



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 decrease 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⁾

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⁾

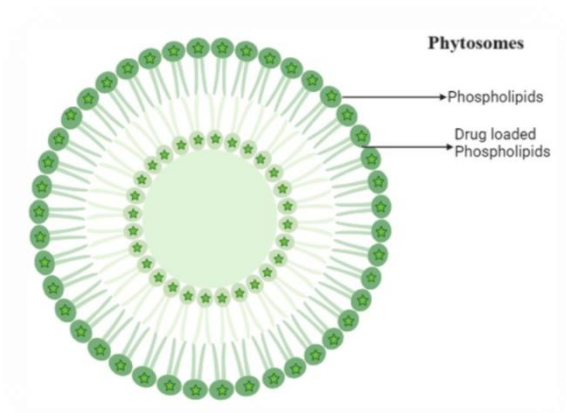


Fig 1: Structure of Phytosome

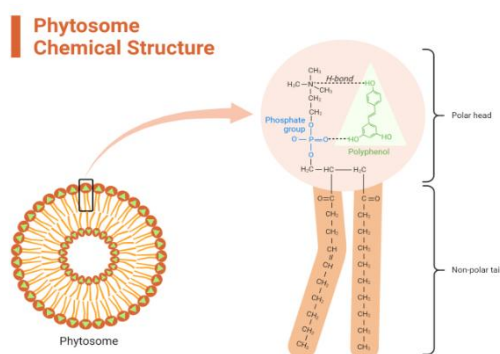


Fig 2: Chemical structure of Phytosome

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)

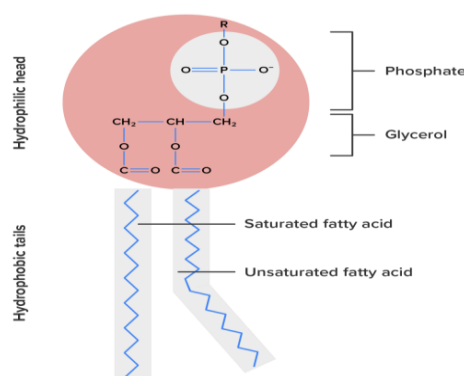


Fig 3: Structure of Phospholipid

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: Curcumin phytosomes - 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 - reveal 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 silymarin phytosomes - 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: Curcumin phytosomes - improved oral absorption. ⁽²⁸⁾
2. Neuroprotective Enhancement: They efficiently cross blood-brain barrier to deliver herbal compounds which can target the brain. Example: Ginkgo biloba phytosomes - treat cognitive impairment. ⁽²⁹⁾
3. Hepatoprotective Liver Protection: These are the phytochemicals which can protect the liver. Example: Silymarin phytosomes - enhance liver function (cirrhosis and hepatotoxicity). ⁽³⁰⁾
4. Dermatology & Cosmetics: UV protection, skin whitening, and anti-aging also contain phytosomes. They enhance penetration through the layers of the skin. Examples: Green tea phytosomes - anti-aging, hyperpigmentation - liquorice phytosomes. ⁽³¹⁾
5. Anti-Inflammatory and Antioxidant Therapy: Antioxidants and anti-inflammatory drugs are also included with phytosomes for improving their actions. Examples: Boswellic acid phytosomes - arthritis, Quercetin phytosomes - oxidative stress. ⁽³²⁾

II. CONCLUSION

Phytosomes 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. Phytosomes 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 phytosomes 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 phytosomes.

