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Smart Herbal Drug Delivery Systems Advances in Phytosomes, Nanomedicine, Stimuli-Responsive Biomaterials and Novel Pharmaceutical Excipients

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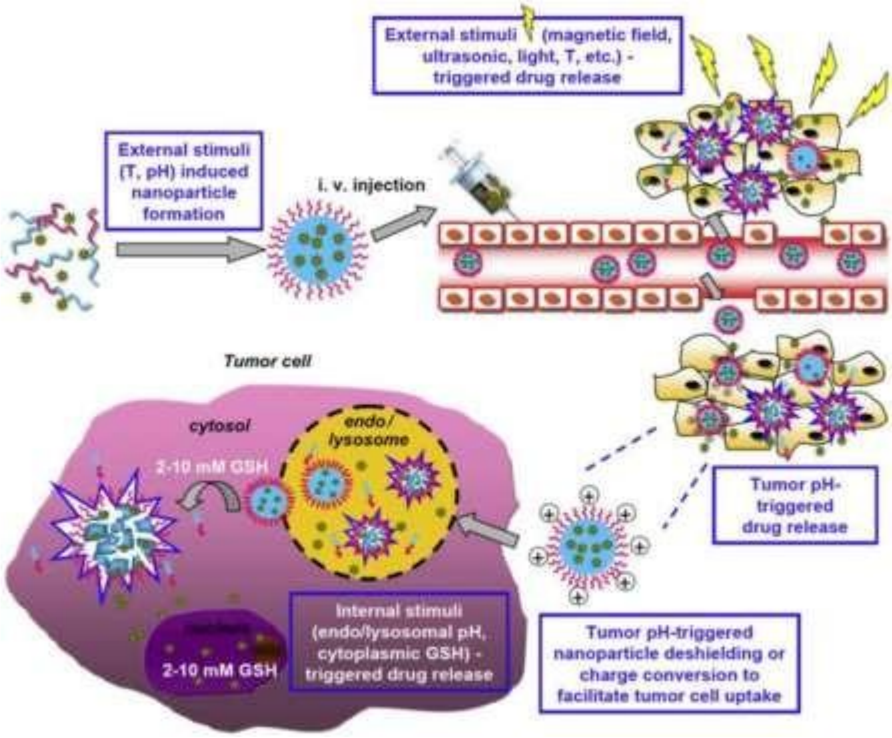
ABSTRACT
Smart herbal drug delivery systems have emerged as promising pharmaceutical strategies for overcoming the limitations associated with conventional administration of plant-derived bioactive compounds. Although phytochemicals possess considerable pharmacological potential, their therapeutic utilisation is frequently restricted by poor aqueous solubility, inadequate membrane permeability, chemical instability, rapid metabolism and low systemic bioavailability. This review examines recent advances in smart delivery approaches, with particular emphasis on phytosomes, nanomedicine, stimuli-responsive biomaterials and novel pharmaceutical excipients. Phytosomes provide improved membrane compatibility and enhanced absorption through phytochemical–phospholipid complex formation, whereas nanomedicine-based systems offer opportunities for improved stability, controlled release, cellular uptake and biodistribution. Stimuli-responsive biomaterials further enable regulated phytochemical release in response to physiological triggers such as pH, temperature, enzymes and redox conditions. Functional pharmaceutical excipients contribute to solubilisation, stabilisation, permeability enhancement and formulation performance. The reviewed literature indicates that integrating herbal bioactives with advanced delivery technologies can substantially improve their pharmaceutical and therapeutic potential. However, challenges concerning botanical standardisation, formulation reproducibility, long-term safety, manufacturing scale-up, regulatory acceptance and clinical validation remain. Continued integration of phytochemistry, nanotechnology and biomaterials science is therefore required to develop stable, reproducible and clinically translatable smart herbal formulations.
Keywords: Smart drug delivery; Herbal bioactives; Phytosomes; Nanomedicine; Phytochemicals; Stimuli-responsive biomaterials; Pharmaceutical excipients; Nanocarriers; Bioavailability; Controlled release.

INTRODUCTION
Herbal medicines have gained sustained scientific and pharmaceutical interest because plants provide a chemically diverse reservoir of biologically active constituents, including flavonoids, phenolic acids, alkaloids, terpenoids, tannins, carotenoids and other polyphenolic compounds. These phytochemicals exhibit a broad range of pharmacological activities,

including antioxidant, anti-inflammatory, antimicrobial, anticancer, cardioprotective and neuroprotective effects, making them attractive candidates for the development of therapeutic interventions (Kyriakoudi et al., 2021). However, the therapeutic translation of many herbal bioactives remains constrained by unfavourable physicochemical and pharmacokinetic characteristics. Poor aqueous solubility, chemical instability, inadequate intestinal permeability, rapid metabolism and limited systemic bioavailability can substantially reduce the concentration of active constituents reaching their intended site of action (Tan et al., 2021).



Recent developments in pharmaceutical nanotechnology and materials science have therefore shifted attention from conventional herbal formulations towards intelligent or "smart" drug delivery systems. Such systems are designed not merely to encapsulate phytochemicals but to modify their solubility, stability, absorption, biodistribution and release behaviour. Phytosomes, lipid-based nanocarriers, polymeric nanoparticles, nanoemulsions, vesicular systems and other nanoscale platforms have demonstrated considerable potential for improving the delivery of poorly bioavailable plant constituents (Pandey et al., 2021). Phytosomes are particularly relevant because phospholipid complexation can enhance the interaction of phytochemicals with biological membranes and improve their absorption characteristics (Raghav et al., 2024).

More recently, stimuli-responsive biomaterials and multifunctional pharmaceutical excipients have expanded the concept of smart delivery by enabling drug release in response to specific physiological or pathological conditions. Consequently, the integration of herbal bioactives with advanced carriers represents an important direction in contemporary pharmaceutical research, aiming to bridge the gap between the recognised pharmacological potential of

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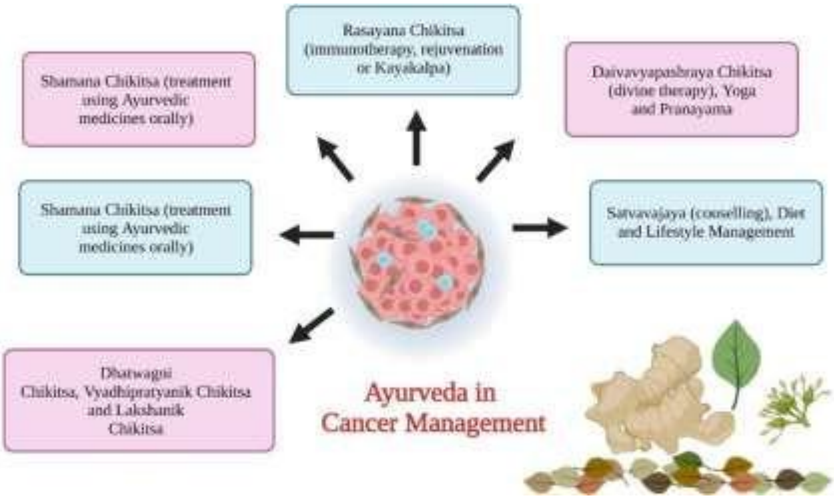
herbal compounds and their effective clinical delivery (Chauhan et al., 2024).

