



A Review on Phytosomes: As A Promising Novel Drug Delivery System for Enhanced Bioavailability

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ABSTRACT:

Herbal medicines have gained significant attention due to their therapeutic efficacy and their safety. However, many phytoconstituents suffer from poor bioavailability, limited membrane permeability, and low stability, all those properties decreases their therapeutic efficacy. To address these challenges, phytosomal drug delivery system is developed. In phytosome systems, the bioactive plant constituents are chemically complexed with phospholipids, leading to improved lipid solubility and enhanced absorption across biological membranes. When it compared to conventional herbal formulations and liposomal systems, the phytosomes demonstrate excellent pharmacokinetic properties and increased therapeutic effectiveness. This review mainly focuses on phytosome technology, methods of preparation, Properties, Characterization and therapeutic applications of phytosome based formulations in the management of various diseases are discussed.

KEYWORDS:

Phytosomes, Novel drug delivery system, Phytoconstituents, Enhanced bioavailability, Phospholipids.

I. INTRODUCTION:

Novel drug delivery systems have been developed to overcome bioavailability-related challenges. Among them, phytosome technology has emerged as a promising approach for enhancing the absorption of phytoconstituents. ⁽¹⁾ Phytosomes are complexes formed by the interaction of plant-derived bioactive compounds with phospholipids, which improves lipid solubility and facilitates better permeation across biological membranes. ⁽²⁾ Unlike liposomes, phytosomes involve a molecular-level interaction between the carrier and the

phytoconstituent, resulting in improved stability and enhanced pharmacokinetic performance.⁽³⁾ The phytosome complex is amphiphilic, it interacts better with lipid cell membranes and aqueous gastrointestinal fluids, enhancing passive diffusion and absorption.⁽⁴⁾

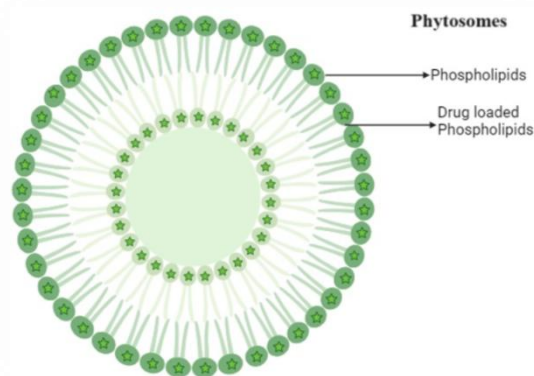


Fig 1: Structure of Phytosome.

Phytosomes:

Definition:

The structure of Phytosome is shown in Figure 1. They represent an advanced type of herbal formulation in which lipids bind and encapsulate the bioactive phytoconstituents of plant extracts.⁽⁵⁾ Phytosomes are also known as herbosomes or phytophospholipid complexes.

They are formed by chemically binding phospholipids, most commonly phosphatidylcholine, to plant-derived active compounds in a specific stoichiometric ratio.⁽⁶⁾ This molecular interaction produces a stable complex that enhances the solubility and absorption of the phytoconstituents.⁽⁷⁾



The chemical structure of Phytosome is shown in Figure 2. These complexes are typically nanostructured, allowing them to efficiently protect the active herbal ingredient from degradation in the gastrointestinal tract.⁽⁸⁾ The lipid envelope facilitates the transfer of the phytoconstituents from an aqueous environment into the lipid-rich cell membranes, thereby improving systemic absorption and bioavailability.⁽⁹⁾

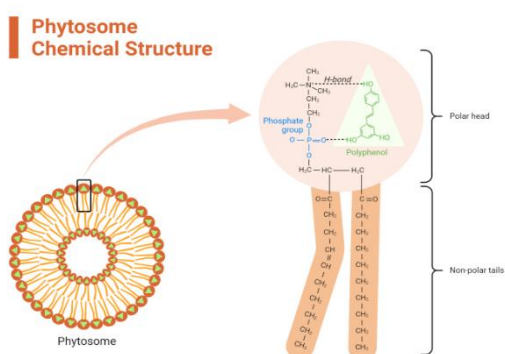


Fig 2: Chemical structure of Phytosome.

