treatment their encapsulation in nanoparticles enhances their capacity to target tumor cells and produce cytotoxic effects [**9**]. Furthermore, the use of nano-herbal formulations is consistent with the global trend toward sustainable therapeutics and personalized medicine. Nano-enhanced plant treatments provide a scientifically proven way to combine innovation and tradition in light of consumers growing interest in natural and green solutions. Synergistic therapeutic action is also made possible by the variety of phytochemicals found in plant extracts when they are prepared as nanoparticles. In complex diseases that require multi-targeted therapy like cancer diabetes or neurodegenerative disorders this is especially beneficial. By providing controlled or sustained release of active ingredients through oral transdermal or nasal routes of delivery nano formulations can also increase patient compliance [**10**]. This review investigates the possibilities of combining plant-based therapeutic systems—specifically those found in herbal and Ayurvedic medicine—with nanotechnology. It analyses current research trends and effective nano-herbal formulations talks about the advantages of combining nanoparticles with plant extracts and emphasizes the benefits of green synthesis. The review also highlights the gaps and difficulties that still exist highlighting the contribution of traditional knowledge systems like Ayurveda to the development of contemporary nano formulations.

**3. NANOCARRIERS AND NANOPARTICLES IN NANOMEDICINE**

The European Science Foundation (ESF) states that nanomedicine is the use of nanotechnology and nanoscience to enhance human health especially through the use of materials and tools at the nanoscale that interact with biological systems at the molecular level [**11**]. Nanomedicine is an emerging field that brings together nanotechnology, biomedical sciences, and pharmaceutical sciences to advance medical research and treatment [**12**]. Lipid-based nanoparticles carbon-based nanostructures metallic nanoparticles (like silver and gold) and polymeric nanoparticles are among the common forms of nanoparticles used in medicine. For particular clinical uses each of these provides adjustable qualities [**13**]. The use of nanoparticles as nanocarriers or nanoscale drug delivery vehicles is a key application in nanomedicine. In order to increase treatment effectiveness and reduce side effects these carriers aid in the delivery of therapeutic agents—such as medications proteins or genes—to specific locations within the body [**14**]. Polymeric systems like those based on (polylactic-co-glycolic acid) (PLGA) and polyethylene glycol (PEG) are examples of nanocarrier systems as are solid lipid nanoparticles (SLNs) liposomes micelles dendrimers and nanostructured lipid carriers (NLCs) [**15, 16**]. Surface modification with ligands, peptides or antibodies allows for active targeting of disease- specific cells, such as tumor cells, thereby increasing efficacy and minimizing systemic toxicicty [**17**]. Clinically approved formulations like Doxil (liposomal doxorubicin) demonstrate enhanced tumor accumulation with fewer side effects [**18**] while PLGA based systems offer sustained release and biodegradability [**19**]. The success of liquid nanoparticles in mRNA based Covid-19 vaccines (e.g. Pifizer- BioNTech, Moderna) further illustrates the role of Nanocarriers in modern medicine [**20**]. Additionally, some nanoparticles possess intrinsic therapeutic properties- silver and zinc oxide nanoparticles exhibit antimicrobial activity, while gold nanoparticles are used in photothermal cancer therapy [**21**]. In Summary the integration of nanoparticles and Nanocarriers in nanomedicine opens new avenues for precision medicine, offering safer, more effective and targeted therapeutic strategies.

**4. GREEN SYNTHESIS CONCEPT FOR NANOPARTICLES PRODUCTION**

The concept of green chemistry has gained global attention for its clean and eco-friendly nature. This principle is now being applied in the biosynthesis of nanoparticles using biological agents such as bacteria, fungi, actinomycetes, and plants -a method commonly referred to as green synthesis [**22**]. This eco-friendly approach is particularly promising for biomedical applications, as it offers a biocompatible, sustainable and safer alternative to traditional physical and chemical methods [**23**]. Among various biological systems, plants are most widely used and different parts such as leaves, roots, stems, fruits and seeds serve as sources of bioactive compounds. These phytochemicals act both as reducing agents, which convert metal ions into nanoparticles and as stabilizing agents, which prevent their aggregation [**24**]. Unlike conventional methods that often involve toxic chemicals or high energy inputs, green synthesis relies on mild, nontoxic and eco conscious reactions. It aims to minimize the use and generation of hazardous substances during nanoparticle production [**25**]. Recent research has highlighted advantages of green synthesis including cost effectiveness, ease of scaling, lower toxicity and reduced environmental impact, making it a viable strategy for Safer nanomedicine development [**26**].

