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REVIEW ARTICLE

Advancing herbal therapeutics through nanotechnology: Innovations in drug delivery and pharmacokinetic enhancement

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Abstract

Herbal medicine has long been integral to global healthcare systems due to its therapeutic versatility and cultural significance. Nevertheless, its clinical utility is hampered by inherent limitations, such as low solubility and instability of numerous herbal bioactive. Nanotechnology has emerged as a modern approach to overcoming these challenges by improving botanical compounds' solubility, stability and targeted delivery. The objective of this review article is to conduct a critical assessment of the application of nanotechnology to enhance the pharmacological properties of plant-derived therapeutics in herbal medicine. This review also includes an analysis of the bioavailability and site-specific delivery of herbal bioactive by examining advancements in Nano formulations, such as liposomes, polymeric nanoparticles, Nano emulsions and lipid-based carriers. Furthermore, the review discusses the obstacles to clinical adoption of nanotechnology, including regulatory issues, production scaling issues and the necessity for longer-term safety investigations. This discussion will be supportive to guarantee nanotechnology's safe and efficient incorporation into herbal medicine. Nanotechnology has noteworthy importance for herbal medicines, like, to improve solubility, pharmacological activity enhancement, bioavailability, stability enhancement and site-specific delivery of herbal bioactives. Nanotechnology's transformative potential for herbal medicine necessitates large-scale human trials and comparative nano-delivery system investigations and interdisciplinary collaboration.

Keywords: bioavailability; drug delivery; herbal medicine; nanotechnology; nano formulations; traditional medicine

Introduction

Herbal medicine remains a cornerstone of global healthcare, offering complementary therapies and natural options for disease prevention and treatment. Its significance is underscored by the fact that numerous modern pharmaceuticals, like aspirin (derived from *Salix alba* bark) and artemisinin (from *Artemisia annua*), originated from plant bioactive (1). Herbs such as *Gymnema sylvestre*, garlic (*Allium sativum*) and turmeric (*Curcuma longa*) demonstrate pharmacological benefits, often with fewer side effects than synthetic drugs, making them valuable for managing chronic conditions like diabetes, cardiovascular disease and inflammation (2). Furthermore, their widespread availability and affordability, particularly in resource-limited regions, solidify their role in diverse healthcare systems. Globally, the World Health Organization estimates approximately 80 % of people rely on herbal medicine for primary healthcare (WHO, 2023). Furthermore, a 2023 WHO survey of 170 member states found that 88 % reported explicitly using traditional and complementary medicine (TCM), with herbal medicines being the most prevalent modality, highlighting its deep integration into national health systems." (WHO Global Report on Traditional and Complementary Medicine 2023). "In the United States alone, consumer spending on herbal supplements reached USD 16.8 billion in 2024, reflecting a significant shift towards natural health products in developed economies." (Statista, US Dietary Supplements, 2024). However, the clinical utility of traditional herbal preparations faces significant limitations such as poor absorbance & instability related with plant-derived compounds (e.g., flavonoids, polyphenols) which will suffer from low water solubility, rapid metabolism and limited gastrointestinal absorption, drastically reducing the amount reaching systemic circulation and the target site (3, 4). Additionally, these bioactive are often susceptible to degradation by light, heat, moisture and microbial contamination during storage and processing, diminishing their potency over time (5). Inconsistent efficacy & lack of standardization including variations in plant species, cultivation conditions, harvesting times, extraction methods and the absence of precise dosage control led to significant batch-to-batch variability in active ingredient content and concentration (2). This inconsistency results in unpredictable therapeutic outcomes and hinders reliable clinical application. These difficulties highlight the necessity of contemporary technological strategies, such as nano-formulation, sophisticated extraction methods and strict quality control, to improve the stability, bioavailability and effectiveness of herbal medications and successfully incorporate them into contemporary healthcare systems (6, 7).

Nanotechnology offers a transformative approach to overcoming these limitations. In this context, nanotechnology involves designing and utilizing materials and delivery systems at the nanometre scale (1-100 nm) specifically for herbal bioactive. Nanocarriers can be modified to accumulate at disease locations (e.g., tumours, inflamed tissues), improving efficacy and decreasing off-target consequences and precisely load active substances and control release characteristics, resulting in more uniform therapeutic blood levels and predictable outcomes (8-9).

This review aims to explore the potential of nanotechnology to enhance the safety, effectiveness and standardization of herbal medicines. By integrating traditional knowledge with modern scientific approaches, we can improve health outcomes and ensure that herbal therapies are safe and effective. Understanding the regulatory challenges and the pathways for clinical acceptance will further strengthen the case for incorporating nanotechnology into herbal medicine.