HERBAL BIOACTIVE COMPOUNDS AND CHALLENGES IN CONVENTIONAL DRUG DELIVERY

Herbal bioactive compounds encompass chemically heterogeneous constituents whose therapeutic effects depend on their molecular structure, concentration, stability and interaction with biological targets. Important groups include flavonoids, phenolic compounds, alkaloids, terpenoids, carotenoids and essential-oil constituents. Despite their considerable pharmacological potential, many of these compounds exhibit physicochemical properties that restrict their effective incorporation into conventional pharmaceutical formulations. In particular, poor aqueous solubility is frequently observed among lipophilic phytochemicals, whereas some hydrophilic compounds demonstrate inadequate membrane permeability and intestinal absorption (Kyriakoudi et al., 2021).

The oral route presents several additional barriers. Following administration, phytochemicals may undergo degradation under gastrointestinal conditions, incomplete dissolution, limited intestinal permeability, enzymatic transformation and extensive first-pass metabolism. Consequently, only a fraction of the administered dose may reach systemic circulation in an active form. Tan et al. (2021) reported that poor intestinal permeability, inadequate solubility or a combination of both are major factors contributing to the low oral bioavailability of medicinal herbal compounds. Large molecular size and strong lipophilicity can further restrict absorption across the intestinal epithelium.

Chemical instability represents another important limitation. Polyphenols and other sensitive constituents may undergo oxidation, hydrolysis or degradation during processing, storage and gastrointestinal digestion, thereby reducing their biological activity. Volatile constituents such as essential oils can additionally suffer from evaporation and instability. Variability in plant species, cultivation conditions, harvesting, extraction procedures and phytochemical composition may also produce inconsistencies in the concentration of active constituents (Kyriakoudi et al., 2021).



Conventional dosage forms such as tablets, capsules and simple extracts often provide limited control over these factors. Although formulation strategies such as solubilisation and solid dispersion can improve dissolution, the complex physicochemical characteristics of herbal extracts frequently require multifunctional delivery approaches (Patel et al., 2021). These limitations have consequently encouraged the development of lipid-based, vesicular and nanoscale systems capable of enhancing solubility, protecting sensitive constituents and improving gastrointestinal absorption (Tan et al., 2021; Pandey et al., 2021).

SMART DRUG DELIVERY SYSTEMS FOR HERBAL THERAPEUTICS

Smart drug delivery systems have emerged as an important strategy for addressing the pharmacokinetic limitations associated with herbal bioactive compounds. Unlike conventional dosage forms, these systems are designed to regulate the solubility, protection, transport, biodistribution and release of active constituents according to their physicochemical characteristics and therapeutic requirements. Liposomes, nanoemulsions, polymeric nanoparticles, solid lipid nanoparticles, nanostructured lipid carriers and phospholipid complexes have therefore been investigated for improving the delivery of poorly soluble and unstable phytochemicals. Such nanoscale systems can increase surface area, facilitate interaction with biological membranes and protect sensitive compounds from premature degradation, thereby potentially improving systemic exposure and therapeutic performance (Gnananath et al., 2017; Lu et al., 2019).

The concept of smart delivery has subsequently expanded beyond simple encapsulation towards responsive and multifunctional platforms. Stimuli-responsive carriers can alter their structure or release behaviour in response to physiological signals such as pH, temperature, enzymes, redox conditions or specific pathological microenvironments. This approach is particularly relevant to herbal therapeutics because many phytochemicals exhibit rapid metabolism and non-specific distribution following administration. Integration with responsive biomaterials can provide greater control over the timing and location of phytochemical release, while surface modification may facilitate tissue-specific delivery (Zhang et al., 2021).

Another important development is the incorporation of functional pharmaceutical excipients capable of enhancing solubilisation, membrane permeability, stability and controlled release. The selection of phospholipids, polymers, surfactants and other functional excipients can consequently determine the performance and stability of smart herbal formulations. Recent research indicates that combining phytochemicals with advanced nanocarriers can improve bioavailability and therapeutic efficacy while creating opportunities for alternative routes of administration (Gaur et al., 2023; Senol Deniz et al., 2024). Thus, smart delivery represents an integrated formulation approach in which carrier architecture, material properties and biological responses are considered together rather than treating the herbal constituent as an isolated active ingredient.

PHYTOSOMES AS ADVANCED HERBAL DRUG DELIVERY SYSTEMS

Phytosomes are phospholipid-based delivery systems developed specifically to improve the absorption and bioavailability of plant-derived bioactive compounds. In a phytosome, the phytoconstituent interacts with a phospholipid, commonly phosphatidylcholine, through molecular interactions including hydrogen bonding, producing a lipid-compatible phytochemical–phospholipid complex. This differs fundamentally from conventional encapsulation because the active constituent becomes associated with the phospholipid structure rather than simply being entrapped within an aqueous or lipidic compartment (Lu et al., 2019). The resulting amphiphilic complex can demonstrate improved partitioning into biological membranes, facilitating absorption of compounds that otherwise exhibit poor permeability or limited bioavailability.

The effectiveness of phytosomes is particularly relevant for polyphenols and flavonoids, whose therapeutic potential is frequently restricted by poor aqueous solubility, inadequate membrane permeability and extensive gastrointestinal or metabolic degradation. Formation of a phospholipid complex can modify the physicochemical characteristics of such compounds and improve their interaction with intestinal membranes. Consequently, increased absorption and systemic exposure have been reported for several phytosomal preparations (Gnananath et al., 2017; Lu et al., 2019). Phytosomes may also provide improved protection of sensitive phytoconstituents against environmental and gastrointestinal degradation.

Recent research has expanded phytosomal applications from traditional herbal extracts towards standardised phytopharmaceuticals and multifunctional nanodelivery platforms. Investigations have explored phytosomes containing compounds such as curcumin, silybin, quercetin and other polyphenolic constituents for applications involving inflammatory, metabolic, neurological and degenerative disorders. Their potential advantages include improved bioavailability, enhanced stability, efficient drug loading and suitability for oral, topical and other administration routes (Gaur et al., 2023). Recent reviews further indicate increasing interest in translating phytosomal systems from experimental formulations towards clinical applications and commercially relevant phytopharmaceutical products (Maddi et al., 2024).

Table 1. Major characteristics of phytosomal drug delivery systems

Characteristic	**Phytosomal system**	**Pharmaceutical significance**
Basic structure	Phytochemical–phospholipid complex	Improves compatibility of phytochemicals with biological membranes
Principal phospholipid	Phosphatidylcholine is commonly used	Provides amphiphilic characteristics
Molecular interaction	Hydrogen bonding and other molecular interactions	Promotes formation of a stable phytochemical complex
Solubility	Can improve apparent solubility of poorly soluble constituents	Facilitates dissolution and absorption
Membrane interaction	Enhanced lipid–membrane affinity	May improve intestinal and cellular uptake
Stability	Provides protection against environmental and gastrointestinal degradation	Helps preserve bioactive constituents

Bioavailability	Generally higher than corresponding free phytoconstituents in suitable formulations	Potentially improves therapeutic exposure
Administration	Oral, topical and other routes have been investigated	Broadens formulation possibilities

Source: Synthesised from Gnananath et al. (2017), Lu et al. (2019), Gaur et al. (2023) and recent phytosome reviews.

