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## A REVIEW ON PHYTOSOMES: NOVEL APPROACHES FOR HERBAL DRUG DELIVERY

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| <p><b>Article History</b><br/>Received on: 14-02-2026<br/>Revised on: 24-03-2026<br/>Accepted on: 02-05-2026</p> | <p>Phytosomes represent a modern and innovative herbal drug delivery system specifically designed to overcome the limitations associated with conventional plant-based formulations. Many bioactive phytoconstituents, such as flavonoids, terpenoids, and polyphenols, exhibit poor lipid solubility and relatively large molecular size, which significantly restricts their absorption through biological membranes. As a result, their therapeutic potential often remains underutilized despite strong pharmacological activity. To address this challenge, phytosome technology was developed, wherein plant-derived active compounds are complexed with phospholipids, most commonly phosphatidylcholine. This unique complexation process enhances the lipophilicity of the phytoconstituents, thereby improving their stability, membrane permeability, and overall bioavailability. The preparation of phytosomes can be achieved through several methods, including solvent evaporation, anti-solvent precipitation, and thin film hydration techniques. Each method ensures effective binding between the phytoconstituent and phospholipid, resulting in a stable molecular complex. Phytosomes offer multiple advantages such as improved absorption, reduced dosage requirements, enhanced therapeutic efficacy, and better patient compliance. However, certain limitations exist, including higher production costs and variability in entrapment efficiency depending on the nature of the plant extract. Applications of phytosomes span across diverse therapeutic areas. They are widely utilized in hepatoprotective formulations (e.g., silybin from milk thistle), anti-inflammatory and antioxidant therapies (curcumin, green tea catechins), cardiovascular support (ginkgo biloba), dermatological preparations, and even as adjuncts in cancer prevention. Their role in nutraceuticals and cosmeceuticals continues to expand, making phytosomes a promising platform for the effective delivery of herbal medicines. In summary, phytosomes bridge the gap between traditional herbal remedies and modern pharmaceutical technology, offering a scientifically validated approach to maximize the clinical benefits of plant-derived compounds.</p> <p><b>Keywords:</b> Phytosomes, herbal drug delivery, bioavailability, phospholipids, novel drug delivery system.</p> |
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### INTRODUCTION

Herbal medicines have been an integral part of healthcare systems across the world for centuries, valued for their natural origin, cultural acceptance, and wide range of therapeutic benefits. Traditional systems such as Ayurveda, Traditional Chinese Medicine (TCM), and Unani have long relied on plant-derived compounds to treat chronic and acute conditions. In recent decades, the global demand for herbal medicines has increased significantly, driven by growing interest in natural therapies, fewer side effects compared to synthetic drugs,

and the perception that plant-based remedies are safer and more holistic. Despite these advantages, one of the major challenges in the clinical application of herbal medicines is their poor bioavailability when administered orally. Many phytoconstituents, including flavonoids, polyphenols, alkaloids, terpenoids, and tannins, exhibit limited absorption due to their hydrophilic nature, large molecular size, and instability in the gastrointestinal environment [1, 2]. This limitation reduces their therapeutic effectiveness and restricts their potential in modern pharmacotherapy.

To overcome these challenges, modern pharmaceutical technologies have developed novel drug delivery systems that enhance the solubility, stability, and absorption of herbal compounds. Among these, phytosomes have emerged as one of the most promising approaches. Phytosomes are lipid-based molecular complexes formed by binding plant extracts or phytoconstituents with phospholipids, most commonly phosphatidylcholine. This unique complexation process transforms hydrophilic plant molecules into lipid-compatible forms, thereby improving their ability to cross biological membranes. The technology is based on the formation of a stable complex between the polar functional groups of phytoconstituents and the polar head of phospholipids. This interaction results in increased lipid solubility, enhanced membrane permeability, improved drug stability, greater bioavailability, and protection of the active compound from enzymatic degradation [3, 4].

