Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 2594-2605 | ISSN:2251-6727

Phytosomes: An Advanced Phytochemical Delivery Platform for Enhanced Bioavailability and Therapeutic Performance

Ravikiran Kanabargi1, Archana S. Patil[1*], Prajwal Patil[1], Yadishma A. Gaude[1]

[1]Department of Pharmaceutics, KLE College of Pharmacy, Belagavi, KLE Academy of Higher Education and Research, Belagavi-591124, Karnataka, India.

(Received: 05 December 2025 Revised: 15 January 2026 Accepted: 10 February 2026)

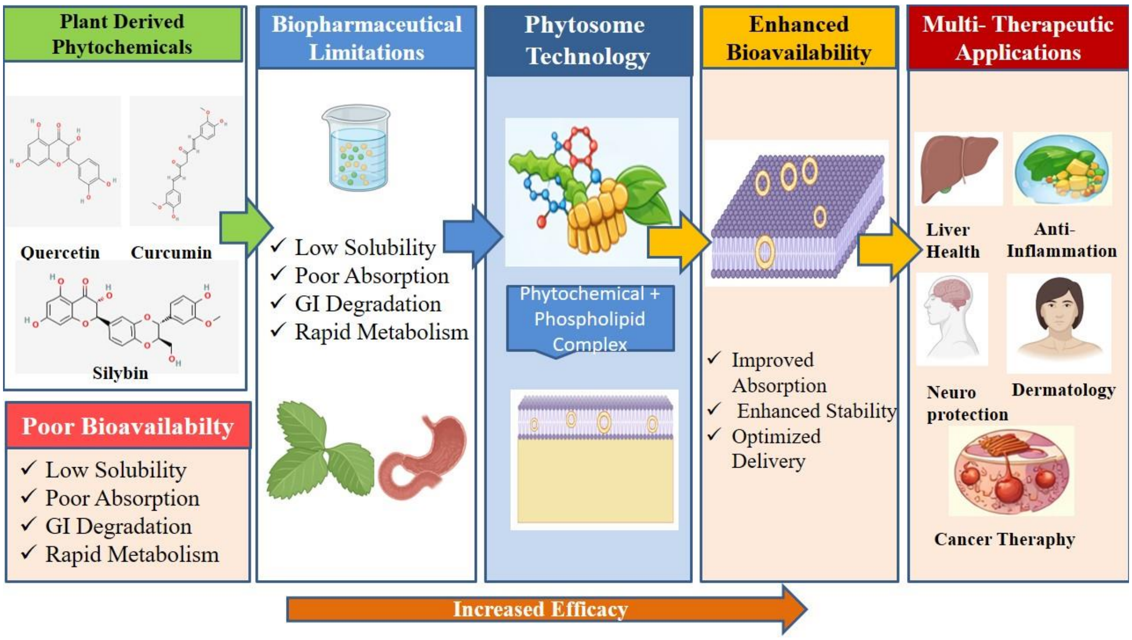
KEYWORDS

Phytosomes;
Phytochemicals;
Phospholipid complexes;
Bioavailability;
Herbal drug delivery;
Nanocarriers;
Pharmacokinetics.

ABSTRACT:

Phytosomes are next-generation lipid-compatible delivery systems designed to enhance the pharmacokinetic and pharmacodynamic performance of plant-derived phytochemicals. Although plant-derived compounds such as polyphenols, flavonoids, and terpenoids exhibit profound therapeutic potential, their clinical translation is often hampered by poor aqueous solubility, limited membrane permeability, gastrointestinal instability, and rapid metabolic degradation. Phytosomal technology circumvents these limitations by forming molecular complexes between phytoconstituents and phospholipids primarily phosphatidylcholine thereby enhancing solubility, membrane integration, systemic absorption, and therapeutic efficacy. This review delineates the structural and functional evolution of phytosomes, detailing their formulation strategies, physicochemical characterization, and mechanistic superiority over conventional herbal extracts and liposomal carriers. Applications span diverse therapeutic domains including pharmaceuticals, nutraceuticals, dermatology, oncology, and metabolic disorders. Consolidated preclinical and clinical data underscore their translational promise. The review also addresses regulatory frameworks, formulation challenges, and strategic directions for scalable implementation.

Graphical abstract



Introduction

Phytochemicals have garnered substantial global attention for their multifaceted therapeutic potential, encompassing antioxidant, anti-inflammatory, hepatoprotective, neuroprotective, antidiabetic, cardioprotective, anticancer, and immunomodulatory activities[1]. Despite their pharmacological promise, the clinical translation of many phytoconstituents is impeded by suboptimal biopharmaceutical properties namely poor aqueous solubility, limited membrane permeability, instability under physiological conditions, rapid metabolic degradation, and diminished systemic bioavailability[2]. These constraints undermine dose-response predictability, attenuate therapeutic efficacy, and hinder the integration of herbal actives into evidence-based pharmacotherapeutics [3].

