Int. J. Sci. R. Tech., 2025 2(11)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Nanoherbals: A Modern Approach in Herbal Medicine

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ABSTRACT

Herbal medicines have long been valued for their therapeutic benefits, minimal side effects, and cost-effectiveness; however, their clinical utility remains constrained by poor solubility, instability, and limited bioavailability. Recent advancements in nanotechnology—encompassing liposomes, nanoemulsions, polymeric nanoparticles, and solid-lipid carriers—have emerged as promising solutions to these challenges. By encapsulating phytoconstituents within nanoscale delivery systems, nanoherbals enhance absorption, protect bioactive compounds from degradation, and enable targeted, controlled release, thereby increasing therapeutic efficacy across a broad spectrum of conditions, including cancer, neurological, inflammatory, and metabolic disorders. Additionally, bibliometric studies illustrate the rapid growth and evolving landscape of herbal nanomedicine research, with significant attention to trends, hot topics, and emerging frontiers in the field. Despite these advances, challenges persist—such as ensuring standardization of herbal materials, evaluating long-term nanotoxicity, scaling up green synthesis processes, addressing regulatory deficits, and ensuring sustainable manufacturing. Thus, while nanoherbals represent a convergence of traditional phytotherapy and modern drug delivery, further rigorous research, safety evaluations, and harmonized regulatory frameworks are essential for their successful translation into mainstream clinical applications.

Keywords: Nanoherbals, Herbal Medicine, Nanocarriers, Bioavailability, Nanotechnology, Drug Delivery, Safety, Future Perspectives

INTRODUCTION

Herbal medicines have been integral to human healthcare for millennia, with documented systems like Ayurveda, Traditional Chinese Medicine, and Unani dating back over 5,000 years [1]. These traditional remedies remain deeply rooted in modern healthcare due to their perceived safety, holistic benefits, and affordability. However, their widespread acceptance is constrained by intrinsic limitations—particularly poor aqueous solubility, instability, and low bioavailability of active phytoconstituents [3]. Nanotechnology has emerged as a transformative solution to these challenges. By integrating herbal constituents into nanoscale delivery systems—such as liposomes, nanoemulsions, polymeric and solid lipid nanoparticles—researchers have significantly enhanced solubility, stability, and absorption, while enabling controlled and targeted release of bioactive compounds [3]. This convergence of nanotechnology and phytotherapy gives rise to the concept of **nanoherbals**—a modern adaptation of herbal medicine utilizing engineering at the nanoscale.

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

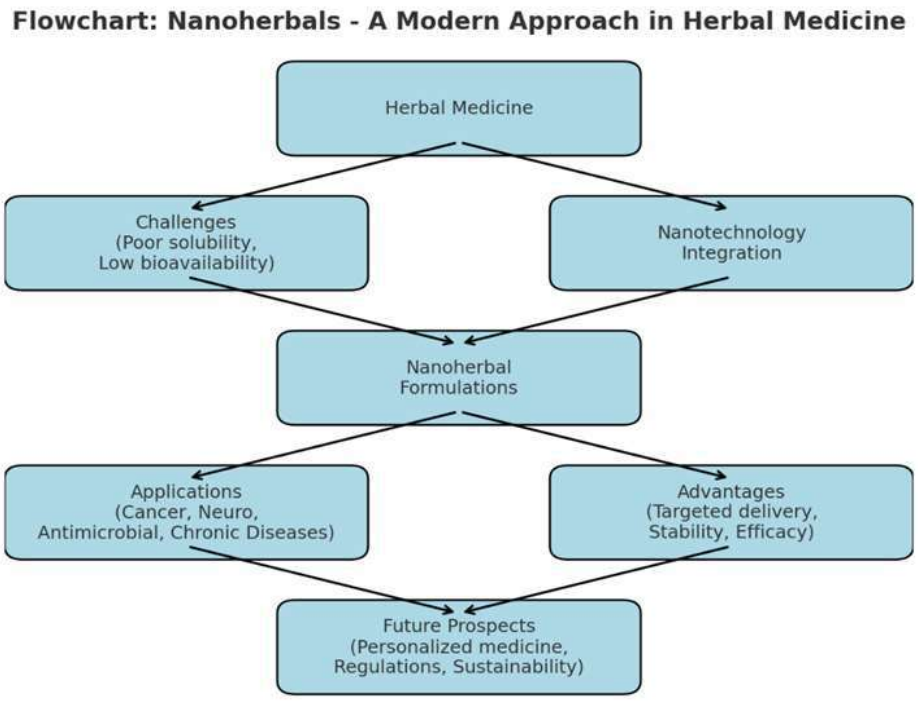

Figure 1: Nanoherbals: A Modern Approach in Herbal Medicine – from traditional herbal challenges to nanotechnology integration, applications, and future prospects

Recent reviews have captured the breadth of these developments. Applications span across diverse herbal nanosystems that bolster therapeutic efficacy, broaden drug delivery routes, and circumvent pharmacokinetic hurdles typical of conventional herbal formulations [1]. A bibliometric analysis of the field further highlights its rapid expansion, identifying key research hotspots, prevalent delivery platforms, and evolving trends in the use of herbal nanoparticles from 2004 to 2023 [6]. Despite their promise, nanoherbals also pose challenges—standardizing herbal raw materials, ensuring long-term safety and biocompatibility, scaling up manufacturing, and navigating regulatory landscapes remain major hurdles [7]. In summary, nanoherbals represent a powerful fusion of age-old medicinal wisdom with cutting-edge nanotechnology. This hybrid approach seeks to enhance therapeutic outcomes, improve pharmacokinetic profiles, and broaden delivery options, heralding a new chapter in herbal medicine. In the following sections, this review will delve deeper into the applications, technical underpinnings, advantages, hurdles, and future prospects of this promising field.

3. What are nanoherbals?

3.1 Concept and Definition

Nanoherbals, also known as *herbal nanoparticles*, represent an advanced delivery system where bioactive compounds from medicinal plants are encapsulated within nanoscale carriers (typically **1–100 nm**) to enhance their therapeutic properties. These nanoparticles are formulated using techniques such as green synthesis, ionic gelation, coacervation, or encapsulation in nanocarriers like liposomes or polymeric nanoparticles [20]. Herbal nanoparticles merge the wisdom of traditional herbal remedies with cutting-edge nanotechnology, aiming to overcome limitations such as poor solubility, instability, and low bioavailability [10]. They deliver herbal actives more effectively, while reducing toxicity and enabling targeted delivery [3].

3.2 Nanotechnology Principles Applied to Herbal Medicine

Nanotechnology enhances herbal medicine through several fundamental principles:

- **Nanosizing for Improved Solubility & Stability**: Reducing the particle size of herbal actives increases surface area, facilitating better dissolution and protecting labile compounds from degradation [1].

- **Encapsulation in Nanocarriers**: Herbal extracts are loaded into liposomes, nanoemulsions, polymeric nanoparticles, solid lipid nanoparticles (SLNs), niosomes, and more—enhancing compatibility, protection, and controlled release [3].

- **Controlled & Sustained Release**: Nanocarriers allow gradual release of the herbal actives, maintaining therapeutic levels and reducing dosage frequency [8].

- **Targeted Delivery & Enhanced Permeability**: Nano-scale particles can pass biological barriers effectively—exploiting the Enhanced Permeability and Retention (EPR) effect for passive targeting and potentially further functionalized for active targeting [10].

- **Biocompatibility & Lower Toxicity**: Many nanocarriers use biodegradable polymers and natural materials, offering safer profiles than conventional systems [14].

