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Review Paper

# Green Nanotechnology in Herbal Medicine: A Review

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## ABSTRACT

Herbal medicine is widely used globally, but many phytoconstituents face challenges such as low solubility, instability, poor bioavailability, and off-target distribution. Green nanotechnology—i.e. the eco-friendly synthesis and application of nanoscale materials—offers a sustainable and biocompatible route to improve herbal therapeutics. In this review, we survey the conceptual basis of green nanotechnology in herbal medicine; types of green nanomaterials employed; mechanistic insights into how nano-herbal systems enhance therapeutic efficacy; sustainability, safety, and toxicological considerations; integration with traditional medicine systems; existing challenges and limitations; and future directions. Emphasis is placed on studies from the last five years (2020–2025). We hope this review serves as a roadmap for researchers to design safe, effective, and scalable herbal nanomedicines..

## INTRODUCTION

Herbal or botanical medicines have long served as a rich resource for bioactive compounds (e.g. flavonoids, terpenoids, phenolics, alkaloids) [1]. However, translating these phytochemicals into clinically effective therapeutics remains challenging due to:

1. **Poor solubility and dissolution** in aqueous environments (many are hydrophobic).
2. **Chemical/physical instability**, including degradation by light, heat, pH, oxidation, or enzymatic action.
3. **Low bioavailability and absorption**, especially by oral routes, often due to first-pass metabolism, efflux transporters, or poor permeability.
4. **Lack of targeting and rapid clearance**, which require high doses and lead to off-target side effects.
5. **Batch variability** in herbal extracts due to plant source, geography, season, and extraction method [2,3].

Nanotechnology has been leveraged to overcome these limitations. Conventional chemical or physical nanoparticle synthesis, however, often involves toxic reagents, organic solvents, high

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energy input, and costly purification, raising environmental and safety concerns. Green nanotechnology is an approach that emphasizes eco-friendly, sustainable, and “safe by design” synthesis and use of nanomaterials [4].

In recent years, especially 2020–2025, there has been rapid growth in research combining green (bio-based) nanoparticle synthesis with herbal medicine, producing nanoformulations that aim to improve absorption, stability, targeting, and therapeutic indices[5]. This review aims to systematically analyze and synthesize that literature, highlight gaps, and propose future directions.


**Figure 1.Application of Green Nanotechnology[6]**

**Conceptual Framework: Green Nanotechnology in Herbal Medicine**

**Definitions and Philosophical Basis:**

- **Green synthesis / biogenic synthesis**: Use of biological systems (plants, microbes, proteins, metabolites) to reduce metal ions or form nanostructures under mild, benign conditions without toxic reagents.
- **Green nanomaterials**: Nanomaterials produced via green routes, ideally biodegradable, non-toxic, derived from renewable sources, and minimal environmental footprint.
- Core principles: minimal use of hazardous reagents; energy efficiency; waste reduction; use of renewable feedstocks; and safe design (i.e. nanoparticles whose byproducts and degradation are benign)[7,8].

**Categories of Nanotechnologies in Herbal Medicine:**

We can broadly classify green nanotechnological systems used in herbal medicine into:

1. **Biogenic metallic / metal-oxide nanoparticles**: e.g. silver (AgNPs), gold (AuNPs), zinc oxide (ZnO), iron oxide (FeOx), etc., synthesized using plant extracts as reducing and stabilizing agents[9].
2. **Carbon-based nanosystems**: e.g. carbon dots or carbon nanoparticles derived from herbal biomass, used for imaging, delivery, or antioxidant roles.
3. **Lipidic / lipid-based carriers**: nanoemulsions, liposomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC)—ideally using biocompatible lipids, natural [10].
4. **Polymeric / biopolymer carriers**: chitosan, alginate, cellulose derivatives, dendrimers (if green), or biodegradable polymers (e.g. PLA, PLGA) formulated under green conditions.

