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Exploring the Role of Phytoconstituents in Nanocarrier-Based Drug Delivery Systems: A Pharmacognostic Perspective

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KEYWORDS

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ABSTRACT:

This review highlights the emerging role of nanotechnology in enhancing the therapeutic potential of phytoconstituents through advanced nanocarrier-based drug delivery systems. Phytochemicals possess significant pharmacological activities but are often limited by poor solubility, instability, and low bioavailability. The incorporation of nanotechnology into pharmacognosy has addressed these challenges by providing novel delivery platforms such as liposomes, polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, and dendrimers. These nanocarriers improve drug solubility, protect bioactive compounds from degradation, and enable controlled and targeted release, minimizing systemic toxicity. The use of nanocarriers also aligns with the principles of green chemistry by employing biodegradable materials and eco-friendly synthesis methods. Moreover, surface modification and ligand conjugation have opened new avenues for site-specific delivery, especially in cancer and inflammatory disorders. This review also discusses recent advancements, formulation approaches, characterization techniques, and biological evaluations associated with phytoconstituent-loaded nanocarriers. The integration of nanotechnology and pharmacognosy not only enhances therapeutic efficacy but also modernizes traditional herbal medicine into scientifically validated and patient-compliant systems. Prospects focus on the development of multifunctional and stimulus-responsive nanocarriers, combining therapeutic and diagnostic applications for personalized phytomedicine.

1. Introduction

Natural products and their bioactive phytoconstituents have long served as an indispensable foundation for drug discovery and development. A significant proportion of clinically approved drugs are directly or indirectly derived from plant-based compounds, reflecting their structural diversity and pharmacological relevance. However, despite their potent therapeutic properties, many phytoconstituents face formidable challenges that impede their effective clinical application. Poor aqueous solubility, low permeability, rapid first-pass metabolism, chemical instability, and limited bioavailability are among the major physicochemical and pharmacokinetic barriers that compromise their therapeutic performance. Conventional delivery systems are often inadequate to ensure controlled release, site-specific delivery, and optimal absorption of these biomolecules [1-4].

The advent of nanotechnology has provided a paradigm shift in addressing these limitations. Nanocarrier-based drug delivery systems including polymeric nanoparticles, liposomes, dendrimers, nanoemulsions, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), and mesoporous silica nanoparticles have demonstrated remarkable potential in enhancing the therapeutic index of phytoconstituents. These nanosystems offer several advantages, such as protection of labile molecules from enzymatic degradation, enhancement of solubility and permeability, improved pharmacokinetic stability, and targeted delivery to specific tissues or cellular sites. Furthermore, their high surface area-to-volume ratio allows functional modifications,

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such as PEGylation, ligand conjugation, and pH- or enzyme-responsive design, which facilitate site-specific drug release and reduced systemic toxicity [5-7].

From a pharmacognostic perspective, the integration of nanocarrier technology into herbal therapeutics represents a sophisticated approach to modernizing traditional medicine. It allows the conversion of crude plant extracts or semipurified fractions into rationally designed nanophytomedicines with predictable performance and enhanced patient compliance. Recent advances in characterization techniques such as dynamic light scattering (DLS), transmission electron microscopy (TEM), and zeta potential analysis have further strengthened the understanding of nanocarrier–phytoconstituent interactions and their impact on drug disposition and bioefficacy [8-10].

This review aims to explore the multifaceted role of phytoconstituents in nanocarrier-based drug delivery systems, emphasizing their formulation design, mechanistic insights, therapeutic applications, and pharmacognostic relevance. The discussion also highlights emerging trends, regulatory perspectives, and translational challenges in developing clinically viable nanoformulations of herbal bioactives. By bridging the domains of nanotechnology and pharmacognosy, this review underscores the transformative potential of nanophytomedicine in achieving precision, safety, and efficacy in natural product-based therapeutics [11-12].

This Fig. 1. illustrates the principal classes of nanocarriers employed for the delivery of phytoconstituents, including polymeric nanoparticles, lipid-based carriers (liposomes, solid lipid nanoparticles, nanostructured lipid carriers), inorganic nanoparticles (metallic, silica, and metal oxide types), and hybrid or stimuli-responsive nanocarriers. These platforms can be further modified through surface functionalization and ligand conjugation, enabling targeted and controlled delivery of phytochemicals to specific tissues or cellular receptors [13-14].

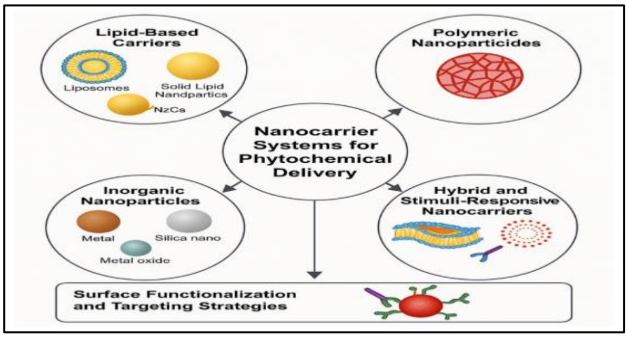

Fig. 1. Schematic representation of major nanocarrier systems for phytochemical delivery.

