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# Phytosomes - An Advanced Herbal Drug Delivery System

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**ABSTRACT:**

Herbal drugs have high polarity and poor lipophilicity; the active contents are poorly absorbed resulting in poor bioavailability. To overcome this problem “Phytosomes” are used. The term ‘phyto’ means plant while ‘some’ means cell-like.Phytosomes are advanced forms of herbal product that are better absorbed, utilized and produce better results than conventional herbal extracts. Based upon absorption only, dosage level of phytosomes is close to dosage recommended for corresponding standardized herbal extracts. Phytosomes contain hydrophilic bioactive phytoconstituents of herbs surround and exhibit better pharmacokinetic and pharmacodyanamic profile than conventional herbal extracts and thus, prevents destruction by digestive secretions and gut bacteria. This process has been applied to herbal extracts like turmeric(*Haridra*), grape seed(*Draksha)*, Green tea etc. This system is mainly used to deliver systemic antioxidant(flavanoid and terpenoid component) and used to treat disease like blood pressure, liver disease, cancer, skin disease and to protect brain lining. This review describes newer technique of drug delivery.

**KEYWORDS:**

Phytosomes, Bioavailability, Phospholipids, Phytoconstituents.

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## INTRODUCTION:

Preparation of herbal medicines has been used for health maintenance since ancient times. It also poses a lot of therapeutic uses. Most of biologically active phytoconstituents such as flavonoids and terpenoids are of highly polar nature or water soluble molecules. These molecules are poorly absorbed due to their poor lipid solubility, thus creating a hurdle to cross the highly lipid rich biological membrane, which finally results in poor bioavailability. Many approaches have been developed for improving bioavailability such as solubility and bioavailability enhancers, structural modification and entrapment with lipophilic carriers. One such approach is phytosome technology.

A) Definition and Historical Context

Phytosomes are advanced herbal drug delivery systems that improve the absorption and bioavailability of plant-based bioactive compounds (phytoconstituents). Derived from "phyto" (plant) and "some" (cell-like structure), they enhance the effectiveness of traditional herbal remedies used for cancer, liver issues, inflammation, and heart diseases, offering a modern solution to age-old therapies.

Despite their potential, phytomedicinals often face poor solubility and absorption due to complex structures, limiting their effectiveness. Phytosome technology, developed by Indena in 1989, addresses these issues by converting water-soluble plant extracts into lipid-compatible complexes, greatly improving bioavailability. This innovation bridges traditional herbal use with modern medicine, overcoming key physicochemical barriers.

B). Fundamental Structure and Composition

Phytosomes, also known as herbosomes, are nano-sized complexes (1–100 nm) formed by chemically binding plant extracts with phospholipids, mainly phosphatidylcholine (PC). This structure features a hydrophilic head (binding water-soluble phytoconstituents) and a hydrophobic tail, creating a lipid-compatible complex that enhances solubility and absorption. Unlike simple encapsulation, the active compound is chemically integrated, allowing better interaction with biological membranes and improved bioavailability.

C). Distinguishing Phytosomes from Liposomes While both phytosomes and liposomes are phospholipid-based nanocarriers employed for drug delivery, their fundamental structural organization and mechanism of interaction with active compounds are distinctly different, leading to significant disparities in their performance.

Phytosomes differ from liposomes by forming chemical bonds between the active compound and phospholipids, making them part of the membrane, unlike liposomes where the compound is just encapsulated. This chemical integration gives phytosomes greater stability, bioavailability, and absorption—with studies showing up to 20x better absorption than traditional extracts. Their structure protects actives from degradation, ensuring more effective and consistent therapeutic results.

## MATERIAL AND METHODS

- Mechanisms of Enhanced Bioavailability and Therapeutic Efficacy

The superior performance of phytosomes arises from a synergistic mechanism that boosts the bioavailability, absorption, and therapeutic effectiveness of plant compounds through chemical bonding, structural stability, and enhanced membrane integration.