- **Green Synthesis Approaches**: Some nanoherbals are produced via eco-friendly methods using plant-derived agents—avoiding toxic chemicals while ensuring enhanced bioactivity, safety, and environmental sustainability [13].

3.3 Key Objectives of Developing Nanoherbals

The development of nanoherbals aims to address multiple therapeutic and formulation challenges:

- **Enhance Solubility and Bioavailability**: Many phytoconstituents are hydrophobic; nanoformulations improve their absorption and systemic availability [1].

- **Protect Herbal Actives**: Encapsulation shields unstable compounds from environmental degradation, preserving efficacy [10].

- **Provide Controlled & Sustained Drug Release**: Offers prolonged therapeutic activity and better dosing compliance [13].

- **Targeted & Site-Specific Delivery**: Enhances delivery precision to disease sites (e.g., tumors, brain, inflamed tissues), improving effectiveness and reducing side effects [10].

- **Improve Safety and Reduce Dosage**: Increased efficiency enables lowering therapeutic doses, minimizing adverse effects [8].

- **Enable Novel Applications**: Nanoherbals extend herbal usage into areas like cancer therapy, neurodegenerative disease management, wound healing, cosmetics, nutraceuticals, and functional foods.

3.4 Traditional Herbal Formulations vs. Nanoherbals

Table 1 Traditional Herbal Formulations vs. Nanoherbals

Aspect	Traditional Herbal Formulation	Nanoherbals (Nano-formulations)
Particle Size	Micron-scale (>1000 nm)	Nano-scale (1–100 nm)
Solubility	Poor, especially for hydrophobic actives	Enhanced, due to larger surface area and encapsulation
Bioavailability	Often low	Significantly improved
Stability	Prone to degradation (light, heat, pH)	Enhanced through protective nanoencapsulation
Targeted Delivery	Non-specific distribution	Passive/active targeting via nanosystems
Control Over Release	Immediate or poorly controlled	Sustained, tunable release profiles
Toxicity & Dosage	Risk of high dosage and side effects	Lower doses, improved safety
Applications	Limited to traditional uses	Expanded into cosmetics, cancer therapy, neuroprotection, etc.

4. Types of Nanoherbals

Nanoherbals encompass a variety of nanoparticulate delivery platforms designed to enhance the bioavailability, stability, and therapeutic efficacy of herbal compounds. Below are key types employed in current research:

4.1 Polymeric Nanoparticles (PNPs)

These are biodegradable particles—often made from polymers such as PLGA, chitosan, or natural polymers—designed to protect herbal actives, enable controlled release, and cross physiological barriers (e.g., for CNS delivery) [14].

4.2 Nanocapsules & Nanospheres

- **Nanocapsules**: Comprise a core–shell architecture where herbal actives reside in the inner core, enclosed within a polymeric shell.
- **Nanospheres**: Dense, matrix-like structures that encapsulate actives within a polymer network [21].

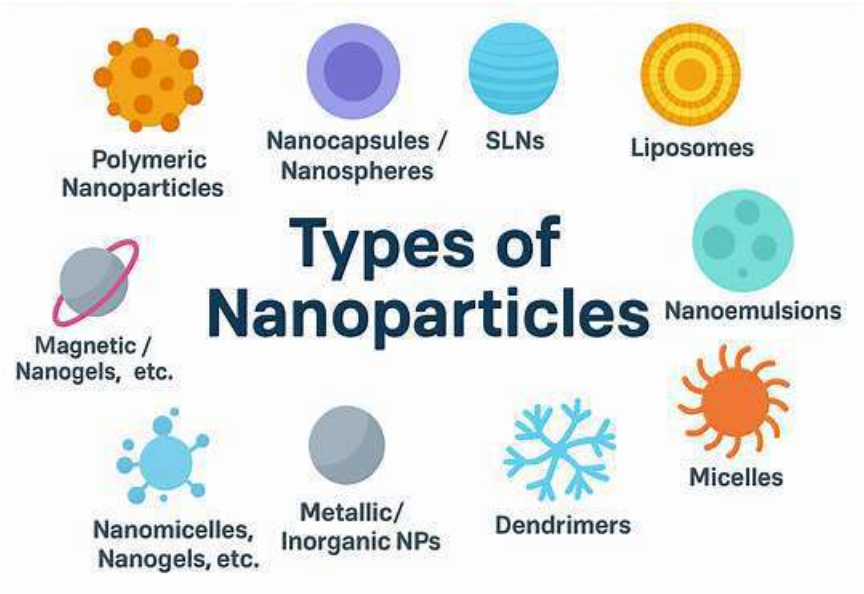

Figure 1 Types of Nanoparticles

4.3 Solid Lipid Nanoparticles (SLNs)

SLNs are made of solid lipids, offering enhanced stability, protection against degradation, controlled release, and improved bioavailability of herbal actives [14].

4.4 Nanostructured Lipid Carriers (NLCs)

These are advanced lipid systems combining solid and liquid lipids, thereby providing higher drug loading, better stability, and improved release profiles compared to SLNs [17].

4.5 Liposomes

Phospholipid bilayer vesicles that encapsulate herbal molecules in an aqueous core—offering biocompatibility and enhanced delivery efficiency [18].

4.6 Nanoemulsions

These are fine oil–water emulsions stabilized by surfactants, excellent for improving the solubility, dissolution, and skin or oral absorption of herbal extracts [19].

4.7 Micelles & Phospholipid Micelles

Self-assembling amphiphilic aggregates that enhance solubilization and delivery of hydrophobic phytochemicals [12].

4.8 Dendrimers

Highly branched, tree-like nanostructures that can load multiple herbal molecules simultaneously, offering high payload and potential for targeted delivery [14].

4.9 Metallic & Inorganic Nanoparticles

Nanoparticles composed of metals like gold or silver, utilized for their unique physicochemical and therapeutic properties—e.g., enhancing anticancer activity when used with herbal compounds [20].

4.10 Magnetic Nanoparticles & Quantum Dots

Used for diagnostics and as specialized payload carriers; quantum dots also serve imaging roles due to their fluorescent properties [14].

4.11 Other Systems (Micelles, Micellar Systems, etc.)

- **Polymeric Micelles**: Stable assemblies for hydrophobic phytochemicals [14].
- **Nanomicellar Systems, Nanotubes, Nanogels**: Emerging platforms explored for their unique structural and functional capabilities [21].

5. Key Characteristics of Nanoherbals

5.1 Enhanced Solubility & Bioavailability

Nanoherbals significantly improve the solubility and bioavailability of poorly water-soluble phytoconstituents. By reducing particle size, these systems increase surface area and facilitate better dissolution and absorption [1].

5.2 Improved Stability & Protection

Encapsulation within nanoparticle systems shields herbal actives from degradation due to light, heat, enzymes, and pH variations—preserving therapeutic potency [10].

5.3 Controlled & Sustained Release

Nanoformulations enable the sustained and controlled release of herbal compounds, maintaining therapeutic levels over prolonged periods and potentially reducing dosing frequency [13].

5.4 Targeted Delivery & Passive Accumulation

Size and surface characteristics allow nanoherbals to exploit the Enhanced Permeability and Retention (EPR) effect, resulting in passive targeting to disease sites such as tumors or inflamed tissues [12].

5.5 Versatile Loading Capacity

Nanoherbal systems can carry both hydrophilic and hydrophobic phytochemicals, offering versatility for formulating diverse herbal extracts in a single carrier [10].