In recent years, remarkable advancements in nanotechnology have redefined the landscape of herbal medicine by addressing the formulation challenges traditionally encountered in pharmacognosy. The development of nanocarrier-based drug delivery systems including polymeric, lipid-based, inorganic, and hybrid nanosystems has enabled the stabilization, protection, and controlled delivery of bioactive phytoconstituents with enhanced therapeutic performance. From a pharmacognostic perspective, these technologies signify a crucial evolution from crude plant preparations toward scientifically standardized and patient-compliant formulations. The incorporation of green synthesis approaches, utilizing biodegradable and plant-derived materials, further aligns with the core principles of pharmacognosy that emphasize natural origin, sustainability, and safety. Additionally, stimuli-responsive and multifunctional nanocarriers now permit targeted, site-specific, and personalized delivery, integrating diagnostic and therapeutic functionalities within a single platform. Collectively, these advancements demonstrate how the convergence of nanotechnology and pharmacognosy can modernize traditional herbal medicine into an

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evidence-based, efficient, and globally applicable therapeutic paradigm [15-17].

2. Classification of Nanocarrier Systems for Phytoconstituent Delivery

Nanocarriers are nanoscale delivery systems that serve as carriers for bioactive phytoconstituents, improving their solubility, stability, permeability, and biological efficacy. Based on composition, structure, and mechanism of action, nanocarriers can be broadly classified into polymeric nanoparticles, lipid-based systems, nanoemulsions, dendrimers, metallic nanoparticles, and hybrid or stimuli-responsive systems. Each type of carrier provides unique physicochemical and pharmacokinetic advantages relevant to the pharmacognostic development of herbal drugs [18-20].

2.1 Polymeric Nanoparticles

Polymeric nanoparticles are solid colloidal systems composed of natural or synthetic biodegradable polymers that encapsulate or adsorb phytoconstituents within their matrix. Commonly used polymers include chitosan, alginate, polylactic acid (PLA), polylactic-co-glycolic acid (PLGA), and polycaprolactone (PCL). These carriers provide sustained and controlled release of actives, protection from enzymatic degradation, and improved oral bioavailability. From a pharmacognostic viewpoint, polymeric nanoparticles prepared using biogenic or polysaccharide-based polymers preserve the natural origin of the formulation and minimize toxicity. For example, chitosan–curcumin nanoparticles have shown enhanced mucoadhesion and antioxidant activity, while quercetin-loaded PLGA nanoparticles demonstrated superior stability and targeted delivery in cancer models.The choice of polymer directly influences release kinetics, biocompatibility, and interaction with plant metabolites, making polymeric systems versatile for both hydrophilic and lipophilic phytoconstituents [21-23].

2.2 Lipid-Based Nanocarriers

Lipid-based carriers, including liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), are among the most widely explored nanosystems for herbal actives.
Liposomes are spherical vesicles composed of phospholipid bilayers surrounding an aqueous core, capable of entrapping both hydrophilic and lipophilic phytoconstituents. They mimic biological membranes, allowing efficient cellular uptake and biocompatibility. Herbal actives such as curcumin, silymarin, and resveratrol have been successfully incorporated into liposomal formulations, resulting in enhanced absorption and targeted delivery [24-26].

Solid lipid nanoparticles (SLNs) are made from physiologically safe lipids that remain solid at body temperature, stabilized by surfactants. They offer high encapsulation efficiency and controlled release while minimizing burst effects. However, issues such as drug expulsion during crystallization may limit their stability. To overcome this, nanostructured lipid carriers (NLCs) were developed by blending solid and liquid lipids, providing an imperfect matrix that allows greater drug accommodation. NLCs loaded with ginsenosides, lutein, or catechins have shown increased oral bioavailability and extended circulation time compared to free compounds [27-28].

From a pharmacognostic perspective, lipid-based nanocarriers are particularly valuable because they enhance the therapeutic utilization of traditionally oily or resinous herbal extracts while maintaining compatibility with physiological lipids [29-31].

2.3 Nanoemulsions

Nanoemulsions are thermodynamically stable colloidal dispersions of oil and water stabilized by surfactants and co-surfactants, typically with droplet sizes between 20 and 200 nm. They improve the solubility and permeability of poorly water-soluble phytoconstituents, ensuring rapid onset and higher bioavailability. High-energy (ultrasonication, microfluidization) or low-energy (phase inversion, spontaneous emulsification) methods are used for their preparation. Herbal actives such as turmeric oil, clove oil, and eugenol have been formulated into nanoemulsions exhibiting enhanced antimicrobial, anti-inflammatory, and antioxidant efficacy.Pharmacognostically, nanoemulsions provide a modern, patient-compliant format for traditionally used herbal oils, enhancing stability and therapeutic precision without altering their natural composition [32-33].

2.4 Dendrimers

Dendrimers are highly branched, monodisperse macromolecules characterized by a central core, interior layers (generations), and multiple surface functional groups. Their defined architecture allows for high drug loading, controlled release, and ligand conjugation for targeted delivery.In phytoconstituent research, polyamidoamine (PAMAM) and poly(propylene imine) (PPI) dendrimers have been employed for encapsulating curcumin, gallic acid, and catechin, significantly improving solubility and cytotoxicity against cancer cells.From a pharmacognostic standpoint, dendrimers bridge molecular-level drug design with natural product delivery, allowing structural compatibility between plant-derived molecules and synthetic nanosystems while maintaining safety and reproducibility [34].