- Preparation Methods of Phytosomes

The formulation of phytosomes requires precise preparation by reacting stoichiometric amounts of phospholipids (mainly phosphatidylcholine) with plant extracts in a suitable solvent system, ensuring

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the formation of stable, lipid-compatible molecular complexes

A) Common Techniques

Several conventional methods are widely employed for phytosome preparation are

a. Solvent Evaporation Method

b. Anti-solvent Precipitation Method (Salting Out)

c. Mechanical Dispersion Method

B). Advanced and Novel Methods

Beyond conventional approaches, advanced methods, particularly those utilizing Supercritical fluids method (SCF) have emerged to address some of the limitations of traditional techniques.This innovative method leverages the unique properties of supercritical fluids, typically carbon dioxide (CO2), as solvents or anti-solvents.

**RESULT**

➢ Therapeutic Applications of Phytosomes

Phytosomes have demonstrated remarkable versatility in enhancing the therapeutic efficacy and safety profiles of a wide array of herbal extracts across diverse disease areas.

A). Applications in Cancer Therapy

Phytosomes enhance the bioavailability and anticancer activity of plant-derived compounds like flavonoids, terpenoids, and alkaloids, enabling better targeting of cancer pathways (e.g., NF-κB, PI3K/AKT) with reduced toxicity. Examples like curcumin and silibinin phytosomes show improved tumor suppression and safety, making phytosomes a promising tool for safer, more effective natural cancer therapies.

B). Applications in Liver Disorders

Phytosomes improve liver targeting by enhancing solubility in bile and uptake by hepatic cells. Silymarin phytosomes show up to 6× higher bioavailability and superior hepatoprotective effects in liver damage models. The use of phosphatidylcholine adds a synergistic benefit, as it also protects the liver, enabling dual-action therapy with reduced drug load and better patient outcomes.

C) Applications in Inflammatory Diseases

Phytosomes enhance the delivery and efficacy of anti-inflammatory phytoconstituents like curcumin and Boswellia serrata, which modulate pathways such as NF-κB and COX-2. They offer improved absorption, broader anti-inflammatory effects, and better outcomes in conditions like arthritis, potentially reducing the need for conventional drugs and their side effects.

D). Applications in Neurological Disorders

Phytosomes enhance brain delivery of neuroactive phytoconstituents, aiding in the treatment of neurological disorders. For example, Ginkgo biloba phytosomes show memory-enhancing, antidepressant, and CNS stimulant effects in animal models. Their ability to cross the blood-brain barrier, combined with brain-supportive phospholipids like phosphatidylserine, makes them a promising tool for cognitive and mood-related therapies.

E). Applications in Metabolic Disorders

Phytosomes aid in managing metabolic disorders like diabetes, dyslipidemia, and obesity by enhancing the delivery of compounds such as berberine, curcumin, and silymarin. Berberine phytosomes improve glucose and lipid metabolism, while curcumin and silymarin phytosomes support liver health in conditions like NAFLD. Improved bioavailability allows for more effective modulation of metabolic pathways and better clinical outcomes.

F) Applications in Skin disorders

Phytosomes improve skin penetration and bioavailability of plant compounds, making them effective in treating conditions like eczema, acne, and psoriasis, while also offering anti-aging and UV-protective benefits. Their lipid compatibility enhances local absorption, reduces systemic side

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effects, and nourishes the skin—making them ideal for dermatology and cosmeceutical use.