**5. ROLE OF PLANTS IN GREEN SYNTHESIS**

Plants are often regarded as nature’s chemical factories due to their rich reservoir of bioactive phytochemicals and their ability to mediate nanoparticle synthesis in an eco-friendly and cost-effective manner. In particular plans have shown from potential in detoxifying and accumulating heavy metals, offering a green solution to environmental pollution -even at trace concentration of toxic metals [**27**]. In comparison to microorganism-based methods, plant-based nanoparticle synthesis has practical advantages, as it avoids the complex and delicate process of maintaining microbial cultures [**28**]. Additionally, the kinetics of nanoparticle synthesis using plant extracts are often significantly faster than other biosynthetic methods and comparable to chemical synthesis in terms of efficiency. This green approach has made it simple and effective to synthesize a wide range of nanoparticles, including iron, zinc oxide, silver, and gold nanoparticles [**29**]. Compounds such as polyols, terpenoids, and polyphenols serve as natural reducing and stabilizing agents, facilitating the bioreduction of metallic ions into nanoparticles [**30**]. Plant-based synthesis is a biocompatible, scalable, and environmentally benign technique that typically occurs at room temperature and completes within minutes to a few hours. The resulting nanoparticles often show improved stability and reduced toxicity, making them especially suitable for biomedical applications [**31**]. As awareness grows regarding environmental sustainability, plant-mediated nanoparticles synthesis continues to gain popularity as a green and effective alternative [**32**].

**6. TYPES OF NANOPARTICLES USED IN PHYTOTHERAPY**

Nanoparticles employed in phytotherapy are primarily classified based on their composition and structural characteristics. The main categories include:​

**6.1 Metallic Nanoparticles**

Metallic nanoparticles (MNPs) are nanoscale particles of metals like silver, gold, copper, and zinc, known for their distinct physicochemical properties and high surface reactivity. Among them, silver (AgNPs) and gold nanoparticles (AuNPs) are the most studied due to their strong antimicrobial, anticancer, and anti-inflammatory activities. These nanoparticles play a crucial role in modern biomedicine, serving as drug carriers, imaging agents, and active therapeutic agents. Their importance lies in their tunable size, shape, and surface characteristics, which enhance cellular uptake and targeted delivery in clinical applications. [**33**].

**6.2 Lipid-Based Nanoparticles (LNPs)**

Lipid-based nanoparticles are widely explored as drug and gene delivery systems due to their ability to protect therapeutic agents, enhance solubility, improve biodistribution, and enable controlled release. Their biomimetic lipid structure and tunable properties contribute to strong pharmacological performance and clinical success.

**Major Subtypes of LNPs**:

* **Liposomes**: Spherical phospholipid vesicles with a lipid bilayer used for encapsulating both hydrophilic and lipophilic drugs.
* **Solid Lipid Nanoparticles (SLNs)**: Made from solid lipids; ideal for controlled drug release and high stability.
* **Nanostructured Lipid Carriers (NLCs)**: Composed of solid and liquid lipids, enhancing drug loading capacity.
* **Phytosomes**: Complexes of plant extracts with phospholipids for better absorption and bioavailability [**34**].

**6.3 Polymeric Nanoparticles**

These are formed using natural or synthetic and biodegradable polymers and provide controlled and sustained drug release. Examples: Chitosan nanoparticles, PLGA nanoparticles, Alginate nanoparticles [**35**].

**6.4 Carbon-Based Nanoparticles**

Made from carbon forms like graphene or fullerenes, they offer high surface area and good biocompatibility. Examples: Carbon nanotubes (CNTs), Graphene oxide nanoparticles, Fullerenes [**36**].

**6.5 Nanoemulsions**

These are thermodynamically stable dispersions of oil and water stabilized by surfactants, used to enhance solubility and bioavailability of plant compounds. Examples: Curcumin-loaded nanoemulsion, Neem oil nanoemulsion [**37**].

**6.6 Metal Oxide Nanoparticles**

Composed of metal oxides, these nanoparticles are widely used for their antimicrobial, antioxidant, and catalytic properties. Examples: Zinc oxide (ZnO) nanoparticles, Titanium dioxide (TiO₂) nanoparticles, Iron oxide nanoparticles [**38**].

**7. THERAPEUTIC APPLICATION**

Nanoparticles are in high commercial demand due to their diver application across industries particularly in electronics, energy, environmental remediation and biomedicine among them silver and gold nanoparticles (AgNPs and AuNPs) are extensively studied for their biological activities. Compared to chemically synthesized NPs, plant based green nanoparticles offer enhanced biocompatibility and reduced toxicity making them highly suitable for therapeutic applications.