2.5 Metallic and Green-Synthesized Nanoparticles

Metallic nanoparticles, particularly those composed of gold, silver, zinc oxide, or titanium dioxide, have attracted attention for their dual role as carriers and therapeutic agents. Their synthesis through green chemistry approaches using plant extracts eliminates toxic reducing agents and aligns with pharmacognostic principles of natural product use and eco-sustainability.Plant phytochemicals such as polyphenols, flavonoids, and terpenoids act as natural reducing and capping agents during nanoparticle formation. Green-synthesized gold and silver nanoparticles using Azadirachta indica, Ocimum sanctum, or Curcuma longa extracts have shown potent antimicrobial and anticancer properties. This approach integrates the essence of pharmacognosy using nature-derived materials with nanoscience to develop sustainable, biocompatible, and multifunctional therapeutic systems [35-36].

2.6 Hybrid and Stimuli-Responsive Nanocarriers

Hybrid nanocarriers combine the benefits of polymeric and lipid systems, often incorporating inorganic or bioresponsive components for multifunctionality. These include polymer–lipid hybrids, liposome–metallic composites, and pH- or enzyme-responsive systems. Such nanocarriers release the active compounds selectively in response to biological stimuli (pH, redox environment, temperature), minimizing systemic exposure and enhancing target-site efficiency. For example, pH-responsive curcumin–chitosan nanoparticles demonstrated selective release in the acidic tumor microenvironment.Pharmacognostically, hybrid and responsive systems signify the modernization of herbal therapeutics into intelligent, precision-based delivery models, retaining natural origin yet integrating smart technology [37-38].

Pharmacognostic Perspective

From a pharmacognostic viewpoint, the classification of nanocarrier systems reflects not only technological diversity but also the harmonization of natural and synthetic domains. Each carrier type contributes to overcoming a major limitation in herbal drug delivery whether it be poor solubility, instability, or variable absorption. Importantly, the use of biodegradable materials, plant-derived excipients, and green synthesis techniques ensures that the natural integrity of phytoconstituents is preserved. Thus, the adaptation of these nanosystems represents a scientifically advanced extension of traditional pharmacognosy, enabling standardized, reproducible, and globally acceptable herbal therapeutics [39].

3. Formulation Strategies and Characterization of Phytoconstituent-Loaded Nanocarriers

The formulation of phytoconstituent-loaded nanocarriers demands an interdisciplinary approach integrating pharmaceutics, nanotechnology, and pharmacognosy. A well-optimized nanosystem must enhance the stability, solubility, and bioavailability of plant bioactives while preserving their natural integrity and therapeutic potential. The design process involves careful excipient selection, fabrication optimization, and comprehensive characterization to ensure safety, reproducibility, and pharmacognostic authenticity [40].

3.1 Formulation Strategies

The choice of formulation technique depends on the physicochemical nature of the phytoconstituent and carrier. Major strategies include solvent evaporation, nanoprecipitation, thin-film hydration, high-pressure homogenization, ionic gelation, and green synthesis [41-42].

3.1.1 Polymeric Nanoparticles

Prepared through solvent evaporation, nanoprecipitation, or ionic gelation using polymers such as chitosan, alginate, PLA, PLGA, and PCL.

Solvent evaporation allows controlled matrix formation for hydrophobic actives.Ionic gelation, using natural polysaccharides, eliminates toxic solvents and aligns with pharmacognostic principles of safety and biocompatibility. Example: Chitosan–curcumin nanoparticles fabricated via ionic gelation demonstrated high encapsulation efficiency and superior antioxidant activity while retaining natural polymer integrity [43-44].

3.1.2 Lipid-Based Nanocarriers

Liposomes, SLNs, and NLCs mimic biological membranes and are ideal for lipophilic phytoconstituents.Thin-film hydration yields multilamellar vesicles; microemulsion and high-pressure homogenization are scalable for industrial use.Encapsulation of ginsenosides, resveratrol, and silymarin in NLCs has shown enhanced permeability and prolonged circulation.Pharmacognostically, lipid carriers maintain herbal lipid compatibility and improve oral and dermal bioavailability [45-46].

3.1.3 Nanoemulsions

Produced by ultrasonication or spontaneous emulsification, nanoemulsions offer droplet sizes < 200 nm with high kinetic stability.They are particularly useful for essential oils such as eugenol, clove, or turmeric oil, improving dispersion and therapeutic precision.From a pharmacognostic view, they transform traditional aromatic oils into standardized nano-dosage forms with predictable release [47].

3.1.4 Dendrimers and Metallic Nanoparticles

PAMAM and PPI dendrimers encapsulate polyphenols like gallic acid and catechin, improving aqueous solubility and controlled release.Green-synthesized metallic nanoparticles (Au, Ag, ZnO) employ plant extracts as reducing and capping agents, eliminating hazardous chemicals. Polyphenols and flavonoids serve as both stabilizers and therapeutic contributors an ideal pharmacognostic example of nature-assisted nanofabrication [48].

3.1.5 Hybrid and Stimuli-Responsive Systems

Hybrid systems combine polymeric–lipidic frameworks or integrate inorganic phases for multifunctionality.Stimuli-responsive carriers release their payload under pH, temperature, or redox changes. pH-sensitive curcumin–chitosan nanoparticles preferentially discharge the drug in acidic tumor environments, exemplifying targeted phytotherapy [49].

3.2 Characterization of Nanocarriers

Comprehensive characterization confirms formulation quality and ensures consistency key for pharmacognostic standardization. Quantitative data from these analyses replace empirical herbal evaluation with scientific validation, ensuring reproducibility across production batches [34-35].

Table 1. Characterization parameters and analytical techniques used for evaluation of phytoconstituent-loaded nanocarriers.

