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Nanotechnology-Enabled Novel Drug Delivery Systems for Herbal Drugs: Design Strategies, Clinical Relevance, and Translational Perspectives

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I. Abstract

In traditional and modern techniques herbal drugs have been widely utilised due to their therapeutic potential and safety profile. However, their clinical application is often limited because their poor solubility, low bioavailability, chemical instability, rapid metabolism, and lack of site-specific delivery. And in order to overcome these limitations, nanotechnology enabled novel drug delivery systems (NDDS) has emerged as a promising strategy to enhance the therapeutic performance of herbal formulations. This review article provided a comprehensive overview of NDDS employed for herbal drugs, focusing on their design strategies, their mechanism of action and clinical relevance. Various carrier systems such as liposomes, phytosomes, nanoparticles, nano emulsions, microspheres, hydrogels, transdermal patches, plant-derived nanovesicles etc. are discussed with representative examples of clinically important phytoconstituents which includes curcumin, silymarin, resveratrol, and epigallocatechin gallate. Additionally, recent advances in marketed formulations, translational challenges, regulatory concerns, and safety considerations are critically examined. The review article also highlights future perspectives, emphasizing green nanotechnology, personalized medicine, and AI-assisted formulation designs too. Overall, nanotechnology-based NDDS offer significant potential to bridge the gap between traditional herbal medicine and modern clinical therapeutics.

II. Introduction

For centuries herbal drugs have been used as therapeutic agents and had remain integral to the traditional medical systems worldwide. The herbal medicines are composed from bioactive phytoconstituents that act synergistically and provide nutritional, cosmetic and medical benefits [1]. But the translation of herbal remedies has been limited due to challenges such as poor solubility, instability, variable bioavailability and difficulties in standardization and formulation [2]. Conventional dosage forms such as tablets, capsules or liquid dosage forms often fail to maintain the effective therapeutic concentration which leads to reduction in efficacy and patient non-compliance. [1,2]

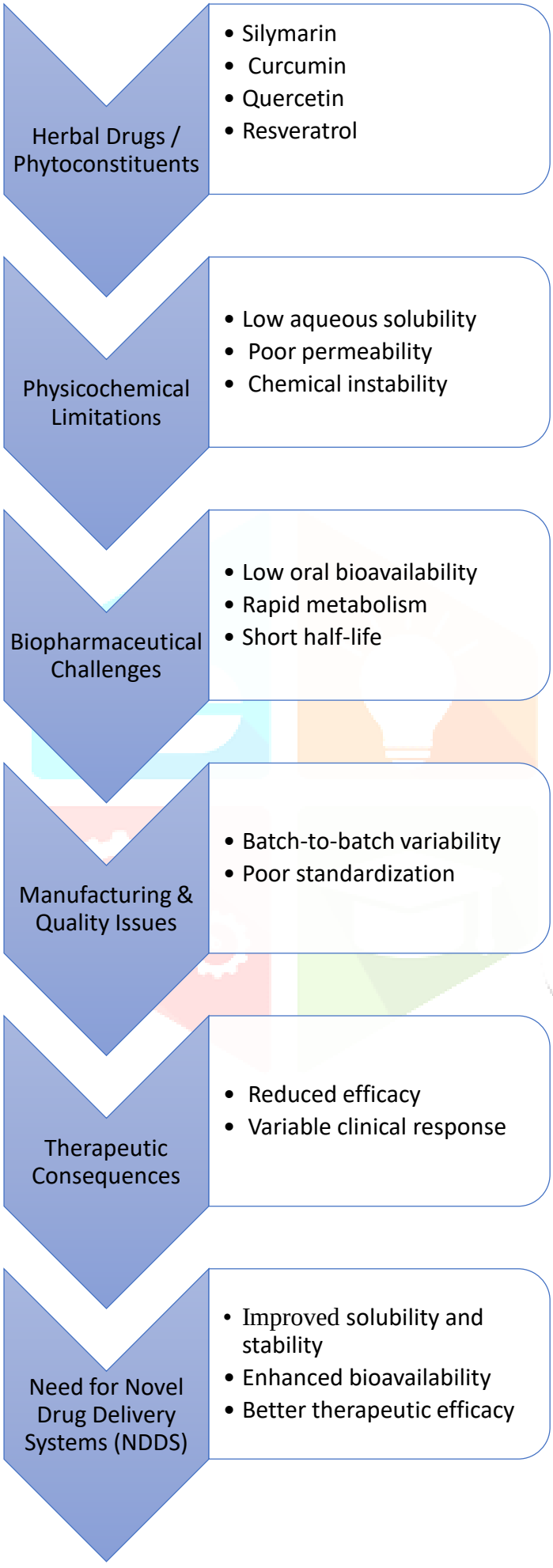
But in recent decades, advancement in pharmaceutical technology have prompted novel drug delivery system (NDDS) to overcome such limitations. NDDS provide sustained or controlled release, site-specific targeting as well as protection from chemical and enzymatic degradation [3]. Techniques such as liposomes, phytosomes, nanoparticles, solid lipid nanoparticles (SLNs), nanoemulsions, microspheres and dendrimers have been successfully applied to herbal formulations [1-4]. These carriers not only enhance the absorption and therapeutic index but also reduce the systemic toxicity and dosing frequency. [3]

Particularly nanotechnology has emerged as a promising strategy for delivering plant based compounds. Nanocarriers – ranging from organic to inorganic and hybrid structures – can modulate solubility, prolonged circulation time and ensured targeted drug delivery [4]. Such systems have been used to encapsulate many phytoconstituents such as silymarin, curcumin, ginsenosides and flavonoids, which showed improved pharmacological outcomes in clinical and preclinical studies. [1,4].