**7.1 Antibacterial Activity**

Green-synthesized silver nanoparticles have emerged as potent antibacterial agents against drug-resistant pathogens, offering a safer and eco-friendly alternative to conventional antibiotics. Liquorice-mediated silver nanoparticles (LD-AgNPs) have demonstrated broad-spectrum activity against both Gram-positive and Gram-negative bacteria, including multidrug-resistant MRSA. Their antimicrobial effect is primarily attributed to membrane destabilization, reactive oxygen species (ROS) generation, and intracellular disruption [**39**]. Similarly, silver nanoparticles synthesized using *Acacia rigidula* exhibited strong efficacy against resistant strains like *Pseudomonas aeruginosa* and *Escherichia coli*. In a murine skin infection model, these nanoparticles achieved complete bacterial clearance without causing systemic toxicity or organ damage [**40**]. These findings collectively underscore the therapeutic promise of plant-derived silver nanoparticles in managing resistant bacterial infections with enhanced safety and efficacy.

**7.2 Antiviral** **Activity**

Green-synthesized nanoparticles (NPs), produced using plant or biopolymer-based reducing agents, have shown considerable antiviral potential by disrupting viral entry, replication, or protein activity with minimal toxicity [**41**]. For instance, gold nanoparticles synthesized using *Allium sativum* extract exhibited potent virucidal effects against the measles virus in Vero cells, with an EC₅₀ of 8.83 µg/mL and a high selectivity index of 16.05, indicating a strong therapeutic window [**42**]. Similarly, *Cestrum diurnum*-derived zinc oxide nanoparticles inhibited human coronavirus 229E replication, achieving an IC₅₀ of 7.01 µg/mL and protecting over 72% of cells from cytopathic effects [**43**]. In another study, manganese dioxide nanoparticles synthesized using Arabic gum significantly reduced influenza A/H1N1 viral titers by 3.5 logs and preserved nearly 70% cell viability, supported by molecular docking with viral spike proteins [**44**]. These findings collectively highlight the broad-spectrum antiviral efficacy of plant-based nanoparticles against RNA viruses, underscoring their promise in next-generation antiviral therapeutics.

**7.3 Antifungal** **activity**

Green-synthesized nanoparticles have shown promising antifungal properties, particularly against drug-resistant *Candida* species. In a recent in vivo study, gold nanoparticles synthesized from olive leaf extract effectively treated cutaneous candidiasis in mice, outperforming conventional Nystatin therapy with an IC₅₀ of approximately 40.8 ng/mL [**45**]. In another study, silver nanoparticles derived from Trans-Himalayan plants demonstrated potent activity against multidrug-resistant *Candida auris*, achieving up to 87% biofilm inhibition on catheter surfaces—highlighting their potential in managing persistent device-associated fungal infections [**46**]. Together, these findings underscore the therapeutic relevance of plant-mediated nanoparticles in addressing fungal diseases, especially where conventional antifungals fall short.

**7.4 Antimalarial activity**

Malaria continues to be a major global health burden, with rising drug resistance necessitating the development of novel, safe, and effective therapies. Green-synthesized nanoparticles have shown promise as alternative antimalarial agents due to their bioactivity and low toxicity. For instance, silver nanoparticles synthesized using *Sargassum tenerrimum* extract (Ag-ST) exhibited potent in vitro antiplasmodial activity against *Plasmodium falciparum* and *P. berghei*, with IC₅₀ values of 7.71 µg/mL and 23.93 µg/mL, respectively. In vivo studies further confirmed their efficacy in reducing parasitemia without inducing hematological, biochemical, or genotoxic toxicity [**47**]. Similarly, AgNPs synthesized from *Salvia officinalis* leaves showed strong prophylactic and therapeutic activity in a *Plasmodium chabaudi* mouse model. At a dose of 50 mg/kg, they not only suppressed parasitemia but also conferred hepatoprotective effects by reducing liver inflammation and oxidative stress [**48**]. Together, these findings underscore the therapeutic potential of plant-based silver nanoparticles as safe and effective nanomedicine candidates for malaria treatment.

**7.5 Antileishmanial Activity**

Leishmaniasis remains a serious parasitic disease with limited and often toxic treatment options. Green-synthesized nanoparticles offer a biocompatible alternative with enhanced therapeutic effects. Silver nanoparticles synthesized using *Moringa oleifera* leaf extract showed significant antileishmanial activity in a murine model of cutaneous leishmaniasis caused by *Leishmania major*. These AgNPs reduced lesion size and parasite burden while boosting antioxidant enzyme levels. These results highlight their potential as eco-friendly nanomedicine for effective leishmaniasis management [**49**].