## DISCUSSION:

Overview of Key Herbal Extracts Formulated into Phytosomes

Many herbal extracts have been successfully formulated into phytosomes, greatly enhancing their bioavailability and efficacy:

- Curcumin (Meriva®) – Anti-inflammatory, antioxidant, anticancer, neuro- and hepatoprotective.
- Silymarin (Siliphos®) – Hepatoprotective, antioxidant, antiviral, anticancer, and metabolic benefits.
- Green Tea (Greenselect®) – Improves fat metabolism, liver health, and antioxidant defense.
- Ginkgo Biloba (Ginkgoselect®) – Boosts memory, cognition, and cerebral circulation.
- Quercetin – Antihistamine, antioxidant, cardiovascular and GI support.
- Berberine – Improves glucose and lipid metabolism, with strong anti-inflammatory effects.
- Boswellia (Casperome®) – Potent anti-inflammatory for joints, GI, and respiratory systems.
- Piperine – Acts as a bioenhancer, improving the absorption of other drugs.

**Challenges and Limitations in Phytosome Technology**

Despite their benefits, phytosomes face challenges in scalability, formulation complexity, cost, and residual solvent concerns, limiting widespread use. Ongoing research and development is essential to address these issues and optimize production for broader commercial and clinical adoption.

a). Stability Issues

Although more stable than liposomes, phytosomes can face leaching, oxidation, hydrolysis, and fusion, especially under poor storage conditions. These issues affect drug release, particle size, and shelf-life, posing challenges for controlled delivery and industrial production, particularly with pH-sensitive formulations.

b). Scalability and Manufacturing Hurdles

Scaling up phytosome production is challenging due to process complexity, cost, and need for specialized equipment (especially in methods like SCF or coacervation). Ensuring batch-to-batch consistency, uniformity, and quality control (e.g., particle size, drug loading) is critical yet difficult for industrial manufacturing.

c). Regulatory Complexities

The regulatory landscape for phytosomes is complex due to a lack of standardized protocols, making approval, classification, and quality control difficult. Their position between supplements and medicines leads to inconsistent regulations. Clear guidelines and robust clinical trials are needed to validate their safety, efficacy, and superiority over pure plant compounds.

d). Other Considerations

Further concerns include possible proliferation risks of phospholipids in some cancer cell lines, high production costs, and a gap between preclinical success and clinical translation—with inconsistent bioavailability outcomes in human trials. These highlight the need for deeper safety testing, cost-reduction strategies, and more robust clinical validation.

**Strategies to Overcome Challenges**

Addressing the limitations of phytosome technology is crucial for its broader adoption and full therapeutic realization. Ongoing research and development are focused on innovative strategies to enhance stability, improve manufacturing scalability, navigate regulatory complexities, and mitigate potential safety concerns.

i) Enhancing Stability and Preventing Leaching

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To enhance phytosome stability and reduce phytoconstituent leaching, key strategies include:

- Optimizing formulation (phospholipid type and ratio),
- Controlling process parameters (e.g., temperature, pH, stirring speed),
- Adding stabilizers (e.g., surfactants, antioxidants), and
- Using advanced drying techniques like spray drying or freeze-drying for better shelf life and storage stability.

ii)Advances in Large-Scale Production

To overcome scalability issues, efforts include:

- Optimizing solvent evaporation for better consistency,
- Refining SCF methods (e.g., GAS, SAS) for industrial use,
- Adopting continuous manufacturing to boost efficiency, and
- Using Process Analytical Technology (PAT) for real-time quality control during production.

iii) Navigating Regulatory Pathways

To navigate regulatory challenges, key strategies include:

- Developing standardized protocols for formulation and quality control,
- Conducting robust clinical trials to prove safety and efficacy,
- Establishing clear product classifications (e.g., supplement vs. medicine), and
- Implementing post-market surveillance for long-term safety tracking.

iv) Mitigating Phospholipid Proliferation Concerns

To address potential proliferative effects of phospholipids in certain cancer cell lines:

- Further research is needed to assess mechanisms and clinical impact,
- Alternative or modified phospholipids may reduce risk,
- Targeted delivery can limit systemic exposure, and
- Combination therapies could help mitigate unwanted proliferation.