According to standard pharmaceutics literature, nanocarrier-based drug delivery systems can significantly modify drug pharmacokinetics by improving absorption, prolonging systemic circulation, and enabling controlled or targeted delivery, thereby enhancing overall therapeutic efficacy of bioactive compounds.[5]

Given the global interests in herbal medicines, integrating them with advanced delivery technologies could revolutionize modern therapy. This review paper aims to provide the comprehensive overview of novel drug delivery systems and also focuses on their design, mechanisms and biomedical applications.

III. Herbal Drugs and Their Limitations

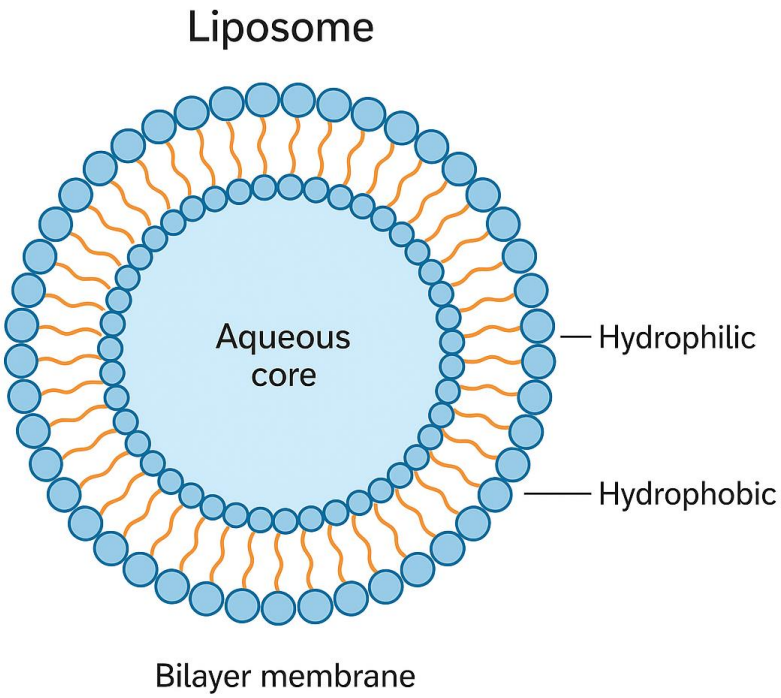


IV. Novel Drug Delivery Systems (NDDS) for Herbal Drugs

Herbal medicines have been widely used across cultures for centuries. However, the therapeutic potential of herbal drugs is often limited by poor solubility, instability, low bioavailability, and rapid metabolism. Novel Drug Delivery Systems (NDDS) provide innovative strategies to overcome these challenges by enhancing solubility, absorption, targeted delivery, and sustained release of herbal compounds. This section highlights different NDDS approaches for herbal drugs, with examples and applications supported by literature.

4.1 Liposomes

- Liposomes are spherical vesicles composed of phospholipid bilayers enclosing an aqueous core. They can encapsulate both hydrophilic and lipophilic herbal compounds, improving solubility and bioavailability(6). Their mechanism involves fusion with biological membranes, facilitating intracellular delivery of active constituents. For example, curcumin-loaded liposomes have been extensively investigated for cancer therapy due to improved stability, enhanced bioavailability, and increased anticancer activity compared to free curcumin (7)



Mechanism:

Liposomes improve the pharmacokinetics of herbal drugs by protecting them from enzymatic degradation and facilitating absorption through cell membranes [11]. They can also be surface-modified for targeted delivery to cancer or inflamed tissues [12].

Example -- Curcumin Liposomes:

Curcumin, derived from Curcuma longa, shows strong anticancer, antioxidant, and anti inflammatory properties. However, its poor solubility and rapid metabolism reduce clinical efficacy. Liposomal formulations enhance its solubility, circulation time, and tumor uptake [13]. Studies show that curcumin-loaded liposomes significantly suppress tumor growth in breast and colon cancer models [14].

Advantages:

- Increased solubility of herbal drugs [15]
- Enhanced tissue targeting
- Protection from degradation
- Reduced dosing frequency

Limitations:

- High production cost
- Instability during storage [16]

4.2 Phytosomes

Phytosomes are complexes formed between plant extracts (or bioactive phytoconstituents) and phospholipids. Unlike liposomes, phytosomes enhance absorption by forming a molecular complex, thereby improving the solubility and membrane permeability of herbal compounds (8). Silymarin phytosomes are a well-documented example, demonstrating improved bioavailability and therapeutic efficacy in liver disorders such as hepatitis and cirrhosis (9).

Mechanism:

The phospholipid--phytoconstituent complex improves lipophilicity, thereby enhancing gastrointestinal absorption and bioavailability[18].