In summary, while traditional herbal medicine offers promising therapeutic options, addressing its limitations through advanced technologies like nanotechnology is essential for maximizing its benefits and ensuring safe clinical use.

Materials and Methods

Researchers conducted an extensive literature review utilizing several online scientific databases, including PubMed, Science Direct, ResearchGate, Wiley and Google Scholar. The literature search was structured and standardized to ensure transparency and reproducibility. The initial search utilized specific keywords such as "Traditional Herbal Medicine," "Nanotechnology," "Herbal Nanocarriers," and "Phytochemical Delivery Systems." These keywords were selected to comprehensively cover the intersection of herbal medicine and nanotechnology.

The inclusion criteria for the literature search were studies published within the last 25 years, ensuring the availability of recent and relevant findings. Only articles published in English were considered to maintain consistency and accessibility of information. Eligible study types included peer-reviewed original research articles, reviews and clinical studies, as these provide reliable data, comprehensive analyses and evidence-based insights.

The exclusion criteria ruled out articles that were not directly related to herbal medicine or nanotechnology, as well as studies that did not provide empirical data or failed to align with the specific research objectives. This ensured that only relevant, evidence-based and contextually significant studies were included in the review.

The selection process followed a systematic approach in line with PRISMA guidelines. Initially, the search yielded a broad range of articles, which were then screened in three stages:

Title and abstract screening

Articles were reviewed based on their titles and abstracts to determine initial relevance. Selected articles underwent a full-text review to assess their alignment with the inclusion criteria and relevance to the research objectives.

Quality assessment

Each selected study was evaluated for methodological quality and scientific rigor, ensuring that only high-quality studies were included.

Through this rigorous screening process, 40 papers were identified as essential for this investigation due to their scientific importance and relevance to the research aims. Comprehensive follow-up investigations were performed on specific herbs highlighted in these studies to provide more precise information on their nanotechnology applications.

By employing this structured literature search strategy, the study aims to contribute to a clearer understanding of how nanotechnology can enhance the efficacy and safety of traditional herbal medicines.

Results and Discussion

Nanotechnology in drug delivery

Nanotechnology has completely transformed contemporary medicine by providing novel approaches to illness diagnosis, treatment and prevention using nanoscale materials and systems. Medicine uses nanotechnology to construct and use nanoparticles, liposomes, dendrimers and nano emulsions (7) to improve medication delivery, increase therapeutic efficacy and lessen adverse effects. Drug delivery systems based on nanoparticles, for example, allow for the targeted delivery of medications to tissues or cells, increasing bioavailability and reducing toxicity. This strategy is beneficial in cancer treatment, as chemotherapeutic drugs are delivered straight to tumour cells by nanoparticles such as liposomes and polymeric micelles. Furthermore, therapeutic applications of poorly water-soluble medications, such as numerous herbal substances, are made possible by nano formulations, which increase their solubility and stability (8).

Categories of nano carriers

Because of their high sensitivity and accuracy, nano-sensors and quantum dots are employed in diagnostics to detect diseases like cancer and infectious disorders early. Furthermore, research is being done on the antibacterial and wound-healing properties of nanomaterials like gold and silver nanoparticles. Nanotechnology in medicine holds enormous promise for improving therapeutic results, enabling individualized medicine and circumventing the drawbacks of traditional treatments. From Table 1, we get a summary of classified nanotechnology.

a) Liposomes are spherical vesicles made of phospholipid bilayers. They are helpful for medication delivery because they can contain both hydrophilic and hydrophobic substances. Table 1 shows that the aqueous core contains hydrophilic medicines, whereas the lipid bilayer contains hydrophobic compounds. Liposomes increase therapeutic efficacy by preventing bioactive substances from degrading, improving their stability and facilitating targeted distribution to specific areas (10).

b) Nanoparticles consist of lipid-based, metal-based and polymeric-based nanoparticles intended for precise and regulated medication administration. Because of their antibacterial and diagnostic qualities, metal nanoparticles, such as gold and silver, are employed extensively. While lipid-based nanoparticles, such as solid lipid nanoparticles (SLNs), shield delicate substances from environmental deterioration and enhance bioavailability, polymeric nanoparticles, such as PLGA (polylactic-co-glycolic acid), guarantee prolonged and regulated drug release (7).

c) Nano-emulsions, defined by oil-in-water or water-in-oil dispersions stabilized by surfactants, are thermodynamically stable. These systems improve the solubility, absorption and bioavailability of herbal components that are weakly soluble by increasing their dispersion. Additionally, nano-emulsions aid in the systemic transport of phyto-compounds and shield them against deterioration (11).