5. **Hybrid systems / composites**: e.g. metallic nanoparticles embedded in polymeric or lipidic matrices, or loaded with herbal extracts.
6. **Other nanosystems**: micelles, phytosomes, nanocrystals, nanogels, etc.[11,12]

## Advantages and Roles of Green Nanoherbal Systems

- **Enhanced solubility**: encapsulation or dispersion improves water compatibility of poorly soluble phytocompounds.
- **Improved stability**: physical protection from degradation by pH, enzymes, light, oxidation[13].
- **Increased permeation / absorption**: nanoscale size facilitates crossing biological barriers, endocytosis.
- **Targeting / accumulation**: passive targeting (e.g. via enhanced permeability and retention, EPR) or active targeting via ligands on nanoparticle surface.
- **Controlled / sustained release**: tunable release profiles help maintain therapeutic concentration over time.
- **Reduced dose and side effects**: by focusing delivery to target tissues, systemic exposure may be lowered[14].
- **Synergy**: the reducing/capping phytochemicals may themselves be bioactive, conferring dual roles (structure + therapeutic).
- **Multiplexing**: combining imaging, diagnostic, or stimuli-responsive features along with therapy (theranostics)[15].

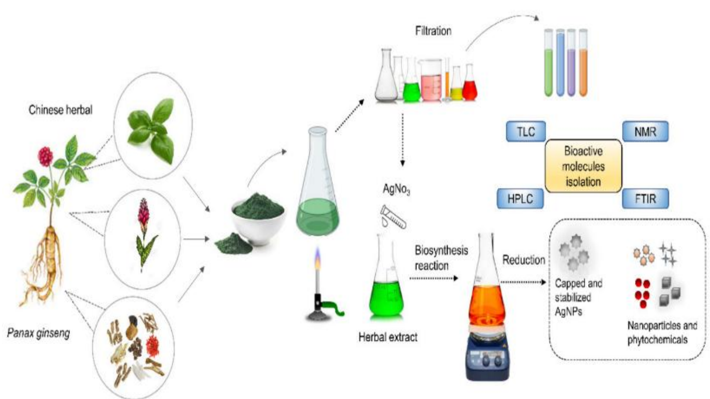


**Figure 2. The conceptual flow: herbal extract → green synthesis → nanoformulation → enhanced uptake/targeting → improved efficacy[16].**

## Green Nanomaterials for Herbal Therapeutics

In this section, we review types of green nanomaterials applied in herbal medicine, along with representative recent studies.

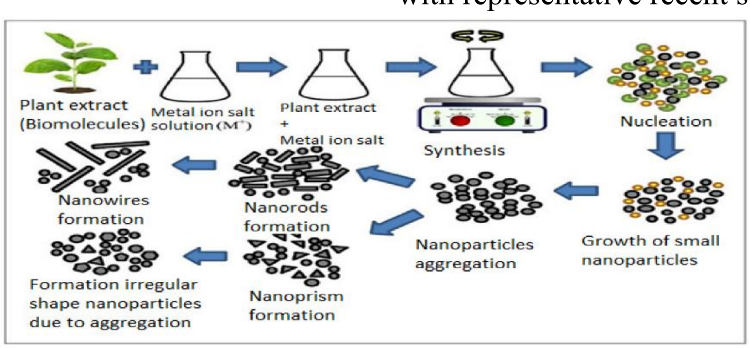


**Figure 3. Metal and Metal Oxide Nanoparticles via Green Routes[17]**

## Metal and Metal Oxide Nanoparticles via Green Routes

### Silver Nanoparticles (AgNPs)

Silver nanoparticles remain among the most studied in green nanoherbal research. Several recent reviews focus on plant-extract mediated green AgNPs, their synthesis parameters, and antimicrobial/biomedical applications.

**Key aspects**:

- Plant extracts supply **reducing** (e.g. phenolics, flavonoids, terpenoids) and **capping/stabilizing** agents (polysaccharides, proteins).
- Reaction parameters such as pH, temperature, concentration, time strongly influence particle size, shape, monodispersity, stability.
- Biomedical applications include antimicrobial, wound healing, anticancer, anti-inflammatory, antioxidant roles[18,19].