Example -- Silymarin Phytosomes:

Silymarin from Silybum marianum (milk thistle) is widely used in treating liver disorders, but suffers from poor oral bioavailability [19]. Phytosomal formulations increase silymarin absorption by 3-5 times compared to conventional extracts [20].

Advantages:

- Enhanced oral bioavailability
- Sustained therapeutic activity
- Better clinical efficacy in hepatoprotection [21]

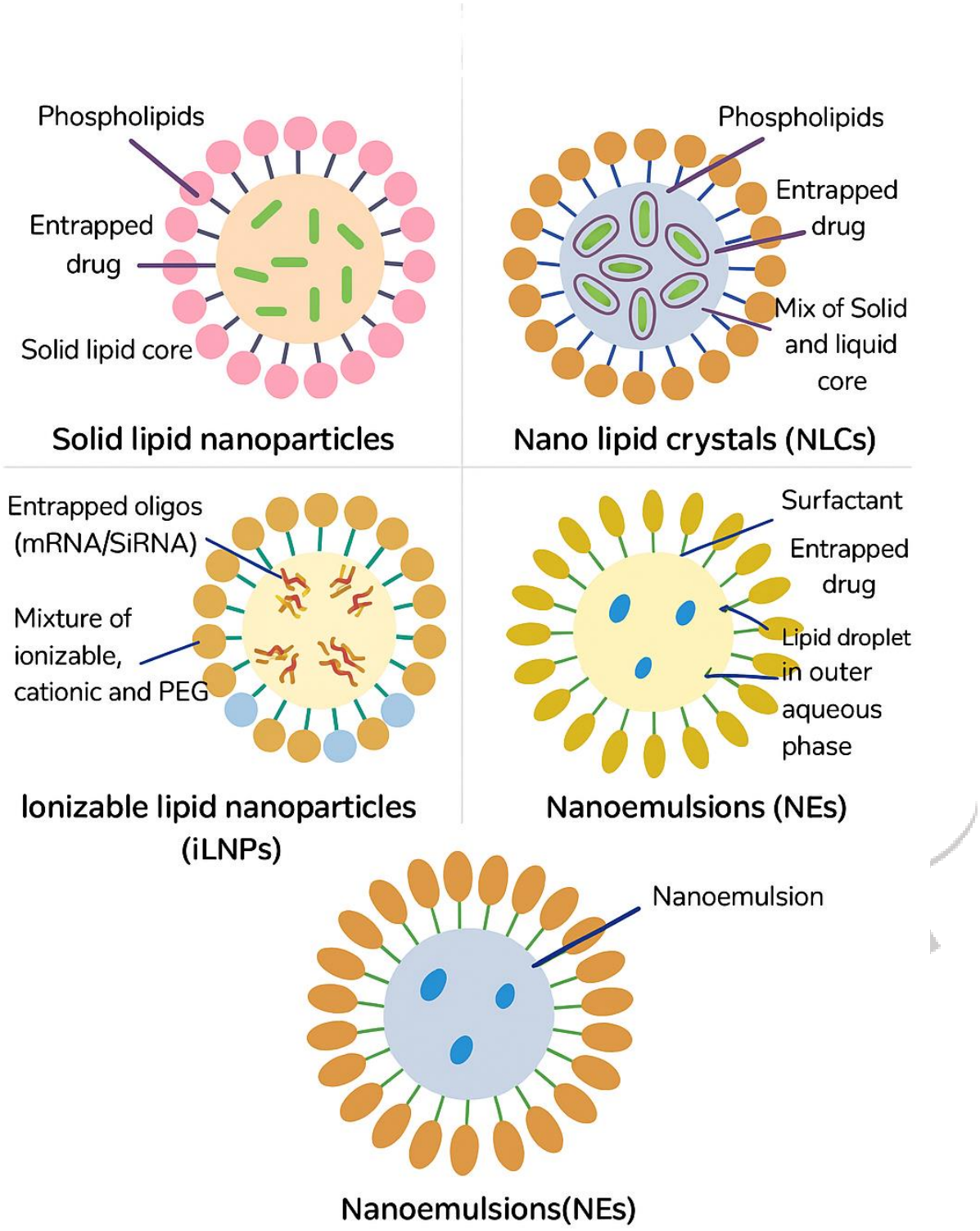
Limitations:

- High cost of production
- Limited data on large-scale clinical applications [22]

4.3 Nanoparticles / Nanoemulsions

Nanoparticles and nanoemulsions are nanoscale carriers that improve the solubility, stability, and targeted delivery of herbal bioactives (10). Polymeric nanoparticles and solid lipid nanoparticles (SLNs) have been widely studied for their controlled drug release properties. Resveratrol nanoparticles, for instance, show enhanced antioxidant, anti-aging, and anticancer properties compared to free resveratrol (11). Similarly, nanoemulsions of poorly soluble herbal extracts improve absorption and therapeutic efficiency (12).

Mechanism:



These carriers increase the surface area, enhance solubility, and allow sustained release of phytochemicals [24]. Nanoemulsions, which are oil-in-water or water-in-oil emulsions stabilized by surfactants, improve solubilization of lipophilic herbal compounds. (25)

Example – Resveratrol Nanoparticles:

Resveratrol, a polyphenol from grapes, has anticancer and anti-aging benefits but suffers from poor oral absorption. Polymeric nanoparticles enhance its stability, prolong circulation time, and increase anticancer efficacy [26].