Table 2. Selected herbal bioactives investigated through phytosomal delivery

Herbal bioactive	**Major formulation challenge**	**Potential benefit of phytosomal delivery**	**Therapeutic relevance**
Curcumin	Poor aqueous solubility and bioavailability	Enhanced absorption and systemic availability	Anti-inflammatory and anticancer research
Silybin	Poor absorption and extensive metabolism	Improved bioavailability	Hepatoprotective applications
Quercetin	Low solubility and limited oral absorption	Improved membrane interaction and absorption	Antioxidant and anti-inflammatory applications
Green tea polyphenols	Instability and limited bioavailability	Improved protection and delivery	Antioxidant and metabolic applications
Grape-seed polyphenols	Poor absorption and rapid metabolism	Enhanced delivery of polyphenolic constituents	Cardiovascular and antioxidant research
Other standardised plant extracts	Variable absorption and stability	Improved lipid compatibility and pharmacokinetic performance	Diverse phytopharmaceutical applications

Phytosomes therefore occupy an important position between conventional herbal formulations and more complex nanomedicine platforms. Their relatively straightforward phospholipid-complex approach allows formulation scientists to modify the delivery characteristics of plant bioactives without fundamentally altering their chemical identity.

BACKGROUND TO THE STUDY

The therapeutic use of medicinal plants has a long history, and modern pharmaceutical research continues to investigate herbal bioactive compounds because of their diverse pharmacological properties. Phytochemicals such as flavonoids, polyphenols, alkaloids, terpenoids and phenolic compounds have demonstrated antioxidant, anti-inflammatory, antimicrobial, anticancer and cardioprotective activities. However, their incorporation into effective pharmaceutical formulations remains challenging because many herbal constituents exhibit poor aqueous solubility, limited gastrointestinal permeability, chemical instability, rapid metabolism and low systemic bioavailability (Kyriakoudi et al., 2021).

Conventional herbal preparations, including crude extracts, powders, tablets and capsules, may therefore fail to provide consistent therapeutic concentrations at the desired biological site. These limitations have encouraged the development of advanced delivery technologies capable of protecting phytochemicals from degradation and improving their absorption and distribution. Nanomedicine has introduced platforms such as liposomes, nanoemulsions, polymeric nanoparticles, solid lipid nanoparticles and nanostructured lipid carriers, while phospholipid-based phytosomes have provided an additional approach for improving the membrane affinity and bioavailability of herbal compounds (Lu et al., 2019).

More recently, smart delivery systems have incorporated stimuli-responsive biomaterials and multifunctional pharmaceutical excipients capable of controlling drug release in response to physiological conditions. Such developments offer opportunities to improve the therapeutic performance of herbal bioactives while reducing limitations associated with conventional formulations. Consequently, systematic evaluation of phytosomes, nanomedicine, stimuli-responsive biomaterials and novel pharmaceutical excipients is important for understanding how advances in pharmaceutical technology can support the development of more effective, stable and targeted herbal therapeutics (Gaur et al., 2023).

SCOPE OF THE RESEARCH

The scope of this research encompasses a comprehensive review of recent advances in smart herbal drug delivery systems, with particular emphasis on technologies developed between 2015 and 2024. The study focuses on the formulation and delivery challenges associated with herbal bioactive compounds, including poor aqueous solubility, low membrane permeability, chemical instability, rapid metabolism and inadequate systemic bioavailability. These limitations provide the basis for examining advanced pharmaceutical approaches designed to improve the therapeutic performance of phytochemicals.

Particular attention is given to phytosomes as phospholipid-based systems for enhancing the absorption and bioavailability of plant-derived compounds. The research also covers nanomedicine-based approaches, including lipidic, polymeric and vesicular nanocarriers used for improving the stability, cellular uptake, controlled release and biodistribution of herbal bioactives (Lu et al., 2019). In addition, the scope incorporates stimuli-responsive biomaterials capable of responding to physiological triggers such as pH, temperature, enzymes and redox conditions, thereby providing opportunities for more controlled and site-specific release.

The review further examines novel pharmaceutical excipients, including functional lipids, polymers, surfactants and other formulation components that contribute to solubilisation, protection, stability and controlled delivery of herbal constituents. Comparative consideration is given to the advantages, limitations, formulation challenges, safety considerations and translational potential of these technologies. Recent developments in formulation optimisation, nanotechnology and biomaterial engineering are also considered to identify emerging directions in smart herbal therapeutics. Overall, the research is intended to establish an integrated understanding of how advanced delivery technologies can address the limitations of conventional herbal formulations and support the development of more effective, stable and bioavailable phytopharmaceutical products.

LITERATURE REVIEW

Barani et al. (2021) described phytosomes as an important nanovesicular approach for improving the delivery of phytochemicals whose clinical application is restricted by poor bioavailability and limited selectivity. Their review highlighted that phytochemicals, particularly polyphenols such as curcumin and silymarin, can benefit from association with phospholipids because the resulting complexes improve interaction with biological membranes. The authors also reported that phytosomal formulations have demonstrated enhanced biological activity and, in some cases, therapeutic effects at lower doses than corresponding conventional preparations. This evidence established phytosomes as an important bridge between traditional phytopharmaceutical preparations and modern nanomedicine. The adaptability of phytosomal systems to different plant constituents has further encouraged their investigation for inflammatory, metabolic, cardiovascular and neurodegenerative conditions (Barani et al., 2021).

Jain et al. (2016) examined the broader expansion of pharmaceutical nanotechnologies for phytopharmaceuticals and demonstrated that nanoscale delivery platforms can address several fundamental limitations of herbal medicines. Their analysis included liposomes, nanoparticles, microspheres and other carrier systems designed to improve solubility, absorption, pharmacokinetic behaviour and bioavailability. An important contribution of this work was the recognition that nanotechnology can provide protection against degradation while also offering opportunities for controlled and targeted delivery. Such characteristics are particularly relevant for herbal extracts, which contain multiple constituents with substantially different physicochemical properties. The authors therefore positioned nanotechnology as a potentially valuable strategy for transforming plant-derived therapeutic substances into more predictable pharmaceutical formulations (Jain et al., 2016).

Afrin et al. (2018) reviewed novel approaches to herbal drug delivery and emphasised the transition from traditional administration towards technologically advanced systems. Their work discussed phytosomes, ethosomes, transfersomes, transdermal systems, nanoparticles and biphasic formulations as approaches for improving the efficacy and stability of herbal medicines. The review suggested that conventional administration may be inadequate where active constituents undergo degradation, poor absorption or rapid elimination. Novel delivery systems can instead provide sustained release, improved patient compliance and, where appropriately designed, more targeted action. The authors also highlighted the importance of formulation standardisation, because the therapeutic performance of herbal delivery systems depends not only on the carrier but also on the quality and consistency of the botanical material incorporated into the formulation (Afrin et al., 2018).

Marella and Tollamadugu (2018) focused on nanotechnological approaches for herbal medicines and demonstrated the growing relevance of nanoformulation to plant-based therapeutics. Their review showed that nanocarriers may overcome poor solubility, limited permeability, instability in biological environments and extensive first-pass metabolism. These limitations are particularly important in chronic disorders where herbal medicines are frequently investigated as complementary or alternative therapeutic agents. Nanoparticle-based delivery can increase the effective exposure of bioactive compounds and may permit controlled or targeted administration. However, the authors also recognised that the development of nanoherbal products requires attention to formulation quality and reproducibility, since differences in herbal composition can influence particle characteristics, drug loading and therapeutic performance (Marella & Tollamadugu, 2018).