5.6 Biocompatibility & Lower Toxicity

Nanoherbals are usually biodegradable, non-toxic, and biocompatible—especially when made using natural polymers or 'green' techniques, making them safer compared to some synthetic carriers [7].

5.7 Dose Reduction & Reduced Side Effects

Improved delivery efficiency and stability can translate into lower required doses and fewer systemic side effects, enhancing patient compliance [8].

5.8 Multifunctional & Application Versatility

Nanoherbals can be tailored for various therapeutic and functional applications—ranging from anticancer and antimicrobial uses to cosmeceuticals, nutraceuticals, functional foods, and environmental uses like water purification [19].

5.9 Adaptable Formulations & Nanocarriers

Common nanoherbal carriers include nanoparticles, nanocapsules, liposomes, micelles, solid lipid nanoparticles (SLNs), dendrimers, nanoemulsions, nanogels, and more—each offering different physicochemical and release properties to suit specific applications [15].

5.10 Green Synthesis & Traditional Integration

Some nanoherbal systems leverage eco-friendly (green) synthesis methods, utilizing plant-based materials, or even draw inspiration from traditional Ayurvedic practices like "bhasma"—metal-based nanomedicines used for targeted delivery and immunomodulation [14].

6. Methods of Preparation of Nanoherbals

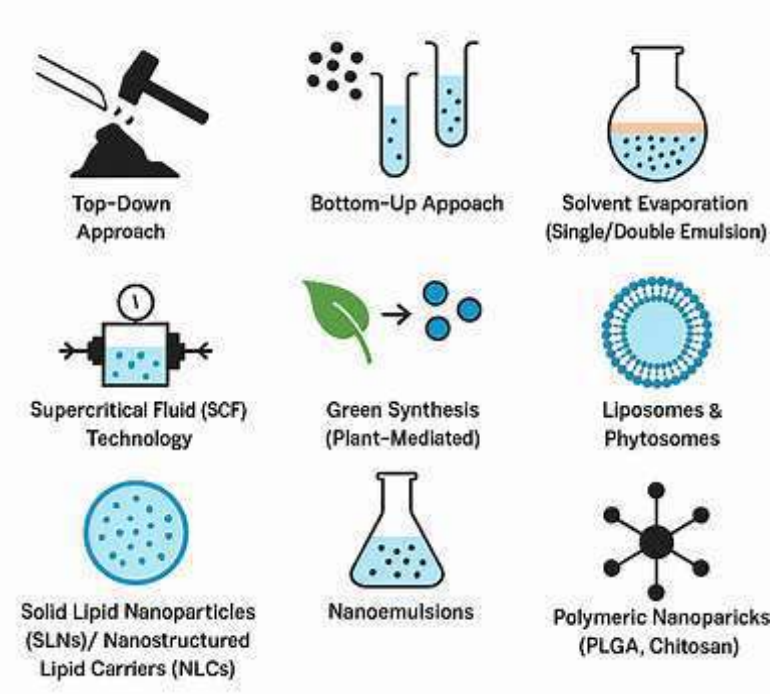

Figure 2 Method of Preparations

6.1 Top-Down vs. Bottom-Up: The Two Master Routes

Top-down approaches start from bulk material and break it down to the nanoscale by mechanical or physicochemical energy (e.g., high-pressure homogenization for solid-lipid nanoparticles; high-energy emulsification for nanoemulsions) [15]. They are attractive for scale-up and regulatory familiarity but can generate broader size distributions and may expose heat-/shear-sensitive phytoconstituents to stress. High-pressure homogenization (HPH) is the workhorse for lipid nanocarriers and has been translated from lab to industrial scales for SLNs and NLCs.

Bottom-up approaches build nanoparticles from molecular or colloidal precursors via precipitation/assembly—e.g., nanoprecipitation (a.k.a. solvent displacement), solvent evaporation (single or double emulsion) for polymeric carriers (PLGA, chitosan), and supercritical CO_2 processes that crystallize or encapsulate actives under mild temperatures. They excel at gentle processing, narrow sizes, and high loading for hydrophobic botanicals but require careful solvent selection, mixing control, and post-processing to meet residual-solvent limits.

6.2 Core Bottom-Up Methods Used in Nanoherbals

6.2.1 Nanoprecipitation (Solvent Displacement)

Concept: A polymer (e.g., PLGA) and the herbal active dissolve in a water-miscible organic solvent (e.g., acetone, acetonitrile, EtOAc). Upon addition to an aqueous phase containing stabilizer (PVA, poloxamer), rapid solvent diffusion reduces polymer solubility, yielding nuclei that grow into nanoparticles. Particle size depends on solvent type, polymer concentration, addition rate, interfacial mixing, and surfactant. Membrane-assisted or microfluidic variants improve mixing and reproducibility.

Why it suits herbal actives: Many phytochemicals (curcuminoids, flavonoids, terpenoids) are hydrophobic; nanoprecipitation provides high encapsulation and narrow size with minimal heat, preserving labile constituents. Recent work underscores how solvent choice (e.g., acetone vs. acetonitrile vs. EtOAc) strongly tunes size and polydispersity—critical for bioavailability and stability [18].

6.2.2 Solvent Evaporation (Single/Double Emulsion)

Single emulsion (O/W): Polymer and hydrophobic herbal actives dissolve in a volatile organic solvent (e.g., EtOAc). Emulsification into an aqueous

surfactant solution creates droplets; solvent removal (stirring or reduced pressure) hardens droplets into nanoparticles.

Double emulsion (W/O/W): For hydrophilic phytoconstituents (glycosides, polyphenolic acids), a first **W/O** emulsion is formed (internal aqueous herbal extract in organic polymer phase), then re-emulsified into an external aqueous phase (**W/O/W**). Solvent removal traps the hydrophilic actives in the polymeric matrix. This route is widely reported for loading delicate biomolecules and botanical hydrophiles.

Advantages/considerations: High entrapment efficiency (with process tuning), tunable size (200–500 nm common), but shear and multiple steps can challenge very labile compounds; surfactant residues and solvent grades must comply with pharmacopeial limits.

6.2.3 Supercritical Fluid (SCF) Technology (e.g., scCO₂)

Principle: Supercritical CO_2 ($T > 31$ °C, $P > 7.38$ MPa) has gas-like diffusivity and liquid-like solvating power. In **RESS**, **SAS**, **SEDS**, or related modes, rapid expansion or anti-solvent action induces precipitation of nanosized drug/polymer composites with narrow PSDs—often at low temperatures, minimizing thermal degradation of phytoactives. Case studies include polyphenols (e.g., resveratrol) and plant pigments [.

Why it's attractive for nanoherbals:

- Green: CO_2 is non-flammable, recyclable, and leaves minimal solvent residues.
- Quality: good control over morphology and crystallinity; potential for continuous manufacture.

Caveats: Capital cost and process tuning (pressure/temperature/co-solvent) are non-trivial; not all polymers/drugs show sufficient solubility without co-solvents.

6.3 Green Synthesis (Plant-Mediated Nanoparticle Synthesis)

Concept: Plant extracts (leaves, peels, barks, seeds) serve as reducing and capping agents to produce metallic or metal-oxide nanoparticles (e.g., Ag, Au, ZnO), where phytochemicals (polyphenols, flavonoids, sugars, proteins) reduce metal ions and stabilize the colloids. Reaction pH, temperature, and extract composition dictate nucleation, growth, and final size/shape.

Relevance to nanoherbals:

- **Bio-origin capping layers** can confer inherent antioxidant/antimicrobial attributes complementary to the herbal payload.
- **Eco-friendly:** avoids toxic reductants/surfactants; fits clean-label/natural product narratives.
- **Versatility:** extensive reports detail Ag/Au NPs made with diverse botanicals, enabling topical antimicrobials, wound-healing gels, and coatings.