- Advantages:

  High loading capacity for herbal drugs

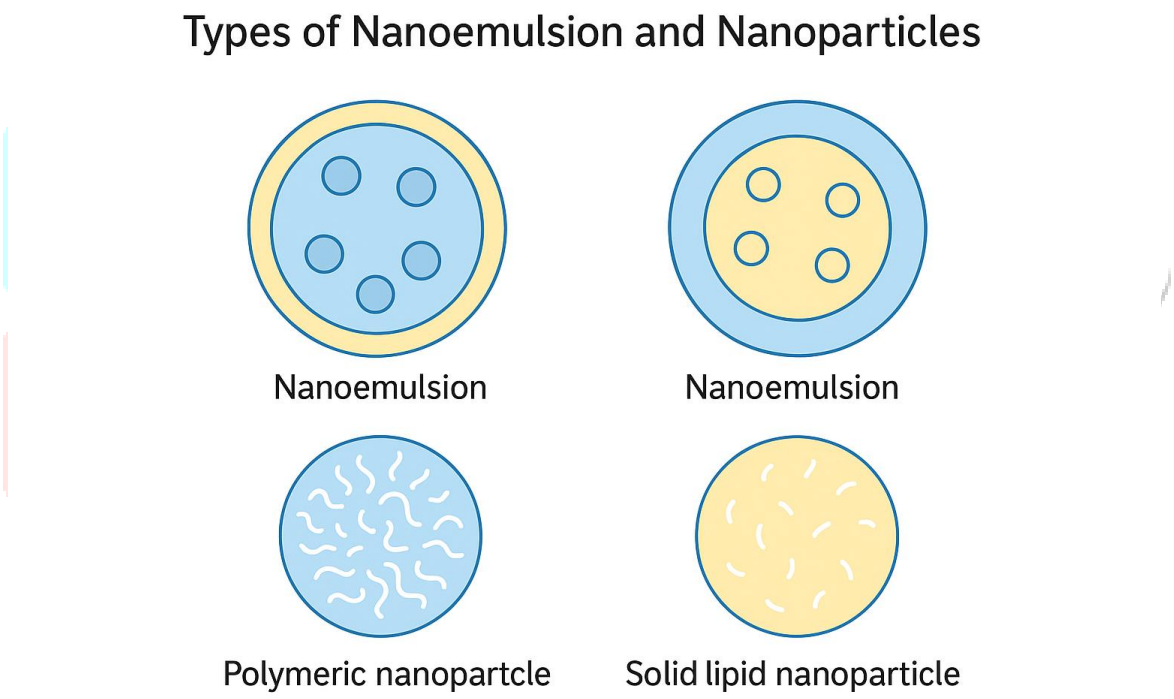
  Targeted and sustained release

  Improved solubility of poorly soluble compounds [27]

- Limitations:

  Risk of toxicity from excipients

  Expensive large-scale production [28]



4.4 Microspheres & Microemulsions

Microspheres are polymeric carriers that encapsulate herbal drugs for controlled and sustained release. Microemulsions, on the other hand, are thermodynamically stable mixtures of oil, water, and surfactants used to enhance solubilization and absorption (13). Aloe vera-based microemulsions have been developed for topical use in cosmetics and wound healing, showing improved penetration and therapeutic action (14).

Microemulsions:

These are thermodynamically stable, clear systems of oil, water, and surfactant, used to improve the solubility of lipophilic herbal actives [30].

Example -- Aloe Vera Microemulsions:

Aloe vera-based microemulsions have shown promise in wound healing and cosmetic applications by improving penetration of bioactive polysaccharides [31].

Advantages:

Uniform distribution of herbal drugs

Enhanced penetration in topical delivery

Reduced dosing frequency [32]

Limitations:

Surfactant toxicity in some cases

Stability issues during long storage [33]

5.5 Hydrogels / Transdermal Patches

Hydrogels are polymeric networks capable of retaining large amounts of water, making them suitable for controlled release formulations of herbal drugs (15). Transdermal patches based on hydrogels allow sustained release through the skin, bypassing first-pass metabolism and improving patient compliance. For example, herbal transdermal patches containing anti-inflammatory plant extracts have demonstrated prolonged therapeutic action and enhanced bioavailability (16).

Transdermal patches:

These patches are applied to the skin and allow sustained systemic delivery of herbal bioactives by bypassing first-pass metabolism [35].

Example -- Herbal Anti-inflammatory Patches:

Formulations containing herbal extracts like curcumin, aloe vera, or capsaicin in transdermal patches have been studied for chronic pain and inflammation, providing long-lasting relief [36].

Advantages:

Non-invasive delivery

Controlled release for prolonged therapy

Patient compliance improved [37]

Limitations:

Not suitable for all herbal molecules (e.g., very large or hydrophilic compounds)

Risk of skin irritation [38]

5.6 Other Systems

Apart from the above, several other NDDS platforms have been explored for herbal drugs. Niosomes, which are vesicles formed from non-ionic surfactants, offer stability and targeted delivery advantages (17). Ethosomes, containing high ethanol concentrations, improve skin permeation of herbal actives (18). Dendrimers, highly branched nanostructures, provide high drug-loading capacity and targeted delivery potential (19). These systems are still under research but hold significant promise for future herbal therapeutics

V. Advantages of NDDS in herbal drugs

- Improved solubility and bioavailability: Liposomes and phytosomes enhance absorption of poorly soluble phytoconstituents such as silybin and curcumin (20)(22).