Table 1. Nanocarrier systems for drug delivery

Nanocarrier	Composition	Key Advantages	Application
Liposomes	Phospholipid bilayers (aqueous core +lipid bilayer)	-Encapsulates both hydrophilic (core) & hydrophobic (bilayer) drugs. -Enhances stability & targeted delivery - Reduces degradation	Cardiovascular drugs, anticancer agents, vaccines, gene therapy
Nanoparticles	-Lipid based (SLNs, NLCs) -Polymeric (PLGA, chitosan) -Metal based (Gold, Silver)	- Controlled/sustained release (polymeric) - Antibacterial and diagnostic (metal NPs) -High bioavailability (lipid NPs)	Cancer therapy, antimicrobials, imaging, oral/vaccine delivery
Nano emulsions	Oil-in-water or water-in-oil droplets surfactants	Improves solubility of poorly soluble drugs -Thermodynamically stable -Enhances absorption and bioavailability	Topical oral delivery of phytochemicals, essestial oils, neutraceuticals
Micelles	Amphiphilic (hydrophobic core + hydrophilic shell) molecules	Solubilizes hydrophobic drugs in aqueous media -Small size (~ 10-100 nm) -Psasive targeting (EPR effect)	Chemotherapy (herbal extracts)
Nanocrystals	Pure drug particles (nanometer size) + stabilizers	-Dramatically increases dissolution rate & saturation solubility -No need for organic solvents -High drug loading	Poorly water soluble drug (eg. Curcumin, flavonoids, antifungal agents)

d) Micelles can solubilize hydrophobic molecules in aqueous conditions because they self-assemble amphiphilic molecules with a hydrophilic shell and a hydrophobic core. In addition to enhancing their stability and transport to the target tissues, they increase the solubility and bioavailability of herbal constituents or medications poorly soluble in water (12).

e) Nanocrystals, pure solid drug particles with diameters in the nanometre range that are stabilized by surfactants, are called nanocrystals. From Table 1, expanding the surface area available for dissolution considerably improves the solubility and bioavailability of herbal components. Nanocrystals, such as curcumin and flavonoids (13), enhance absorption and therapeutic benefits and are especially advantageous for phyto-compounds that are poorly soluble in water.

Rights to intellectual property and commercialization of nano-herbal formulation

Nanotechnology in herbal medicine has catalysed advancements in medication transport and formulation, generating prospects for patentable inventions (PI) and commercial enterprises. This convergence also presents issues in intellectual property protection, regulatory compliance and market scalability. Here, some lists were given in Table 2.

Curcumin (Turmeric)

Turmeric contains curcumin, a polyphenolic molecule with anti-inflammatory and anti-cancer effects. Nevertheless, its therapeutic potential is limited by its low solubility and poor absorption.

a) Nanotechnology approaches: Utilizing nanotechnology, particularly polymeric nanoparticles, has shown promise in improving curcumin's solubility and stability. These nanoparticles enhance their dispersion in water, increase gastrointestinal absorption and protect them from rapid degradation. Studies have demonstrated that curcumin encapsulated in polymeric nanoparticles exhibits enhanced anti-inflammatory and anticancer activities, leading to better therapeutic outcomes in conditions like arthritis and cancer (14).

b) Liposomal curcumin: To improve curcumin's bioavailability, incorporating it into liposomes spherical vesicles with a lipid bilayer has been explored. This method enhances curcumin's transport and absorption in the body, potentially increasing its therapeutic efficacy (15).

c) Natural Deep Eutectic Solvents (NADES): Research into dissolving curcumin in NADES has indicated potential benefits in enhancing its solubility and stability. This approach may offer a viable method for improving curcumin's bioavailability and therapeutic application (16). These advancements suggest that employing such strategies can significantly improve the therapeutic potential of curcumin in treating various inflammatory and cancerous conditions.

Table 2. List of patent formulations based on herbal medicine with nanotechnology

Bioactive Compound	Source	Therapeutic Properties	Limitations	Nanotechnology Approach	Enhanced Effects	References
Curcumin	Turmeric	Anti-inflammatory, anticancer	Low solubility, poor absorption, rapid degradation	Polymeric nanoparticles, liposomal curcumin, Natural Deep Eutectic Solvents (NADES)	Improved solubility, bioavailability and stability; enhanced anti-inflammatory and anticancer effects	(23–25)
Resveratrol	Grapes	Antioxidant, neuroprotective	Low bioavailability, difficulty crossing the blood-brain barrier (BBB)	Liposomal encapsulation	Better solubility, improved BBB penetration, enhanced neuroprotective effects (e.g., Alzheimer's, Parkinson's)	(26)
Quercetin	Flavonoid (fruits, vegetables)	Antioxidant, anti-inflammatory, antiviral	Poor water solubility, low bioavailability	Nanoemulsions (oil-water interface stabilized by surfactants)	Increased solubility, absorption and distribution; stronger anti-inflammatory and antioxidant effects	(27–29)
Silymarin	Milk Thistle	Hepatoprotective (liver diseases like hepatitis, cirrhosis)	Poor solubility, rapid metabolism, low bioavailability	Lipid nanoparticles	Enhanced absorption, protection from metabolism, improved liver protection	(30–32)
Berberine	Berberis species	Antidiabetic, antimicrobial	Low bioavailability, poor water solubility	Polymeric nanocarriers, gum-based nanocomplexes, shellac nanoparticles, Pluronic F127 micelles	Increased solubility, stability, cellular uptake; stronger antimicrobial and antidiabetic effects	(33–35)