Considerations: Batch-to-batch variability from plant extract composition (seasonality, extraction method) can affect reproducibility; robust characterization (UV-Vis, DLS, TEM, FTIR, XRD) and specification of extract chemistry are essential for translation.

6.4 Encapsulation Platforms Widely Used for Herbal Actives

6.4.1 Liposomes & Phytosomes

Preparation methods:

- **Thin-film hydration (Bangham):** dissolve lipids in organic solvent → evaporate to a thin film → hydrate with aqueous herbal extract → size-reduce (sonication or extrusion).
- **Ethanol/ether injection:** rapid injection of lipid solution into aqueous phase yields small unilamellar vesicles.
- **Reverse-phase evaporation, detergent depletion, microfluidics, and even SCF-assisted liposomes** are additional routes.

Why for nanoherbals: Amphiphilic bilayers can solubilize both hydrophilic and lipophilic phytochemicals; vesicle size (80–200 nm) and

lamellarity control release/targeting. Phospholipid complexes ("phytosomes") improve oral absorption of flavonoids and saponins.

6.4.2 Solid Lipid Nanoparticles (SLNs) / Nanostructured Lipid Carriers (NLCs)

Preparation: Hot or cold **high-pressure homogenization** of a lipid melt (plus surfactant) dispersed in water; for NLCs, a solid lipid is blended with liquid lipid to increase payload and prevent expulsion. Suitable for thermosensitive herbs with careful temperature control and brief exposure. Industrial homogenizers enable scale-up.

Use-case: Oral and topical nanoherbals (e.g., curcumin, essential-oil components) benefit from improved solubility, occlusive effect on skin, and controlled release.

6.4.3 Nanoemulsions

High-energy methods: high-pressure homogenization or ultrasonication breaks coarse emulsions into nano-droplets (typically 50–200 nm).

Low-energy methods: phase-inversion temperature/ composition or spontaneous emulsification leverage interfacial phenomena and surfactant chemistries to self-assemble nano-droplets. For volatile essential-oil actives (eugenol, thymol), nanoemulsions enhance dispersion and stability.

Trade-offs: High-energy routes are robust and food/ cosmetic friendly; low-energy routes save energy but may require higher surfactant loads—important in nutraceutical contexts.

6.4.4 Polymeric Nanoparticles (e.g., PLGA, chitosan)

Routes: Nanoprecipitation (Section 2.1), **single/double emulsion–solvent evaporation** (Section 2.2), ionic gelation for chitosan, or microfluidics to refine sizes/PDIs. PLGA is favored for its biodegradability and regulatory track record; double emulsion is especially useful for hydrophilic herbal polysaccharides and phenolics.

6.5 Surface Modification (Functionalization) for Stability & Targeting

Improve colloidal stability (salt/serum), extend blood circulation, reduce opsonization, and achieve **active targeting** to tissues/cells (e.g., tumors, inflamed endothelium, gut mucosa).

- **PEGylation:** grafting polyethylene glycol reduces protein adsorption, prolongs circulation, and can mitigate immunogenicity—used across liposomes and polymeric NPs.
- **Ligand conjugation:** attaching folate, peptides, antibodies, or sugars (e.g., mannose for macrophage targeting) enables receptor-mediated uptake; orientation and density of ligands critically influence binding and biodistribution.
- **Charge/hydrophobicity tuning:** surface charge (ζ-potential) and hydrophobic domains modulate mucus penetration, cellular uptake, and hemocompatibility; excessive cationic character may trigger toxicity, so balanced designs are advised.
- **Metallic NP coatings:** biopolymers, lipids, proteins, and phytochemical shells improve stability and biocompatibility of plant-mediated Ag/Au NPs and allow further ligand coupling.
- **Analytical confirmation:** FTIR/XPS (surface chemistry), DLS/ζ (size/charge), TEM/cry-EM (morphology), DSC/XRD (crystallinity for lipid/drug), and in-vitro protein corona assays map how coatings alter biological identity.

6.6 Practical Selection Guide for Nanoherbal Methodology

- **Hydrophobic, labile actives (e.g., curcuminoids, resveratrol):** polymeric NPs via nanoprecipitation or SLN/NLC via HPH; consider SCF for solvent-lean processing.
- **Hydrophilic phytoconstituents (glycosides, polysaccharides):** double emulsion (W/O/W) PLGA or liposomes (aqueous core).
- **Volatile/essential-oil actives:** nanoemulsions (high-energy HPH/sonication for food/cosmetic compliance).

- **Antimicrobial topical systems:** plant-mediated Ag/Au NPs (green synthesis) with biopolymer capping; confirm reproducibility of extract chemistry.

- **Need for long circulation/targeting:** add PEGylation and ligand decoration post-encapsulation.

7. Applications of Nanoherbals

7.1 Cancer therapy

Principle

Multiple plant-derived compounds modulate oncogenic signaling (PI3K/Akt/mTOR, Wnt/β-catenin, JAK/STAT, MAPK), apoptosis, ferroptosis, and tumor microenvironment. Nanoformulation of these hydrophobic molecules consistently improves tumor exposure and antitumor readouts in vivo; early clinical studies are emerging [17].

Example: Curcumin (nanocurcumin)

- **Evidence base:** Systematic reviews (2021–2024) conclude nanocurcumin enhances antitumor efficacy and safety versus free curcumin in preclinical cancer models; early clinical signals include symptom relief and improved quality of life, supporting further trials.

- **Mechanisms enhanced by nanoformulation:** greater cellular uptake, sustained release, and pathway modulation (e.g., PI3K/Akt/mTOR, JAK/STAT), with reports of ferroptosis induction.

- **Case studies:**

    - **PLGA/other polymeric nanoparticles:** Curcumin-loaded PLGA NPs showed anti-metastatic activity; several formulations decrease invasion and metastasis in breast cancer models.

    - **PGMD–curcumin NPs (≈110–218 nm):** Demonstrated cytotoxicity against breast cancer lines, illustrating polymer choice and size control for efficacy.

    - **Targeted protein nanocages (H-ferritin):** pH-sensitive Cur@HFn delivered curcumin selectively to breast cancer cells, boosting potency.

Other herbal actives in oncology

- **EGCG (green tea catechin):** Low oral bioavailability limits free EGCG; nano-EGCG (lipid/polymeric) improves stability and cytotoxicity in breast, cervical, and lung cancer models; reviews discuss nano-encapsulation to bridge bench-to-bedside.

- **Resveratrol:** Nanoparticle delivery elevates anticancer potency vs. free compound; comprehensive 2023–2024 reviews summarize design trends and advantages (solubility, controlled release).

Takeaway: Across tumor types, nano-herbal systems most robustly improve **exposure** and **tumor uptake**; clinical translation is advancing fastest for curcumin and catechins, with multiple formulations poised for larger trials.

7.2 Neurological disorders (Alzheimer's, Parkinson's)

Principle

The **blood–brain barrier (BBB)** excludes most small molecules and nearly all macromolecules. Nanocarriers (lipid/polymer micelles, SLNs, exosomes, ligand-decorated NPs) can leverage receptor-mediated transcytosis, adsorptive transport, or cell-membrane cloaking to cross the BBB and/or restore BBB integrity, enabling delivery of herbal neuroactives (curcumin, resveratrol, berberine, ginsenosides).