Example: Aconitum violaceum leaf extract was used to prepare AuNPs and AgNPs via green means; the antioxidant potential was confirmed via radical assays.

Another study: Green and environmentally friendly synthesis of silver nanoparticles using *Artemisia wilhelmsii*, *Matricaria chamomilla*, *Curcuma longa* extracts, producing spheres <50 nm, and demonstrating antibacterial activity.

Comprehensive recent review: "Green Synthesis of Silver Nanoparticles: A Comprehensive Review of Methods, Influencing Factors and Applications" (2024) discusses the design parameters and biomedical uses [20].

### Other Metals / Metal Oxides (Au, ZnO, Fe, $TiO_2$, etc.)

- Gold nanoparticles (AuNPs) via green routes: e.g. using herbal extracts, combining antioxidant properties (e.g. via A. violaceum)
- ZnO nanoparticles synthesized using plant extracts have been increasingly explored for antimicrobial or UV protection roles (less in strictly herbal therapeutics but important in green nanotech reviews).
- Iron nanoparticles: a review covering green synthesis and environmental/biomedical applications (though many for remediation)
- More general: Radulescu et al. (2023) review green synthesis of metal and metal oxide nanoparticles, summarizing routes, biomedical applications, and design considerations.

These metallic/metal oxide NPs can be integrated or loaded with herbal actives to produce hybrid nanoherbal systems[21-24].

### Carbon-based Nanoherbal Systems

- Carbon dots / carbon nanoparticles from plant biomass (including herbal biomass) are emerging for imaging, sensing, and delivery roles.
- Plant-derived nanoparticles (PNPs) more broadly include carbon-based materials derived from plants, which often are biocompatible, multifunctional, and eco-friendly.
- The review "Nano-particles of natural product-derived medicines" (2025) also discusses carbonaceous nanomaterials for antiviral herbal therapies.
- The review in JDDT (2025) also discusses polymeric nanoparticles, nanoemulsions, liposomes in herbal contexts.
- Researchers apply green surfactants or natural lipids to match the green philosophy[25-27].

### Polymeric / Biopolymer-based Green Nanocarriers

- Chitosan, alginate, cellulose derivatives, starch, pectin, etc., are natural biopolymers

that can be processed under "green" conditions for nanoencapsulation of herbal actives.
- Some studies combine biogenic metallic NPs with polymer carriers to form composites with synergistic effects.
- The review "Biofabrication of nanoparticles: sources, synthesis, and biomedical applications" addresses the use of phytochemicals in NP formation and the possible polymer supports[28].

**Hybrid / Composite Nanoherbal Systems**

Combining metallic NPs with biopolymer or lipid matrices offers advantages:
- Stabilization of metallic NP core
- Controlled release of herbal actives from polymer shell
- Synergistic action: metallic NP + herbal drug together
- Examples: metallic NP embedded in a polymer matrix loaded with herbal extract, or metallic NP coated with herbal extract capping molecules[29-30].

**Mechanistic Insights and Therapeutic Enhancements**

In this section, we explore how green nanoherbal systems exert their improved effects mechanistically.

**Mechanisms Underlying Enhanced Efficacy**

Improved Cellular Uptake and Penetration
- Nanoparticles can enter cells via endocytosis, phagocytosis, or other uptake pathways more readily than free small molecules.
- Surface functionalization (e.g. with targeting ligands) can mediate receptor-mediated uptake.
- Nanoscale size can allow crossing of biological barriers (e.g. blood–brain barrier, mucosal barriers)[31].

Controlled / Sustained Release
- Multi-layer or polymer-encapsulated nanoparticles allow controlled release kinetics, reducing burst release and maintaining therapeutic levels over time.
- Stimuli-responsive release (pH, redox, enzymes) enables triggered release at target tissue microenvironment.

Protection from Degradation
- Encapsulation or physical embedding protects phytocompounds from enzymatic degradation, oxidation, hydrolysis, and photodegradation.
- Metallic NP cores may act as stabilizers for the active compound[32].