- Protection from degradation: Phospholipid complexes shield herbal actives from gastric and enzymatic breakdown (22).
- Controlled and sustained release: Nanoparticles and microspheres allow prolonged drug action and reduced dosing frequency (21)(23).
- Targeted delivery: Liposomes exploit the enhanced permeability and retention effect, directing drugs to tumour tissues (20).
- Reduced toxicity and side effects: Encapsulation minimizes systemic exposure and improves therapeutic index (21)(23).
- Versatility of administration routes: Novel Drug Delivery System enable oral, topical, transdermal, intranasal, and parenteral delivery (22).
- Alopecia management: Nanocarriers, liposomes, microneedles, and nanostructured lipid carriers improve follicular targeting and transdermal penetration of phytochemicals like EGCG, curcumin, rosemary oil, and ginseng (25).
- Asthma nano-phytomedicine: Liposomes, polymeric nanoparticles, and solid lipid nanoparticles enhance pulmonary delivery of phytochemicals (quercetin, curcumin, ginseng), reducing oxidative stress and airway inflammation (26).
- Sugar-based herbal nanoparticles: Naturally occurring polysaccharide nanoparticles in boiling herbal extracts act as immunostimulants, suggesting traditional herbal medicine may already function as "oldest nanomedicine" (27).
- Herbal antioxidants: Nanocarriers improve stability and bioavailability of antioxidant phytochemicals (quercetin, tocopherols, curcumin), enhancing their role in managing oxidative stress-related diseases (28).
- Natural products in Alzheimer's disease: Compounds such as ginsenoside Rg1, EGCG, resveratrol, and oleuropein reduce neuroinflammation, modulate NF-κB/NLRP3 pathways, and improve cognitive function (29).
- Polyherbal anti-aging skincare: Formulations combining Curcuma longa, Glycyrrhiza glabra, Calendula officinalis, Withania somnifera, and Matricaria chamomilla act synergistically to enhance collagen synthesis, hydration, and antioxidant defence (30).
- Phytosomes in cancer therapy: Phytosomes improve solubility and bioavailability of poorly soluble phytochemicals like curcumin and silybin, enabling better tumor targeting via the EPR effect (31).
- Nanomedicine for breast cancer: Liposomes, solid-lipid nanoparticles, and polymeric carriers enhance stability and targeted delivery of phytoconstituents such as quercetin, curcumin, and berberine (32).
- Sildenafil/glycyrrhizin nanofibers: Electrospun buccal nanofibers provide rapid disintegration (<5s), bypass first pass metabolism and improves patient compliance (33).
- Green synthesis of Au/Fe_3O_4 nanocomposites: Myrtus communis extract provides dual functionality (reduction + stabilization), enabling eco-friendly fabrication of magnetic gold nanocomposites with strong antibacterial activity against Gram-positive and Gram-negative strains (34).
- Nanocochleates for oral bioavailability: Lipid-based nanocochleates protect hydrophilic and hydrophobic drugs from enzymatic degradation, enhance stability, and improve oral absorption of poorly soluble drugs (35).
- Herbal actives + endogenous lipids in nanocarriers: Co-loading capsaicin with oleoylethanolamide (OEA) or phenylalaninol oleamide (PAO) in lipid nanocarriers improves

anti-obesity efficacy, reduces glucose and triglyceride levels, and enhances gastric tolerability (36).

- Pulmonary nano/micro-carriers: Nanocarriers (liposomes, polymeric nanoparticles, SLNs) enable targeted lung delivery, bypass hepatic metabolism, improve solubility, and reduce systemic side effects in respiratory diseases (37).
- Plant-derived exosome-like nanovesicles: Plant-derived Exosome Like Nanovesicles are biocompatible, non-immunogenic, and naturally enriched with bioactive lipids; they show anti-inflammatory, anti-tumor, and antiviral effects, and can serve as novel drug carriers (38).
- Microneedle-assisted nano formulations for Rheumatoid Arthritis:
    - Microneedles bypass the stratum corneum barrier, enabling painless, localized drug delivery.
    - Nanoformulations improve solubility, stability, and targeting efficiency, enhancing Rheumatoid Arthritis therapy (39).
- Hypericin-loaded silica nanoparticles:
    - HP-SiNPs show high entrapment efficiency (~95%), sustained release
    - Improved antioxidant activity and reduced serum creatinine, BUN, and uric acid compared to free hypericin (40).
- Hydrogel platforms for Inflammatory Bowel Disease:
    - Smart hydrogels provide stimuli-responsive release (pH, ROS), mucosal barrier repair, and immunomodulation (41).
    - Multifunctional hydrogels integrate drug delivery, microbiota regulation, and epithelial regeneration (41).
- Herbal nanogels for skin cancer:
    - Nanogels encapsulate bioactive herbal compounds, enabling targeted, stimuli-responsive release (42).
    - Reduce systemic toxicity compared to chemotherapy, while enhancing localized efficacy (42).
- Transdermal drug delivery systems:
    - Transdermal Drug Delivery System bypasses first-pass metabolism, improves patient compliance, and allows sustained release (43).
    - Microneedles and solid lipid nanocarriers enhance permeability and bioavailability (43).
- Nano-formulated Chinese Herbal Medicines for cancer immunotherapy:
    - Nanocarriers improve solubility, stability, and half-life of herbal actives (44).
- Active ingredients (e.g., polysaccharides, flavonoids, alkaloids) modulate innate and adaptive immunity, enhancing anti-tumour responses (44).
- Exosome-based delivery for glioblastoma: Homologous U87 cell-derived exosomes cross the BBB efficiently and target glioblastoma cells specifically (45). Co-delivery of temozolomide and resveratrol enhances apoptosis and downregulates PI3K/AKT signalling (45).
- Pulmonary micro/nano-carriers: Inhalation route bypasses first-pass metabolism, offers rapid onset, and localized treatment (46). Nanocarriers (liposomes, SLNs, polymeric nanoparticles) improve solubility, sustained release, and patient compliance (46).