Nano-curcumin for AD/Parkinson's (preclinical and clinical signals)

- **BBB & disease modulation:** Recent reviews detail nanocarriers that ferry neuroprotective agents across the BBB and even **repair** BBB dysfunction—a relevant AD/PD pathology.

- **Preclinical case study:** Nanoencapsulated curcumin reversed memory impairment and

neuroinflammation in a validated AD rat model (ICV-STZ), outperforming free curcumin.

- **Clinical signal (nanocurcumin):** Triple-blind randomized trials of curcumin-containing nanomicelles have reported immunomodulatory effects in CNS disease contexts, suggesting systemic immune-neuro crosstalk benefits; broader reviews of AD trials provide context for where phytochemical nanosystems fit among disease-modifying strategies.

Takeaway: For neurodegeneration, nanoherbals principally address **BBB penetration** and **neuroinflammation/oxidative stress**, with encouraging animal data and early human signals for nanocurcumin.

7.3 Cardiovascular diseases (CVD)

Principle

Cardiovascular indications benefit from anti-inflammatory, antioxidant, antiplatelet, lipid-lowering, and anti-fibrotic effects of polyphenols (resveratrol, quercetin, curcumin). Nano-delivery can target plaques or injured myocardium, improve bioavailability, and enable combination therapies.

Clinical and translational highlights

- **Nanocurcumin & CVD risk factors:** A meta-analysis of placebo-controlled RCTs found nano-curcumin interventions improve lipid profiles, glycemic control, inflammatory mediators, and sometimes BP—validating a nutraceutical-to-cardiometabolic bridge.

- **Microvascular angina model:** In patients with coronary slow flow phenomenon (a microvascular ischemia model), 80 mg/day nanocurcumin for 8 weeks improved endothelial function and inflammatory markers versus placebo.

- **Quercetin clinical pilot (STEMI):** Add-on quercetin limited infarct size and reduced intramyocardial hemorrhage in first anterior STEMI patients (pilot study)—a signal for flavonoid cardioprotection that motivates nano-quercetin development.

Nano-resveratrol and nano-quercetin for atherosclerosis & MI (preclinical/engineering)

- **Resveratrol nanocarriers:** Reviews emphasize that nanoparticle delivery resolves resveratrol's solubility/PK issues; recent studies show plaque-modulating actions and mechanistic links (e.g., LDLR upregulation, ferroptosis pathways).

- **Targeted delivery:** Biomimetic, macrophage-membrane-coated NPs carrying resveratrol show MI-site targeting and cardioprotection in preclinical models.

- **Quercetin & ischemia-reperfusion:** Reviews summarize antioxidant/antiapoptotic mechanisms relevant to MI; nanoformulations are being engineered to enhance delivery to ischemic myocardium.

Takeaway: In CVD, the strongest human data today are **risk-factor improvements** with nano-curcumin and **pilot cardioprotection** with quercetin; nanocarrier engineering for **plaque targeting** and **injury-site homing** is rapidly evolving (preclinical).

7.4 Antimicrobial & Antiviral therapies

Principle

Essential oils (EOs) and phenolics (thymol, carvacrol, eugenol, oregano or eucalyptus oils) show broad antimicrobial activity but are volatile, hydrophobic, and unstable. **Nanoemulsions, SLNs, and polymer-encapsulated systems** increase dispersion in aqueous environments, control release, and enhance contact with microbial membranes/biofilms; **plant-mediated silver nanoparticles (AgNPs)** provide a green-synthesized, inorganic nano-antimicrobial option.

Representative case studies

- **EO nanoemulsions (food and biomedical contexts):**
    - Oregano/carvacrol/thymol nanoemulsions (50–85 nm) prepared by ultrasound showed enhanced antibacterial and antibiofilm activities, supporting food and oral-health applications.

- Thymus vulgaris oil nanoemulsions overcome volatility/hydrophobicity limits, improving antimicrobial performance versus free oil.
- Comparative studies and reviews conclude nano-sizing increases active surface area and can amplify antimicrobial effects, though formulation details (surfactant, droplet size) critically determine outcomes; a 2024–2025 literature stream documents improved control of **S. aureus**, **E. coli**, **C. perfringens** and foodborne pathogens.

- **Green-synthesized AgNPs:**
  - **Plant-mediated AgNPs** (using phenolic-rich extracts from neem, turmeric, Ficus spp., etc.) display potent antimicrobial activity with eco-friendly synthesis routes; recent reviews detail synthesis parameters, phytochemical roles, and biomedical applications.

Caveat: Antimicrobial claims depend strongly on **assay conditions**; method papers emphasize standardization challenges for EOs. Formulation and testing protocols must be carefully controlled to ensure reproducible MIC/MBC values.

7.5 Anti-inflammatory & Immunomodulatory uses

Principle

Herbal actives frequently modulate NF-κB, Nrf2, COX/LOX, cytokine networks, and immune cell phenotypes. Nano-encapsulation enhances tissue exposure at inflamed sites and can shift systemic immune markers in clinical studies.

Examples & evidence

- **Nanocurcumin in inflammatory conditions:** Clinical and translational studies report reductions in CRP and pro-inflammatory cytokines and improvements in clinical symptoms in inflammatory milieus (e.g., autoimmune contexts), attributed partly to improved bioavailability and immune pathway modulation.

- **Arthritis models:** Curcumin nanocarriers (polymer/lipid) demonstrate better joint targeting, stability, and anti-inflammatory efficacy than free curcumin; reviews summarize platform choices and release kinetics.

Takeaway: For inflammation, the most mature nanoherbal is **nanocurcumin**, with human biomarker improvements and robust preclinical disease-model benefits.

7.6 Nutraceuticals & Functional foods

Principle

Functional foods often require **aqueous processing**, **thermal/photostability**, and **palatability**—a poor fit for many hydrophobic botanicals. Food-grade nano-delivery (nanoemulsions, casein micelles, plant-protein nanoparticles, biopolymer complexes) improves **dispersibility**, **stability**, and **bioaccessibility** of polyphenols and essential oils in drinks, dairy, and snacks.

Human PK and formulation exemplars

- **Theracurmin® (colloidal curcumin nanoparticles):** In a randomized crossover PK study, a 30 mg nano-curcumin dose achieved a **~27-fold increase in AUC** over unformulated curcumin—often cited as proof-of-concept for nutraceutical nano-delivery.

- **Across nano-curcumin products:** A review of 11 clinical studies reported **9–185×** higher relative bioavailability for nanoformulations, albeit with heterogeneity in designs and analytics—important when comparing products.

- **Co-encapsulation strategies:** Co-loading **resveratrol + curcumin** in nano-systems improves photostability and antioxidant performance; micro/nanocapsules enable controlled release profiles for functional foods.

- **Protein/biopolymer carriers:** Soy-protein and dual-polysaccharide-coated micro/nanocapsules achieve high curcumin encapsulation efficiency (≈95%), with improved stability for beverage/dairy applications.

Food safety and antimicrobial packaging

- EO-loaded nanocarriers and **curcumin-active packaging films** provide antimicrobial action and freshness indicators, extending shelf life while potentially delivering bioactives.

Takeaway: In foods, nanoherbals primarily deliver **higher, more consistent systemic exposure** and **product stability**, with human PK advantages well documented for nano-curcumin; careful formulation selection and regulatory compliance (food-grade excipients, GRAS status) are essential.

7.7 Selected recent case studies (quick-scan)

- **Oncology:** Comprehensive 2024 systematic review—nanocurcumin improves preclinical efficacy; early clinical signals support QoL/toxicity mitigation.