Targeted Delivery and Accumulation
- Passive targeting: via enhanced permeability and retention (EPR) effect in tumors or inflamed tissues.
- Active targeting: ligand conjugation (e.g. folate, antibodies, peptides) directs nanoparticles to specific cell types.
- Surface modifications can reduce off-target binding (stealth coatings, PEGylation etc., provided green-compatible).

Synergistic / Additive Effects
- The plant extract used for NP synthesis often contains bioactive molecules (e.g. flavonoids, phenolics) which remain on the NP surface and contribute therapeutic effect.
- Metallic NPs may act through ROS generation, membrane disruption (in antimicrobial contexts) or catalytic effects, complementing phytochemical activity[33-34].

**Examples of Therapeutic Enhancements**

- In neurodegenerative disease models, green-synthesized nanoparticles have been used to deliver herbal antioxidants, reduce amyloid aggregation, oxidative stress, and neuroinflammation. It discusses these applications.

- In antimicrobial applications: green AgNPs synthesized using plant extracts show strong inhibition zones. The capping phytochemicals may enhance binding to microbial membranes and generate ROS.
- In anticancer applications: nanoherbal delivery systems demonstrate better in vitro cytotoxicity, better internalization in cancer cells, and in some cases in vivo tumor suppression (though more such in vivo data is needed). The bibliometric analysis “Collision of herbal medicine and nanotechnology” emphasizes “drug delivery”, “curcumin,” “wound healing” as hot areas.
- The “Nano-particles of natural product-derived medicines” review also details enhancement of antiviral herbal medicine efficacy when delivered via nanocarriers[35-36].

These examples show that the synergy of green nanotechnology with herbal actives can significantly boost therapeutic outcomes.

**Sustainability, Toxicology, and Safety Considerations:-**

While green nanotechnology aims to be safer and more sustainable, it is not free from challenges. This section discusses environmental and toxicological perspectives, and regulatory aspects.

**Sustainability and Environmental Impact**

- Green synthesis reduces or eliminates toxic reagents, uses milder conditions, and often reduces waste and energy consumption.
- Use of biodegradable materials and natural capping agents helps minimize persistent nanowaste.
- However, sourcing of plant materials must avoid overexploitation; batch-to-batch consistency and sustainable harvesting are critical[37].
- Life cycle assessment (LCA) of nanoherbal products is rarely done; such assessments (from raw material to disposal) are needed.
- Environmental fate: even “green” nanoparticles may accumulate, dissolve, or transform in ecosystems, with unknown ecotoxicity[38].

**Toxicological and Safety Concerns**

- **In vitro** cytotoxicity, ROS generation, membrane damage, genotoxicity: metallic NPs may generate reactive species, cause oxidative stress.
- **In vivo** biodistribution, accumulation (liver, kidney, brain), clearance, long-term retention, immunogenicity.
- Surface properties, size, shape, charge, and coating heavily influence toxicity.
- Biodegradation and metabolite products must be assessed for safety.
- Standardization and reproducibility are lacking in many reported studies; many do not evaluate full toxicological profiles[39-40].

For example, the review “Revisiting the Green Synthesis of Nanoparticles” explores the roles of phytochemicals in stabilizing NPs and the factors that influence NP safety profiles.

**Regulatory, Quality, and Ethical Issues**

- Lack of clear regulatory guidelines for herbal-nano products in many jurisdictions.
- Need for Good Manufacturing Practice (GMP) standardization, batch control, traceability.
- Ethical issues around nanomedicine deployment, especially in resource-limited settings.
- Intellectual property and equitable access: many herbal resources are traditional; benefit

sharing and intellectual property must be handled ethically[41].