## CONCLUSION:

**Phytosomes: A Paradigm Shift in Herbal Drug Delivery**

Phytosomes are advanced nanocarriers that chemically bond plant-derived phytoconstituents with phospholipids (notably phosphatidylcholine), overcoming traditional barriers such as poor solubility, low bioavailability, and degradation. Unlike liposomes, where compounds are merely encapsulated, phytosomes integrate the active compound into the lipid membrane—yielding superior absorption, stability, and pharmacokinetics.

**Core Mechanism & Advantages**

- Chemical bonding enables stable, targeted, and efficient delivery.
- Nanostructure (1–100 nm) enhances membrane permeability.
- Phosphatidylcholine adds synergistic therapeutic benefits, especially in liver health.
- Enables controlled release, reduced dosage, and fewer side effects.

**Key Therapeutic Applications**

- Oncology: Curcumin, silibinin phytosomes show enhanced anticancer activity.
- Liver Disorders: Silymarin phytosomes offer hepatoprotection with 6× better absorption.
- Neurological Disorders: Ginkgo biloba phytosomes improve memory, mood, CNS activity.
- Inflammation: Boswellia and curcumin phytosomes modulate NF-κB, COX-2 pathways.
- Metabolic Conditions: Berberine and quercetin phytosomes improve glucose/lipid profiles.

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- Dermatology: Enhance delivery in eczema, acne, psoriasis, anti-aging treatments.

**Innovations & Future Directions**

- Nanotechnology: Stimuli-responsive, ligand-targeted, and hybrid phytosome systems.
- AI & In Silico Modeling: Predicts formulation compatibility and accelerates design.
- Personalized Medicine: Tailoring phytosomes to genetic/metabolic patient profiles.
- Sustainability: Eco-friendly solvents and biodegradable phospholipids reduce impact.

**Challenges & Solutions**

- Stability: Improved with excipients, process control, and freeze-drying techniques.
- Scalability: Solvent evaporation optimized; SCF methods and continuous processing explored.
- Regulatory Hurdles: Need standardized protocols, robust clinical trials, post-market surveillance.
- Safety Concerns: Investigating phospholipid proliferation effects and refining formulations.

Phytosomes modernize and legitimize herbal medicine, merging ancient botanical wisdom with cutting-edge pharmaceutical science. With ongoing innovation and cross-disciplinary collaboration, phytosomes are set to become cornerstones of next-generation natural therapeutics—offering safer, more effective, and patient-friendly alternatives in global healthcare.

**CONFLICT OF INTEREST**

The field of phytosome technology is dynamic, with ongoing research and development poised to unlock its full potential in modern healthcare. The future trajectory is expected to be shaped by interdisciplinary approaches that integrate cutting-edge technologies and personalized medicine principles

A). Integration with Nanotechnology for Targeted Delivery

Nanotech innovations in phytosomes include:

- Stimuli-responsive phytosomes for targeted, controlled drug release based on pH, enzymes, or light,
- Ligand-conjugated phytosomes for active targeting of diseased cells (e.g., cancer), and
- Hybrid nanosystems combining phytosomes with other carriers for improved stability, drug loading, and therapeutic performance in complex diseases.

B). Personalized Herbal Medicine Approaches

The future of phytosomes lies in personalized medicine, using:

- Pharmacogenomics to tailor formulations based on genetic/metabolic profiles, and
- AI & in silico modeling to predict optimal designs and therapeutic outcomes—especially for chronic diseases like diabetes and autoimmune disorders.

C). Green and Sustainable Formulation Methods

Sustainable phytosome development focuses on:

- Using eco-friendly solvents (e.g., ethanol, ethyl lactate) and low-energy methods to reduce environmental impact, and
- Employing biodegradable phospholipids for safer, more biocompatible formulations.

D). Role of Artificial Intelligence and Computational Modeling

AI and in silico tools are revolutionizing phytosome research by enabling:

- Predictive modeling for selecting optimal phytoconstituent–phospholipid combinations,

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- Process optimization for stability and efficiency, and
- Drug discovery/design of novel phytosome formulations. These innovations accelerate development and improve therapeutic precision.

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