REFERENCES

- [1]. Barani, M., Sangiovanni, E., Angarano, M., Rajizadeh, M. A., Mehrabani, M., Piazza, S., Gangadharappa, H. V., Pardakhty, A., Mehrbani, M., Dell'Agli, M., & Nematollahi, M. H. (2021). Phytosomes as Innovative Delivery Systems for Phytochemicals: A Comprehensive Review of Literature. *International journal of nanomedicine*, 16, 6983–7022.
- [2]. Rayate, Yogita, Shital Shewale, Aishwarya V. Patil, Manojkumar M. Nitalikar and Shrinivas Krishna Mohite. "Phytosomes—A Novel Approach in Herbal Drug Delivery System." *Asian Journal of Research in Pharmaceutical Science* 8 (2018): 151-154.
- [3]. Gaikwad, Sachin S., Yogita Y. Morade, Akshada M. Kothule, Sanjay J. Kshirsagar, Umesh D. Laddha, and Kishor S. Salunkhe. "Overview of phytosomes in treating cancer: Advancement, challenges, and future outlook." *Heliyon* 9, no. 6 (2023).
- [4]. Mane, Kavita, Shrikrishna Baokar, Atul Bhujbal, Swapnali Pharande, Gauri Patil, Rajendra Patil, Prabhat Jain, and Adityanath Pandey. "Phyto-phospholipid complexes (phytosomes): a novel approach to improve the bioavailability of active constituents." *Journal of Advanced Scientific Research* 11, no. 03 (2020): 68-78.
- [5]. Ahmad, S. "Engineered nanomaterials for drug and gene deliveries-A review." *Journal of Nanopharmaceutics and Drug Delivery* 3, no. 1 (2016): 1-50.
- [6]. Singh, Sudarshan, Yogesh V. Ushir, and Bhupendra Prajapati. "Phytosomes and herbosomes: a vesicular drug delivery system for improving the bioavailability of natural products." In *Lipid-Based Drug Delivery Systems*, pp. 423-460. Jenny Stanford Publishing, 2023.
- [7]. Gnananath, Kattamanchi, Kalakonda Sri Nataraj, and Battu Ganga Rao. "Phospholipid complex technique for superior bioavailability of phytoconstituents." *Advanced pharmaceutical bulletin* 7, no. 1 (2017): 35.
- [8]. Chavda, Vivek P., Aayushi B. Patel, Kavya J. Mistry, Suresh F. Suthar, Zhuo-Xun Wu, Zhe-Sheng Chen, and Kaijian Hou. "Nano-drug delivery systems entrapping natural bioactive compounds for cancer: recent progress and future challenges." *Frontiers in oncology* 12 (2022): 867655.



- [9]. Udapurkar, Prachi, Omprakash Bhusnure, Santosh Kamble, and Kailash Biyani. "Phyto-phospholipid complex vesicles for phytoconstituents and herbal extracts: A promising drug delivery system." *Int J Herbal Med* 4, no. 5 (2016): 14-20.
- [10]. Sahu, Ram Kumar, and Vinod Nautiyal. "Phytosomes." In *Advanced Pharmaceutical and Herbal Nanoscience for Targeted Drug Delivery Systems Part II*, pp. 94-115. Bentham Science Publishers, 2022.
- [11]. Singh, Rudra Pratap, H. V. Gangadharappa, and K. Mruthunjaya. "Phospholipids: Unique carriers for drug delivery systems." *Journal of Drug delivery science and technology* 39 (2017): 166-179.
- [12]. KS, Salunkhe, and Khalkar Aditi. "Phytosome as a novel drug delivery system for bioavailability enhancement of phytoconstituents and its applications: A review." *Journal of Drug Delivery & Therapeutics* 11, no. 3 (2021).
- [13]. Gaurav, Vishal, Shivangi Paliwal, Arpita Singh, Swarnima Pandey, and M. Siddhiqui. "Phytosomes: Preparation, evaluation and application." *Int J Res Eng Sci* 9, no. 2 (2021): 35-9.
- [14]. Mane, Kavita, Shrikrishna Baokar, Atul Bhujbal, Swapnali Pharande, Gauri Patil, Rajendra Patil, Prabhat Jain, and Adityanath Pandey. "Phyto-phospholipid complexes (phytosomes): a novel approach to improve the bioavailability of active constituents." *Journal of Advanced Scientific Research* 11, no. 03 (2020): 68-78.
- [15]. Lu, Mei, Qiujun Qiu, Xiang Luo, Xinrong Liu, Jing Sun, Cunyang Wang, Xiangyun Lin, Yihui Deng, and Yanzhi Song. "Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents." *Asian journal of pharmaceutical sciences* 14, no. 3 (2019): 265-274.
- [16]. Sharafan, Marta, Anna Dziki, Magdalena Anna Malinowska, Elżbieta Sikora, and Agnieszka Szopa. "Targeted Delivery Strategies for Hydrophilic Phytochemicals." *Applied Sciences* 15, no. 13 (2025): 7101.
- [17]. Gandhi, Arijit, Avik Dutta, Avijit Pal, and Paromita Bakshi. "Recent trends of phytosomes for delivering herbal extract with improved bioavailability." *J. Pharmacogn. Phytochem* 1, no. 4 (2012): 6-14.
- [18]. Alharbi, Waleed S., Fahad A. Almughem, Alshaimaa M. Almeahady, Somayah J. Jarallah, Wijdan K. Alsharif, Nouf M. Alzahrani, and Abdullah A. Alshehri. "Phytosomes as an emerging nanotechnology platform for the topical delivery of bioactive phytochemicals." *Pharmaceutics* 13, no. 9 (2021): 1475.
- [19]. Jacob, Shery, Fathima Sheik Kather, Sai HS Boddu, Rekha Rao, and Anroop B. Nair. "Vesicular carriers for phytochemical delivery: A comprehensive review of techniques and applications." *Pharmaceutics* 17, no. 4 (2025): 464.
- [20]. Peanparkdee, Methavee, and Ratchadaporn Yooying. "Enhancement of solubility, thermal stability and bioaccessibility of vitexin using phosphatidylcholine-based phytosome." *NFS Journal* 31 (2023): 28-38.
- [21]. Mardiana, Lia, Tiana Milanda, Yuni Elsa Hadisaputri, and Anis Yohana Chaerunisaa. "Phytosome-Enhanced Secondary Metabolites for Improved Anticancer Efficacy: Mechanisms and Bioavailability Review." *Drug Design, Development and Therapy* (2025): 201-218.
- [22]. Breen, Sibilah, Sarah Kofoed, David Ritchie, Tracey Dryden, Roma Maguire, Nora Kearney, and Sanchia Aranda. "Remote real-time monitoring for chemotherapy side-effects in patients with blood cancers." *Collegian* 24, no. 6 (2017): 541-549.
- [23]. Maiti, Kuntal, Kakali Mukherjee, Arunava Gantait, Bishnu Pada Saha, and Pulok K. Mukherjee. "Curcumin-phospholipid complex: preparation, therapeutic evaluation and pharmacokinetic study in rats." *International journal of pharmaceuticals* 330, no. 1-2 (2007): 155-163.
- [24]. Daghman, Mohamed Ibrahim. "Comparison of the physicochemical characteristics and flavonoid release profiles of *Sutherlandia frutescens* phytosomes versus liposomes." (2016).
- [25]. Hashemzadeh, Hassan, Mohammad Yahya Hanafi-Bojd, Milad Iranshahy, Asghar Zarban, and Heidar Raissi. "The combination of polyphenols and phospholipids as an efficient platform for delivery of natural products." *Scientific Reports* 13, no. 1 (2023): 2501.
- [26]. El-Batal, Ahmed Ibrahim, Shahira F. Elmenshawi, Ahmed M. Abdelhaleem Ali,