**Integration with Traditional Medicine Systems:-**

For green nanoherbal products to be accepted and used in traditional medical systems (Ayurveda, TCM, Unani, etc.), certain considerations apply:

- **Preservation of traditional knowledge**: ensure that nanoformulation does not violate or erode traditional practices; rather, it augments them.
- **Formulation integrity**: some traditional formulations involve complex multi-ingredient mixtures—nanoformulating whole formulations (rather than isolating single actives) may preserve synergy.
- **Acceptability among practitioners and patients**: demonstration of safety, efficacy, familiarity in terms of dosage forms (e.g. similar to traditional decoctions but in nano form)[41].
- **Standardization of herbal inputs**: chemotype profiling, fingerprinting, consistency are critical in traditional systems.
- **Bridging with modern regulatory frameworks**: need for safety and clinical validation to integrate with mainstream medicine[42].

The bibliometric review "Collision of herbal medicine and nanotechnology" discusses how nanosizing and nanodelivery are key modes of integration.

**Challenges and Limitations:-**

Despite the promise, many challenges hinder translation:

1. **Scalability and reproducibility**: laboratory green synthesis is often small-scale; scaling up while maintaining uniformity is nontrivial.
2. **Batch variability**: herbal extracts vary with season, location, species, extraction method, affecting nanoparticle formation and performance[43].
3. **Stability and shelf life**: nanoformulations may aggregate, degrade, or lose efficacy over time.
4. **Incomplete toxicology and pharmacokinetics data**: many papers stop at in vitro; few progress to rigorous animal or human studies.
5. **Regulatory and safety constraints**: lack of standardized guidelines for herbal-nano systems.
6. **Cost and commercialization**: translation from lab to market requires investment, partnerships, regulatory approval, scale manufacturing.
7. **Intellectual property and benefit sharing**: particularly sensitive if using traditional knowledge.
8. **Public perception and acceptance**: concerns about "nano" in context of herbal medicine; need for education and transparency[44-45].

Addressing these limitations is essential to move from bench to bedside.

**Future Perspectives and Research Directions:-**

Based on the current literature and gaps, the following directions are promising:

1. **More in vivo and clinical studies**: Strong need for animal pharmacokinetics, long-term safety, and ultimately human clinical trials.
2. **Fully biodegradable and metabolizable nanocarriers**: Design NPs whose breakdown products are benign[46].
3. **Stimuli-responsive and smart nanoherbal systems**: e.g. pH, redox, enzyme-responsive release in specific tissues.
4. **Multifunctionality / theranostics**: Combining imaging (e.g. fluorescence, MRI),

diagnostic markers, and therapy in one nanoherbal platform.

5. **Personalized nanoherbal medicine**: Tailoring herbal phytochemical profiles and nanoformulation to individual patient needs (precision herbal nanomedicine).
6. **Standardization, quality control, and regulatory frameworks**: Adopting guidelines for herbal-nano products, reference monographs, stability criteria.
7. **Life cycle and sustainability assessments**: Evaluate environmental impact from manufacture to disposal[47].
8. **Integration of computational modeling**: In silico modeling of nanoparticle behavior, interactions, and ADMET (absorption, distribution, metabolism, excretion, toxicity).
9. **Cross-disciplinary collaboration**: Bringing together experts in pharmacognosy, nanotechnology, toxicology, regulatory science, formulation engineering.
10. **Community engagement and acceptance studies**: Understanding social, cultural dimensions in traditional medicine contexts[48].

If these areas are addressed, green nanoherbal medicine may emerge as a viable class of therapeutics in coming decades.

## CONCLUSION

Green nanotechnology holds tremendous potential to transform herbal medicine by overcoming key limitations (poor solubility, stability, targeting, bioavailability) while adhering to sustainable and biocompatible design principles. The synergy between plant-derived materials and nanoscale carriers can yield enhanced therapeutic systems with lower doses and improved safety indices. However, significant challenges remain: scaling, standardization, safety validation, regulatory acceptance, and commercial viability. The next decade of research must focus on rigorous in vivo/clinical studies, regulatory frameworks, sustainable manufacturing, and ethical integration with traditional medicine systems.

When fully matured, green nanoherbal therapeutics might bridge the best of traditional medicine and modern nanomedicine—delivering safe, effective, and eco-friendly therapies to global populations.

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