- **Neurology:** Nano-curcumin improved cognition/inflammation in an AD rat model; BBB-targeted nano-delivery is a major translational avenue.

- **Cardiology:** RCT meta-analysis—nano-curcumin improves cardiometabolic risk factors; CSFP trial shows endothelial benefit; pilot STEMI trial supports quercetin cardioprotection (basis for future nano-quercetin).

- **Antimicrobial:** Thymol/carvacrol/oregano oil nanoemulsions demonstrate increased anti-pathogen and antibiofilm activity; green-synthesized AgNPs offer broad antimicrobial potential with eco-friendly fabrication.

- **Functional foods:** Nano-curcumin PK ↑27× (Theracurmin®); co-encapsulation of curcumin/resveratrol enhances stability and antioxidant power in food matrices.

8. Advantages of Nanoherbals

8.1 Improved Solubility and Bioavailability

Nanoherbals enhance solubility and bioavailability by significantly decreasing particle size, boosting surface area, and optimizing absorption mechanisms. Techniques such as nanocrystals, nanoemulsions, and lipid/polymer carriers elevate dissolution rates, leading to improved pharmacokinetics versus traditional formulations. Specifically, solid lipid nanoparticle (SLN) systems loading puerarin revealed over threefold higher bioavailability compared to suspensions, confirmed by a shorter Tmax. Nanocrystals circumvent the need for carriers, enabling high drug loading and reducing toxicity.

8.2 Controlled and Sustained Release

Nanoherbals can be engineered to deliver phytochemicals at controlled and sustained rates, reducing dose frequency and ensuring maintained therapeutic concentrations. Systems like nanohydrogels, lipid carriers, and NDDS (novel drug delivery systems) support prolonged release and better bioavailability.

8.3 Targeted Delivery (Site-Specific Action)

The nanoscale of these formulations allows enhanced tissue penetration and targeted delivery, either actively (using ligands) or passively via enhanced permeability and retention (EPR) effect—particularly useful in tumor targeting. Additionally, nanotheranostic platforms combine therapy and diagnostics in one system.

8.4 Reduced Toxicity & Enhanced Safety Profile

Nanoherbals enhance safety by reducing systemic exposure and toxicity. Higher targeting precision helps minimize adverse effects, while carrier-free approaches like nanocrystals further lower carrier-related toxic risks. Moreover, using biocompatible, biodegradable, and plant-derived carriers (green synthesis) reinforces favorable safety profiles.

8.5 Improved Patient Compliance

By increasing bioavailability, achieving sustained release, and reducing dosing frequency, nanoherbals make herbal therapies more convenient and improve adherence. NDDS helps reduce repeated dosing and enhance effectiveness, addressing a major gap in conventional herbal treatments.

9. Limitations and Challenges

9.1 Standardization of herbal raw materials

Unlike single-molecule APIs, botanicals are chemically heterogeneous and influenced by species, genotype, soil, climate, harvest time, and post-harvest processing. This variability alters the concentrations of marker compounds and co-constituents, making it difficult to ensure consistent pharmacological performance when herbs are converted into nanoformulations. WHO's monographs and handbooks underscore the need for stringent identity, purity, and contaminant testing (macroscopy/ microscopy, chromatographic fingerprints, residual pesticides/metals, microbial limits) to control this variability—requirements that many herbal supply chains still struggle to meet. Even when good botanical control is applied, translating a complex extract into a nanosystem adds another layer of variability: the "effective payload" in a nanocarrier depends on the extract's batch chemistry (e.g., polyphenol content) which in turn affects encapsulation efficiency, stability, and release. Contemporary reviews on herbal quality control emphasize that fingerprints/multi-marker assays are often necessary (single-marker standardization is insufficient) and that lack of harmonized standards hinders interchangeability across regions and manufacturers. Regulatory guidance in Europe (EMA) similarly highlights the special quality problems of herbal medicinal products and the need to specify starting materials, preparation methods, and stability in detail—issues that become more exacting for nano-enabled versions.

9.2 Toxicity and safety concerns of nanoparticles

Nanocarriers can shift biodistribution and biological interactions in ways that are difficult to predict from conventional herbal preparations. A central issue is the **protein corona**—adsorption of biomolecules onto nanoparticle surfaces—which can modify "identity," uptake, immune recognition, and organ distribution, sometimes undermining targeting and creating off-target effects. Recent reviews delineate how corona composition is context-dependent and dynamic, complicating translation and safety assessment. Broader nanosafety literature flags potential immunotoxicity, oxidative stress, and long-term accumulation concerns, which must be assessed for each nanoherbal system, its materials (lipids, polymers, inorganics), and its route of administration. Healthcare-focused reviews also emphasize environmental safety (manufacturing/ disposal) as part of risk assessment. Regulators (FDA) stress that products containing nanomaterials may exhibit attributes distinct from non-nano comparators and therefore warrant tailored characterization (size/shape, surface chemistry, aggregation, release, in vitro–in vivo correlations) and risk-based evaluation; there is no blanket presumption of safety or harm.

9.3 Scale-up and manufacturing issues

Reproducibly producing nanoformulations at industrial scale remains challenging. Batch methods often suffer from size/polydispersity drift, mixing/heat-transfer limitations, and batch-to-batch variability as equipment scales up. Reviews of nanomedicine scale-up (including experiences from liposomes and polymeric/lipid nanoparticles) document how process parameters that work at bench scale can fail in large reactors, jeopardizing critical quality attributes (CQAs). Recent analyses argue for continuous manufacturing and intensified/controlled mixing (e.g., microfluidics) to improve reproducibility, yet adoption is still evolving and requires significant process development, modeling, and regulatory engagement. Moreover, nanosystems with multi-step fabrication (core formation, loading, surface modification, sterilization, lyophilization) are especially hard to scale without compromising stability and performance—an obstacle noted across contemporary nanomedicine manufacturing reviews.

9.4 High cost of production

Complex processes, specialized equipment (e.g., high-shear/ microfluidic mixers), advanced analytics (DLS, electron microscopy, nanoparticle tracking, hyphenated chromatography), sterile operations, and often low process yields contribute to higher COGS versus conventional herbal dosage forms. Economic and policy reviews note that high R&D and manufacturing costs remain a major barrier to widespread adoption and equitable access—especially in low- and middle-income settings. Industry-oriented assessments and pharmacoeconomic reviews add that while manufacturing costs are elevated, cost-effectiveness can still be achieved if nanoformulations produce clinically meaningful benefits (e.g., fewer

administrations, lower toxicity management costs). Nonetheless, the upfront investment and per-unit costs are typically higher than for non-nano analogs, demanding a clear value proposition.

9.5 Regulatory & ethical concerns

Regulatory. For nano-enabled drug products (including botanicals formulated as drugs), agencies expect robust, case-by-case characterization and control strategies. FDA's 2022 *Guidance for Industry* outlines considerations spanning material attributes, manufacturing controls, in vitro/ in vivo testing, and comparability when changes occur. EMA's horizon-scanning and scientific advice frameworks encourage early dialogue because nanomedicines often raise unique CMC and clinical questions (e.g., bioequivalence criteria for complex nanosystems). For herbal nanosystems, these expectations layer on top of existing herbal quality guidance.

Ethical. Scholarship on nanomedicine ethics highlights: (i) uncertainty and transparency in risk communication; (ii) privacy and data issues for nano-enabled diagnostics/theranostics; (iii) environmental stewardship across the lifecycle; and (iv) **equity**, to avoid a "nano-divide" where benefits accrue primarily to wealthier populations. Responsible innovation frameworks urge stakeholder engagement and fair access as the field advances.