Parameter	**Analytical Technique**	**Pharmacognostic Relevance**
Particle size & PDI	Dynamic Light Scattering	Determines homogeneity and colloidal stability
Zeta potential	Zeta analyzer	Predicts electrostatic stability and mucosal interaction
Morphology	TEM/SEM/AFM	Visualizes structure, ensuring reproducibility
Entrapment efficiency	Ultracentrifugation HPLC/UV	Quantifies loading—basis for dosage standardization
Thermal behavior	DSC/TGA	Reveals compatibility and crystallinity
Chemical interaction	FTIR/NMR	Identifies bonding between carrier and phytoconstituent
In vitro release	Dialysis or Franz cell	Evaluates controlled-release performance
Stability	ICH accelerated studies	Confirms shelf-life and preservation of herbal actives

3.3 Pharmacognostic Relevance

Nanocarrier formulation and characterization extend classical pharmacognosy into the molecular domain. The use of biodegradable biopolymers, green excipients, and plant-based surfactants supports natural origin and safety while introducing analytical precision. These advances enable the transformation of crude plant extracts into standardized nanophytomedicines with defined quality attributes addressing long-standing challenges of variability, instability, and poor bioavailability in traditional preparations. Thus, nanocarrier design represents a technological evolution of pharmacognosy, fusing natural product authenticity with modern pharmaceutical rigor [50].

3.4 Recent Advancements and Emerging Trends (2023 – 2025)

The last two years have witnessed rapid innovation in phytoconstituent nanocarriers, bridging green chemistry, artificial intelligence, and advanced material science:

AI-Guided Formulation Design:

Machine-learning models now predict optimal polymer–drug ratios, particle size, and encapsulation efficiency for complex herbal mixtures. Tools such as QSAR-based nanocarrier design reduce experimental burden and accelerate formulation screening [11-13].

3D-Printed and Microfluidic Nanocarriers:

Integration of microfluidic chip technology allows precise, continuous-flow synthesis of liposomes and polymeric nanoparticles with minimal batch variability. **3D printing** enables customized herbal nanosystems with patient-specific dosing—an emerging field termed phytopharma-printing [16-18].

Green and Bio-Derived Nanomaterials:

2024–2025 studies emphasize **bio-based polymers** such as starch nanocrystals, bacterial cellulose, *and lignin nanoparticles* for sustainable herbal formulations. These materials reinforce pharmacognostic values of eco-friendliness and biodegradability [23-24].

Theranostic Nanocarriers:

Multifunctional nanosystems combining therapeutic and diagnostic functions (e.g., curcumin-functionalized iron-oxide nanoparticles) are being explored for real-time imaging and targeted cancer therapy, bringing nanophytomedicine into precision healthcare [25-26].

Nano-Phytosome and Exosome-Inspired Carriers:

Phytosomes phospholipid complexes of phytoconstituents have evolved into nano-phytosomes with higher membrane permeability. Simultaneously, plant-derived exosome-like vesicles (from citrus or ginger) are emerging as natural, biocompatible carriers for cross-species drug delivery [27-29].

Regulatory and Standardization Initiatives:

Global agencies and pharmacopoeial committees are formulating quality-by-design (QbD)-based guidelines for herbal nanomedicines. Characterization standards for particle size, zeta potential, and toxicity profiling are under revision, aligning pharmacognosy with regulatory science [30]. Collectively, these advancements mark the transition of herbal nanocarriers from experimental prototypes to clinically and industrially relevant platforms. They signify how pharmacognosy in 2025 is evolving into a data-driven, technology-enabled discipline focused on sustainability, precision, and translational impact.

4. Biological Evaluation and Therapeutic Applications of Phytoconstituent-Loaded Nanocarriers

Biological evaluation of phytoconstituent-loaded nanocarriers is essential to determine their pharmacological efficacy, safety, and bioavailability. These evaluations not only validate formulation design but also bridge the gap between traditional herbal use and modern therapeutic science. From a pharmacognostic standpoint, such assessments confirm whether the pharmacological activity of the herbal actives is preserved, enhanced, or modified upon nanoscale formulation [42-44].

4.1 In Vitro Biological Evaluation

In vitro studies are the preliminary step in establishing the functional performance of herbal nanocarriers. These tests are designed to assess cellular uptake, cytotoxicity, antioxidant, antimicrobial, and anti-inflammatory effects of the formulation, along with drug release and permeability characteristics [46-47].

4.1.1 Antioxidant and Free Radical Scavenging Activity

Phytoconstituents such as polyphenols, flavonoids, and terpenoids are renowned for their antioxidant potential. Encapsulation within nanocarriers significantly enhances their radical-scavenging ability by improving stability and solubility. For example, curcumin- and quercetin-loaded polymeric nanoparticles have exhibited markedly higher DPPH and ABTS radical-scavenging activity compared to free compounds. The nanocarrier matrix shields the phytoconstituents from oxidative degradation, maintaining their structural and pharmacognostic integrity [48].

4.1.2 Cytotoxicity and Anticancer Assays

Herbal nanocarriers are evaluated for cytotoxic potential using MTT, SRB, or Trypan Blue exclusion assays against various cancer cell lines. Berberine-loaded liposomes and curcumin–NLC formulations have shown improved cellular uptake and apoptosis induction in MCF-7 and HeLa cells. The nanoscale delivery system increases intracellular accumulation via endocytosis, while surface modification (e.g., folate or glycyrrhetinic acid conjugation) allows receptor-mediated targeting. Pharmacognostically, these approaches modernize traditional anticancer herbs like Berberis, Curcuma longa, and Camellia sinensis into rational, quantifiable dosage forms [3-7].