To overcome these limitations, advanced drug-delivery modalities such as nanoparticles, micelles, solid lipid carriers, nanoemulsions, and liposomes have been investigated[3]. Among these, phytosomes, phospholipid-compatible molecular complexes have emerged as a superior delivery paradigm for enhancing the bioavailability and stability of plant-derived actives[4]. Originally developed by Indena in the early 1990s, phytosomes (also termed phyto-phospholipid complexes) involve the stoichiometric conjugation of phytoconstituents with phosphatidylcholine[5], yielding lipid-soluble complexes with enhanced membrane affinity and systemic absorption. Unlike liposomes, which encapsulate compounds within vesicular structures, phytosomes establish true molecular interactions via hydrogen bonding and polar affinity, conferring enhanced physicochemical stability and improved pharmacokinetic behaviour[6].

This review provides a critical appraisal of phytosome technology, elucidating its developmental trajectory, structural and mechanistic attributes, formulation methodologies, and physicochemical characterization. Emphasis is placed on its translational relevance across diverse therapeutic domains, supported by consolidated preclinical and clinical evidence[7].

Phytochemicals and Their Therapeutic Importance

Phytochemicals such as flavonoids (e.g., quercetin, rutin, kaempferol), terpenoids, phenolic acids, lignans, alkaloids, glycosides, and tannins are bioactive secondary metabolites that confer the sensory attributes and therapeutic efficacy of medicinal plants. Their pharmacological repertoire includes antioxidant defense, enzymatic modulation, cytokine regulation, apoptotic induction, metabolic homeostasis, and cytoprotection. However, despite compelling in vitro efficacy[8], many phytoconstituents exhibit suboptimal pharmacokinetics in vivo due to poor aqueous solubility, limited membrane permeability, instability under physiological conditions, and rapid metabolic clearance exemplified by curcumin's <1% oral bioavailability[4], quercetin's extensive glucuronidation, silymarin's hydrophobicity, and catechins' pH sensitivity. Phytosome technology mitigates these limitations by transforming hydrophilic phytochemicals into lipid-compatible molecular complexes, thereby enhancing membrane integration, solubility, hepatocellular uptake, and metabolic resilience[9].

Structural Biology and Composition of Phytosomes

Phytosomes are advanced molecular assemblies wherein bioactive phytoconstituents form stable complexes with phospholipids primarily phosphatidylcholine via hydrogen bonding and polar interactions[10]. This structural integration distinguishes phytosomes from conventional liposomal systems, as the phytochemicals are not merely encapsulated but embedded within the phospholipid bilayer[11]. The amphiphilic nature of these complexes enhances membrane fluidity, facilitates transcellular permeability, and promotes efficient partitioning into biological membranes, thereby improving systemic uptake and pharmacological performance[12].

The bilayer architecture of phytosomes mimics cellular membranes, offering protective encapsulation against oxidative, hydrolytic, and photolytic degradation while enabling enhanced gastrointestinal absorption. The vesicular size, typically ranging from 50 to 200 nm, provides an optimal surface area for interaction with epithelial barriers, contributing to superior bioavailability and extended circulation time[13]. This structural versatility allows for the incorporation of diverse phytochemicals—both hydrophilic and lipophilic—making phytosomes applicable across therapeutic domains such as anti-inflammatory, antioxidant, and anticancer interventions[14].

Comparatively, guggulosomes share a similar phospholipid-based framework but differ in the spatial orientation of the active constituents. In phytosomes, the phytochemical is molecularly integrated within the bilayer, whereas in guggulosomes, it may reside within the aqueous core or the lipid membrane, depending on its physicochemical properties. Both systems leverage the lipophilic exterior of the phospholipid bilayer to traverse biological barriers and enhance bio efficacy[15].

Key Components of Phytosomes

- **Phytoconstituents:** Plant-derived actives, particularly polyphenols, often exhibit poor solubility and limited membrane permeability. Phytosome formation enhances aqueous solubility for lipophilic compounds and improves membrane transport for hydrophilic molecules, while also shielding them from metabolic degradation[3].
- **Phospholipids:** Predominantly phosphatidylcholine (PC), valued for its amphipathic character, biocompatibility, and membrane affinity. Other phospholipids like phosphatidylserine (PS) and phosphatidylethanolamine (PE) are employed in specialized formulations to tailor pharmacokinetic profiles[16].
- **Solvents:** Protic solvents such as ethanol, methanol, and hydroalcoholic mixtures are preferred for complex synthesis due to their efficiency and eco-compatibility. Emerging green technologies, including supercritical CO_2, are gaining traction for sustainable production[17].

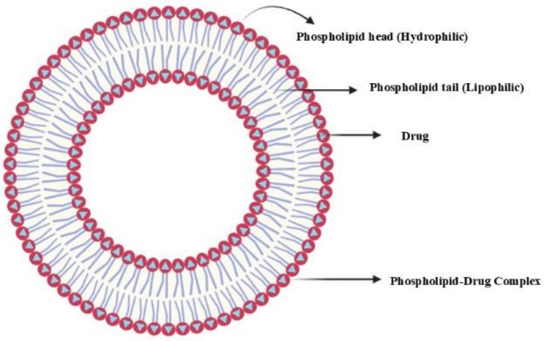


Figure 1: Structure of Phytosomes

Selection Criteria for Phytosomal Drug Candidates

The successful integration of herbal extracts or active pharmaceutical ingredients (APIs) into phytosomal delivery systems necessitates adherence to specific physicochemical and biopharmaceutical parameters that govern complexation efficiency and therapeutic performance:

Lipophilicity: A pronounced lipophilic character is essential for effective interaction with phospholipid molecules, particularly phosphatidylcholine, which forms the structural matrix of phytosomes. Hydrophilic compounds exhibit limited affinity for lipid bilayers, thereby compromising encapsulation efficiency and systemic delivery[18].