Pati et al. (2018) further reported that nanoformulation can improve the delivery characteristics of plant-derived therapeutic molecules affected by poor solubility, low permeability, instability and extensive first-pass metabolism. Their review considered nanoparticles, nanocapsules, nanospheres, nanocrystals and related systems as potential approaches for achieving sustained delivery of herbal constituents. An important issue identified in their work was standardisation. Unlike many single-molecule synthetic drugs, herbal preparations may contain numerous constituents, and variations in chemical composition can influence formulation performance. Consequently, successful nanoherbal development requires simultaneous consideration of phytochemical standardisation, particle characteristics and biological activity rather than relying solely on nanoscale size as an indicator of formulation quality (Pati et al., 2018).

Baskar et al. (2018) examined herbal nanogels and highlighted the importance of nanostructured polymeric systems in improving the delivery and permeation of phytoconstituents. Nanogels combine nanoscale dimensions with the three-dimensional network characteristics of hydrogels, providing opportunities for incorporating active substances while regulating their release. Their relevance is particularly evident for topical and transdermal applications, where the skin represents a major biological barrier. The review indicated that advanced gel systems can improve drug permeation and maintain therapeutic compounds within the intended application site for longer periods. Such systems consequently represent an intermediate technology between conventional semisolid herbal preparations and more sophisticated responsive biomaterial-based delivery platforms (Baskar et al., 2018).

Baradaran et al. (2021) provided a detailed assessment of phytosomes as innovative delivery systems for phytochemicals and reported that the formation of phytochemical–phospholipid complexes can substantially influence the absorption and biological performance of plant compounds. Phospholipids provide an amphiphilic environment that can improve the interaction of poorly absorbed phytochemicals with biological membranes. The authors noted that curcumin and silymarin have been among the most extensively investigated phytosomal compounds, reflecting the strong interest in improving the delivery of poorly bioavailable polyphenolic and flavonoid constituents. The review also demonstrated that phytosomes have progressed beyond theoretical formulation concepts, with both commercial and experimental preparations being investigated for diverse pathological conditions (Baradaran et al., 2021). A similar perspective was presented by Ragab et al. (2021), who examined phytosomes as an emerging platform for topical delivery of bioactive phytochemicals. Their analysis identified poor penetration through biological barriers, particularly the skin, as a major obstacle to the effective topical use of many phytochemicals. Phytosomes can modify the physicochemical characteristics of plant compounds and facilitate their interaction with lipid-rich biological barriers. This characteristic is relevant to topical formulations intended for antioxidant, anti-inflammatory and wound-related applications. The literature therefore suggests that the potential of phytosomes extends beyond oral bioavailability enhancement and includes localised delivery where improved tissue penetration is required (Ragab et al., 2021).

Siddiqui et al. (2021) emphasised the importance of stimuli-responsive delivery systems in improving the performance of bioactive plant compounds. Stimuli-responsive carriers are capable of modifying their structure, permeability or release characteristics following exposure to particular environmental conditions. Relevant stimuli include pH, temperature, enzymes, oxidative conditions and external irradiation. Such mechanisms are particularly attractive for phytochemicals because they can potentially protect unstable compounds during transport while promoting release under specific physiological or pathological conditions. The development of multi-stimuli-responsive systems further expands this concept by integrating two or more triggers into a single carrier, potentially increasing the precision of bioactive delivery (Shishir et al., 2021).

Chatterjee and Hui (2021) reviewed stimuli-responsive hydrogels based on thermoresponsive biopolymers and demonstrated the increasing role of naturally derived biomaterials in intelligent drug delivery. Materials such as chitosan, cellulose derivatives, xyloglucan, gelatin and related biopolymers can undergo temperature-dependent transitions that alter their physical state and influence drug release. Their biodegradability, biocompatibility and comparatively favourable safety profiles make such materials attractive for pharmaceutical applications. For herbal therapeutics, these biomaterials can provide a matrix within which phytochemicals are protected and subsequently released under controlled conditions. The combination of herbal bioactives with responsive biopolymers therefore provides an opportunity to integrate the biological activity of plant compounds with the functional characteristics of modern biomaterials (Chatterjee & Hui, 2021).

Samadian et al. (2021) investigated stimuli-responsive drug delivery systems based on natural gums and highlighted their potential as biodegradable and biocompatible materials. Natural gums possess properties that can be modified through chemical or physical functionalisation to generate responsiveness to environmental conditions. Their low cost, availability and biodegradability are particularly relevant to the development of sustainable pharmaceutical delivery systems. However, limitations such as inadequate mechanical strength and excessive hydration can restrict their direct application. Modification through grafting or incorporation of responsive polymers can therefore improve their functionality. These findings are relevant to herbal delivery because plant-derived gums and polysaccharides may function simultaneously as pharmaceutical excipients and structural components of smart delivery

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platforms (Samadian et al., 2021). Zhou et al. (2021) demonstrated the broader potential of stimuli-responsive nanomaterials through their review of metal–organic framework nanoparticles. These systems can be engineered to release their payload following chemical, physical or biological triggers, including pH changes, reducing conditions, ions, heat, light and disease-associated biomarkers. Although metal–organic frameworks are not exclusively herbal delivery systems, the underlying design principles are applicable to phytochemical delivery. Their porous structures provide opportunities for high loading, while responsive surface modifications can regulate release. Such approaches illustrate the movement of drug delivery research from passive carriers towards systems capable of responding dynamically to the biological environment (Zhou et al., 2021).

Wang et al. (2021) examined the multifaceted role of plant-derived polyphenols within nanodrug delivery systems and demonstrated that phytochemicals can function not only as therapeutic payloads but also as functional components of nanocarriers. Polyphenols possess chemical groups capable of interacting with proteins, metal ions, polymers and nucleic acids, allowing their incorporation into multifunctional delivery architectures. This approach represents an important conceptual development because the phytochemical may contribute both pharmacological activity and carrier functionality. Polyphenols can also provide antioxidant protection and influence the physicochemical properties of polymeric systems, suggesting opportunities for developing delivery platforms in which the carrier and active compound are more closely integrated (Wang et al., 2021).

Lu et al. (2022) highlighted the continuing development of nanomedicine-mediated delivery for herbal and plant-derived medicines. The literature indicates that herbal medicines present unique formulation difficulties because they frequently contain complex mixtures rather than single active pharmaceutical ingredients. Nanocarriers can address several of these difficulties by improving gastrointestinal stability, protecting constituents from enzymatic degradation and facilitating membrane transport. Lipid nanoparticles, polymeric nanoparticles, nanoemulsions and vesicular systems have therefore been explored for different classes of phytochemicals. The authors also stressed the importance of evaluating nanophytomedicines using appropriate physicochemical, pharmacological and toxicological parameters, since improvements in particle size or encapsulation efficiency alone do not necessarily establish clinical effectiveness (Lu et al., 2022).