The importance of phytosomes lies in their ability to bridge the gap between traditional herbal medicine and modern pharmaceutical science. Conventional herbal extracts often require high doses to achieve therapeutic effects, which can lead to variability in patient response and reduced compliance. By contrast, phytosome formulations allow for lower doses with higher efficacy, ensuring more consistent pharmacological outcomes. For example, curcumin, a polyphenolic compound from turmeric, is known for its potent anti-inflammatory and antioxidant properties but suffers from extremely poor oral bioavailability. When formulated as a phytosome, curcumin demonstrates significantly higher plasma concentrations and improved therapeutic activity. Similarly, silybin from milk thistle widely used for liver protection, shows enhanced absorption and hepatoprotective effects when delivered as a phytosome complex [5].

Phytosome preparation methods include solvent evaporation, anti-solvent precipitation, and thin film hydration techniques, each designed to ensure effective binding between phytoconstituents and phospholipids. These methods not only improve entrapment efficiency but also allow for controlled particle size distribution, which is critical for stability and absorption. Characterization of phytosomes involves evaluating parameters such as particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug content, and in-vitro drug release profiles. Together, these analyses confirm the quality, stability, and therapeutic potential of the formulation [6].

The advantages of phytosomes are multifaceted. They provide enhanced absorption, improved pharmacokinetics, greater therapeutic efficacy, and better patient compliance. Additionally, phytosomes protect sensitive plant compounds from degradation in the gastrointestinal tract, thereby extending their shelf life and clinical utility. However, certain limitations exist, including higher production costs, variability in entrapment efficiency depending on the nature of the extract, and the need for specialized equipment during preparation. Despite these challenges, phytosomes are increasingly being adopted in pharmaceutical and nutraceutical industries due to their superior

performance compared to conventional herbal formulations [7].

Applications of phytosomes span across diverse therapeutic areas. They are widely used in hepatoprotective formulations (e.g., silybinphytosome for liver disorders), anti-inflammatory and antioxidant therapies (curcuminphytosome, green tea catechins), cardiovascular support (ginkgo bilobaphytosome), cognitive enhancement, metabolic regulation, dermatological preparations, and even as adjuncts in cancer prevention and therapy. Their role in nutraceuticals and cosmeceuticals continues to expand, with commercial products such as Meriva® (curcuminphytosome) and Ginkgo Select® gaining global recognition. These formulations demonstrate how phytosome technology can transform traditional herbal remedies into scientifically validated clinically effective products [8].

## COMPONENTS

**Phytoconstituents:** Flavonoids, polyphenols, alkaloids, terpenoids, and glycosides. Specific examples are curcumin, quercetin, silymarin, and Ginkgo extract, which have shown improved pharmacokinetic and therapeutic profiles when formulated as phytosomes [9].

**Phospholipids:** Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine. These phospholipids enhance drug solubility and facilitate transport across biological membranes [10].

Table 01: Components of Phytosomes

| Component                                  | Description   | Function   |
|--|---|--|
| Plant extract (bioactive compound)         | Derived from medicinal plants such as turmeric, milk thistle, or ginkgo biloba.         | Provides the therapeutic or nutritional effect.  |
| Phospholipid (usually phosphatidylcholine) | A natural lipid found in cell membranes.  | Acts as a carrier molecule; binds with the plant extract to improve lipid solubility and absorption. |
| Solvent system                             | Organic solvents like ethanol, acetone, or dichloromethane are used during preparation. | Facilitates the reaction and formation of the phytosome complex.                                     |

### Advantages

- Improved bioavailability
- Enhanced drug absorption
- Better stability
- Reduced dose requirement
- Increased therapeutic efficacy
- Suitable for herbal drugs
- Improved patient compliance

### Limitations

- High manufacturing cost
- Limited drug loading capacity
- Possible stability issues
- Need for specialized equipment

## PREPARATION METHODS

Common methods for preparing phytosomes include:

### 1. Solvent Evaporation Method

In this method, the phytoconstituent (active herbal compound) and phospholipid are dissolved in a suitable organic solvent. The solvent is then evaporated under controlled conditions, resulting in the formation of a phytosome complex [11, 12].

#### Procedure

- The drug (plant extract or phytoconstituent) and phospholipid (commonly phosphatidylcholine) are dissolved in an organic solvent such as ethanol, chloroform, or acetone.
- The mixture is stirred to ensure complete dissolution and interaction between the components.
- The solvent is removed using a rotary evaporator under reduced pressure.
- A thin film of the drug–phospholipid complex is formed.
- The dried complex is collected and may be hydrated or further processed into dosage forms.