Molecular Size and Conformation: The molecular weight and steric configuration of the candidate compound must be conducive to integration within the phospholipid bilayer. Excessively bulky or structurally complex molecules may encounter steric hindrance, impeding stable complex formation. Ideal molecular weights typically fall within a moderate range to ensure compatibility and uniform dispersion[19].

Biopharmaceutical Limitations: APIs characterized by poor aqueous solubility, low membrane permeability, or rapid metabolic turnover are prime candidates for phytosomal encapsulation. The platform is specifically designed to overcome these limitations by enhancing dissolution kinetics, transmembrane transport, and metabolic resilience[20].

Stability Profile: The compound must exhibit chemical and physical stability throughout the formulation process and subsequent storage. Resistance to oxidative degradation, hydrolysis, and photolytic breakdown is critical to maintaining therapeutic integrity and shelf-life viability[21]**.**

Purity and Consistency: High-purity extracts or APIs are imperative to ensure reproducible complexation and formulation performance. Impurities can disrupt molecular interactions, destabilize the phytosomal structure, and attenuate pharmacological efficacy[22].

Particle Size and Surface Characteristics: Phytosomes typically exhibit particle sizes ranging from 100 to 700 nm, with optimal formulations falling between 231.0 and 701.4 nm. This nanoscale dimension enhances surface

area for membrane interaction, facilitating efficient cellular uptake. Zeta potential values within ±20–35 mV indicate colloidal stability, while entrapment efficiencies exceeding 70–90% particularly for flavonoids reflect robust encapsulation and delivery potential[23].

Advantages of Phytosomes

Phytosomes offer a unique set of benefits that make them superior for delivering plant-derived bio actives:

- Enhanced Bioavailability: Phytosomes form molecular complexes with phospholipids, improving solubility, membrane permeability, and systemic absorption especially for poorly soluble phytochemicals[24].
- Improved Stability: The chemical bonding between phytoconstituents and phospholipids provides higher thermodynamic and chemical stability compared to physical entrapment systems[25].
- Targeted Delivery: Their lipid-compatible nature allows better interaction with biological membranes, facilitating targeted cellular uptake and reduced off-target effects[25].
- Protection from Degradation: Phytosomes shield sensitive phytochemicals from hydrolysis, oxidation, and enzymatic degradation during gastrointestinal transit[26].
- Biocompatibility and Safety: Use of natural phospholipids like phosphatidylcholine ensures compatibility with cell membranes and minimizes toxicity[19].
- Versatility: Suitable for a wide range of phytochemicals both hydrophilic and lipophilic and applicable across oral, topical, asnd transdermal routes[27].

Comparison with Other Delivery Systems

Feature	Phytosomes	Liposomes	Nanoparticles	Micelles	Nanoemulsions
Drug Incorporation	Chemically bound to phospholipids	Physically entrapped	Adsorbed or encapsulated	Solubilized in core	Dispersed in oil/water phase
Stability	High thermodynamic stability	Prone to leakage and fusion	Moderate to high	Moderate	Moderate
Bioavailability	Significantly enhanced	Variable	Improved but depends on surface design	Enhanced for hydrophobic drugs	Enhanced for lipophilic compounds
Membrane Permeability	Excellent due to lipid compatibility	Moderate	Depends on surface modification	Good for small molecules	Good for lipophilic molecules
Size Range	100–700 nm	50–1000 nm	10–1000 nm	10–100 nm	20–500 nm
Manufacturing Complexity	Moderate	High	High	Moderate	Moderate
Cost Efficiency	Relatively cost-effective	Expensive	Expensive	Moderate	Moderate

Methods for Phytosome Preparation

Phytosomes are sophisticated molecular complexes formed through the strategic conjugation of standardized plant extracts with phospholipids—primarily phosphatidylcholine (PC), phosphatidylethanolamine (PE), or phosphatidylserine (PS)—via polar interactions and hydrogen bonding. The preparation techniques are designed to optimize complexation efficiency, physicochemical stability, and therapeutic performance. Key methodologies include:

1. Solvent Evaporation Technique

This conventional method involves dissolving both the phytoconstituent and phospholipid in a compatible organic solvent system (e.g., methylene chloride, ethyl acetate, dioxane). The mixture is subjected to mechanical agitation and gradual solvent evaporation under controlled temperature (typically 40–60 °C), facilitating molecular complex formation. Stoichiometric ratios ranging from 1:1 to 3:1 (drug: phospholipid) are optimized to enhance encapsulation efficiency and bioavailability[24].

2. Lyophilization (Freeze-Drying) Process

In this technique, natural or synthetic phospholipids and phytoconstituents are dissolved separately in suitable solvents and then combined under continuous stirring to form a stable complex. The mixture is subsequently subjected to lyophilization, which removes solvent under low temperature and vacuum, yielding a dry, amorphous phytosomal powder. This method preserves thermolabile compounds and enhances shelf-life stability. Fatty acids such as stearic, oleic, palmitic, and linoleic acids contribute to the phospholipid backbone, offering structural diversity[27].