- and Enas Goodha. "Preparation and characterization of silymarin nanocrystals and phytosomes with investigation of their stability using gamma irradiation." *Indian J. Pharm. Educ. Res* 52 (2018): S174-S183.
- [27]. Metkari, Vijay, Rohit Shah, Nitin Salunkhe, and Shailendra Gurav. "QBD approach for the design, optimization, development, and characterization of naringenin-loaded phytosomes to enhance solubility and oral bioavailability." *Journal of Pharmaceutical Innovation* 18, no. 4 (2023): 2083-2097.
- [28]. Kidd, Parris M. "Bioavailability and activity of phytosome complexes from botanical polyphenols: the silymarin, curcumin, green tea, and grape seed extracts." *Altern Med Rev* 14, no. 3 (2009): 226-246.
- [29]. Tiwari, Prashant, K. M. Geetha, Shweta Shrivastava, Yogita Kumari, Rajni Kant Panik, Pankaj Kumar Singh, Dileep Kumar, and Pratap Kumar Sahu. "Phytosome for Targeted Delivery of Natural Compounds: Improving Efficacy, Bioavailability, and Delivery across BBB for the Treatment of Alzheimers disease." *Frontiers in Clinical Drug Research-CNS and Neurological Disorders: Volume 11* 11 (2023): 262.
- [30]. Mahmoudabad, Arezoo Gohari, Fatemeh Gheybi, Mohsen Mehrabi, Alireza Masoudi, Zeinab Mobasher, Hamid Vahedi, Anneh Mohammad Gharravi, Fatemeh Sadat Bitaraf, and Seyed Mahdi Rezayat Sorkhabadi. "Synthesis, characterization and hepatoprotective effect of silymarin phytosome nanoparticles on ethanol-induced hepatotoxicity in rats." *BioImpacts: BI* 13, no. 4 (2023): 301.
- [31]. Dwivedi, Jyotsana, Pranay Wal, Shubhi Kaushal, Arpan Kumar Tripathi, Priyanka Gupta, and Surada Prakash Rao. "Phytosome based cosmeceuticals for enhancing percutaneous absorption and delivery." *Journal of Research in Pharmacy* 29, no. 1 (2025): 242-271.
- [32]. Prabha, Jyoti, Mohit Kumar, Devesh Kumar, Shruti Chopra, and Amit Bhatia. "Nano-platform strategies of herbal components for the management of rheumatoid arthritis: A review on the battle for next-generation formulations." *Current Drug Delivery* 21, no. 8 (2024): 1082-1105.