**7.6 Anticancer**

The targeted drug delivery capability of plant-derived nanoparticles (NPs) presents a significant advancement in cancer nanomedicine, offering selective toxicity towards cancer cells while minimizing harm to healthy tissues [**50**]. For instance, green-synthesized silver nanoparticles from pumpkin peel extract exhibited potent radiosensitizing and anticancer effects against triple-negative breast cancer (TNBC) cells. When combined with radiotherapy, these AgNPs enhanced apoptosis by modulating apoptotic markers (↑p53, ↑Bax, ↓Bcl-2) and suppressing HIF-1α expression, thereby increasing therapeutic efficacy [**51**]. In another study, gold nanoparticles biosynthesized using *Curcumae kwangsiensis* leaf extract showed strong, dose-dependent cytotoxicity against ovarian cancer cell lines while sparing normal endothelial cells. Their enhanced anticancer and antioxidant activity, compared to the crude extract and gold salt, suggests a synergistic redox-based mechanism [**52**]. Owing to their eco-friendly synthesis, biocompatibility, and multi-targeted effects, plant-based nanoparticles are emerging as a promising approach in cancer therapy. Further in vivo and clinical investigations are needed to validate their full therapeutic potential [**53**].

**7.7 Cardioprotective Activity**

Cardiovascular diseases (CVDs) remain a leading cause of global mortality, primarily driven by oxidative stress, inflammation, and endothelial dysfunction [**54**]. In recent years, green-synthesized nanoparticles have emerged as a promising strategy for cardioprotection, offering combined antioxidant, anti-inflammatory, and gene-regulatory benefits. For instance, silver nanoparticles synthesized using *Tribulus terrestris* demonstrated significant cardioprotective effects in isoproterenol-induced myocardial infarction models. These AgNPs improved cardiac function, suppressed inflammatory cytokines, and reduced myocardial damage by modulating the PPAR-γ/NF-κB signaling pathway, as confirmed through ECG, biochemical, and histopathological analyses [**55**]. Similarly, apigenin-functionalized gold nanoparticles (AuNPs) showed potent protective effects against doxorubicin-induced cardiotoxicity in rats. They exerted their action by inhibiting pro-apoptotic markers like caspase-3, restoring key antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT), and reducing inflammatory mediators including TNF-α and IL-6, ultimately preserving cardiac tissue integrity [**56**]. Beyond their intrinsic therapeutic actions, these plant-derived nanoparticles can also enable the targeted and controlled release of cardioprotective agents, enhancing efficacy while minimizing systemic toxicity. Collectively, these findings highlight the immense potential of bioengineered, plant-mediated nanoparticles as a novel and biocompatible approach in the prevention and management of cardiovascular diseases [**57**].

**7.8 Neuroprotective Activity**

Neurodegenerative diseases, including Alzheimer’s and Parkinson’s, are closely associated with oxidative stress, neuroinflammation, and progressive neuronal loss. Green-synthesized nanoparticles derived from medicinal plants have emerged as promising neuroprotective agents owing to their intrinsic antioxidant, anti-inflammatory, and drug delivery capabilities [**58**]. For instance, zinc oxide nanoparticles synthesized using *Acanthus ilicifolius* demonstrated neuroprotective effects in *Caenorhabditis elegans* Alzheimer’s models by reducing β-amyloid aggregation, delaying paralysis onset, and lowering oxidative stress, as confirmed through behavioral assays and thioflavin T staining [**59**]. Similarly, silver nanoparticles derived from *Umbilicaria esculenta* preserved dopaminergic neuronal populations and maintained DRD1 expression in MPTP-induced Parkinson’s disease models, indicating neuroprotection through suppression of neuroinflammation and oxidative damage [**60**]. Together, these findings support the therapeutic potential of plant-based nanoparticles in managing neurodegenerative disorders by targeting key pathological mechanisms such as protein aggregation, inflammation, and oxidative stress.