3. Gas Anti-Solvent (GAS) Technique

This advanced method utilizes supercritical fluids (e.g., CO_2) as antisolvents to precipitate the phytosome complex. Drug and phospholipid solutions are introduced into a high-pressure reaction vessel, where supercritical CO_2 induces rapid precipitation by reducing solubility. Conditions are maintained at ~10 mPa and 38 °C for several hours to ensure uniform particle formation. GAS offers precise control over particle size and morphology, making it suitable for scale-up and industrial applications[19].

4. Anti-Solvent Precipitation

This method involves dissolving the active compound and phospholipid in a primary solvent (e.g., dichloromethane), followed by the addition of an anti-solvent (e.g., n-hexane) to induce precipitation. The resulting complex is isolated via vacuum drying to remove residual solvents. Variants such as anhydrous co-solvent lyophilization have been employed to produce amorphous phytosomal complexes, as demonstrated in rutin-PC systems. Optimal drug-to-phospholipid ratios (e.g., 1:3) are critical for maximizing therapeutic efficacy and dissolution properties[28].

5. Rotary Evaporation Technique

In this method, plant extracts and phospholipids are co-dissolved in tetrahydrofuran within a rotating round-bottom flask. The mixture is stirred at sub-ambient temperatures (<40 °C) to form a thin film. Subsequent addition of n-hexane facilitates precipitation, and the final product is collected and stabilized under ambient conditions. This technique is valued for its simplicity and reproducibility in laboratory-scale formulations[25].

Characterization Techniques for Phytosomes

Comprehensive characterization of phytosomes is essential to evaluate their physicochemical integrity, structural morphology, encapsulation efficiency, and biological performance. These analytical techniques provide critical insights into formulation stability, drug–phospholipid interactions, and therapeutic potential.

Parameter	Analytical Technique	Purpose / Insights
Morphological Analysis refers to the examination of the shape, surface structure, and physical appearance of phytosomes. It helps determine whether the vesicles are spherical, irregular, aggregated, or uniformly dispersed. Techniques such as	Transmission Electron Microscopy (TEM) Scanning Electron Microscopy (SEM)	Visualizes surface topology, vesicle shape, and lamellar structure

Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM) are commonly used[19].		
Particle Size and Zeta Potential Particle size is the measurement of the average diameter of phytosomal vesicles, typically expressed in nanometers (nm). It is commonly determined using Dynamic Light Scattering (DLS). Zeta potential is the measurement of the surface charge of phytosomal particles, expressed in millivolts (mV)[27].	Dynamic Light Scattering (DLS) Photon Correlation Spectroscopy (PCS)	Determines hydrodynamic diameter, polydispersity index, and colloidal stability
Entrapment Efficiency (%) represents the percentage of drug or phytoconstituent successfully incorporated within the phytosome complex relative to the total amount used during formulation[24].	Ultracentrifugation UV-Vis Spectrophotometry	Quantifies the percentage of phytoconstituent successfully complexed
Thermal Behaviour refers to the study of heat-induced physical and chemical changes in phytosomes. It is commonly analyzed using Differential Scanning Calorimetry (DSC)[24].	Differential Scanning Calorimetry (DSC) Thermogravimetric Analysis (TGA)	Assesses phase transition temperature, thermal stability, and crystallinity
Surface Properties include evaluation of surface morphology, roughness, texture, and charge characteristics of phytosomes. These properties influence interaction with biological membranes[28].	Contact Angle Measurement Surface Tension via Tensiometry	Evaluates wettability and interfacial behaviour relevant to absorption
Spectroscopic Evaluation involves the use of techniques such as Fourier Transform Infrared Spectroscopy (FTIR) to study molecular interactions, hydrogen bonding, and functional group changes between the phytoconstituent and phospholipid[25].	Fourier Transform Infrared Spectroscopy (FTIR) Proton & Carbon NMR (^{1}H-NMR, ^{13}C-NMR) UV-Vis Spectroscopy Mass Spectrometry (MS)	Confirms molecular interactions, complex formation, and structural elucidation
Crystallinity & Phase Analysis This analysis determines whether the drug remains crystalline or converts into an amorphous form after complexation. Techniques such as X-Ray Diffraction (XRD) and sometimes DSC are used[24].	X-ray Diffraction (XRD)	Differentiates amorphous vs crystalline states of the complex
In-vitro Evaluation In-vitro evaluation refers to laboratory testing performed outside a living organism to assess: • Drug release profile (dissolution studies) • Stability • Permeation studies • Antioxidant or cytotoxic activity (if applicable)[24]	Dissolution Testing Permeation Studies (e.g., Franz Diffusion Cell)	Measures release kinetics and membrane transport efficiency

In-vivo Evaluation In-vivo evaluation involves testing the phytosomal formulation in animal models or clinical subjects to assess: • Pharmacokinetics (absorption, distribution, metabolism, elimination) • Bioavailability • Therapeutic efficacy • Safety and toxicity[24]	Pharmacokinetic Profiling Anti-hepatotoxicity Assays Skin Sensitization Studies	Assesses systemic absorption, therapeutic efficacy, and biocompatibility