Resveratrol (Grapes): The polyphenolic chemical resveratrol present in grapes is well known for its antioxidant and neuroprotective properties. However, the entire therapeutic potential of this substance is limited by its low bioavailability. Resveratrol's solubility and bioavailability are improved when it is encapsulated in liposomes, making it easier to pass through the blood-brain barrier (BBB) and have neuroprotective effects. The chemical is now a promising therapeutic candidate due to its improved ability to fight neurological illnesses, including Parkinson's and Alzheimer's, due to liposomal formulations (17).

Quercetin (Flavonoid): The flavonoid quercetin, which has antiviral, anti-inflammatory and antioxidant qualities, has problems since it is not very soluble in water. Nano emulsions have been created to increase quercetin's solubility and therapeutic effectiveness. Using surfactants to stabilize the oil-water interface, nano emulsions improve quercetin's bioavailability, facilitating improved absorption and distribution throughout the body. These formulations also improve the compound's anti-inflammatory and antioxidant properties, increasing its potential to treat ailments like diabetes, inflammatory disorders and cardiovascular diseases (18-20).

Silymarin (Milk thistle): Milk thistle's primary component, silymarin, is well-known for its hepatoprotective properties, especially when it comes to treating liver conditions like cirrhosis and hepatitis. However, its therapeutic usage is limited by its poor bioavailability, which is caused by its quick metabolism and poor solubility. From Table 2, lipid nanoparticle application has demonstrated encouraging outcomes in enhancing silymarin's bioavailability. Lipid-based nanocarriers boost silymarin's absorption and shield it from metabolic breakdown, improving liver protection and therapeutic effectiveness (21-23).

Berberine (Berberis species): A substance called berberine, present in many plants, including *Berberis* species, has been shown to have antibacterial and antidiabetic properties. Low bioavailability, however, prevents it from being used in clinical settings. Developing polymeric nanocarriers has enhanced berberine's solubility, stability and bioavailability. These nanocarriers increase the compound's antibacterial activity through improved absorption into cells and tissues, increasing its efficacy against infections and metabolic diseases. In comparison to pure berberine, berberine's *in vitro* antidiabetic and antibacterial properties are much increased when it is nano encapsulated in gum-based nanocomplexes, indicating increased bioavailability (24). Scientists created shellac nanoparticles functionalized with octadecyl trimethylammonium bromide and Poloxamer 407 to encapsulate berberine. Due to the enhanced attraction between the cationic nanocarriers and anionic cell surfaces, which results in a larger local concentration of berberine, these nanocarriers demonstrated a strong amplification of berberine's antimicrobial efficacy across various bacteria (25). To address berberine's poor water solubility and bioavailability, Pluronic F127 micelles containing berberine were developed in earlier studies. According to the micelles' enhanced drug loading, stability and sustained release profile, polymeric micelles may be a viable nanocarrier for boosting the therapeutic effectiveness of berberine (26). Table 2 highlights the patent formulations based on herbal medicine with nanotechnology.

Herbal drugs with Artificial Intelligence (AI)

The design and optimization of nanocarriers using AI and Machine Learning (ML) have the potential to transform the herbal medicine industry completely. AI algorithms can process large preclinical and clinical research datasets to forecast the best way to formulate herbal compounds using nanotechnology. These algorithms can all aid in selecting the most appropriate materials for nanocarriers, the creation of nanoparticles with surface characteristics and predicting their biological interactions within the body. Furthermore, AI could help customize herbal treatments according to a person's genetic or molecular profile and maximize the scalability of nanocarrier production by identifying effective manufacturing processes. The development of innovative herbal formulations that are safer, more effective and customized to each patient's needs can be significantly accelerated by AI's capacity to analyze complex datasets.