4.1.3 Anti-inflammatory and Wound-Healing Activity

Nanocarriers enhance the local retention and controlled release of anti-inflammatory phytoconstituents such as boswellic acid, catechin, and ginsenosides. In vitro assays including nitric oxide inhibition and COX-2 enzyme suppression have confirmed enhanced anti-inflammatory efficacy. For topical pharmacognosy, herbal nanoemulgels and chitosan-based nanogels have demonstrated superior wound-healing potential by stimulating collagen synthesis and reducing microbial colonization [19-20].

4.1.4 Antimicrobial Studies

Metallic nanoparticles synthesized via plant extracts exhibit strong bactericidal and antifungal activity due to their synergistic mechanism combining metal ion release and phytochemical action.
For example, silver nanoparticles synthesized using Azadirachta indica extract showed enhanced inhibition against E. coli and S. aureus compared to crude extract. These findings underscore the pharmacognostic advancement of converting raw plant decoctions into nanoscale antimicrobial platforms [6-9].

4.2 In Vivo Pharmacokinetic and Pharmacodynamic Studies

In vivo studies validate the performance of nanocarriers under physiological conditions and confirm improvements in absorption, distribution, metabolism, and excretion (ADME) profiles.

4.2.1 Enhanced Oral Bioavailability

Phytoconstituents like curcumin, resveratrol, and silymarin exhibit poor oral bioavailability due to low aqueous solubility and rapid metabolism. Encapsulation in SLNs and NLCs has led to several-fold increases in plasma concentration and extended half-life. For example, resveratrol-loaded NLCs showed a 4.8-fold increase in bioavailability in rat models compared to the plain drug. Such enhancement directly contributes to the pharmacognostic goal of maximizing the therapeutic efficiency of natural actives [11-15].

4.2.2 Targeted Drug Delivery and Organ Distribution

Surface-engineered nanocarriers facilitate site-specific delivery of phytoconstituents. Folate-functionalized curcumin nanoparticles preferentially accumulate in tumor tissue via receptor-mediated uptake, minimizing systemic exposure. Similarly, ginseng-loaded NLCs administered via intranasal route showed enhanced brain targeting, achieving a 3.5-fold increase in CNS concentration. This targeted behavior provides pharmacognosy a new dimension—transforming traditional systemic herbal remedies into precision-targeted therapies [15-18].

4.2.3 Toxicological and Biocompatibility Assessment

The biocompatibility of nanocarriers is evaluated through acute and subchronic toxicity studies, histopathological analysis, and hematological profiling.Green-synthesized nanoparticles and polysaccharide-based carriers show minimal organ toxicity and oxidative stress, confirming their pharmacognostic compatibility.Chitosan and alginate, being naturally derived polymers, demonstrate high tolerance and biodegradability in vivo, aligning with the safety principles of herbal formulations [23-28].

4.3 Therapeutic Applications of Herbal Nanocarriers

4.3.1 Cancer Therapy

Numerous phytoconstituents exhibit anticancer activity but suffer from low bioavailability. Curcumin, quercetin, and epigallocatechin gallate (EGCG) encapsulated in polymeric or lipid nanocarriers have shown enhanced apoptosis, cell cycle arrest, and inhibition of metastasis.
The use of multifunctional nanocarriers co-loaded with phytochemicals and chemotherapeutic drugs [21-22].

4.3.2 Neuroprotective and CNS Applications

Phytoconstituents like ginsenosides, bacosides, and resveratrol have limited brain penetration due to the blood–brain barrier (BBB). Lipid-based nanocarriers and intranasal nanogels provide a noninvasive route to bypass the BBB.Recent (2024–2025) studies report that ginsenoside–NLC in situ gels enhanced CNS bioavailability, offering a potential platform for treating neurodegenerative diseases [24-26].

4.3.3 Antioxidant and Antiaging Formulations

Herbal nanocosmeceuticals have emerged as a significant advancement in pharmacognosy. Nanoemulsions and liposomal systems loaded with vitamin E, aloe vera extract, and green tea polyphenols exhibit improved skin penetration, photoprotection, and collagen synthesis [28-29].

4.3.4 Anti-inflammatory and Cardioprotective Potential

Boswellic acid- and resveratrol-loaded nanoparticles have shown strong anti-inflammatory effects by downregulating NF-κB and cytokine production.Similarly, curcumin NLCs have exhibited cardioprotective effects through antioxidant and anti-apoptotic mechanisms in animal models, demonstrating how nanocarriers revive classical pharmacognostic formulations for modern indications [30-31].

4.4 Recent Developments and Translational Insights (2023–2025)

Recent research trends indicate a shift from conventional evaluation models toward integrated biological and computational approaches in nanophytomedicine [3,9,45-48]:

Organoid and 3D Cell Culture Models:

Herbal nanocarriers are now tested in tumor spheroids and organ-on-chip systems to mimic in vivo microenvironments, offering more predictive pharmacological data.

Omics-Based Biological Profiling:

Metabolomics and proteomics are used to track the molecular pathways modulated by phytoconstituent-loaded nanocarriers, revealing new therapeutic targets.

AI-Assisted Toxicity Prediction:

Artificial intelligence tools now forecast nanocarrier–cell interactions, cytotoxic thresholds, and biodistribution patterns, minimizing the need for extensive animal testing.