Applications of phytosomes

Pharmaceutical Drug Delivery and Oral Bioavailability Enhancement

Phytosomes have redefined the paradigm of oral drug delivery by addressing the pharmacokinetic limitations of plant-derived bioactives. Through the formation of lipid-compatible molecular complexes, phytosomes significantly enhance solubility, gastrointestinal permeability, and lymphatic transport. This results in markedly improved systemic bioavailability, as demonstrated by formulations like Meriva® (curcumin-phosphatidylcholine) and Siliphos® (silybin-phosphatidylcholine), which exhibit multi-fold increases in plasma exposure compared to their unformulated counterparts. The phospholipid matrix also facilitates sustained and controlled release, optimizing therapeutic windows and minimizing dosing frequency[29].

Hepatoprotective Therapy and Liver Disease Management

In hepatology, phytosomes have emerged as a gold standard for delivering hepatoprotective agents with enhanced efficacy. Silymarin-based phytosomes, particularly silybin-phosphatidylcholine complexes, exhibit superior hepatocellular uptake and membrane integration, leading to improved outcomes in conditions such as liver cirrhosis, non-alcoholic fatty liver disease (NAFLD), and drug-induced hepatotoxicity. These formulations enhance bile secretion, attenuate hepatic inflammation, and bolster antioxidant defenses, as validated by multiple clinical investigations. Their targeted delivery to hepatic tissues underscores their therapeutic precision in liver-centric interventions[30,31].

Cardiometabolic and Endocrine Disorder Modulation

Phytosomes have demonstrated considerable promise in the management of cardiometabolic syndromes, including dyslipidemia, hypertension, and type 2 diabetes mellitus. By enhancing the intestinal absorption and systemic retention of bioactives such as berberine, ginseng saponins, and green tea catechins, phytosomes potentiate metabolic regulation via mechanisms like AMPK activation, oxidative stress attenuation, and endothelial function restoration. These effects translate into improved lipid profiles, glycemic control, and vascular health, positioning phytosomes as a strategic adjunct in integrative metabolic therapy[32,33].

Neurotherapeutics and Cognitive Enhancement

The delivery of neuroprotective phytochemicals across the blood–brain barrier (BBB) remains a formidable challenge in neuropharmacology. Phytosomes offer a viable solution by increasing lipophilicity and facilitating transcellular transport. Formulations such as Ginkgo biloba, Bacopa monnieri, and green tea catechin phytosomes have demonstrated enhanced central nervous system bioavailability, leading to improved cognitive performance, memory retention, and neuroprotection in models of neurodegeneration. These systems extend plasma half-life and promote lymphatic circulation, making them ideal for long-term neurological applications[34,25].

Dermatological and Cosmeceutical Applications

In the realm of dermal therapeutics and cosmetic science, phytosomes have gained traction for their ability to enhance the cutaneous delivery of botanical actives. The amphiphilic nature of phospholipids facilitates deeper

epidermal penetration, improving the efficacy of agents targeting skin aging, pigmentation, inflammation, and barrier repair. Phytosomal formulations of Centella asiatica, grape seed proanthocyanidins, and arbutin have shown superior outcomes in collagen synthesis, UV protection, and melanogenesis inhibition. Their biocompatibility and natural origin align with the growing demand for clean, effective skincare technologies[35,36].

Oncology and Adjunctive Cancer Therapeutics

Phytosomes have emerged as a promising nanocarrier system in oncology, offering a strategic advantage in the delivery of plant-derived anticancer agents that typically suffer from poor solubility, rapid systemic clearance, and limited tumor targeting. By forming stable lipid-compatible complexes, phytosomes enhance the bioavailability, cellular uptake, and intracellular retention of phytochemicals such as curcumin, quercetin, and epigallocatechin gallate (EGCG). These formulations facilitate deeper penetration into tumor tissues, promote mitochondrial accumulation, and potentiate reactive oxygen species (ROS)-mediated apoptosis. Preclinical studies have demonstrated that phytosomal curcumin exhibits superior chemopreventive and cytotoxic effects in various cancer models, while EGCG and quercetin phytosomes have shown enhanced efficacy in prostate and breast cancer lines, respectively. The ability of phytosomes to modulate oncogenic signaling pathways while minimizing systemic toxicity positions them as a compelling adjunct or alternative to conventional chemotherapeutics[37].

Wound Healing and Tissue Regeneration

In regenerative medicine, phytosomes offer a novel approach to accelerating wound healing and tissue repair by enabling targeted delivery of bioactive phytoconstituents directly to the site of injury. Their nanoscale size and lipid compatibility facilitate deep dermal penetration and sustained release of therapeutic agents, enhancing their interaction with cellular targets. Phytosomes encapsulating flavonoids and triterpenoids—such as those derived from *Centella asiatica* and curcumin—have demonstrated significant efficacy in promoting fibroblast proliferation, stimulating collagen synthesis, reducing oxidative stress, and modulating inflammatory cascades. These mechanisms collectively contribute to faster re-epithelialization, improved angiogenesis, and reduced scar formation. The enhanced therapeutic index and biocompatibility of phytosomal formulations make them a promising platform for the development of next-generation wound care products[34].