Chauhan et al. (2024) reviewed recent advances in nanotechnology for phytochemical delivery and reported that phytosomes have become particularly prominent because of their capacity to improve the stability and bioavailability of herbal compounds. Their review emphasised the amphiphilic characteristics of phospholipids, which facilitate interactions with both hydrophilic and lipophilic components and can improve the delivery of poorly absorbed phytochemicals. The authors also identified the continuing expansion of phytosome research towards diverse therapeutic areas and highlighted the importance of optimising formulation parameters and demonstrating consistent pharmacokinetic benefits. This progression illustrates how phytosome technology is increasingly being incorporated into the broader field of phytochemical nanomedicine rather than being considered solely as a specialised herbal formulation approach (Chauhan et al., 2024).

Chowdhury et al. (2024) further described nanotechnology-based herbal drug delivery as an emerging field in which carrier design is increasingly linked with the physicochemical properties of specific phytoconstituents. The review highlighted nanoparticles and related systems as potential tools for improving bioavailability, controlled release and therapeutic targeting. At the same time, the authors identified formulation complexity, standardisation and translation as important considerations. This is particularly significant for herbal products because variations in extraction procedures and botanical composition can affect drug loading and release characteristics. Consequently, the successful development of smart herbal systems requires integration of pharmacognosy, pharmaceutics, nanotechnology and analytical standardisation rather than isolated optimisation of the carrier system (Chowdhury et al., 2024).

Koppula et al. (2024) identified phytosomes as an increasingly important nanotechnology platform for phytopharmaceutical development and highlighted their potential to improve solubility, absorption, stability and therapeutic effectiveness. The review considered applications involving inflammatory, neurological, metabolic, cardiovascular and infectious disorders and indicated that phytosomal systems can be adapted to several routes of administration. At the same time, the authors identified stability, large-scale manufacturing, regulatory requirements and clinical translation as continuing barriers. These observations are important because promising laboratory results do not automatically translate into commercially reproducible products. Greater emphasis on pharmacokinetic validation, quality control, manufacturing scale-up and well-designed clinical investigations is therefore necessary for broader pharmaceutical adoption (Koppula et al., 2024).

Raghav et al. (2024) further reviewed phytosomes and ethosomes as advanced vesicular approaches for delivering plant-derived phytochemicals. Their analysis reinforced the capacity of phospholipid association to improve the absorption and stability of phytoconstituents that otherwise demonstrate limited therapeutic availability. The authors also discussed preparation methods, characterisation parameters and applications across different therapeutic areas. Importantly, the continuing development of vesicular systems demonstrates that carrier selection must be matched to the physicochemical characteristics of the phytochemical, intended route of administration and desired release profile. This supports a broader movement towards rational formulation design rather than the use of a single universal delivery platform for all herbal compounds (Raghav et al., 2024).

Maddi et al. (2024) emphasised that the current direction of phytosome research is moving towards more clinically relevant and technologically integrated phytopharmaceutical systems. Their review identified improved bioavailability and therapeutic efficacy as major advantages while also drawing attention to manufacturing, stability and regulatory challenges. This is particularly relevant to the concept of smart herbal drug delivery because future systems are likely to combine several functions, such as phospholipid complexation, nanoscale transport, controlled release and physiological responsiveness. Such multifunctional platforms could potentially overcome several barriers simultaneously rather than addressing solubility, stability or targeting as isolated formulation problems (Koppula et al., 2024).

Analysis Table: Review of Smart Herbal Drug Delivery Systems

Author(s) and year	**Delivery system/approach**	**Herbal bioactive or application**	**Major findings**	**Key limitation/gap**
Jain et al. (2016)	Nanotechnology-based delivery	Various phytochemicals	Nanocarriers can improve solubility, stability, absorption and bioavailability	Standardisation and translation require further investigation
Gnananath et al. (2017)	Phytosomes	Plant-derived phytoconstituents	Phospholipid complexation can improve membrane interaction and bioavailability	Formulation optimisation and stability remain important
Afrin et al. (2018)	Novel herbal delivery systems	Herbal extracts and phytochemicals	Phytosomes, nanoparticles and vesicular systems can overcome limitations of conventional formulations	Variability in herbal materials affects formulation reproducibility
Marella and Tollamadugu (2018)	Herbal nanotechnology	Plant-based therapeutics	Nanoformulations can improve solubility, permeability and pharmacokinetic performance	Safety, reproducibility and scale-up require attention
Pati et al. (2018)	Nanoparticles and nanostructures	Herbal bioactives	Nanoscale systems may provide sustained and controlled delivery	Phytochemical standardisation remains a major challenge
Baskar et al. (2018)	Nanogels	Herbal constituents	Nanogels offer controlled release and improved topical/transdermal delivery	Mechanical and formulation stability can limit applications

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Baradaran et al. (2021)	Phytosomes	Curcumin, silymarin and other phytochemicals	Phospholipid complexes can enhance absorption and biological performance	More clinical and regulatory evidence is needed
Ragab et al. (2021)	Phytosomes	Topical phytochemicals	Improved interaction with biological barriers can enhance topical delivery	Limited clinical translation of many formulations
Chatterjee and Hui (2021)	Stimuli-responsive hydrogels	Bioactive compounds	Thermoresponsive biopolymers provide opportunities for controlled release	Material properties require optimisation for pharmaceutical use
Samadian et al. (2021)	Responsive natural gums	Bioactive compounds	Natural gums offer biodegradable and biocompatible platforms for smart delivery	Weak mechanical properties and hydration can restrict use
Siddiqui et al. (2021)	Stimuli-responsive systems	Phytochemicals and bioactives	pH-, temperature-, enzyme- and redox-responsive systems can regulate release	Complex formulation and manufacturing requirements
Zhou et al. (2021)	Stimuli-responsive nanomaterials	Nanomedicine applications	Responsive nanomaterials permit environmentally triggered drug release	Further evaluation of safety and clinical applicability is required
Wang et al. (2021)	Polyphenol-functionalised nanocarriers	Plant polyphenols	Polyphenols may act as both therapeutic agents and functional components of nanocarriers	Carrier–phytochemical interactions require detailed characterisation
Lu et al.	Nanomedicine	Herbal medicines	Nanocarriers can	Complex herbal

(2022)			improve gastrointestinal stability, absorption and controlled delivery	composition complicates standardisation
Chauhan et al. (2024)	Phytosomes and nanotechnology	Phytochemicals	Phytosomes demonstrate potential for enhancing stability and bioavailability	Optimisation and pharmacokinetic validation remain necessary
Chowdhury et al. (2024)	Nanotechnology-based herbal delivery	Herbal bioactives	Carrier characteristics can be tailored to phytochemical properties	Manufacturing, standardisation and regulatory translation remain challenges
Koppula et al. (2024)	Advanced phytosomes	Multiple phytochemicals	Increasing evidence supports improved solubility, absorption and therapeutic performance	Scale-up, stability, regulation and clinical validation remain unresolved
Raghav et al. (2024)	Phytosomes and ethosomes	Plant-derived phytochemicals	Vesicular systems can improve delivery and stability through phospholipid association	Optimal carrier selection depends on bioactive and administration route