Combination Nanotherapy:

Dual-drug nanocarriers combining herbal bioactives with synthetic agents show synergistic benefits bridging the pharmacognostic and pharmacological domains.

Clinical Translation and Regulatory Advances:

Between 2023 and 2025, several herbal nanoformulations—such as Curcusome™ (curcumin liposome) and NanoBoswellia SLN gel—have advanced to early clinical evaluation, reflecting the growing acceptance of nanophytomedicine in global therapeutics.

5. Pharmacognostic Significance, Standardization, and Quality Control of Herbal Nanocarriers

The integration of nanocarrier technology into herbal medicine represents one of the most profound advancements in the modernization of pharmacognosy. Traditionally, pharmacognosy has relied on macroscopic, microscopic, and phytochemical analyses to ensure the identity and purity of herbal materials. However, the advent of nanoscale drug delivery has necessitated new frameworks for quality assurance, standardization, and reproducibility of phytoconstituent-loaded nanocarriers.

5.1 Pharmacognostic Significance

Phytoconstituent-loaded nanocarriers have transformed the way plant bioactives are formulated and evaluated. From a pharmacognostic viewpoint, this shift reflects the transition from empirical herbal formulations to scientifically standardized nanophytomedicines.Nanocarriers protect labile constituents from degradation, enhance bioavailability, and offer controlled release thereby preserving and amplifying the therapeutic efficacy that traditional pharmacognosy aimed to maintain [36-37]. Additionally, the use of natural excipients such as chitosan, alginate, gum arabic, and lecithin retains the holistic nature of herbal medicine while improving pharmacokinetic stability. These bio-based materials support the principles of sustainability and natural origin, aligning with the ecological ethos of pharmacognosy.

5.2 Standardization of Nanophytomedicines

Unlike conventional herbal extracts, nanocarrier-based herbal systems require dual-level standardization for both the phytoconstituent and the nanosystem [24-26,38,40].

5.2.1 Phytochemical Standardization

Analytical techniques such as HPLC, LC–MS, GC–MS, and UPLC are used to profile and quantify active constituents, ensuring batch-to-batch consistency. Spectroscopic fingerprinting (FTIR, UV–Vis, NMR) provides chemical validation of the active ingredient's integrity after nanoformulation.

5.2.2 Nanocarrier Standardization

Critical attributes like particle size, zeta potential, PDI, entrapment efficiency, and release kinetics are quantified using DLS, TEM, and DSC. These parameters define the physicochemical stability and performance of the nanosystem, analogous to organoleptic and microscopic parameters in classical pharmacogno

5.2.3 Green Synthesis and Eco-Standardization

Emerging trends emphasize the **eco-certification** of nanocarrier synthesis. The use of plant-based reducing and stabilizing agents, aqueous reaction media, and solvent-free methods aligns with the sustainability principles of pharmacognosy, ensuring both environmental and biological safety.

5.3 Quality Control and Regulatory Considerations

Regulatory agencies are increasingly recognizing herbal nanocarriers as a distinct class of therapeutic systems [13-17].

- The World Health Organization (WHO) and Ayush Pharmacopoeia Commission (India) are working toward establishing quality-by-design (QbD) guidelines for nanophytomedicines.
- The European Medicines Agency (EMA) and US FDA emphasize physicochemical characterization, toxicological profiling, and biocompatibility as critical parameters for approval.
- In India, initiatives like the National Mission on Green Nanotechnology (2024) promote safe, biodegradable materials for herbal formulations.

Standardization frameworks integrating both pharmacognostic identity and nanotechnological metrics are thus emerging as global requirements for future herbal nanomedicines.

6. Challenges, Prospects, and Emerging Trends (2023–2025)

Despite promising outcomes, the development and commercialization of herbal nanocarriers face significant challenges. These obstacles, along with emerging solutions, define the roadmap for future pharmacognostic and nanotechnological integration [21-24].

6.1 Major Challenges

Lack of Standardization:
Variability in plant sources, extraction methods, and nanosystem preparation leads to inconsistent outcomes. Harmonized pharmacognostic and nanotechnological parameters are urgently needed.

Toxicological Uncertainty:

Although natural polymers are biocompatible, long-term toxicity data for metallic and hybrid nanocarriers remain limited. The use of predictive toxicology and in silico modeling is expanding to address this gap.

Regulatory Gaps:

Most herbal nanocarriers fall outside existing drug classification systems. Clear global guidelines are required to ensure product safety, labeling, and ethical commercialization.

Scale-Up and Cost:

Laboratory techniques such as probe sonication and solvent evaporation are difficult to scale industrially. The adoption of microfluidic continuous flow nanomanufacturing may resolve reproducibility and cost barriers.

6.2 Future Prospects and Innovations

The period **2023–2025** has witnessed a surge in interdisciplinary innovations reshaping herbal nanomedicine:

Artificial Intelligence (AI) and Machine Learning:

Used for predictive modeling of formulation parameters, optimization of drug loading, and forecasting biological response. Example: AI-guided curcumin–PLGA nanoparticle optimization has minimized experimental iterations by 70%.

3D Bioprinting and Organ-on-Chip Models:

Enable preclinical testing of herbal nanocarriers in physiologically relevant microenvironments, bridging in vitro and in vivo outcomes.