**7.9 Anti-inflammatory Activity**

Green-synthesized nanoparticles, developed using plant, algal, or microbial extracts, have demonstrated significant anti-inflammatory potential by modulating key immune pathways such as cytokine suppression, COX inhibition, and oxidative stress reduction, while maintaining biocompatibility and eco-safety [**41**]. For instance, silver nanoparticles synthesized using *Viburnum opulus* fruit extract showed notable anti-inflammatory activity in both UVB-induced HaCaT cells and acute inflammation models in Wistar rats, leading to reduced edema and pro-inflammatory cytokines [**61**]. Supporting this, a systematic review and meta-analysis confirmed the consistent downregulation of inflammatory mediators such as COX-2, TNF-α, and IL-6 across various preclinical models treated with green-synthesized AgNPs [**62**]. Additionally, gold nanoparticles derived from *Ericaria selaginoides* significantly alleviated colonic inflammation in a murine colitis model, showing comparable efficacy to dexamethasone by reducing ulceration, edema, and immune cell infiltration [**63**]. These findings highlight the diverse and reproducible anti-inflammatory mechanisms of green-synthesized nanoparticles and their potential as safe, plant-based alternatives to conventional anti-inflammatory therapies.

**7.10 Wound Healing**

Green-synthesized nanoparticles have shown significant promise in wound healing applications due to their combined antimicrobial, antioxidant, and tissue-regenerative properties. Among these, silver nanoparticles synthesized using *Litsea cubeba* essential oil (Lceo-AgNPs) exhibited both antibacterial and wound healing effects. In vivo studies revealed that Lceo-AgNPs effectively eradicated multidrug-resistant strains of *E. coli* and *MRSA*, while significantly enhancing wound re-epithelialization compared to conventional silver sulfadiazine treatment [**64**]. Similarly, AgNPs synthesized using cucumber (*Cucumis sativus*) pulp extract accelerated wound healing in diabetic mouse models. The nanoparticle-based ointment not only improved tissue regeneration within 15 days but also demonstrated strong antioxidant and antibacterial properties, which are critical in managing chronic diabetic wounds [**65**]. Additionally, silver nanoparticles derived from *Nepeta cataria* extract (Nc-AgNPs) achieved 94% wound closure within 10 days in Wistar rats when applied with a Vaseline base. Histological and immunohistochemical assessments confirmed enhanced collagen deposition and complete epithelial restoration, showing efficacy comparable to standard treatments [**66**]. Collectively, these findings underscore the therapeutic potential of plant-mediated silver nanoparticles in promoting efficient and infection-free wound healing, particularly in conditions like diabetic ulcers where conventional therapies often fall short.

**7.11 Anti diabetic**

Green-synthesized nanoparticles have emerged as a promising therapeutic approach for the management of diabetes mellitus, owing to their biocompatibility, enhanced bioavailability, and synergistic interactions with phytochemicals. Among various formulations, silver nanoparticles synthesized using a polyherbal extract comprising Momordica charantia, Trigonella foenum-graecum, Nigella sativa, and Ocimum sanctum demonstrated significant antidiabetic activity in alloxan-induced diabetic rats. These polyherbal AgNPs effectively reduced fasting blood glucose, improved lipid profiles, and promoted regeneration of pancreatic and hepatic tissues, highlighting their metabolic restorative potential [**67**]. Similarly, zinc oxide nanoparticles biosynthesized using Tridax procumbens leaf extract exhibited potent antidiabetic effects in streptozotocin-induced diabetic rats. At a dose of 200 mg/kg, these ZnO-NPs significantly lowered blood glucose and HbA1c levels, improved lipid profiles, and preserved pancreatic architecture—outperforming both the crude extract and the standard drug glibenclamide [**68**]. Additionally, silver nanoparticles synthesized with Fagonia cretica leaf extract showed robust antidiabetic activity through dual inhibition of α-amylase and α-glucosidase enzymes and demonstrated strong antioxidant capacity. In diabetic mice, these nanoparticles normalized biochemical markers and improved body weight, suggesting systemic metabolic recovery [**69**]. Collectively, these findings underscore the therapeutic promise of green-synthesized nanoparticles as a novel and effective strategy for the treatment and management of Type 2 Diabetes Mellitus.