METHODOLOGY

This review-based research adopted a systematic narrative approach to examine advances in smart herbal drug delivery systems, with particular emphasis on phytosomes, nanomedicine, stimuli-responsive biomaterials and novel pharmaceutical excipients. Relevant scientific literature published between 2015 and 2024 was considered to maintain contemporary coverage of technological developments. Literature was identified through searches of Google Scholar and relevant peer-reviewed scientific databases using combinations of keywords including “smart herbal drug delivery”, “phytosomes”, “herbal nanomedicine”, “phytochemical nanoparticles”, “stimuli-responsive drug delivery”, “responsive biomaterials", and "novel pharmaceutical excipients". Studies were selected according to their relevance to herbal bioactive delivery, formulation strategies, bioavailability enhancement, controlled release, targeting, stability and therapeutic applications. Peer-reviewed research articles and authoritative review papers were prioritised, while publications lacking sufficient scientific relevance or focusing exclusively on non-herbal synthetic drug delivery were excluded. The retrieved literature was critically analysed according to delivery mechanism, carrier characteristics, therapeutic application, formulation advantages and limitations. Comparative interpretation was subsequently undertaken to identify technological developments, recurring challenges and research gaps. The review also considered issues related to formulation optimisation, standardisation, safety, scalability and clinical translation to provide an integrated assessment of the potential of smart delivery technologies for advancing herbal therapeutics.

FINDINGS

1. Advances in Phytosomes and Nanomedicine for Herbal Bioactive Delivery

The reviewed literature demonstrates that the principal contribution of smart delivery technologies is their ability to address the physicochemical and pharmacokinetic limitations that frequently restrict the therapeutic application of herbal bioactives. Phytochemicals such as curcumin, quercetin, silybin, resveratrol, catechins and other polyphenols commonly exhibit poor aqueous solubility, inadequate intestinal absorption and susceptibility to chemical or enzymatic degradation. Consequently, conventional administration may result in low systemic exposure despite substantial pharmacological activity. Recent evidence indicates that nanocarrier systems can improve the apparent solubility, stability, permeability and bioavailability of these compounds by modifying their interaction with biological environments (Jain et al., 2016; Lu et al., 2022).

Phytosomes represent one of the most distinctive approaches within herbal nanomedicine because they rely on the formation of a phytochemical–phospholipid complex rather than simple physical entrapment. The phospholipid component, commonly phosphatidylcholine, provides amphiphilic characteristics that facilitate interaction with biological membranes. This structural feature can improve the absorption of poorly bioavailable phytochemicals and protect them from adverse gastrointestinal conditions. Recent literature reports improvements in bioavailability, stability and therapeutic performance for several phytosomal formulations, supporting their continued development as herbal delivery systems (Baradaran et al., 2021; Chauhan et al., 2024).

The evidence also suggests that the performance of phytosomes depends strongly on the nature of the phytochemical and formulation parameters. Particle size, polydispersity, surface charge, phospholipid-to-phytochemical ratio, preparation technique, encapsulation efficiency and release behaviour can substantially influence biological performance. A 2024 meta-analysis involving 93 studies reported significant differences in physicochemical characteristics according to phytochemical class, with flavonoid-, terpenoid-, alkaloid- and polyphenol-based phytosomes exhibiting different particle and performance characteristics.

This finding is important because it indicates that phytosomal formulation cannot be treated as a universal technology; carrier composition must be rationally matched to the chemical characteristics of the active constituent (Nurbaiti et al., 2024).

Table 2. Stimuli-responsive biomaterials and novel pharmaceutical excipients in herbal drug delivery

Material/system	**Stimulus or functional property**	**Role in herbal drug delivery**	**Potential advantage**	**Major formulation challenge**
pH-responsive polymers	Changes in environmental pH	Regulates release according to gastrointestinal or tissue pH	Potential site-specific release	Precise control of transition and release behaviour
Thermoresponsive polymers	Temperature variation	Controls gel formation and phytochemical release	Useful for localised and injectable delivery	Appropriate transition temperature must be maintained
Enzyme-responsive biomaterials	Specific enzymes	Enables biologically triggered release	Greater biological specificity	Requires an appropriate enzyme-rich target environment
Redox-responsive polymers	Oxidative/reducing conditions	Promotes release under specific intracellular or pathological conditions	Potential intracellular targeting	Chemical stability and reproducibility
Chitosan-based systems	Mucoadhesion and permeability enhancement	Improves retention and transport across mucosal barriers	Biocompatibility and mucoadhesion	Molecular-weight and formulation-dependent performance
Natural gums	Hydration and matrix formation	Provides controlled-release matrices for herbal compounds	Biodegradable and relatively accessible materials	Batch-to-batch variability
Phospholipids	Amphiphilic and membrane-compatible	Forms phytosomes and lipid-based	Improves membrane interaction and	Lipid-to-phytochemical ratio

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	properties	carriers	bioavailability	requires optimisation
Surfactants	Solubilisation and interfacial stabilisation	Supports nanoemulsions and self-emulsifying systems	Improves dispersion of poorly soluble phytochemicals	Concentration-dependent toxicity and instability
Hydrogels	Three-dimensional hydrated network	Provides controlled and prolonged phytochemical release	Suitable for topical and local applications	Swelling, mechanical strength and release control
Functional polymers	Controlled degradation or responsiveness	Protects and regulates release of phytoconstituents	Enables customised delivery profiles	Manufacturing and regulatory complexity

The wider herbal nanomedicine literature supports this interpretation. Nanocarriers including polymeric nanoparticles, solid lipid nanoparticles, nanoemulsions, nanomicelles, liposomes, phytosomes, ethosomes and nanofibres have been investigated according to the solubility and permeability characteristics of individual herbal extracts and phytoconstituents. Importantly, appropriate characterisation requires evaluation of particle size, surface area, zeta potential, polydispersity, drug loading, encapsulation efficiency and release characteristics rather than relying solely on the nominal nanoscale dimensions of a formulation (Lu et al., 2022). Recent reviews similarly emphasise that novel carriers can improve solubility, permeability, elimination half-life, pharmacokinetics and therapeutic efficacy, although clinical translation remains incomplete (Koppula et al., 2024).

The therapeutic implications are particularly relevant in diseases where prolonged exposure or improved intracellular delivery is required. Phytosome-based systems have been investigated for inflammatory, metabolic, neurological, hepatic and oncological applications. In cancer research, phytosome-based delivery of compounds such as curcumin, quercetin, silibinin and luteolin has been associated with improved cellular uptake and enhanced anticancer activity in experimental models. Nevertheless, these findings should be interpreted cautiously because increased in vitro activity does not necessarily establish improved clinical efficacy. Large-scale manufacturing, long-term stability, reproducibility and clinical validation remain important translational barriers (Sadr et al., 2024).

2. Stimuli-Responsive Biomaterials and Novel Pharmaceutical Excipients

The development of stimuli-responsive biomaterials represents a further progression from passive delivery towards intelligent drug-release systems. Conventional nanocarriers generally release their payload according to diffusion, degradation or carrier erosion, whereas stimuli-responsive systems are designed to respond to specific physicochemical or biological signals. Common triggers include pH, temperature, enzymes and redox conditions. Such systems can potentially provide spatial and temporal control over phytochemical release, which is particularly useful when a bioactive compound requires protection during circulation or gastrointestinal transit but should be released at a specific biological location (Dheer et al., 2024).

pH-responsive systems are particularly relevant to oral herbal delivery because the gastrointestinal tract exhibits substantial variation in pH. A carrier can theoretically remain relatively stable in the stomach and undergo structural changes in the intestinal environment, thereby modifying the release profile of the encapsulated phytochemical. Enzyme-responsive systems provide another level of biological specificity because certain enzymes are expressed at higher concentrations in particular tissues or pathological environments. Redox-responsive materials similarly exploit differences in oxidative and reducing conditions between extracellular and intracellular environments. These mechanisms provide opportunities for protecting sensitive phytochemicals while reducing premature release.