Structural composition:

1. Phospholipids:

The structure of phospholipid is shown in Figure 3. Typically, glycerophospholipids such as phosphatidylcholine, phosphatidylethanolamine, and phosphatidylserine are used in the formulation of

phytosomes.⁽¹⁰⁾ Among these, phosphatidylcholine is the most commonly employed phospholipid due to its excellent biocompatibility, amphipathic nature, and natural presence in biological membranes.⁽¹¹⁾

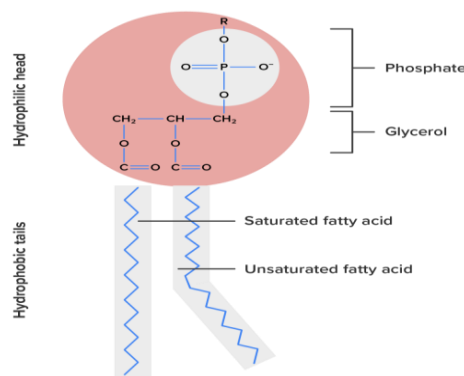


Fig 3: Structure of Phospholipid

2. Phytoconstituent:

It describes the bioactive substance derived from plants, such as terpenoids, polyphenols, and flavonoids that complex with phospholipid. A stable "phyto phospholipid" complex is created by molecular binding, typically by hydrogen bonds between the hydroxyl groups of the phytoconstituent and the phosphate or ammonium groups of phospholipids.⁽¹²⁾

PREPARATION METHODS⁽¹³⁾

Method	Process
1. Solvent (Rotary) Evaporation	Drug + phospholipid dissolved in organic solvent → solvent evaporated → thin film → hydrated to form phytosomes.
2. Anti-Solvent Precipitation	Organic solution of complex added to non-solvent (e.g., hexane) → phytosome complex precipitates.
3. Lyophilization (Freeze Drying)	Phytosome dispersion frozen → sublimation of water → stable dry powder.
4. Salting Out Technique	Salt added to aqueous solution → reduces solubility of complex → phytosomes separate out.
5. Supercritical Fluid (SCF) Method	Phytoconstituent + Phospholipid → Exposure to Supercritical CO ₂ → Molecular Interaction & Complex Formation → Controlled Depressurization → Phytosome Powder
6. Reflux Method	Phytoconstituent + Phospholipid → Dissolve in organic solvent → Reflux at 50–60°C (1–3 hours) → Phytosome Complex Formation → Concentration of Solution → Drying

Table 1: Various Methods of Preparation of Phytosomes



PROPERTIES OF PHYTOSOMES:

a. Physicochemical Properties :

Amphiphilic Nature:The amphiphilic nature of phytosomes is a result of the combination of nonpolar phospholipid tails and polar phytoconstituents. They can effectively interact with lipophilic and hydrophilic environments, improving medication absorption and solubility. ⁽¹⁴⁾

Stoichiometric Complexation:Phytosomes are created by complexing bioactive phytochemicals with phospholipids, often phosphatidylcholine, in a specific molar ratio, usually 1:1 or 2:1. This process is known as stoichiometric complexation. ⁽¹⁵⁾

Improved Lipophilicity: Hydrophilic phytochemicals have improved lipophilicity due to the development of phytosomes, which facilitates their better partitioning into lipid bilayers of cell membranes. ⁽¹⁶⁾

b. Biological Properties :

Enhanced Bioavailability: In terms of improved tissue permeability, phytosomes considerably increase the oral bioavailability of herbal extracts that are not well absorbed. ⁽¹⁷⁾

Improved Absorption and Distribution: Because of their lipid-based structure, phytosomes exhibit improved absorption across the skin and gastrointestinal barriers, which enables more effective delivery of phytochemicals to their intended tissues. ⁽¹⁸⁾

ADVANTAGES OF PHYTOSOMES

a. Increased Bioavailability:

Compared to traditional herbal extracts, phytosomes greatly increase the bioavailability of phytoconstituents by generating lipid-compatible molecular complexes that facilitate improved absorption across biological membranes. ⁽¹⁹⁾

b. Better Solubility and Stability:

Hydrophilic phytochemicals are more soluble in lipid environments thanks to phytosome complexes, which also provide protection against chemical deterioration, extending their shelf life and stability in storage. ⁽²⁰⁾

c. Targeted and Enhanced Therapeutic Efficacy:

Through mechanisms such as enhanced cellular uptake and inhibition of signalling pathways phytosome-encapsulated secondary metabolites. ⁽²¹⁾

d. Effective Drug Transport through Membrane Fusion:

Phytosomes enable contact-facilitated drug delivery (CFDD), which permits deeper integration and improved diffusion of active compounds into target cells because of their structural resemblance to biological membranes and amphiphilic micelle-like nature. ⁽²²⁾

CHARACTERIZATION AND EVALUATION

1. Particle Size and Size Distribution:It is used to determine the average size and uniformity of phytosomes, which influences absorption and bioavailability. Technique - dynamic light scattering (DLS) are commonly used. Evaluation: Smaller and uniformly distributed particles are enhancing the membrane permeation.

Example:Curcuminphytosomes - average particle size of 150 to 300 nm. ⁽²³⁾

2. Morphological Characterization: Surface morphology and shape of phytosomes are determined by using scanning electron microscopy (SEM) or transmission electron microscopy (TEM).Evaluation:Confirms vesicular structure and uniformity.

Example: TEM images of quercetin phytosomes -reveale spherical vesicles. ⁽²⁴⁾

3. Encapsulation / Complexation Efficiency: This determines the percentage of phytoconstituent successfully complexed with phospholipids. Evaluation: Higher efficiency shows effective formation.

Example: Green tea polyphenol phytosomes showed more than 80% complexation efficiency. ⁽²⁵⁾

4. Differential Scanning Calorimetry (DSC): It is conducted to determine thermal behavior and physical state changes. Evaluation: Disappearance of melting peaks confirms complex formation.

Example: DSC thermograms of silymarinphytosomes - absence of the drugs melting peak.⁽²⁶⁾

5. X-Ray Diffraction (XRD): It is used to evaluate the crystalline or amorphous nature of phytosomes. Evaluation: Reduction in crystallinity shows improved solubility.

Example: XRD patterns of phytosomal formulations shows less intensity peaks compared to the empty phytoconstituents. ⁽²⁷⁾

APPLICATIONS OF PHYTOSOMES:

1. Improved Bioavailability of Herbal Compounds: Lots of active ingredients, such as flavonoids and polyphenols, are poorly soluble in water. Phytosomes in this case enhance the bioavailability and also absorption.

Example: Curcuminphytosomes - improved oral absorption. ⁽²⁸⁾

2. Neuroprotective Enhancement: They efficiently cross blood-brain barrier to deliver herbal compounds which can target the brain.

Example:Ginkgo bilobaphytosomes - treat cognitive impairment. ⁽²⁹⁾



3. Hepatoprotective Liver Protection: These are the phytochemicals which can protect the liver.

Example: Silymarin phytoosomes - enhance liver function (cirrhosis and hepatotoxicity).⁽³⁰⁾

4. Dermatology & Cosmetics: UV protection, skin whitening, and anti-aging also contain phytoosomes. They enhance penetration through the layers of the skin.

Examples: Green tea phytoosomes - anti-aging, hyperpigmentation - liquorice phytoosomes.⁽³¹⁾

5. Anti-Inflammatory and Antioxidant Therapy: Antioxidants and anti-inflammatory drugs are also included with phytoosomes for improving their actions.

Examples: Boswellic acid phytoosomes - arthritis, Quercetin phytoosomes - oxidative stress.⁽³²⁾

II. CONCLUSION

Phytoosomes are a revolutionary advancement in the field of herbal medicine delivery systems that greatly improves the limited bioavailability, low permeability, and poor solubility of several phytoconstituents. Phytoosomes improve the therapeutic and pharmacokinetic characteristics of bioactive substances by complexing plant extracts with phospholipids, which guarantee more effective absorption. This cutting-edge technique, which provides targeted distribution and sustained release of active ingredients, fills the gap between traditional herbal treatment and contemporary pharmaceutical needs. They are used in a variety of therapeutic fields, including as skin health, neuroprotection, anti-inflammatory, anti-cancer, and hepatoprotection. The potential of phytoosomes is being further expanded by continuous advancements in formulation science and nanotechnology, despite some formulation and scale-up challenges. Their potential is still being expanded by continuous research and integration with nanotechnology, despite persistent obstacles like cost and scalability. The clinical efficacy of herbal medications can thus be advanced thanks to phytoosomes.

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