- Natural product draggability via Drug Delivery System: DDSs enhance bioavailability, stability, and targeting of bioactive natural products (47). Paclitaxel liposomes, curcumin nanoparticles, and resveratrol-loaded carriers show improved pharmacokinetics (47).
- Nanotoxicity assessment: Advanced in vitro/in vivo models (zebrafish, C. elegans) allow safer nanoparticle design (48). High-throughput screening improves risk evaluation while enabling innovation in nanomedicine (48).
- Electrospun nanofibers for cutaneous delivery: Nanofibers mimic extracellular matrix, promote wound healing, and allow controlled release (49). Multifunctional fibers can incorporate antimicrobials, growth factors, and diagnostic sensors (49)

VI. Challenges and Future Perspectives

6.1 Challenges

- Standardization issues: Herbal extracts vary due to cultivation, harvesting, and processing, complicating reproducibility (21)(24).
- Formulation complexity: Encapsulation of diverse phytochemicals with varying polarity and stability is technically demanding (20)(23).
- Stability concerns: Herbal bioactives are prone to oxidation, microbial contamination, and degradation during storage (24).
- Regulatory hurdles: Lack of harmonized guidelines for herbal NDDS complicates clinical translation (21)(24).
- Safety and toxicology gaps: Limited data on long-term safety of nanocarriers combined with herbal actives (23).
- Cost-effectiveness: Advanced nanocarrier systems are expensive compared to conventional herbal formulations (22).
- Skin penetration limits: Even with nanocarriers, hydrophobic phytochemicals face formulation hurdles (25).
- Pulmonary toxicity risks: Nano-phytomedicine for asthma shows promise but requires more clinical validation to ensure safety (26).
- Variability in plant chemistry: Sugar-based nanoparticles differ depending on herbal source, complicating reproducibility (27).
- Oxidative stress models: Antioxidant nanomedicine often relies on in vitro assays (DPPH, FRAP, ORAC), which may not fully predict clinical outcomes (28).
- Alzheimer's phytotherapy: Safety concerns include EGCG hepatotoxicity at high doses and celastrol hepatotoxicity/nephrotoxicity; BBB penetration remains limited (29).
- Polyherbal skincare: Standardization is difficult due to chemical interactions among phytoconstituents, and stability requires advanced validation (30).
- Phytosomes: Low drug-loading capacity and storage stability issues compared to other nanocarriers hinder clinical translation (31).
- Breast cancer nanomedicine: Toxicity risks from cationic lipids and carbon nanotubes, plus complexity of tumor microenvironment, challenge effective targeting (32).

- Nanofiber buccal delivery: Scalability of electrospinning and dose optimization for sildenafil remain hurdles for clinical application (33).
- Nanocomposites: Conventional synthesis of Au/Fe_3O_4 requires toxic chemicals ($NaBH_4$, hydrazine) and costly equipment; scalability and reproducibility remain barriers (34).
- Nanocochleates: Despite stability, limitations include restricted permeability, slow release, and challenges in large-scale production (35).
- Anti-obesity nanocarriers: Co-loading multiple actives risks competition for encapsulation, variable entrapment efficiency, and requires precise dose optimization (36).
- Pulmonary nanocarriers: Biological barriers (mucociliary clearance, enzymatic degradation) and short half-life of inhaled formulations hinder sustained therapeutic efficacy (37).
- Plant-derived Exosomes Like Nanovesicles: Isolation and purification methods (ultracentrifugation, polymer precipitation) yield variable purity; heterogeneity of plant sources complicates standardization (38).
- Microneedles:
    - Limited for drugs with poor solubility/stability (39).
    - Risk of high local concentration for cytotoxic drugs (39).
    - Targeting efficiency remains suboptimal (39).
- Hypericin nanoparticles:
    - Hypericin's inherent hydrophobicity complicates formulation (40).
    - Long-term biosafety of silica nanoparticles requires further validation (40).
- Hydrogels for Inflammatory Bowel Disease:
    - Biocompatibility and scalability issues (41).
    - Clinical translation hindered by variability in patient microbiota and immune responses (41).
- Herbal nanogels:
    - Risk of metastasis if systemic targeting is insufficient (42).
    - Complex synthesis methods (photolithography, micromoulding) limit scalability (42).
- Transdermal Drug Delivery System:
    - Skin irritation, variability in regional permeability, and difficulty delivering large molecules (43).
    - Regulatory challenges in standardizing permeation enhancers (43).
- Nano-formulated Chinese Herbal Medicines:
    - Hydrophobicity and poor stability of herbal actives (44).
    - Industrial-scale production and safety concerns remain unresolved (44).
- Exosome systems:
    - Exosome systems suffer from large-scale production and purification difficulties (45).
    - Risk of immunogenicity and variability in exosome cargo (45).