Temperature-responsive biomaterials represent another important category. Thermoresponsive polymers and hydrogels can undergo reversible physicochemical transitions in response to temperature changes, allowing formulation scientists to regulate drug release. Natural polymers and biopolymers are particularly attractive because of their biodegradability and compatibility with biological systems. However, the incorporation of natural materials introduces challenges relating to batch-to-batch variation, mechanical strength, swelling behaviour and reproducibility. Therefore, the pharmaceutical usefulness of a biomaterial depends not only on its responsiveness but also on its physicochemical consistency and ability to maintain an appropriate release profile.

Novel pharmaceutical excipients play a central role in these developments because the carrier itself frequently determines the solubility, stability, permeability and release behaviour of a herbal formulation. Phospholipids, polymers, surfactants, natural gums and hydrogel-forming materials can function as more than inert formulation components. Their molecular interactions with phytochemicals can influence drug loading, protection against degradation, membrane transport and release kinetics. This has encouraged a shift towards functional excipients specifically selected according to the physicochemical characteristics of the herbal bioactive.

Table 3. Critical evaluation of smart herbal drug delivery systems

Evaluation parameter	**Conventional herbal formulation**	**Phytosomes**	**Nanomedicine-based systems**	**Stimuli-responsive systems**
Solubility enhancement	Limited to moderate	High for suitable poorly soluble phytochemicals	Generally high, depending on carrier	Potentially high through carrier

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				engineering
Bioavailability improvement	Often limited	Frequently demonstrated	Frequently demonstrated in preclinical studies	Potentially high but system-dependent
Protection from degradation	Limited	Moderate to high	High	High
Controlled release	Generally poor	Moderate	High	Very high
Site-specific delivery	Limited	Limited to moderate	Moderate to high	Potentially high
Formulation complexity	Low	Moderate	Moderate to high	High
Manufacturing requirements	Relatively simple	Manageable with optimisation	More demanding	Highly demanding
Standardisation requirements	High	Very high	Very high	Very high
Scalability	Relatively straightforward	Generally feasible but requires process optimisation	Can be challenging	More challenging
Clinical translation	Established for some herbal products	Promising but still developing	Predominantly preclinical for many systems	Early-stage for many applications
Principal research gap	Poor pharmacokinetic performance	Long-term stability and clinical validation	Safety, scale-up and reproducibility	Complexity, safety and regulatory validation

A major advantage of responsive biomaterials is that they can potentially integrate several delivery functions within a single platform. For example, a phytochemical may first be protected through encapsulation, subsequently transported through a biological barrier and finally released following exposure to a disease-associated stimulus. Such multifunctionality is consistent with the broader transition towards smart drug delivery systems, where carrier design is based on the biological environment rather than solely on the physical protection of the active compound.

At the same time, greater complexity can introduce new pharmaceutical risks. Each additional component may influence toxicity, stability, manufacturing reproducibility and regulatory assessment. Herbal formulations already present standardisation challenges because botanical composition may vary according to species, geographical origin,

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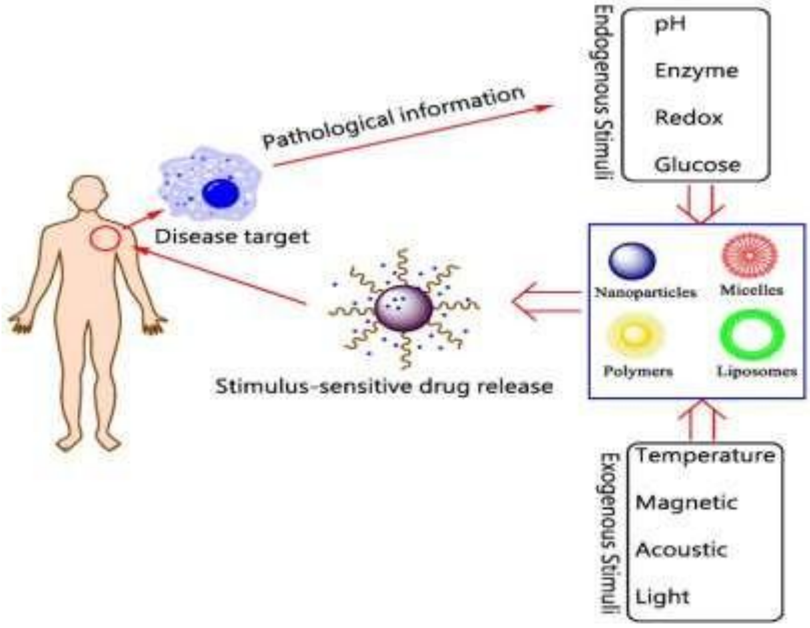
cultivation conditions, harvesting and extraction methods. Introducing a sophisticated nanocarrier therefore requires simultaneous control of both the botanical starting material and the delivery system. This reinforces the need for rigorous analytical characterisation and quality-by-design principles during formulation development.

3. Therapeutic Potential, Translational Challenges and Future Direction

The combined evidence indicates that smart delivery technologies can substantially modify the therapeutic behaviour of herbal bioactives. Improved solubility and permeability may increase systemic exposure, while protection against chemical and enzymatic degradation can preserve bioactive compounds during administration. Controlled-release and responsive systems additionally offer opportunities to reduce fluctuations in drug concentration and maintain therapeutic exposure over longer periods. These characteristics are particularly valuable for phytochemicals whose conventional pharmacokinetic profiles are characterised by rapid absorption followed by extensive metabolism and elimination.

The recent development of phytosome technology illustrates this transition particularly clearly. A comprehensive 2024 review reported that phytosomes can address several limitations of herbal products, including poor solubility, absorption and stability, while supporting oral, topical and intranasal administration. The same review identified applications across inflammatory diseases, neurological disorders, cancers, metabolic syndrome and liver disorders, demonstrating the broad therapeutic scope of the platform.



One of the most important findings from the reviewed literature is therefore that improved physicochemical performance does not automatically establish clinical superiority. Many smart herbal delivery systems demonstrate encouraging results in cell culture and animal models, but considerably fewer have progressed through robust clinical evaluation. Recent literature specifically identifies scale-up, formulation stability and clinical validation as persistent barriers to phytosome-based nanomedicine (Sadr et al., 2024).

Another important consideration is the relationship between formulation complexity and therapeutic benefit. A highly sophisticated carrier may provide responsive release and targeting but can also increase production costs, analytical requirements and regulatory complexity. Conversely, relatively simple phospholipid complexes may provide substantial bioavailability enhancement without requiring an excessively complicated manufacturing process. The optimal approach should therefore be selected according to the properties of the phytochemical, intended route of administration, therapeutic objective and required release behaviour rather than according to technological novelty alone.