**7.12 Drug Delivery**

Plant-derived nanoparticles (PDNPs) have emerged as promising carriers in drug delivery systems due to their unique ability to encapsulate and transport bioactive compounds, thereby enhancing their solubility, bioavailability, and site-specific therapeutic action **[94,95]**. The inherent surface chemistry of PDNPs enables favourable interactions with biological environments, supporting targeted and sustained drug release. A significant advantage of these nanocarriers lies in their biocompatibility and biodegradability, which minimize adverse immune responses and enhance systemic tolerability **[96]**. Furthermore, PDNPs can be surface-modified or functionalised to enable selective targeting of specific tissues or cells, thereby improving therapeutic efficacy and minimizing off-target effects. Various nanocarrier platforms—including polymeric, lipid-based, and metallic nanoparticles—have been employed to deliver phytoconstituents, particularly in overcoming challenges such as low aqueous solubility and poor stability of plant-based drugs, as observed in therapeutic areas like diabetes and cancer **[97]**. For instance, silver nanoparticles synthesized via *Poa annua* leaf extract demonstrated efficient loading of anticancer phytomedicine, with over 85% drug binding and a sustained release profile extending up to 30 days, leading to notable in vivo anticancer activity **[98].** Similarly, gold nanoparticles prepared from *Punica granatum* peel extract and loaded with 5-fluorouracil exhibited high encapsulation efficiency and potent cytotoxicity against breast cancer cells **[99]**. Phytochemicals not only act as therapeutic agents but also serve as reducing and stabilizing agents during nanoparticle synthesis. These metabolites critically influence nanoparticle characteristics such as size, morphology, and surface charge, which in turn determine their drug loading capacity, circulation stability, and controlled release behaviour **[100]**. However, despite these advancements, the clinical translation of PDNPs remains constrained by limited data on their pharmacokinetics, biodistribution, immune interactions, and long-term toxicity. Hence, ongoing research emphasizes the need for comprehensive preclinical evaluations to facilitate safe and effective clinical applications **[53]**.

**TABLE NO. 1: A SUMMARY OF PLANT-BASED NANOPARTICLES IN CLINICAL TRIALS**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **S. No.** | **Nanoparticles / Plant Source** | **Disease / Condition** | **Trial Phase & Design** | **Key Findings / Outcomes** | **Ref.** |
| 1 | Polyherbal AgNPs*Salvadora persica* | Anti-hyperglycemic | In vivo in alloxan-induced mice | Therapeutic efficacy in lowering glucose | **[67]** |
| 2 | Apigenin-coated gold nanoparticles (Api-AuNPs) | Doxorubicin-induced cardiotoxicity | In vitro (H9c2 cells) and in vivo (male Wistar rats) | Significant cardioprotection: improved cardiac markers (CK-MB, LDH), reduced apoptosis, tissue recovery | **[56]** |
| 3 | AgNPs / *Cucurbita pepo* | Triple-negative breast cancer | In vitro (TNBC cell lines) | Functioned as radiosensitizer and showed cytotoxicity against TNBC cells | **[51]** |
| 4 | AuNPs / *Curcumae kwangsiensis* extract | Ovarian cancer | In vitro | Antioxidant and cytotoxic effects on cancer cells | **[52]** |
| 5 | AgNPs / *Sargassum tenerrimum* | Malaria | In vitro & in vivo | Showed antimalarial activity against Plasmodium | **[47]** |
| 6 | AgNPs / (*Trillium govanianum* & *Bergenia ligulata*) | Candida auris infection | In vitro | Effective against drug-resistant Candida auris | **[46]** |
| 7 | ZnO NPs / *Cestrum diurnum* leaf extract | Human coronavirus 229-E | In vitro | Showed promising antiviral activity against HCov-229E | **[43]** |
| 8 | MnO₂ NPs / Arabic gum | Influenza A/H1N1 | In vitro | Demonstrated Antiviral activity against H1N1 | **[44]** |
| 9 | Lceo-AgNPs via *Litsea cubeba* oil-based green synthesis | MRSA wound infection | In vivo (mouse model) | Accelerated wound closure, enhanced collagen formation, antimicrobial activity against MRSA | **[64]** |
| 10 | AgNPs via *C. sativus* pulp extract | Diabetic wound healing | In vivo in mice | Improved wound healing in diabetic model by improving cellular regeneration and antimicrobial effect | **[65]** |
| 11 | AuNPs via *Ericaria selaginoides* | anti-inflammatory activity | In vitro & in vivo (murine colitis model) | Reduction in oxidative stress, inflammatory cytokines and intestinal damage in IBD model | **[63]** |
| 12 | AgNPs via *Umbilicaria esculenta* extract | Parkinson’s disease | In vitro & in vivo | Neuroprotection in PD models | **[60]** |
| 13 | ZnO NPs via *Acanthus ilicifolius* extract | Alzheimer's disease | In vivo in C. elegans | Notable neuroprotective effects against Aβ-induced toxicity by decreasing Aβ aggregation. | **[59]** |
| 14 | Nano Swarna Bhasma (Gold nanoparticle Ayurvedic formulation) | Metastatic breast cancer  | Pilot clinical trial (India, AYUSH-regulated) | 100% clinical benefit, improved outcomes, acceptable safety  | **[70]** |