Previous studies

To substantiate the pharmacological advantages of phytosomal drug delivery systems, a series of preclinical investigations have been conducted across diverse therapeutic domains. These studies encompass both in vitro and in vivo models, demonstrating the enhanced bioavailability, cellular uptake, and therapeutic efficacy of phytoconstituents when complexed with phospholipids. The following table presents a curated selection of peer-reviewed studies that exemplify the translational potential of phytosomes. Each entry includes the phytochemical involved, experimental models used, therapeutic indication, and key outcomes, thereby offering a comprehensive overview of the mechanistic and functional validation of phytosomal technology[38].

Table: Consolidated Preclinical Studies on Phytosomal Formulations

Source Extract	In Vitro Model	In Vivo Model	Significance / Key Outcomes	Reference
Curcuma longa	Caco-2 cell permeability assay	—	8-fold increase in intestinal permeability vs. free curcumin[39]	[39]
Rubia cordifolia	SH-SY5Y neuroblastoma cells	Neuropathic pain rat model	Improved cellular uptake; reduced oxidative stress; significant pain attenuation in vivo[3].	[3]

Vitis vinifera	Skin permeation assay	UV-induced dermal damage in rats	Enhanced skin penetration; reduced oxidative stress and collagen degradation in UV-exposed skin[40.]	[40]
Pongamia pinnata	—	Streptozotocin-induced diabetic rats	Improved glycemic control; reduced blood glucose and oxidative stress markers[32.]	[32]
Hydroalcoholic leaf extract	Antibacterial zone of inhibition	—	Effective against *E. coli*, *S. aureus*, and *P. aeruginosa*; enhanced antibacterial activity vs. crude extract[41.]	[41]

Table: Published Patents on Phytosomal Formulations

Title	**Source Extract**	**Year**	**Application Domain**	**Key Innovation / Claim**	**Patent Reference**
Rutin and Phyllanthin	*Polyherbal formulation*	2024	Pharmaceutical / Nutraceutical	Enhanced solubility and absorption of herbal actives via phytosome encapsulation	[42]
Nanoscale phytosome system	—	—	Drug delivery / Nanotechnology	Method for producing nanoscale phytosomes with improved dispersion and stability	[43]

Future Perspectives

The evolution of phytosome technology is anticipated to be shaped by multidisciplinary innovations spanning lipid chemistry, green processing, and personalized therapeutics. One promising direction involves the incorporation of synthetic and semi-synthetic phospholipids to enhance the physicochemical stability and shelf-life of phytosomal formulations. Parallel to this, the adoption of environmentally sustainable manufacturing techniques such as supercritical fluid extraction and solvent-free protocols will support the development of eco-friendly delivery systems[47]. The integration of phytosomes into personalized and precision herbal medicine is another frontier, where formulations can be tailored to individual genetic, metabolic, and disease profiles[48]. Moreover, the emergence of hybrid nanocarriers combining phytosomes with polymeric nanoparticles, micelles, cubosomes, and hydrogels offers the potential for multi-targeted therapeutic interventions. Artificial intelligence is also poised to play a transformative role in formulation science, enabling predictive modelling of phytochemical–lipid interactions and accelerating the rational design of optimized delivery platforms[49].

Conclusion

Phytosomes represent a paradigm shift in the delivery of poorly soluble phytochemicals, offering a robust platform for enhancing bioavailability, membrane permeability, and therapeutic efficacy. Their validated performance across pharmaceutical, nutraceutical, and cosmeceutical domains has led to widespread application in the management of inflammation, metabolic disorders, hepatoprotection, oncology, neurodegeneration, and dermatological conditions. Supported by a growing body of preclinical and clinical evidence, phytosomes have demonstrated superior pharmacokinetic profiles and improved patient outcomes. As research continues to advance in areas such as green manufacturing, regulatory harmonization, and precision medicine, phytosomes are expected to become foundational to next-generation botanical therapeutics, bridging the gap between traditional herbal remedies and modern drug delivery science.