Benefits of nanotechnology in medicine

Enhanced solubility and stability

Nanotechnology greatly enhances the solubility and stability of weakly water-soluble compounds frequently found in pharmaceutical formulations and herbal remedies. By increasing the surface area of bioactive chemicals, nanocarriers like liposomes, nanoparticles and nano emulsions facilitate improved solubility in biological fluids. This increased solubility allows for better absorption in the gastrointestinal tract, which improves bioavailability. Furthermore, nanocarriers extend the shelf life and therapeutic efficiency of sensitive substances by shielding them from environmental deterioration brought on by oxidation, light, or heat (27).

Targeted drug delivery to specific tissues

Nanotechnology makes targeted medicine delivery possible, lowering systemic exposure and adverse effects. By altering their surface properties to identify specific receptors or using external stimuli like magnetic fields or pH changes, nanoparticles and nanocarriers can target specific tissues or cells, like cancer cells or areas of inflammation. By providing the therapeutic chemicals precisely to the site of action, this focused method maximizes therapeutic efficacy and minimizes off-target effects (6, 28).

Controlled release mechanisms

Nanocarriers allow the controlled and sustained release of bioactive chemicals, which ensures a consistent and long-lasting therapeutic effect. This technique is invaluable for chronic illnesses, where stable medication levels are necessary for effectiveness. By gradually releasing their payloads, nanoparticles, liposomes and micelles can be made to administer drugs less often and increase patient compliance. Controlled release also reduces toxicity by preventing high peak drug concentrations (29-31).

Studies and advances in pharmacokinetics and pharmacodynamics

Pharmacokinetics: Enhanced absorption and prolonged half-life of herbal extracts with nanocarriers

Several studies have demonstrated how nanotechnology enhances the pharmacokinetics of herbal extracts by improving absorption, bioavailability and prolonging half-life. For example, curcumin, a poorly soluble compound, has been encapsulated in polymeric nanoparticles to improve its bioavailability. Curcumin, a polyphenol compound extracted from the turmeric rhizome, exhibits various biological activities, including antibacterial, anti-inflammatory, anti-cancer and antioxidant properties. However, its poor solubility leads to low bioavailability. Previous studies (32) showed that curcumin-loaded nano-liposomes coated with chitosan and alginate have been developed, resulting in enhanced intestinal absorption and improved therapeutic efficacy compared to conventional curcumin formulations.

Similarly, resveratrol, a polyphenol with strong antioxidant capacity but poor bioavailability and light instability, benefits from encapsulation in liposomes. Resveratrol-encapsulated liposomes maintain an intact membrane structure during digestion, improving cellular absorption and enhancing therapeutic effects (33).

Pharmacodynamics: Increased potency of herbal drugs due to targeted delivery

Nano carriers improve the pharmacokinetic properties of herbal compounds and enhance their pharmacodynamics by enabling targeted delivery. For instance, resveratrol-loaded PEGylated liposomes have demonstrated increased systemic circulation time and improved brain distribution, enhancing their potential for treating neurological disorders (34).

Comparative analysis of traditional vs. nano-formulations in preclinical/clinical trials

Comparative studies have shown that nano formulations often outperform traditional herbal formulations. For example, curcumin-loaded nano gels are at least twice as potent as free curcumin, possibly due to enhanced uptake (35). Similarly, resveratrol nano formulations have shown improved bioavailability and therapeutic efficacy compared to traditional formulations (36).

In contrast, traditional herbal formulations often suffer from poor absorption, low bioavailability and short half-lives, which limit their therapeutic efficacy. Nanotechnology-based drug delivery systems overcome these limitations, offering targeted, controlled and sustained drug release that maximizes therapeutic outcomes and minimizes side effects.

Commercial applications and patents

Review of commercially available nanotechnology-based herbal formulations

Nanotechnology-based formulations have been developed to enhance herbal compounds' bioavailability and therapeutic efficacy. Below are references related to the mentioned formulations: A review discusses curcumin's bioavailability challenges and nanoparticle technology's potential to enhance its absorption and therapeutic effects (37). A comprehensive overview of curcumin's bioavailability issues and the advancements in nanoparticle formulations to improve its therapeutic efficacy (38).

A study explored how reducing the particle size of silymarin can improve its solubility, absorption and therapeutic performance. Another review summarized recent formulation techniques designed to enhance the bioavailability of silymarin through modern drug delivery approaches (21). These references provide insights into the advancements in nanotechnology-based herbal formulations, explicitly focusing on curcumin and silymarin and their improved therapeutic potentials.

Patents filed for nanotechnology in herbal medicine

Numerous patents aiming at improving the delivery, bioavailability and therapeutic efficacy of herbal compounds have resulted from incorporating nanotechnology into herbal medicine. Famous instances consist of:

Numerous patent applications have been filed to increase the solubility and bioavailability of nanocurcumin. Theracurmin®, for example, filed patent US7348187B2, which describes a preparation of curcumin that uses nanoparticles to increase its solubility in water. This allows for improved absorption and therapeutic effects. This formulation has overcome curcumin's limitations for clinical use.