Comparison: Traditional vs Nanoherbal Formulations

Table 2 Comparison: Traditional v/s Nanoherbal Formulation

Aspect	Conventional Herbal Formulations	Nanoherbals (Nano-formulations)
Solubility & Absorption	Low water solubility; poor GI absorption	Nanoemulsions, liposomes, micelles dramatically enhance solubility and absorption
Bioavailability	Very limited systemic exposure	Enhanced exposure—often several-fold higher AUC/C_{max}
Release Kinetics	Immediate release; fluctuations in plasma levels	Controlled or sustained release via nanoparticles, nanosuspensions, nanoemulsions
Targeting	Non-specific systemic distribution	Passive (EPR) and active targeting achievable with functionalized nanoparticles
Stability	Susceptible to degradation (light, heat, enzymes)	Nano-encapsulation offers protection and improved chemical stability
Dose Requirements	Typically, high doses needed	Lower doses can be effective due to improved PK/PD profile
Consistency	Batch-to-batch variability	More reproducible if manufacturing and quality controls are robust
Complexity & Cost	Simple, low-cost methods (powders, decoctions, capsules)	Complex and higher-cost manufacturing; scale-up challenges

10. Case Examples

1. Curcumin

- **Conventional**: Curcumin displays very poor solubility and minimal oral absorption—e.g., only about *0.05 μg/mL* detected in plasma even after high oral dosing.
- **Nanoformulated**:
  - A novel **solid dispersion** of curcumin increased bioavailability by **8–16×** in rats compared to standard curcumin.
  - In human trials comparing formulations, one phytosome product (CW8) achieved a **~39×** AUC boost; another (CHC) yielded a **~46×** increase versus unformulated standard curcumin.
  - A nanoemulsion-based system (pH-driven) showed superior GI tract bioaccessibility (~74–79%) versus commercial preparations, suggesting better absorption potential.

2. Quercetin

- **Conventional**: Oral quercetin has low bioavailability, often below 5%.

- **Nanoformulated**: Nanosuspensions incorporating metabolic inhibitors (e.g., piperine) improved bioavailability up to **23.6%**, versus just **3.6%** from a standard water suspension.
    - A nanocochleate formulation further achieved sustained release, better C_{max}, and AUC, with higher cytotoxicity against MCF-7 cancer cells.

3. Ginseng (Nano-Enhanced)

- Though detailed studies are limited, one self-reported example involving fermented Panax ginseng (GS15-4™) claimed:
    - **↑15× absorption**, **4× faster uptake**, and **4× consistency** compared to conventional extracts, attributed to improved metabolic profile post-fermentation.
    - While not strictly "nano", such metabolic processing can mimic nanoscale enhancement approaches in improving bioavailability.

11. Recent Developments and Research Trends in Nanoherbals (2004–2025)

11.1 Bibliometric landscape (2004–2023)

A comprehensive bibliometric analysis in *Journal of Nanobiotechnology* mapped 1,876 publications (2004–2023) on herbal-based nanomedicine. Output accelerated steeply after ~2016, with China emerging as the leading contributor by volume; highly active institutions included the Chinese Academy of Sciences and Tehran University of Medical Sciences. Frequently used keywords and hotspots were "green synthesis," "curcumin," "wound healing," "silver nanoparticles," "anticancer," "antimicrobial," "carbon dots," and "electrospinning." The most productive outlets were *Journal of Nanobiotechnology*, *Scientific Reports*, *RSC Advances*, and *Materials Science and Engineering C*. The analysis also highlighted a strong methodological cluster in **green/biogenic nanoparticle synthesis** and an application cluster around **anti-infective and anticancer uses**.

Interpretation. The field has shifted from exploratory synthesis to translational themes: (i) solvent-free/plant-mediated fabrication, (ii) delivery of poorly soluble phytochemicals (e.g., curcumin, quercetin), and (iii) skin/tissue repair, antimicrobial coatings, and adjunct oncology.

11.2 Patents and clinical trials: signals of translation

11.2.1 Patents (illustrative)

- **Curcumin nano-micelles** (block-copolymer micelles; film-dispersion + hydration/sonication). Claims improved solubility, <100 nm size, and ~8% drug loading. (CN102274163A/B).
- **PEG-PCL curcumin nanoparticles** (amphiphilic copolymer carrier). (CN104414976A).
- **Quercetin nanoformulations**, including hyaluronate–quercetin nanocomplexes (CN109172543A) and quercetin-phosphate in lipid nanoparticles (WO2018172942A1).
- Platform-level prior art on **lipid carriers** (liposomes, lipid nanocapsules) and green liposome methods (e.g., Mozafari method) continues to underpin phytochemical IP filings.

Takeaway. Patent activity clusters around micelles, lipid/polymer hybrids, and biocompatible polysaccharide complexes for canonical actives (curcumin, quercetin), indicating emphasis on **solubility, stability, and scalable processes**.

11.2.2 Clinical trials (selected)

- **Colloidal submicron curcumin (Theracurmin®)**: human bioavailability studies (double-blind crossover) showed markedly higher plasma exposure versus other DDS forms; RCTs in knee osteoarthritis reported symptom and NSAID-sparing benefits with acceptable safety.
- **Nanocurcumin in inflammatory disease & infection**: RCTs and prospective trials (2020–2025) explored nanomicellar curcumin as an adjunct in COVID-19 (reduced inflammatory markers and oxygen need in some cohorts) and ulcerative colitis (2025 double-blind RCT signals efficacy; peer-reviewed publication accepted Aug 18, 2025).

Caveats. Many studies are small, heterogeneous in formulation, and not yet pivotal; nonetheless, they demonstrate clinical-grade manufacturing and regulatory engagement for nanoherbal products.

11.3 Emerging nanocarrier systems and design trends

11.3.1 Hybrid and next-gen carriers

- **Polymer–lipid hybrid nanoparticles (PLHNPs/LPHNPs)** combine a stabilizing polymeric core (e.g., PLGA) with a lipid shell to enhance **encapsulation, colloidal stability, mucus permeation, and controlled release** of phytochemicals. Recent reviews emphasize their promise for phytochemical delivery (cancer, inflammatory and metabolic diseases) and topical/transdermal use.

- **Stimuli-responsive hybrids** (pH/light/redox) and surface-decorated systems (peptides, polysaccharides, hyaluronate, mannose) are being used to target tumors or inflamed tissues, reduce off-target exposure, and enhance bio adhesion.

- **Electrospun nanofibers** incorporating herbal actives (e.g., curcumin, plant antimicrobials) are rising for wound dressings and mucosal delivery, leveraging large surface area and tunable release. Bibliometric hotspots also list "electrospinning" as a growth keyword.

- **Plant-derived nanoparticle/exosome-like vesicles** (PDNVs/PDENs) are attracting attention for **biogenic delivery and nutraceutical interfacing**, with early reports on biocompatibility and multifunctionality.

- **MOFs and porous inorganic–organic hybrids** are explored as **high-payload, controlled-release hosts** for hydrophobic phytochemicals like curcumin (e.g., ZIF-8), although clinical translation remains early.

11.3.2 Green/biogenic fabrication

Green synthesis using **plant extracts as reducing/capping agents** remains a dominant research stream—especially for **AgNPs, AuNPs, and metal oxides**—owing to lower toxicity of residual reagents and alignment with herbal/natural product positioning. Applications concentrate on antimicrobial coatings, wound care, and adjunct anticancer strategies.