References

1. Andreicut AD, Pârvu AE, Mot AC, Pârvu M, Fischer Fodor E, Cătoi AF, Feldrihan V, Cecan M, Irimie A. Phytochemical analysis of anti-inflammatory and antioxidant effects of Mahonia aquifolium flower and fruit extracts . Oxidative Medicine and Cellular Longevity. 2018;2018(1):2879793.
2. Aqil F, Munagala R, Jeyabalan J, Vadhanam MV. Bioavailability of phytochemicals and its enhancement by drug delivery systems. Cancer letters. 2013 Jun 28;334(1):133-41.
3. Barani M, Sangiovanni E, Angarano M, Rajizadeh MA, Mehrabani M, Piazza S, Gangadharappa HV, Pardakhty A, Mehrbani M, Dell'Agli M, Nematollahi MH. Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of literature. International journal of nanomedicine. 2021 Oct 15:6983-7022.
4. Lu M, Qiu Q, Luo X, Liu X, Sun J, Wang C, Lin X, Deng Y, Song Y. Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents. Asian journal of pharmaceutical sciences. 2019 May 1;14(3):265-74
5. https://www.indena.com/indena_files/2020/01/wp_phytosome_int.pdf
6. Karimi N, Ghanbarzadeh B, Hamishehkar H, KEYVANI F, Pezeshki A, Gholian MM. Phytosome and liposome: the beneficial encapsulation systems in drug delivery and food application.
7. Reddy S, Sharma A. characterization, properties and formulation of Phytosomes. International Journal of Multidisciplinary Trends. 2022;4(2):229-34.
8. Hossain MS, Wazed MA, Asha S, Amin MR, Shimul IM. Dietary phytochemicals in health and disease: Mechanisms, clinical evidence, and applications—a comprehensive review. Food Science & Nutrition. 2025 Mar;13(3):e70101.
9. Talebi M, Shahbazi K, Dakkali MS, Akbari M, Ghale RA, Hashemi S, Sashourpour M, Mojab F, Aminzadeh S. Phytosomes: A promising nanocarrier system for enhanced bioavailability and therapeutic efficacy of herbal products. Phytomedicine Plus. 2025 May 1;5(2):100779.
10. https://thisvsthat.io/liposomes-vs-phytosomes
11. Babazadeh A, Jafari SM, Shi B. Encapsulation of food ingredients by nanophytosomes. InLipid-based nanostructures for food encapsulation purposes 2019 Jan 1 (pp. 405-443). Academic Press.
12. Dutt Y, Pandey RP, Dutt M, Gupta A, Vibhuti A, Raj VS, Chang CM, Priyadarshini A. Liposomes and phytosomes: Nanocarrier systems and their applications for the delivery of phytoconstituents. Coordination Chemistry Reviews. 2023 Sep 15;491:215251.
13. Patil SR, Chhajed SS. Phytosomes, A versatile Phyto-Phospholipid Nanocarriers: A Review. Biosciences Biotechnology Research Asia. 2025 Dec 1;22(4):1337.
14. Karimi N, Ghanbarzadeh B, Hamishehkar H, KEYVANI F, Pezeshki A, Gholian MM. Phytosome and liposome: the beneficial encapsulation systems in drug delivery and food application.
15. Jafari SM. Lipid-Based Nanostructures for Food Encapsulation Purposes: Volume 2 in the Nanoencapsulation in the Food Industry series. Academic Press; 2019 Aug 3.
16. Likhitwitayawuid K. Oxyresveratrol: Sources, productions, biological activities, pharmacokinetics, and delivery systems. Molecules. 2021 Jul 11;26(14):4212.
17. Kumar A, P N, Kumar M, Jose A, Tomer V, Oz E, Proestos C, Zeng M, Elobeid T, K S, Oz F. Major phytochemicals: recent advances in health benefits and extraction method. Molecules. 2023 Jan 16;28(2):887.
18. Krishnaswami V, Regunathan S, Natarajan B, Arthanari S, Natesan S. Phytosomes, an Emerging Platform for Herbal Based Drug Delivery.
19. Dave P, Jani R, Chakraborthy GS, Jani KJ, Upadhye V, Kahrizi D, Mir MA, Siddiqui S, Saeed M, Upadhyay TK. Phytosomes: A promising delivery system for anticancer agents by using phytochemicals in cancer therapy. Cellular and Molecular Biology. 2023 Dec 20;69(14):1-8.
20. Gaikwad SS, Morade YY, Kothule AM, Kshirsagar SJ, Laddha UD, Salunkhe KS. Overview of phytosomes in treating cancer: Advancement, challenges, and future outlook. Heliyon. 2023 Jun 1;9(6).
21. Human C, Aucamp M, de Beer D, van Der Rijst M, Joubert E. Food-grade phytosome vesicles for nanoencapsulation of labile C-glucosylated xanthones and dihydrochalcones present in a plant

extract matrix—Effect of process conditions and stability assessment. Food Science & Nutrition. 2023 Dec;11(12):8093-111.