Figure 01: Flow chart of solvent evaporation method

#### Advantages

- Simple and widely used method
- Produces stable phytosome complexes
- Suitable for both laboratory and industrial scale
- Enhances bioavailability of herbal drugs

#### Limitations:

- Requires use of organic solvents
- Needs specialized equipment (rotary evaporator)
- Possible residual solvent if not properly removed

### 2. Anti-solvent Precipitation Method

In this method, the drug (phytoconstituent) and phospholipid are first dissolved in a suitable organic solvent. An anti-solvent (in which the components are poorly soluble) is then added, causing the phytosome complex to precipitate out of the solution [13].

#### Procedure

- The plant extract or active phytoconstituent and phospholipid are dissolved in an organic solvent such as ethanol or acetone.
- The solution is stirred to ensure proper mixing and complex formation.
- An anti-solvent (commonly water or n-hexane) is slowly added to the solution under continuous stirring.
- The sudden decrease in solubility leads to precipitation of the phytosome complex.
- The precipitated phytosomes are collected by filtration or centrifugation and then dried.



Figure 02: Flow chart of anti-solvent precipitation method

#### Advantages

- Simple and cost-effective method
- Produces fine particles with uniform size
- Suitable for temperature-sensitive phytoconstituents
- Requires relatively less sophisticated equipment

#### Limitations

- Particle aggregation may occur if conditions are not optimized
- Careful control of solvent–anti-solvent ratio is required
- Additional drying step needed

### 3. Thin Film Hydration Method

In this method, the phospholipid and phytoconstituent are dissolved in an organic solvent to form a thin lipid film after solvent evaporation. This film is then hydrated with an aqueous medium, resulting in the formation of phytosome vesicles [14].

#### Procedure

- The drug (plant extract or active phytoconstituent) and phospholipid are dissolved in an organic solvent such as chloroform, methanol, or ethanol.
- The solvent is evaporated using a rotary evaporator under reduced pressure to form a thin lipid film on the wall of a round-bottom flask.
- The formed thin film is dried further to remove residual solvent.
- The film is hydrated with an aqueous phase (distilled water or buffer solution) at a controlled temperature with gentle stirring.
- The resulting suspension is sonicated or homogenized to obtain uniform phytosome vesicles.



Figure 3: Flow chart of thin film hydration method

#### Advantages

- Produces stable and uniform phytosome vesicles
- High entrapment efficiency
- Widely used and reproducible method
- Suitable for controlled drug delivery systems

#### Limitations

- Requires specialized equipment (rotary evaporator, sonicator)
- Time-consuming process

- Possible degradation of heat-sensitive compounds during hydration

### Characterization of Phytosomes

**i. Particle size analysis:** To determine the average diameter and size distribution of phytosome particles. Helps assess homogeneity and stability of the formulation. Smaller and uniform particles generally lead to better absorption and enhanced therapeutic efficacy. Particle size analysis is one of the most critical characterization parameters for phytosomes because it directly influences their bioavailability, stability, and absorption efficiency. The size of phytosome particles determines how well they can penetrate biological membranes and how uniformly they disperse in formulations. Typically ranges from 50 nm to 500 nm for phytosomes [15-17].

Table 02: Techniques and principle's involved in particle size analysis

| Technique                              | Principle  | Typical Output  | Advantages   |
|--|--|---|--|
| Dynamic Light Scattering (DLS)         | Measures fluctuations in light scattering due to Brownian motion of particles in suspension. | Average particle size (Z-average) and polydispersity index (PDI). | Rapid, non-destructive, suitable for nano-range particles. |
| Photon Correlation Spectroscopy (PCS)  | Similar to DLS; analyzes intensity fluctuations of scattered light.                          | Particle size distribution and PDI.                               | High precision for sub-micron particles.                   |
| Laser Diffraction (LD)                 | Based on angular variation of light intensity scattered by particles.                        | Size distribution over a wide range (0.1–3000 μm).                | Suitable for both nano and micro-scale particles.          |
| Scanning Electron Microscopy (SEM)     | Direct imaging of particle morphology and size.  | Visual confirmation of shape and size.                            | Provides detailed surface structure information.           |
| Transmission Electron Microscopy (TEM) | Uses electron transmission through thin samples.   | High-resolution particle size and internal structure.             | Ideal for nanoscale visualization.                         |