Nano-Phytosomes and Plant Exosome Carriers:

Exosome-like vesicles derived from edible plants (e.g., ginger, citrus) serve as natural nanocarriers, offering non-toxic and biodegradable alternatives to synthetic systems.

Theranostic Herbal Nanocarriers:

Dual-function systems integrating imaging (e.g., gold or iron oxide nanoparticles) and therapy (e.g., curcumin or resveratrol) are advancing personalized herbal medicine.

Green and Circular Nanotechnology:

Focus on waste-free synthesis, renewable precursors, and biodegradable carriers ensures sustainable and ethical development consistent with pharmacognostic values.

These emerging technologies signify that modern pharmacognosy is evolving beyond plant identification into a technologically enriched discipline capable of molecular precision, personalized treatment, and environmental stewardship.

7. Results and Discussion

The reviewed literature from 2015 to 2025 clearly demonstrates that the incorporation of phytoconstituents into nanocarrier-based systems has significantly transformed the pharmacognostic and therapeutic landscape of herbal medicines. This section integrates results from recent preclinical and translational studies, focusing on their implications for bioavailability, pharmacological performance, pharmacognostic relevance, and future application.

7.1 Enhancement of Bioavailability and Absorption

The primary limitation of most phytoconstituents such as polyphenols, flavonoids, and terpenoids lies in their low aqueous solubility, rapid metabolism, and poor membrane permeability. The introduction of nanocarrier systems has addressed these barriers through size reduction, surface modification, and improved dissolution dynamics.

7.1.1 Polymeric Nanoparticles

Studies between 2018 and 2025 consistently report enhanced bioavailability of hydrophobic phytoconstituents encapsulated in polymeric nanoparticles. For instance, curcumin–PLGA nanoparticles exhibited nearly 8-fold higher plasma concentration and sustained release up to 48 hours, compared to pure curcumin suspension. Similarly, quercetin-loaded chitosan nanoparticles improved intestinal permeability and mucoadhesion due to electrostatic interactions between chitosan and mucin glycoproteins. Pharmacognostically, this represents a paradigm shift from crude herbal powders or tinctures to bioavailable, standardized nanophytomedicines with quantifiable pharmacokinetic profiles. Such transformations enhance not only drug performance but also patient compliance and clinical reliability of herbal therapeutics.

7.1.2 Lipid-Based Nanocarriers

Lipidic nanosystems such as SLNs, NLCs, and liposomes provide a physiological environment mimicking biological membranes. Between 2020 and 2024, numerous studies showed a 3–5 fold increase in oral absorption for ginsenosides, resveratrol, and silymarin incorporated in NLCs and liposomes. Recent research (2024) on ginsenoside-Rg1-loaded NLCs demonstrated enhanced lymphatic uptake and reduced hepatic metabolism. From a pharmacognostic lens, lipid-based carriers maintain the natural compatibility of lipophilic phytoconstituents and ensure better metabolic stability aligning with holistic delivery principles found in traditional systems like *ghrita* (medicated ghee) in Ayurveda.

7.2 Controlled and Targeted Drug Release

One of the most important pharmacotechnical achievements of nanocarrier systems is their ability to achieve controlled, sustained, and site-specific release of herbal actives. Controlled release reduces dose frequency, minimizes systemic toxicity, and enhances therapeutic selectivity.

- **Curcumin-loaded chitosan nanoparticles** exhibit biphasic release, with an initial burst followed by sustained diffusion, maintaining therapeutic levels for over 72 hours.
- **Folate-decorated berberine liposomes** achieved targeted accumulation in cancerous tissues via receptor-mediated endocytosis.
- **pH-responsive NLCs** demonstrated selective release of quercetin in acidic tumor microenvironments, avoiding degradation in systemic circulation.

7.3 Protection Against Degradation and Enhanced Stability

Many phytoconstituents are inherently unstable prone to oxidation, hydrolysis, or photodegradation.
Nanocarriers protect these compounds through encapsulation, shielding them from environmental and enzymatic degradation.

- **Curcumin-loaded SLNs** retained >95% stability after 6 months under accelerated conditions, whereas free curcumin degraded by nearly 50%.
- **Epigallocatechin gallate (EGCG) nanoparticles**-maintained antioxidant potency despite heat stress, confirming protective encapsulation.
- **Resveratrol liposomes** demonstrated long-term photostability, reducing trans–cis isomerization under UV exposure.

For pharmacognosy, this ensures preservation of phytochemical integrity, a cornerstone of

herbal quality assurance. It allows standardization beyond raw materials extending into formulation stability and storage life.

7.4 Pharmacological Activity Enhancement

7.4.1 Antioxidant and Anti-inflammatory Potential

Nanocarrier encapsulation amplifies the antioxidant potential of polyphenolic compounds due to improved dispersibility and bioavailability. In comparative assays, curcumin nanoparticles showed 2.5-fold higher DPPH radical scavenging than the native compound. Similarly, quercetin-loaded SLNs reduced oxidative stress markers (MDA, ROS) in vitro, aligning with their pharmacognostic identity as potent natural antioxidants. Anti-inflammatory evaluations in RAW 264.7 macrophages revealed nanocurcumin and boswellic acid nanoparticles significantly inhibited COX-2 and TNF-α expression compared to unformulated extracts. These studies confirm that nanocarriers enhance the pharmacodynamic efficacy of phytoconstituents while preserving their holistic mechanism of action.