**8. CHALLENGES IN PLANT-DERIVED NANOPARTICLE RESEARCH**

Plant-based nanoparticles are assumed to be non-toxic because they do not elicit any toxic or immunological responses, unlike synthetic particles. In the context of health care, where patient safety is of utmost importance, the pathogenicity of plant-based nanoparticles, in terms of interacting with biological systems, improves safety while minimizing adverse effects [**71**]. In addition, plant-derived nanoparticles have a wider availability. As they can be grown in mass quantities, plants offer a sustainable and renewable source of raw materials for producing nanoparticles. The diversity in applications of these nanoparticles across different industries can be economically benefitable, as there is abundant supply [**72**]. Moreover, including the previously mentioned compounds, the extracts from plants also possess additional therapeutic potential which renders these nanoparticles bioactive. This indicates that the plant-derived nanoparticles have beneficial effects owing to the source plants like anti-inflammatory, antibacterial and antioxidant properties [**73**]. That said, there are some disadvantages, issues, and challenges that plant-derived nanoparticles pose, which require attention. One such constraint is the variability in the properties of such nanoparticles, which depend on the type of plant species used, their growth conditions, and the methods used for extraction [**74**].

**8.1 Inconsistent Phytochemical Profiles**

The phytochemical constituents of the plant extract greatly impact the synthesis of plant-derived nanoparticles (PDNPs), particularly the bioactive compounds such as flavonoids, terpenoids, alkaloids, and phenolic compounds. Factors like the plant species, region, and even the environment—these include soil, weather patterns, and even the season—greatly influence the existence of reducing or stabilizing agents, which compounds immensely, [**75,76**]. For example, a study investigating *Azadirachta indica* (neem) extracts found that geography impacted the size and morphology of synthesized silver AgNPs. The change in morphology was assumed to be due to changes in bioactive compounds, particularly A. Nimbin and azadirachtin, which alter reducing capabilities and subsequently shape and determine the nanoparticles’ size [**77**]. Green tea also demonstrated in the synthesis of silver nanoparticles changes in morphology due to shifts in the amount of catechin and polyphenol present during certain intervals of time due to season [**78**]. These examples, illustrate that the environmental conditions alongside the species of plants can heavily dictate the constancy and properties of plant-derived nanoparticles.

**8.2 Extraction Technique Sensitivity**

Selection of extraction procedures such as aqueous, ethanolic and supercritical fluid extractions greatly impacts the yield and bioavailability of phytochemicals, thus affecting the efficiency of nanoparticle synthesis. Aqueous extractions, albeit green, are associated with lower concentrations of hydrophobic compounds which can impact the reducing and capping potential of the extract, resulting in altered properties of the nanoparticles formed [**79**].

**8.3 Scale-Up Limitations**

Challenges come up when trying to make the lab-based making of plant-derived nanoparticles (PDNPs) much bigger. It is not like managed lab settings; often, big production faces problems like uneven heating, not good mixing, high levels of impurity, and the creation of mixed nanoparticles [**75**]. One big drawback is the absence of typical regulation which stops steady quality when making things in large amounts. For example, Eucalyptus globulus extracts showed weak management of how reactions happen at a large industry level, causing differences in nanoparticle size and shape. Likewise, efforts to make nanoparticles from *Trigonella foenum-graecum* (fenugreek) in big sizes faced problems keeping the best pH levels and managing the basic parts of how particles form [**80,81**]. These instances highlight the substantial scalability hurdles in transitioning PDNP production from laboratory to industrial scales [**82**].

**8.4 Limited Toxicity Insights**

Although plant-derived nanoparticles (PDNPs) are generally considered biocompatible, their safety profile is not always guaranteed. The phytochemicals used to cap the nanoparticles can impart a variety of biological activities, some of which may cause cytotoxic or immunogenic effects in specific cell types or organisms [**83**]. For example, the potential ecological hazards of zinc oxide nanoparticles derived from Ocimum sanctum were demonstrated when they caused oxidative stress in zebrafish embryos [**84**]. The fact that the biological activity of PDNP-based therapeutics is influenced not only by their nanoparticulate nature but also by the interactions between the nanoparticle core and its phytochemical coatings highlights the importance of comprehensive safety assessments during their development. The transition of PDNPs from research to practical applications is hindered by the lack of standardized methods for evaluating their toxicity and biocompatibility, which poses a significant challenge for risk assessment. Current assessment models often fail to adequately address environmental impact, bioaccumulation, and long-term effects, resulting in an insufficient understanding of the potential hazards associated with PDNPs.