**ii. Zeta potential:** Often measured alongside particle size to evaluate stability; higher absolute values imply better dispersion stability. It measures the electrostatic potential at the slipping plane around phytosome particles. Indicates colloidal stability-higher absolute values (positive or negative) mean stronger repulsion between particles, reducing aggregation. Helps predict shelf life and dispersion quality of phytosome formulations [18-20].

### METHODS OF MEASUREMENT

**Electrophoretic Light Scattering (ELS):** Most

common technique. It measures particle velocity under an applied electric field and converts mobility into zeta potential using the Smoluchowski equation.

**Micro-electrophoresis:** Direct observation of particle movement under a microscope.

**Streaming Potential/Current Methods:** Used for porous materials or surfaces rather than suspensions

**Note:** ±30 mV or higher shows good stability (particles repel each other strongly) and from -30 mV and +30 mV shows poor stability, prone to aggregation.

**Typical Phytosome Values:** Often range between -40 mV to -50 mV, indicating strong negative surface charge and good stability.

**Influencing Factors:** Type of phospholipid used, pH of the medium and ionic strength of the suspension.

**iii. The Polydispersity Index (PDI):** It is a crucial parameter in phytosome characterization because it reflects the uniformity of particle size distribution within the formulation. PDI is a dimensionless number that indicates how evenly particle sizes are distributed in a sample. It is derived from Dynamic Light Scattering (DLS) measurements. Low PDI ensures that phytosome particles are consistent in size, leading to predictable drug release, reliable pharmacokinetics and better stability during storage. High PDI suggests aggregation or poor formulation control, which can reduce bioavailability and therapeutic effectiveness [21].

**Note:** PDI < 0.1 indicates highly monodisperse (very uniform particle size). 0.1 – 0.3 shows narrow size distribution, considered acceptable for stable nanoformulations like phytosomes. > 0.3 shows broad size distribution, indicating heterogeneity and possible instability.

**iv. Entrapment efficiency (EE):** EE is critical for dose optimization, stability, and consistency of phytosome formulations. It is a vital parameter in phytosome characterization because it measures how much of the active plant extract is successfully incorporated into the phospholipid complex. It reflects the effectiveness of the preparation method and the quality of the final formulation. EE is the percentage of bioactive compound bound within the phytosome compared to the total amount initially used. It indicates how well the phytosome system captures and retains the therapeutic molecules [22, 23].

$$EE\% = \frac{\text{Amount of drug entrapped}}{\text{Total drug added}} \times 100$$

### METHODS OF DETERMINATION

**Ultracentrifugation method:** Phytosome suspension is centrifuged at high speed. Free (unbound) drug remains in the supernatant, while entrapped drug is in the pellet. Supernatant is analyzed (e.g., by UV spectroscopy or HPLC) to calculate EE%.

**Dialysis method:** Phytosome suspension is placed in a dialysis bag. Free drug diffuses out, while entrapped drug remains inside. The amount of drug retained is measured.

**Chromatographic methods (HPLC/UV Spectroscopy):** Used to quantify the concentration of free vs. bound drug and provides precise measurement of entrapment efficiency [24-26].

Phytosomes generally show high entrapment efficiency (70–95%), depending on the type of plant extract, the phospholipid used (commonly phosphatidylcholine), the

preparation method (solvent evaporation, anti-solvent precipitation, thin film hydration).

**Note:** High EE% ensures the maximum therapeutic benefit with minimal waste and low EE% indicates poor binding, leading to reduced bioavailability.

**v. Drug content:** It determines the actual amount of bioactive compound present in the phytosome formulation, ensuring that the dosage is accurate and consistent. Drug content refers to the quantitative measurement of the active plant extract incorporated into the phytosome complex. It verifies whether the formulation contains the expected concentration of the therapeutic compound. It confirms the accuracy of formulation and compliance with quality standards. Ensures dose reliability, which is critical for therapeutic effectiveness. It helps in batch-to-batch consistency during large-scale production. Complements entrapment efficiency by showing not just how much is bound, but how much is actually present in the final product [27-31].