Another well-known application of nanotechnology patenting is encapsulating resveratrol in liposomes or nano emulsions for improved bioavailability. US20170203532A1, a noteworthy patent in this field, explains how liposomal resveratrol can improve pharmacokinetics and delivery, increasing its potential for treating cardiovascular and neurodegenerative diseases (39, 40).

Silymarin nano-formulation, particularly with nanostructured lipid carriers (NLCs), has been the subject of patent applications. The US20170239278A1 patent, for instance, describes a process for creating nanoscale silymarin particles for enhanced bioavailability and liver protection (41).

Numerous patents, including US9512237B2, have addressed the formulation of berberine in a polymeric nanoparticle for improved absorption and increased antimicrobial activity, as well as polymeric nano carriers for improved berberine delivery. By improving berberine's solubility and bioavailability, this invention strengthens its defences against infections and metabolic diseases (23).

These patents highlight the noteworthy developments in nanotechnology-based herbal formulations, which enable better therapeutic results and broader global commercialization of conventional herbal compounds.

Challenges and limitations of nano-herbal formulations

Variable pharmacokinetics

Changes in gastrointestinal circumstances, enzyme activity and first-pass metabolism can also affect the pharmacokinetics of herbal substances, resulting in notable alterations in the plasma concentrations of these compounds. For instance, curcumin's limited absorption and quick elimination contribute to low and irregular systemic levels despite its strong pharmacological activities (42, 43).

These pharmacokinetic irregularities may compromise the effectiveness and dependability of herbal remedies. Advanced medication delivery methods, like formulations based on nanotechnology, may help with these issues by making herbal ingredients more soluble, encouraging regulated release and increasing their systemic availability.

Dose escalation and toxicity risks

Because of the high dosages needed to provide therapeutic results, dose escalation and toxicity risks are significant issues in herbal therapy. Large doses are required for clinical efficacy since several herbal components, including polyphenols, flavonoids and terpenoids, have poor pharmacokinetic characteristics and low bioavailability (2). Furthermore, when used without appropriate regulation or medical supervision, the unpredictability and lack of standardization of herbal medicines might increase the danger of overdosing and unintentional toxicity. Long-term high-dose treatment may compromise patient safety by causing nephrotoxicity, hepatotoxicity, or herb-drug interactions (44). To overcome these obstacles, bioavailability must be increased using cutting-edge delivery methods like nanotechnology. These methods can lower the necessary therapeutic dosage, lower the risk of toxicity and guarantee safer administration of herbal medications.

Stability issues

Since many phyto-compounds are susceptible to deterioration when exposed to light, heat, moisture and oxidative stress, stability problems are a significant problem in herbal therapy. These environmental elements may cause the active ingredients to degrade, which would lessen their potency and therapeutic effectiveness (45). For example, polyphenols, flavonoids and essential oils are highly vulnerable to oxidation, reducing their bioactivity and shortening their shelf life (46).

Likewise, substances like catechins and curcumin break down quickly in heat and light, reducing their usefulness in traditional formulations. The quality and uniformity of the final product are compromised by oxidative stress, which speeds up the deterioration process even more, particularly in herbal medicines that are not adequately preserved. Advanced formulation techniques like encapsulation, nano emulsions and solid lipid nanoparticles (SLNs) are used to overcome these obstacles. These techniques aim to protect phyto-compounds from environmental stressors, improve their stability and extend their shelf life for better therapeutic results (7).

Cost and scalability of nanotechnology for herbal medicine

Scalability and production costs are two major obstacles to the use of nanotechnology in herbal medicine. Creating in lipid-based carriers, nanoparticles and nano emulsions frequently require sophisticated technologies, specialized tools and strict quality control procedures, raising production costs. For example, creating polymeric liposomes and nanoparticles requires expensive materials and intricate procedures, making it challenging to produce at reasonable costs. Furthermore, maintaining consistency in the size, shape and surface properties of nanoparticles may be difficult for large-scale manufacturing, which could affect the safety and effectiveness of the particles. These elements may limit the widespread use of nano formulated herbal medicines, particularly in low-income markets, by making them unaffordable(47-49).

Regulatory hurdles and safety concerns regarding nanocarrier formulations

Since many nations lack precise nanomedicines' safety and approval procedures, the regulatory environment for nanotechnology-based herbal formulations is still developing. Manufacturers are uncertain because regulatory bodies such as the European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have not yet set precise guidelines for nanotechnology-enhanced herbal products. This delays the commercialization of nano-based herbal formulations, making it difficult to get approval. Furthermore, little is known about the long-term safety of nanocarriers, particularly about the risks associated with their possible buildup in the body. Toxicity concerns include the potential for organ toxicity, immunological responses and cellular damage from nanoparticles. The absence of thorough research on the safety profile of nano herbal formulations could endanger public health and make the approval process more difficult (50-52).