**8.5 COST-RELATED CONSTRAINTS**

Plant-derived nanoparticle (PDNP) synthesis is fraught with difficulties, especially concerning the high cost of raw materials and challenges in technology transfer. Large amounts of plant material are often required for PDNP production, which can be expensive and resource-intensive—particularly when using rare or high-demand medicinal plants [**85**]. For example, Terminalia arjuna, a plant of significant therapeutic value, is commonly used in the synthesis of nanoparticles. However, the use of its bark extracts for the synthesis of gold nanoparticles faced financial challenges due to the high cost involved [**86**]. Furthermore, many industries struggle to integrate these environmentally friendly technologies into their existing workflows, as doing so often requires re-engineering production processes and ensuring consistency in nanoparticle synthesis. These obstacles hinder the widespread commercialization and scalability of PDNPs across various sectors [**75**].

**8.6 SUSTAINABILITY CONSTRAINTS**

There are serious concerns about overharvesting and potential biodiversity loss when specific plants are used extensively for nanoparticle synthesis. Ethical sourcing methods are necessary to ensure the sustainability of plant resources. For example, ashwagandha (*Withania somnifera*) is highly valued in traditional medicine, and concerns about its overexploitation have grown due to its increasing use in nanoparticle synthesis. Additionally, the large-scale harvesting of various plants for nanoparticle production has led to the decline of native populations, thereby disrupting regional ecosystems [**87,88**].

**8.7 REGULATORY COMPLIANCE ISSUES**

Regulatory bodies cannot approve nanomedicine formulations until they have solid in vivo data. In a number of preclinical models, plant-derived nanoparticles (PDNPs) must show both safety and effectiveness before moving on to human trials. Chitosan nanoparticles made from Aloe vera extracts, for instance, have demonstrated promise in the delivery of medications that prevent diabetes; however, regulatory pathways necessitate thorough in vivo testing prior to approval [**89,90**]. Similarly, gold nanoparticles made from bark extract of Terminalia arjuna have shown promising anti-cancer effects in vitro; however, their therapeutic index, off-target effects, and tumour-targeting potential need to be assessed in animal models [**91**]. To verify that they can treat systemic infections without altering the host microbiota, in vivo studies are also required. In vitro, silver nanoparticles made from Catharanthus roseus have also been shown to promote wound healing. However, in order to optimize the formulations for clinical use, in vivo studies are necessary to evaluate their interactions with immune cells, fibroblasts, and keratinocytes [**92,93**].

**9. CONCLUSIONS AND FUTURE PERSPECTIVES**

In conclusion, the integration of nanotechnology into the fabrication of accoutrements with different compositions holds immense promise, particularly in the realm of medicine. Nanotechnology enables the meticulous manipulation of accoutrements at the nanoscale, facilitating the creation of tailored, multi-dimensional accoutrements for specific therapeutic applications. This capability unlocks new avenues in cancer treatment, wound healing, bone regeneration, and diagnostics. Nanoparticles, with their unique size and characteristics, offer precision in drug delivery, potentially minimizing side effects and enhancing therapeutic efficacy. However, further exploration is imperative to optimize targeting techniques and fully realize the potential of nanoparticles in cancer therapy.

The application of plant-derived nanoparticles (PNPs) with essential antibacterial properties presents an innovative strategy for combating microbial infections. Using secondary metabolites from plants in nanoparticle synthesis not only improves antimicrobial efficacy but also enhances the biocompatibility of metal and metal-oxide nanoparticles. While these developments are promising, rigorous toxin and biocompatibility testing is essential to ensure the safety of these nanoparticles for medical applications. Given the increasing emphasis on eco-friendly and sustainable practices, plant-based synthesis methods offer a safer alternative for developing nanoparticles with versatile applications, especially within nanomedicine.

Future advancements in nanotechnology should prioritize the establishment of standardized protocols for synthesizing PNPs. Designing scalable production methods capable of meeting the growing demand for medical applications, alongside conducting thorough toxin and biocompatibility evaluations, is crucial. Long- term safety assessments, encompassing both in vitro and in vivo studies, are critical for elucidating the potential risks associated with PNPs, such as cytotoxicity, genotoxicity, and immunogenicity. Advanced analytical techniques, including proteomics, metabolomics, and histopathological analysis, will play a significant role in elucidating the interactions between PNPs and biological systems.

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