- Pulmonary carriers:
    - Pulmonary carriers suffer from short half-life due to clearance and enzymatic degradation (46).
    - Resistant strains in infectious diseases limit effectiveness (46).
- Bioactive Natural Products druggability :
    - BNPs face poor solubility, instability, and multi-target complexity hindering clinical translation (47).
    - Naked BNPs often fail to achieve synergy due to unfavourable pharmacokinetics (47).
- Nanotoxicity:
    - Nanotoxicity testing lacks standardized protocols across labs (48).
    - Nanoparticles may cause oxidative stress, genotoxicity, and unintended organ accumulation (48).
- Nanofibers:
    - Nanofiber scalability and reproducibility remain unresolved (49).
    - Burst release or poor encapsulation efficiency for certain drugs (49).

6.2 Future Perspectives

- Nanotechnology integration: Smart nanocarriers (phytosomes, solid lipid nanoparticles, nanocrystals) for precision delivery (22)(23).
- Personalized medicine: Tailoring NDDS formulations based on genetic and metabolic profiles (21).
- AI-driven formulation design: Computational modeling to predict stability, release kinetics, and efficacy (22).
- Green nanotechnology: Eco-friendly synthesis of carriers using plant-derived materials (23).
- Regulatory evolution: Development of specific international guidelines for herbal NDDS (24).
- Commercialization potential: Expansion into nutraceuticals, cosmeceuticals, and mainstream pharmaceuticals (22).
- Integrative therapies: Combining synthetic drugs (minoxidil, finasteride) with phytochemicals in nanocarriers for alopecia (25).
- Eco-friendly nanotechnology: Plant-mediated nanoparticle synthesis offers sustainable alternatives to chemical methods (26).
- Vaccine adjuvants: Sugar-based herbal nanoparticles could serve as natural immunostimulant adjuvants (27).
- Personalized antioxidant therapy: Tailoring nanocarrier-based herbal antioxidants to individual oxidative stress profiles (28).
- Alzheimer's therapy: Nanoparticle encapsulation and self-assembly carriers may improve CNS delivery of natural products (29).
- Anti-aging cosmeceuticals: Combining liposomes, ethosomes, and emulgels with omics-based profiling will strengthen polyherbal skincare efficacy (30).
- Cancer phytosomes: Personalised phytosome formulations and integration with chemotherapy could reduce toxicity and enhance therapeutic outcomes (31).

- Breast cancer nanomedicine: Multifunctional nanocarriers (theranostics) and integration with immunotherapy hold promise for future treatment (32).
- Buccal nanofibers: Smart dual-drug delivery systems and clinical validation could expand applications of glycyrrhizin nanofibers beyond Erectile Disfunction (33).
- Green nanocomposites: Plant-mediated synthesis offers scalable, eco-friendly alternatives; combining magnetic targeting with Au antibacterial activity could combat multidrug resistance (34).
- Nanocochleates: Emerging applications in cancer, diabetes, malaria, and vaccines highlight potential for personalized oral therapies (35).
- Anti-obesity nanocarriers: Integration of herbal actives with lipid mediators may enable safer long-term obesity management; clinical validation is needed (36).
- Pulmonary nanocarriers: Smart polymers, hydrogels, and controlled microparticles could overcome clearance barriers and provide sustained lung drug release (37).
- PELNVs: Plant exosome-like vesicles may revolutionize drug delivery, offering natural targeting, oral stability, and therapeutic effects in cancer, inflammation, and viral infections (38).
- Microneedle + nanoformulation:
    - Smart MNs with biosensing materials could enable personalized RA therapy (39).
    - Integration with biodegradable polymers for safer delivery (39).
- Hypericin nanoparticles:
    - Potential clinical application as nephroprotective adjunct in psychiatric therapy (40).
    - Exploration of other herbal actives with silica nanocarriers (40).
- Hydrogels for Inflammatory Bowel Disease:
    - Development of multifunctional hydrogels combining anti-inflammatory and regenerative agents (41).
    - Personalised hydrogel therapy based on patient microbiota profiles (41).
- Herbal nanogels:
    - Combination with systemic immunotherapy to balance local and systemic effects (42).
    - Exploration of acid-activatable prodrug nanogels for tumour microenvironment targeting (42).
- Transdermal Drug Delivery System:
    - Electronic patches and reservoir systems for controlled multi-drug release (43).
    - Hypoallergenic adhesives and optimized microneedle safety (43).
- Nano-formulated Chinese Herbal Medicines:
    - Integration with checkpoint inhibitors and CAR-T therapy for synergistic cancer immunotherapy (44).
    - Industrial-scale production with standardized nanocarrier systems (44).
- Exosome systems:
    - Personalised exosome therapy with engineered ligands for precision GBM targeting (45).
    - Clinical translation in CNS diseases (45).