FUTURE PERSPECTIVES

12.1 Personalized herbal nanomedicine

The next wave of nanoherbals will move beyond "one-size-fits-all" extracts toward **patient-stratified delivery**—matching phytochemical payloads and nanocarriers to individual biology (genotype, microbiome, metabolic status) and disease endotypes. In oncology and neurology, reviews on **precision nanomedicine** describe how modular carriers (polymer–lipid hybrids, ligand-decorated systems) can be tuned for specific targets (e.g., tumor receptors, inflamed endothelium) and adjusted to inter-patient variability in permeability and immune milieu—exactly the kind of heterogeneity that has blunted effects of conventional herbal products. For herbal actives, "personalization" also means selecting chemically fingerprinted extracts (or purified phytochemical mixes) aligned with a patient's metabolic phenotype and drug–herb interaction profile, then optimizing the nano-delivery (size, surface, release) for that context. Emerging analyses argue that such personalization is feasible when linked to **digital biomarkers** and **theranostic** carriers that report exposure while dosing.

What's new since 2023: Perspectives explicitly frame nano-phytomedicine as a bridge between traditional knowledge and precision therapeutics, highlighting safer, more effective, and potentially **personalized** formulations as evidence matures.

12.2 Integration with AI & precision medicine

AI/ML is rapidly becoming the "operating system" for nanoherbals:

(i) Formulation design. ML models (QSAR, Bayesian optimization, neural nets) predict how polymer/lipid composition, solvent ratios, and mixing regimes influence size, PDI, loading, and release—shrinking experimental search space. Recent reviews outline how AI links **nanoparticle design →**

performance → toxicity across discovery, CMC, and clinical development.

(ii) Patient matching. AI-assisted PBPK/QSP pipelines are being combined with QSAR to simulate phytochemical disposition and to match formulations to patient phenotypes (e.g., transporter polymorphisms, gut metabolism).

(iii) Personalized nanocarriers. Fresh 2025 work explores AI-guided "personalized nanocarrier" selection for (herbal) drugs, tying formulation knobs to individual needs and predicted outcomes.

(iv) CNS applications. Reviews on AI-enabled nanomedicine for brain disorders survey biomarker discovery, image-guided targeting, and adaptive dosing—relevant to nano-curcumin, resveratrol, and ginsenosides aimed at neuroinflammation and BBB transport.

Bottom line: Expect AI copilots to accompany nanoherbal development from DoE-like recipe generation to in-silico patient trials, accelerating iteration and de-risking translation.

12.3 Sustainable and green nanotechnology approaches

Sustainability has moved from "nice-to-have" to a design constraint. Green nanoscience emphasizes biogenic synthesis (plant extracts as reducing/capping agents), safer solvents, energy-lean processes, and biodegradable carriers—all closely aligned with the ethos of herbal medicine. Recent reviews catalogue plant-mediated Ag/Au/oxide nanoparticles for antimicrobial and wound applications and argue that green routes can reduce toxic residues and process energy while preserving performance.

Broader sustainability agendas now include life-cycle assessment (LCA) and circularity: sourcing botanicals responsibly, minimizing waste streams, and designing eco-benign hybrids (e.g., polysaccharide/graphitic carbon nitride composites) for biomedical use.

Future pivot: Expect "green by design" checklists in papers and dossiers (renewable inputs, solvent/reagent metrics, degradability, and environmental fate) to become standard for nanoherbals.

12.4 Need for global regulatory frameworks

Regulators increasingly treat nanomedicines as **case-by-case** products requiring enhanced characterization (size/shape, surface chemistry, aggregation), mechanism-aware nonclinical programs, and manufacturing controls. The EMA EU-Innovation Network Horizon-Scanning Report (Jan 2025) summarizes regulatory support pathways (e.g., innovation offices, scientific advice) and flags emerging issues for nanotechnology-based medicinal products—highly relevant to nano-enabled botanicals. Companion horizon-scanning on new approach methodologies (NAMs) signals where toxicology, in-vitro/in-silico tools, and real-world evidence can augment risk assessment for complex nanosystems. National agencies echo the need to clarify expectations early and to standardize comparability when sponsors tweak materials or processes.

Implication for developers: Build dossiers that integrate **CMC-to-clinical continuity** (critical quality attributes tied to clinical performance), leverage NAMs where appropriate, and engage regulators **before** pivotal studies.

12.5 Industrial & commercial prospects

Commercial success hinges on scalable, reproducible, and cost-aware manufacturing. The strongest trend is toward continuous manufacturing (CM) using microfluidics (including 3D-printed mixers) for narrow-PDI nanoparticles; 2025 reviews highlight CM's potential to improve quality, reduce shortages, and enable real-time release testing. Technically, microfluidic synthesis is now recognized as superior to many batch routes for mixing control and heat/mass transfer, and current work couples CM with CFD-guided design to predict and lock in particle attributes at scale.

Commercial pathways:

- **Nutraceutical/functional foods:** GRAS-leaning carriers and human PK wins (e.g., nano-curcumin) make near-term market entries realistic—provided labeling and claims stay within local rules.

- **Rx therapeutics:** Oncology, inflammatory bowel disease, and CNS adjuncts are closest, but will require standardized compositions, validated biomarkers, and multicenter RCTs to justify premium pricing. Horizon-scanning documents and industry perspectives underscore this evidence bar.

Industrial to-do list:

I. Invest in cm/microfluidics;

II. Adopt **design-space + AI** for rapid tech-transfer;

III. Embed **green metrics**;

IV. Plan for **global regulatory convergence** and early scientific advice.0

CONCLUSION

Nanoherbals represent a transformative evolution of traditional herbal medicine, merging the time-tested therapeutic potential of botanicals with the precision of nanotechnology. By overcoming intrinsic limitations of conventional formulations—such as poor solubility, instability, and low bioavailability—nano-enabled delivery systems provide enhanced absorption, targeted action, and controlled release of herbal actives. These advantages translate into improved therapeutic efficacy, reduced dosing requirements, and better patient compliance. At the same time, several challenges remain. Standardization of herbal raw materials, long-term safety evaluation of nanoparticles, high costs, and the complexity of scaling up manufacturing hinder widespread adoption. Regulatory frameworks for herbal nanomedicines are still evolving, leaving gaps in quality, safety, and efficacy assessment. Ethical considerations—including equitable access and sustainability—must also be addressed to prevent widening disparities in healthcare. Despite these limitations, the potential of nanoherbals in modern healthcare is substantial. Early clinical trials, particularly with nanocurcumin and nanoquercetin, already demonstrate promising results in cancer, inflammatory, and infectious diseases. Emerging technologies such as AI-driven formulation design, personalized nanomedicine, and green synthesis approaches are expected to accelerate translation from laboratory to clinic. Furthermore, industrial adoption of continuous and sustainable manufacturing could reduce costs and improve reproducibility, strengthening the commercial viability of these systems. In outlook, nanoherbals may become an integral part of precision and integrative medicine, complementing synthetic drugs and offering safer, more effective alternatives for chronic and lifestyle-related diseases. By uniting the wisdom of traditional herbal therapy with the rigor of nanotechnology, nanoherbals have the potential to redefine the role of natural medicines in 21st-century global healthcare.

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HOW TO CITE: Parth Khandelwal*, Vikram Saruk, Hrishikesh Bhakade, Huzaifa Patel, Amol Jadhav, Sohail Shaikh, Nanoherbals: A Modern Approach in Herbal Medicine, Int. J. Sci. R. Tech., 2025, 2 (11), 587-606. https://doi.org/10.5281/zenodo.17668066