### METHODS OF DETERMINATION

**UV-Visible Spectrophotometry:** Measures absorbance of the active compound at a specific wavelength. It is a simple and cost-effective for plant extracts with known absorption peaks [32].

**High-Performance Liquid Chromatography (HPLC):** Separates and quantifies the active compound with high precision. It is commonly used for complex phytosome formulations [33].

**Mass Spectrometry (MS):** Provides highly sensitive detection and quantification. Useful for compounds present in very small amounts.

**Gravimetric Analysis (less common):** Involves weighing the dried phytosome complex after extraction.

**vi. In-vitro drug release:** To evaluate how effectively and at what rate the active compound is released from phytosomes under simulated biological conditions. This is critical for predicting bioavailability, therapeutic performance, and dosage consistency. Parameters to be measured as cumulative drug release (%) over time, release kinetics models (Zero-order, First-order, Higuchi, Korsmeyer-Peppas) to understand the mechanism and comparison with pure extract to demonstrate improved release and absorption potential. It helps to optimize formulation for maximum therapeutic effect with minimal dosing frequency [34, 35].

### METHODS OF STUDY

**Dialysis bag method:** Phytosome suspension is placed inside a dialysis bag. The bag is immersed in a release medium (e.g., phosphate buffer, simulated gastric fluid). Samples are withdrawn at intervals and analyzed for drug content.

**Franz diffusion cell method:** Phytosome formulation is placed in the donor compartment. A membrane separates it from the receptor compartment filled with release medium. Drug diffusion across the membrane is monitored over time.

**USP dissolution apparatus (Type II paddle method):** Phytosome capsules or suspensions are placed in dissolution medium. Paddle rotation ensures uniform mixing. Samples are collected periodically and analysed [36, 37].

## APPLICATIONS OF PHYTOSOMES

Table 03: Herbal extracts and uses

| Application Area                    | Herbal Extracts Commonly Used                              | Purpose / Benefit  |
|-------------------------------------|--|--|
| Liver Protection                    | Milk Thistle (Silybin)                                     | Enhances hepatoprotective activity, supports detoxification, and improves liver function.    |
| Anti-inflammatory & Antioxidant     | Turmeric (Curcumin), Green Tea Catechins                   | Reduces inflammation, combats oxidative stress, and improves bioavailability of polyphenols. |
| Cardiovascular Health               | Ginkgo Biloba, Green Tea Extract                           | Improves circulation, reduces platelet aggregation, and supports heart health.               |
| Cognitive Function                  | Ginkgo Biloba  | Enhances memory, concentration, and neuroprotection.   |
| Metabolic Support                   | Green Tea Extract, Silybin                                 | Aids in weight management, improves lipid metabolism, supports glucose regulation.           |
| Skin Care / Dermatology             | Grape Seed Extract, Curcumin                               | Provides antioxidant protection, reduces UV damage, supports anti-aging formulations.        |
| Cancer Prevention / Adjunct Therapy | Curcumin, Green Tea Catechins                              | Enhances anticancer activity by improving absorption and cellular uptake.                    |
| Immune Support                      | Various polyphenolic extracts (e.g., Echinacea, Green Tea) | Boosts immune response, protects against infections.   |

### CONCLUSION

Phytosomes are an innovative herbal drug delivery system that significantly enhances the bioavailability and therapeutic performance of plant-derived compounds. By forming stable complexes with phospholipids, phytoconstituents gain improved lipid solubility, membrane permeability, and protection from degradation, resulting in better absorption and clinical outcomes. Their advantages, including enhanced stability and wide-ranging applications in liver health, cardiovascular support, antioxidant therapy, and dermatology, have made them increasingly important in pharmaceutical and nutraceutical development. Continued research is expected to expand their role in modern healthcare, positioning phytosomes as a reliable platform for next-generation herbal therapeutics.

### AUTHOR CONTRIBUTIONS

All authors contributed equally.

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