Standardization and quality control challenges in combining nanotechnology with herbal medicine

Standardizing the finished product is a significant challenge when developing herbal medicine nano formulations. Due to variables like location, growing conditions and harvesting time, herbal medicines naturally differ in their chemical makeup, which results in uneven therapeutic outcomes. Because of the intricate nano formulation procedures required, applying nanotechnology to these variable compounds makes maintaining consistent quality and potency even more difficult. Size distribution, surface charge and encapsulation efficiency must be described for nano carriers and it can be challenging to guarantee the reproducibility of these parameters on a large scale. The need for standardized manufacturing procedures and rigorous testing for each batch produced makes quality control even more crucial. Furthermore, new challenges in formulation stability, bioavailability and safety are introduced when nanotechnology is combined with herbal products; these issues need careful testing and validation before commercial marketing.

Future prospects of nanotechnology in herbal medicine

Emerging trends and smart nano carriers (Stimuli-responsive delivery systems)

Recent advancements in nanotechnology have led to the development of stimuli-responsive nanocarriers (also known as innovative delivery systems), which enable precise, controlled release of herbal therapeutics in response to environmental cues such as P^H, temperature, light, or enzymatic activity (53, 54). These systems enhance therapeutic efficacy by targeting specific biological microenvironments. For instance, pH-sensitive nanoparticles can selectively release herbal compounds in acidic tumour tissues or the gastrointestinal tract, minimizing off-target effects (55). Similarly, temperature-responsive carriers release payloads in hyperthermic or inflammatory regions, while light-triggered systems allow spatiotemporal control over drug delivery (56, 57). Such innovations improve bioavailability and reduce systemic toxicity, addressing longstanding challenges in herbal medicine delivery (54).

Enhancing personalized herbal medicine with nanotechnology

Nanotechnology holds transformative potential for personalized herbal medicine by integrating pharmacogenomics and genomic data to tailor treatments to individual patient profiles (58, 59). Smart nanocarriers can be engineered to target cellular or tissue-specific markers influenced by genetic variations, optimizing therapeutic outcomes. For example, AI-driven algorithms enable the design of nanocarriers that accommodate genetic polymorphisms affecting drug metabolism, thereby enhancing efficacy while mitigating adverse effects (60, 61). This approach facilitates precision dosing, timing and delivery, creating patient-specific regimens that maximize therapeutic benefits (62). The convergence of AI, genomics and nanotechnology may redefine herbal medicine by enabling data-driven, individualized therapies (59). Integrating AI-driven design, stimuli-responsive nanocarriers and personalized medicine represents a paradigm shift in herbal therapeutics. These technologies promise to enhance therapeutic precision, reduce side effects and improve patient adherence through tailored formulations. Future research should prioritize clinical validation of these systems and address scalability challenges to ensure translational viability (Table 3).

Potential for personalized herbal medicine through nanotechnology

The development of customized herbal medicine could be significantly aided by nanotechnology. Nanocarriers combined with developments in pharmacogenomics and genomics can be used to create customized herbal treatments tailored to each patient's particular requirements. To maximize the delivery and effectiveness of herbal medications, nanocarriers can target specific cells or tissues according to a person's genetic profile or current state of illness. Herbal formulations, for instance, might be modified to address genetic variations that affect drug metabolism or response, improving therapeutic results while reducing side effects. Nanotechnology-enabled personalized medicine presents the potential for creating customized treatment regimens that maximize the dosage, timing and targeting of herbal remedies, which could