22. Prabu SL, Suriyaprakash TN. Impurities and its importance in pharmacy. Int. J. Pharm. Sci. Rev. Res. 2010 Jul;3(2):66-71.
23. Varsha M, Devika R. Formulation and Evaluation of Phytosome, A Novel Biomedicine. Int. J. Pharm. Sci. Rev. Res. 2023;79(1):06.
24. Shriram RG, Moin A, Alotaibi HF, Khafagy ES, Al Saqr A, Abu Lila AS, Charyulu RN. Phytosomes as a plausible nano-delivery system for enhanced oral bioavailability and improved hepatoprotective activity of silymarin. Pharmaceuticals. 2022 Jun 24;15(7):790.
25. Kalaivani P, Kamaraj R. Phytosome technology: a novel breakthrough for the health challenges. Cureus. 2024 Aug 30;16(8).
26. Koppula S, Shaik B, Maddi S. Phytosomes as a new frontier and emerging nanotechnology platform for phytopharmaceuticals. *Phytother Res.* 2025;39(5):2217-2249.
27. Chauhan D, Yadav PK, Sultana N, Agarwal A, Verma S, Chourasia MK, Gayen JR. Advancements in nanotechnology for the delivery of phytochemicals. Journal of Integrative Medicine. 2024 Jul 1;22(4):385-98.
28. Yadav AK, Kamal R, Agarwal V, Sharma PK. Phytosomes: advancing herbal medicine through innovative integration. Current Pharmaceutical Design. 2025 Apr 16.
29. Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. Foods. 2017 Oct;6(10):92.
30. Loguercio C, Federico A, Trappoliere M, Tuccillo C, Sio ID, Leva AD, Niosi M, D'Auria MV, Capasso R, Blanco CD, Real Sud Group. The effect of a silybin-vitamin e-phospholipid complex on nonalcoholic fatty liver disease: a pilot study. Digestive diseases and sciences. 2007 Sep;52(9):2387-95.
31. Koppula S, Shaik B, Maddi S. Phytosomes as a new frontier and emerging nanotechnology platform for phytopharmaceuticals: therapeutic and clinical applications. Phytotherapy Research. 2025 May;39(5):2217-49.
32. Belcaro G, Ledda A, Hu S, Cesarone MR, Feragalli B, Dugall M. Greenselect phytosome for borderline metabolic syndrome. Evidence-Based Complementary and Alternative Medicine. 2013;2013(1):869061.
33. Toma L, Deleanu M, Sanda GM, Barbălată T, Niculescu LŞ, Sima AV, Stancu CS. Bioactive compounds formulated in phytosomes administered as complementary therapy for metabolic disorders. International journal of molecular sciences. 2024 Apr 9;25(8):4162.
34. Sbrini G, Brivio P, Fumagalli M, Giavarini F, Caruso D, Racagni G, Dell'Agli M, Sangiovanni E, Calabrese F. Centella asiatica L. Phytosome improves cognitive performance by promoting bdnf expression in rat prefrontal cortex. Nutrients. 2020 Jan 29;12(2):355.
35. Alharbi WS, Almughem FA, Almehmady AM, Jarallah SJ, Alsharif WK, Alzahrani NM, Alshehri AA. Phytosomes as an emerging nanotechnology platform for the topical delivery of bioactive phytochemicals. Pharmaceutics. 2021 Sep 15;13(9):1475.
36. Susilawati Y, Chaerunisa AY, Purwaningsih H. Phytosome drug delivery system for natural cosmeceutical compounds: Whitening agent and skin antioxidant agent. Journal of advanced pharmaceutical technology & research. 2021 Oct 1;12(4):327-34.
37. Sadr S, Hajjafari A, Lotfalizadeh N, Lotfalizadeh M, Laein SS, Abbasi AM, Jafroodi PP, Moghadam ER, Rahdar A, Fathi-karkan S, Sohbatzadeh Z. Phytosome-based nanotechnology for enhanced efficacy of anticancer phytocompounds: Challenges and prospects. Journal of Drug Delivery Science and Technology. 2025 Feb 1;104:106543.
38. Talebi M, Shahbazi K, Dakkali MS, Akbari M, Ghale RA, Hashemi S, Sashourpour M, Mojab F, Aminzadeh S. Phytosomes: A promising nanocarrier system for enhanced bioavailability and therapeutic efficacy of herbal products. Phytomedicine Plus. 2025 May 1;5(2):100779.
39. Jamwal R. Bioavailable curcumin formulations: A review of pharmacokinetic studies in healthy volunteers. Journal of integrative medicine. 2018 Nov 1;16(6):367-74.

40. Zaboronok A, Khaptakhanova P, Uspenskii S, Bekarevich R, Mechetina L, Volkova O, Mathis BJ, Kanygin V, Ishikawa E, Kasatova A, Kasatov D. Polymer-stabilized elemental boron nanoparticles for boron neutron capture therapy: Initial irradiation experiments. Pharmaceutics. 2022 Mar 31;14(4):761.
41. Jain S, Rathod N, Nagi R, Sur J, Laheji A, Gupta N, Agrawal P, Prasad S. Antibacterial effect of Aloe vera gel against oral pathogens: An in-vitro study. Journal of clinical and diagnostic research: JCDR. 2016 Nov 1;10(11):ZC41.
42. Vakilsearch Patent 202421005424
43. RU2680809C2 – Google Patents
44. SAKURE K, PATEL A, PRADHAN M, Badwaik HR. Recent trends and future prospects of phytosomes: A concise review. Indian journal of pharmaceutical sciences. 2024 May 1;86(3).
45. Krishnaswami V, Regunathan S, Natarajan B, Arthanari S, Natesan S. Phytosomes, an Emerging Platform for Herbal Based Drug Delivery.
46. Riva A, Petrangolini G, Allegrini P, Perna S, Giacosa A, Peroni G, Faliva MA, Naso M, Rondanelli M. Artichoke and bergamot phytosome alliance: A randomized double blind clinical trial in mild hypercholesterolemia. Nutrients. 2021 Dec 27;14(1):108.
47. Chemat F, Vian MA, Cravotto G. Green extraction of natural products: Concept and principles. International journal of molecular sciences. 2012 Jul 11;13(7):8615-27.
48. Li Shao LS, Zhang Bo ZB. Traditional Chinese medicine network pharmacology: theory, methodology and application.
49. Zhavoronkov A. Artificial intelligence for drug discovery, biomarker development, and generation of novel chemistry. Molecular Pharmaceutics. 2018 Oct 1;15(10):4311-3.