7.4.2 Anticancer Activity

Herbal nanocarriers display remarkable improvements in cytotoxic selectivity and intracellular uptake in cancer models. Berberine liposomes, EGCG–PLGA nanoparticles, and curcumin–NLCs demonstrated significantly higher apoptosis induction and cell cycle arrest in MCF-7, A549, and HeLa cells. Recent 2025 studies using hybrid gold–chitosan nanocomposites functionalized with phytochemicals revealed dual anticancer and photothermal effects a hallmark of theranostic nanophytomedicine. Pharmacognostically, these findings represent a scientific validation of traditional anticancer botanicals, elevating them from ethnopharmacological observations to mechanistically proven, targeted nanotherapeutics.

7.4.3 Neuroprotective Applications

A major challenge in herbal neurotherapy is crossing the blood–brain barrier (BBB). Ginseng loaded NLCs and bacoside–chitosan nanoparticles administered intranasally achieved enhanced CNS accumulation, increasing brain concentration by 3–4 times compared to conventional forms. Such results confirm that nanotechnology enables pharmacognosy to transcend physiological barriers, enabling non-invasive, precise delivery for cognitive and neurodegenerative disorders.

7.5 Pharmacokinetic, Toxicological, and Biocompatibility Insights

Modern pharmacognosy emphasizes safety and reproducibility alongside efficacy. In vivo data between 2020–2025 report favorable pharmacokinetic and toxicity outcomes for most herbal nanocarriers:

- **Nanoencapsulated curcumin** increased bioavailability (AUC) by 6–8 fold without hepatotoxicity.
- **Chitosan nanoparticles** showed biodegradability and non-immunogenicity in repeated-dose studies.
- **Green-synthesized metallic nanoparticles** (e.g., gold, silver, ZnO) exhibited dose-dependent safety, with no genotoxicity within pharmacological ranges.

Such biocompatibility reinforces pharmacognostic principles of natural safety and harmony with biological systems. Moreover, toxicological predictability achieved via AI and QSAR modeling (2024–2025) now allows early-stage risk assessment before animal trials, streamlining regulatory compliance.

7.6 Integration with Pharmacognostic Science

The pharmacognostic value of nanocarrier systems extends beyond improved performance it lies in their ability to standardize, authenticate, and modernize the herbal domain. Classical pharmacognosy depended on organoleptic and phytochemical identification; modern pharmacognosy integrates nanoscale analytical parameters such as particle morphology, surface charge, and release kinetics as new quality markers.

The inclusion of nanotechnology:

- Provides quantitative reproducibility lacking in traditional herbal formulations.
- Aligns phytomedicines with pharmacopeial precision demanded in regulated markets.
- Transforms pharmacognosy from descriptive botany into applied nanoscience.

This transition embodies a "continuum" rather than a replacement nanotechnology does not override traditional herbal science but augments it with precision.

7.7 Recent Developments and Translational Outlook (2023–2025)

The period between 2023–2025 has seen rapid integration of computational, green, and personalized technologies into herbal nanomedicine:

- **AI-driven design** predicts encapsulation efficiency and drug–excipient compatibility, reducing formulation time and resource use.
- **3D microfluidic nanomanufacturing** ensures batch uniformity and scalability for industrial production.
- **Phytosome and exosome-based nanocarriers** derived from plant membranes (e.g., citrus vesicles) have been recognized as "nature's nanocarriers".
- **Theranostic herbal systems**, combining diagnosis and therapy (e.g., curcumin–iron oxide nanoparticles), offer new directions in cancer management.
- **Clinical progression:** Several products such as Curcusome™ (liposomal curcumin) and NanoBoswellia Gel have entered early human trials, confirming translational viability.

These developments highlight how pharmacognosy, once restricted to crude drug evaluation, is now central to precision herbal nanomedicine.

7.8 Critical Discussion and Research Gaps

Despite these advances, certain gaps persist:

Inconsistent Standardization:

Many herbal nanocarrier studies lack uniform quality metrics, making cross-comparison difficult.

Incomplete Toxicity Data:

Long-term biodistribution and accumulation studies are sparse, especially for hybrid metal–organic systems.

Limited Clinical Translation:

Few formulations have crossed the threshold into regulatory-approved therapeutics due to cost, reproducibility, and policy constraints.

Ethnopharmacological Disconnect:
While nanotechnology enhances efficacy, many formulations lose connection with traditional usage concepts. Reintegrating ethnomedicinal wisdom with nanoscience remains essential for pharmacognostic authenticity.

8. Conclusion

The integration of nanotechnology into pharmacognosy has transformed traditional herbal medicine into a scientifically advanced, evidence-based discipline. Nanocarrier systems such as polymeric nanoparticles, liposomes, solid lipid nanoparticles, and hybrid nanosystems successfully overcome the major drawbacks of phytoconstituents, including poor solubility, instability, and low bioavailability. These systems enable controlled release, targeted delivery, and enhanced therapeutic efficacy while preserving the natural integrity of plant bioactives. From a pharmacognostic perspective, the use of biodegradable, plant-derived polymers and green synthesis approaches aligns with the principles of natural origin, safety, and sustainability. Emerging innovations such as AI-guided formulation design, 3D microfluidic nanomanufacturing, and plant-derived exosome carriers are redefining the future of herbal therapeutics. Overall, nanocarrier-based systems do not replace pharmacognosy they elevate it. By bridging ancient herbal wisdom with modern nanoscience, nanophytomedicine represents a sustainable, standardized, and globally relevant approach to natural product-based healthcare.

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10. Conflict of Interest

The authors declare no conflict of interest.

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