Recent research also indicates that future herbal nanomedicine is moving towards personalised and mechanism-oriented delivery. Instead of developing a generic carrier for a broad herbal extract, formulation scientists are increasingly considering the specific solubility, permeability, metabolism and target-site requirements of individual phytochemicals or standardised fractions. This approach could improve reproducibility and facilitate more rational selection of pharmaceutical excipients. The 2024 literature on novel carriers further demonstrates that contemporary research is increasingly concerned with clinical trial status, analytical methods, loading capacity, encapsulation efficiency and in vivo validation rather than merely demonstrating successful nanoparticle preparation (Koppula et al., 2024).

The integration of phytosomes, nanomedicine, responsive biomaterials and novel excipients consequently represent a multidimensional approach to herbal drug delivery. Phytosomes offer an established strategy for improving membrane compatibility and bioavailability; nanoparticles provide opportunities for controlled and targeted transport; responsive biomaterials introduce environmental sensitivity; and functional excipients provide the physicochemical foundation required for formulation stability and performance. The most promising future systems are therefore likely to combine complementary functions while maintaining an acceptable balance between therapeutic benefit, formulation simplicity, safety, scalability and regulatory feasibility. This integrated approach may be particularly important for translating the extensive pharmacological potential of herbal bioactives into reproducible pharmaceutical products.

CONCLUSION

Smart herbal drug delivery systems represent an important advancement in the pharmaceutical development of plant-derived therapeutics. The reviewed evidence demonstrates that phytosomes, nanomedicine-based carriers, stimuli-responsive biomaterials and novel pharmaceutical excipients can address major limitations of conventional herbal formulations, particularly poor solubility, instability, inadequate permeability and low bioavailability. Phytosomes have emerged as a particularly promising approach because phospholipid complexation can improve membrane interaction and enhance the absorption of several phytochemicals. Nanomedicine further provides opportunities for controlled, sustained and potentially targeted delivery, while stimuli-responsive biomaterials introduce greater control over the timing and location of phytochemical release. Functional excipients increasingly contribute to solubilisation, protection, stability and carrier performance rather than acting merely as inactive formulation components. However, substantial challenges remain concerning botanical standardisation, formulation reproducibility, long-term safety, manufacturing scale-up, regulatory acceptance and clinical validation. Future research should therefore prioritise rational carrier design, quality-by-design approaches, pharmacokinetic evaluation and well-designed clinical studies. Integrating advanced delivery technologies with standardised herbal bioactives may ultimately facilitate the development of more predictable, effective and clinically translatable phytopharmaceutical products.

REFERENCES

1. Afrin, S., Jahan, I., Hasan, A. H. M. N., & Deepa, K. N. (2018). Novel approaches of herbal drug delivery. Journal of Pharmaceutical Research International, 21(5), 1–11. https://doi.org/10.9734/JPRI/2018/39143
2. Alexander, A., Ajazuddin, Patel, R. J., Saraf, S., & Saraf, S. (2016). Recent expansion of pharmaceutical nanotechnologies and targeting strategies in the field of phytopharmaceuticals for the delivery of herbal extracts and bioactives. Journal of Controlled Release, 241, 110–124. https://doi.org/10.1016/j.jconrel.2016.09.017
3. Barani, M., Sangiovanni, E., Angarano, M., Rajizadeh, M. A., Mehrabani, M., Piazza, S., Gangadharappa, H. V., Pardakhty, A., Mehrbani, M., Dell'Agli, M., & Nematollahi, M. H. (2021). Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of literature. International Journal of Nanomedicine, 16, 6983–7022. https://doi.org/10.2147/IJN.S318416
4. Chatterjee, S., & Hui, P. C.-L. (2021). Review of applications and future prospects of stimuli-responsive hydrogel based on thermo-responsive biopolymers in drug delivery systems. Polymers, 13(13), 2086. https://doi.org/10.3390/polym13132086
5. Chauhan, N. S., et al. (2024). Recent advances in phytosome-based delivery systems for phytochemicals.
6. Chen, Z., Farag, M. A., Zhong, Z., Zhang, C., Yang, Y., Wang, S., & Wang, Y. (2021). Multifaceted role of phyto-derived polyphenols in nanodrug delivery systems. Advanced Drug Delivery Reviews, 176, 113870. https://doi.org/10.1016/j.addr.2021.113870
7. Chowdhury, H., et al. (2024). Nanotechnology-based approaches for herbal drug delivery: Recent advances and challenges.
8. Gnananath, K., Nataraj, K. S., & Rao, B. G. (2017). Phospholipid complex technique for superior bioavailability of phytoconstituents. Advanced Pharmaceutical Bulletin, 7(1), 35–42. https://doi.org/10.15171/apb.2017.005
9. Koppula, S., et al. (2024). Phytosomes as advanced nanocarriers for herbal bioactive delivery.
10. Lu, M., Qiu, Q., Luo, X., Liu, X., Sun, J., Wang, C., Lin, X., Deng, Y., & Song, Y. (2019). Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents. Asian Journal of Pharmaceutical Sciences, 14(3), 265–274. https://doi.org/10.1016/j.ajps.2018.05.011

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ISSN (Print): 2321-7510 | ISSN (Online): 2321-7529

| An ISO 9001:2015 Certified Journal |

11. Marella, S., & Tollamadugu, N. V. K. V. P. (2018). Nanotechnological approaches for the development of herbal drugs in treatment of diabetes mellitus: A critical review. IET Nanobiotechnology, 12(5), 549–556. https://doi.org/10.1049/iet-nbt.2017.0242
12. Nurbaiti, N., et al. (2024). Phytosome formulations: A systematic/meta-analytical evaluation of physicochemical and delivery characteristics.
13. Pati, R. Y., Patil, S. A., Chivate, N. D., & Patil, Y. N. (2018). Herbal drug nanoparticles: Advancements in herbal treatment. Research Journal of Pharmacy and Technology, 11(1), 421–426. https://doi.org/10.5958/0974-360X.2018.00078.1
14. Ragab, D. M., et al. (2021). Phytosomes as innovative delivery systems for phytochemicals and their topical applications.
15. Raghav, R., et al. (2024). Phytosomes and ethosomes as advanced vesicular systems for phytochemical delivery.
16. Sadr, S., et al. (2024). Phytosome-based delivery systems in cancer therapy: Current perspectives and future prospects.
17. Samadian, H., et al. (2021). Stimuli-responsive natural polymer-based systems for controlled drug delivery.
18. Siddiqui, S. A., et al. (2021). Stimuli-responsive drug delivery systems: Recent advances and future perspectives.
19. Wang, H., Wang, C., Zou, Y., Hu, J., Li, Y., & Cheng, Y. (2020). Natural polyphenols in drug delivery systems: Current status and future challenges. Giant, 3, 100022.
20. Zheng, Y., Wang, Y., Xia, M., Gao, Y., Zhang, L., Song, Y., & Zhang, C. (2021). The combination of nanotechnology and traditional Chinese medicine (TCM) inspires the modernization of TCM: Review on nanotechnology in TCM-based drug delivery systems. Drug Delivery and Translational Research, 12, 1–20. https://doi.org/10.1007/s13346-021-01029-x
21. Zhou, H., et al. (2021). Metal–organic framework nanoparticles for drug delivery and biomedical applications. Chemical Society Reviews.