Table 3. Future prospects of nanotechnology in herbal medicine

Aspect	Key Concepts	Mechanism/Example	Advantages	Future Focus/Outlook	References
Stimuli-Responsive Nanocarriers (Smart Delivery Systems)	pH, temperature, light and enzyme-responsive nanocarriers for controlled drug release	pH-sensitive nanoparticles release herbal compounds in acidic tumor or GI environments; temperature-responsive systems act in inflamed areas; light-triggered allow spatiotemporal delivery	- Targeted delivery - Controlled release - Enhanced bioavailability -Reduced systemic toxicity	Clinical validation and optimization for scalable, cost-effective production	(53-57)
Integration with Pharmacogenomics & Genomic Data	Use of patient-specific genetic information to design tailored nanocarriers	Nanocarriers designed to target tissue/cell markers based on genetic variations influencing drug metabolism	- Personalized therapy - Optimized efficacy - Minimized side effects	Research on gene-drug-nanocarrier interaction ns; precision herbal formulation	(58-59)
AI-Driven Nanocarrier Design	Artificial intelligence used to predict, model and optimize nanocarrier structures and responses	AI algorithms simulate drug-carrier-tissue interactions for individualized formulation	- Precision dosing and timing - Enhanced targeting - Improved adherence	Integration of AI, genomics and nanotechnology for personalized herbal therapeutics	(60-61)
Personalized Herbal Medicine	Customized formulations based on patient's genetic and physiological profile	Adjust herbal therapy to genetic polymorphisms affecting drug metabolism or response	- Higher therapeutic outcomes - Fewer adverse effects - Data-driven personalization	Translation to clinical settings; ethical and regulatory frameworks	(62)
Overall Future Outlook	Convergence of smart nanocarriers, AI and genomics	Development of precision herbal nanomedicine	- Enhanced therapeutic precision - Reduced side effects - Improved patient outcomes	Validation, scalability and global implementation	(56, 63-66)

result in more potent therapies with fewer adverse effects. As this field develops, combining genomic data and nano medicine may create new opportunities for creating safer and more effective precision herbal treatments.

In summary, advances in smart nanocarriers, AI-driven design and personalized medicine are opening the door to more individualized and efficient treatment options, making the future of nanotechnology in herbal medicine extremely bright (Table 4). As these technologies advance, they could significantly improve the therapeutic effectiveness of herbal remedies while reducing adverse effects and improving patient outcomes (56, 63-72).

Conclusion

Nanotechnology has the potential to revolutionize the field of herbal medicine by addressing key challenges such as poor bioavailability, instability and variability in efficacy. Using advanced nanocarriers, such as liposomes, polymeric nanoparticles, nano emulsions and micelles, nanotechnology enhances the solubility, stability and bioavailability of phyto-compounds, making them more effective in therapeutic applications. Moreover, the ability to target specific tissues and organs with stimuli-responsive systems further improves the precision and potency of herbal treatments, paving the way for personalized medicine.

Integrating traditional herbal knowledge with modern nanotechnology represents a powerful synergy that can unlock the full therapeutic potential of plant-based medicines. By bridging these two worlds, we can optimize the efficacy of herbal compounds, enhance their pharmacokinetic profiles and mitigate risks associated with traditional formulations. This combination of ancient wisdom and cutting-edge science offers a promising path to developing more effective, safe and patient-tailored herbal therapies.

However, significant challenges remain, including cost, regulation, scalability and the need for standardization in manufacturing and quality control. Further research is essential to overcome these hurdles and translate nanotechnology-based herbal formulations into routine clinical use. With continued innovation, collaboration between the fields of pharmacognosy, nanotechnology and pharmaceutical sciences and rigorous clinical trials, the integration of nanotechnology into herbal medicine has the potential to transform healthcare, offering enhanced therapeutic outcomes and personalized treatments that were once thought to be beyond reach.

Table 4. Integration of nanotechnology and artificial intelligence in the modification of herbal drugs for enhanced delivery, targeting and therapeutic efficacy

Herbal Compound	Application	Nanotechnology Used	AI Application	Research Reference
Curcumin (Turmeric)	Cancer therapy, anti-inflammatory	Polymeric nanoparticles, liposomes	AI-driven optimization of nanoparticle synthesis & drug in controlled release kinetics	(67)
Resveratrol (Grapes)	Anti-aging, neuroprotection	Nanoemulsions, solid lipid nanoparticles	Machine learning for formulation stability prediction	(68)
Epigallocatechin Gallate (EGCG) (Green Tea)	Antioxidant, cancer prevention	Gold nanoparticles, nanoliposomes	AI modeling of drug release profiles	(69)
Paclitaxel (Taxus spp.)	Breast cancer treatment	Albumin-bound nanoparticles (e.g., Abraxane®)	AI-guided pharmacokinetic modeling	(70)
Berberine (Berberis spp.)	Diabetes, antimicrobial therapy	Chitosan nanoparticles	AI-based toxicity and efficacy prediction	(71)
Withanolides (Ashwagandha)	Neuroprotection, stress reduction	Nanoemulsions, polymeric micelles	AI-driven neuroprotective activity screening	(72)

Authors' contributions

FR conceptualized the study, conducted the literature review and prepared the initial draft of the manuscript. SS and SZ contributed to literature synthesis, improved the review structure and provided critical revisions. IJB finalized the manuscript, supervised the overall project and offered expert guidance. All authors read and approved the final version of the manuscript.

Compliance with ethical standards

Conflict of interest: The authors declare that there is no conflict of interest regarding the publication of this manuscript.

Ethical issues: None

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