- Pulmonary carriers:
- Smart inhalable formulations with stimuli-responsive release for respiratory infections (46).
- Combination therapies for MDR-TB and viral infections (46).
- Bioactive Natural Products druggability:
    - Hybrid DDS integrating BNPs with immunotherapy, photodynamic, or sonodynamic approaches (47).
    - Synergistic formulations mimicking TCM "JUN-CHEN-ZUO-SHI" principles (47).
- Nanotoxicity:
- Development of global regulatory frameworks for nanomedicine safety (48).
- AI-driven predictive toxicology models (48).
- Nanofibers:
    - Multifunctional nanofiber patches with diagnostic-therapeutic dual roles (49).
    - Personalized dermatological therapy and skin cancer management (49)

VII. Recent Studies and Marketed Formulations

Over the last five years, research on integrating herbal actives into novel drug delivery systems (NDDS) has focused on improving solubility, stability, oral bioavailability, targeted delivery, and sustained release (50,55). Curcumin remains the most intensively studied herbal compound: a steady stream of nanoparticle, lipid-based, micellar and phytosome approaches have demonstrated improved pharmacokinetics and enhanced biological activity compared with unformulated curcumin (50,54).

Notable marketed formulations that illustrate translation from technology to product include Theracurmin®, a sub-micron curcumin dispersion developed to increase oral absorption (commercial product and PK comparisons available), and several phospholipid-complex (phytosome) or oil-complex curcumin products (e.g., Meriva®, BCM-95®/Longvida®) that claim enhanced systemic exposure versus raw curcumin (50,52,54). Clinical and pharmacokinetic studies comparing these preparations underscore measurable gains in plasma curcumin levels for nanoparticulate/micellar/phytosome technologies (50,54).

Green-tea catechins (primarily EGCG) have been formulated in lipid-based nanocarriers (liposomes, solid lipid nanoparticles, nanoemulsions) and polymeric nanoparticles to improve chemical stability and intestinal uptake; recent reviews and preclinical studies demonstrate enhanced antioxidant, anti-inflammatory and weight-management relevant bioactivities for EGCG in NDDS (51,56). While several dietary supplements now market “liposomal” or enhanced-EGCG products for wellness/weight management, rigorous clinical evidence for marketed nano-EGCG products remains more limited than for curcumin formulations (51).

Other herbal actives showing strong NDDS interest in the past five years include berberine, silymarin (silybin), quercetin, and andrographolide (53,56). Berberine nanoformulations (polymeric/lipid nanoparticles, metal-conjugates) show improved cellular uptake and promising preclinical efficacy (e.g., anticancer, metabolic effects), although clinical translation is still emerging (53). Phytosome technology has already produced marketed silymarin-phospholipid complexes (e.g., Siliphos®/Siliphos-containing supplements) that improve silybin bioavailability and are widely used in liver-support products (52,56)

Herbal drug	NDDS type (example)	Therapeutic use / target indication
Curcumin (Theracurmin®)	Sub-micron nanoparticle dispersion / micellar powder (commercial) Recent Studies and Marketed Formulations	Improved oral bioavailability; anti-inflammatory / antioxidant (supplement & adjunct uses)
Curcumin (Meriva®, BCM-95®/Longvida®)	Phytosome / oil-complex / lecithin-complex (marketed)	Enhanced systemic exposure; trials in inflammatory and metabolic conditions
EGCG (green tea catechins)	Liposomes, solid lipid nanoparticles, nanoemulsions (research & some supplement products)	Antioxidant, chemoprevention, weight management (preclinical + limited clinical)
Silymarin / silybin	Phytosome (Siliphos® and other phospholipid complexes; marketed)	Liver support, antioxidant; improved absorption versus raw extract
Berberine	Polymeric/lipid nanoparticles; engineered conjugates (recent preclinical studies)	Metabolic modulation, anticancer, anti-fibrotic effects (preclinical)

VIII. Conclusion

The growing integration of herbal medications with advanced drug delivery technologies reflects a significant shift in modern pharmaceutical development. Rather than focusing solely on enhancing bioavailability, nanotechnology-based delivery platforms also offer opportunities to redesign how herbal medicines are formulated, administered, and evaluated. Delivery systems such as lipid-based carriers, polymeric matrices, transdermal platforms, and stimulus-responsive systems enable us to have greater control over release behavior, tissue interaction, and patient-centric dosing regimens. In parallel, increasing evidence from marketed products highlights the feasibility of translating selected herbal nanomedicines into real-world use. Even so, the complexity of herbal matrices, batch-to-batch variability, and uncertainties surrounding nanocarrier–biological interactions continue to challenge formulation reproducibility and regulatory acceptance. Addressing these issues will require interdisciplinary collaboration, standardized characterization protocols, and alignment between pharmaceutical scientists, clinicians, and regulatory authorities. As the research progresses, emphasis should shift toward scalable manufacturing, long-term safety assessment, and rational design frameworks which balances efficacy, safety, and cost. With such advancement, nanotechnology has the potential to reposition herbal drugs as credible components of evidence-based pharmaceutical therapy rather than adjunct traditional remedies.

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