Phytosomes and their role in bioavailability enhancement

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Abstract:
A well-turned, self-assembling vesicular drug delivery system based on phospholipids is called a phytosome. The bioactive phytoconstituents of the herbal extract are encased and bound by a lipid in this sophisticated form of herbal preparation. We also go over current developments in the production, characterisation, structural validation, and enhanced bioavailability of phyto-phospholipid complexes. For many years, medicinal herbs have been used to treat a variety of illnesses. Compounds derived from plants are known to have less adverse effects than traditional medications and to have therapeutic benefits. However, the usefulness of active herbal components has been restricted due to problems with their absorption. A potential way to maximize the medical efficiency of herbal substances is by the use of phytosomes, also known as herbosomes, a drug delivery method that improves the absorption and bioavailability of these plant-based compounds. Due to largely unbalanced hydrophilicity and lipophilicity concerns, the scientific community finds it nearly impossible to supply phytoconstituents efficiently. The majority of phytoconstituents are hydrophilic, have high molecular sizes, and have low bioavailability and absorption. Vesicular systems, such as phytosomes, are acknowledged as a special and innovative method to improve the solubility and bioavailability of herbal extracts and phytoconstituents. These are complexes of phospholipid molecules and phytoconstituents, commonly known as herbosomes or phytophospholipid complexes. In this paper we will discuss. Phytosomes and their role in bioavailability enhancement

Keywords:
Phytosomes, Bioavailability Enhancement, Herbal Extract, Lipid, Substances, Pharmacokinetics, Solubility, Plant Compounds, Cell Membranes, Phospholipids

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Introduction:

One lipid-based vesicular delivery technology that can be utilized to encapsulate medications and plant-derived nutraceuticals such polyphenolic chemicals is the phytosome. The phytosome, a recently developed food-grade delivery mechanism, may lessen issues related to the solubility and bioavailability of polyphenolic substances, making them useful in the creation of novel food and medication compositions. Pharmaceutical businesses may benefit from this delivery platform in terms of encapsulating enough active phyto-ingredients to create novel supplements. For many years, a wide range of illnesses have been treated with medicinal plants and the therapeutic components they contain. [1]

The fact that modern medicine is unable to treat every human ailment, that synthetic drug assurance and safety are gaining more attention, and that many natural products have been shown to perform better than synthetic medications with no negative side effects are the main reasons for the growing use of herbal medicines. Many active plant compounds have poor oral bioavailability, which makes their therapeutic usage questionable. "Some" refers to something that resembles a cell, and "Phyto" indicates a plant. Herbosomes, sometimes referred to as phytosomes, are vesicular drug delivery systems that increase low-soluble medications' bioavailability. Phytosomes are created when plant extracts and phosphatidylcholine (or any other hydrophilic polar head group) react in an aprotic solvent. Over the years, numerous plant extracts have been the focus of pharmacological and chemical research to identify their chemical components and validate the applications of traditional medicine. Many plants include polar or water-soluble bioactive components. However, water-soluble plant compounds (such as flavonoids, tannins, and terpenoids) are poorly

absorbed either because of their large molecule size, which inhibits passive diffusion, or because of their poor lipid solubility, which severely restricts their ability to pass through biological membranes that are rich in lipids and leads to poor bioavailability. When extracts are taken orally, the stomach environment may break down some of their constituents. Over the past century, phytochemical and phyto-pharmacological investigations have established the compositions, biological functions, and health-wellness characteristics of plant extracts and their derivatives. [2]

Benefits of phytosomes in formulations

When taken orally, phytosomes improve systemic bioavailability and the active absorption of active substances. Compared to traditional herbal extracts, this sophisticated type of herbal goods offers more efficacy. Compared to straightforward herbal medications, phytosomes have better pharmacokinetics. Additionally, phytosomes have a longer shelf life than any other herbal product on the market and are naturally transformed into vital phytonutrients, giving them an advantage in assimilation. Phytosomes can be prepared in a variety of ways, such as by altering them to target particular organs prior to the release of pharmacological drugs. Additionally, it is anticipated that using disease modeling to apply these preventive measures will speed up patient recovery and raise levels of care satisfaction. [3]

Enhanced bioavailability

Phytosome technology can improve the solubility and permeability of poorly soluble phytochemicals by making them soluble and able to pass through the intestinal epithelial barrier. Similar outcomes can be obtained by administering tablets with a reduced active ingredient quantity due to the higher bioavailability.

Advantages of phytosomes:

Phytosomes have the following advantages

- It improves the oral and topical absorption of lipid-insoluble polar phytoconstituents, demonstrating improved bioavailability and thus much larger therapeutic efficacy.
- The dose requirement for the active ingredient or ingredients decreases as their absorption improves.
- Phosphatidylcholine, which is utilized to prepare phytosomes, has a synergistic impact when hepatoprotective chemicals are used since it functions as both a carrier and a hepatoprotective.
- The phytosomes exhibit a better stability profile because phosphatidylcholine molecules and phytoconstituents create chemical connections.
- Phospholipids have additional nutritional benefits.

Disadvantages of Phytosomes

- Phytoconstituents is quickly eliminated from phytosomes
- Phospholipid (lecithin) can encourage proliferation on MCF breast cancer cell line
- Leaching of phytoconstituents off the "same" is a major disadvantage of phytosomes that reduces the expected medication concentration. [4]

Review of Literature:

Many plant compounds with a variety of biological activities and health-promoting benefits, such as anti-mutagenicity, anti-carcinogenicity, and anti-oxidative activity, for age-related diseases like memory loss, osteoporosis, diabetic wounds, immune and liver disorders, etc., have been discovered over the past century by phytochemical and phytopharmacological science. Since ancient times, people have been aware of the safety, effectiveness, folk acceptability, and reduced side effects of herbal treatments. Since the chemical components they contain are involved in the physiological processes of living plants, it is thought that they are more compatible with the human body. (Minakshi S., 2013) [5]

A variety of pharmacological carriers, including polymeric micelles, particulate systems, macromolecules, and micromolecules, are included in novel drug delivery systems. Lipid particles, micro- and nanoparticles, micro- and nanospheres, polymeric micelles, and vesicular systems such as liposomes, sphingosomes, niosomes, transfersomes, aquasomes, ufasomes, and so on are examples of particulate type carriers, also referred to as colloidal carrier systems. When specific amphiphillic building blocks come into contact with water, vesicular systems—highly organized assemblies of one or more concentric lipid bilayers—are created. These mechanisms help prolong the drug's duration in the bloodstream, lessen toxicity, and postpone the removal of medicines that are quickly metabolized. (Jadhav S., 2012) [6]

Herbal products must have appropriate homeostasis between hydrophilic (for absorption into gastrointestinal tract fluid) and lipophilic (to pass lipid biomembrane balance) in order to increase bioavailability. Both ancient and contemporary medical systems make extensive use of plant preparations. Many plant extracts and their constituents have been the subject of numerous pharmacological investigations throughout history to determine their potential for medicinal use. The development of innovative drug delivery systems (NDDS) for different plant extracts and their active ingredients has advanced significantly within the last year. Innovative drug delivery methods, such targeted drug delivery, which directs the active ingredient directly to the site of action, may provide prolonged

and focused drug release, allowing for the achievement of pharmacological effects at lower dosages. Herbal medicine began to advance earlier in order to treat human illnesses with fewer adverse effects. [7]

Objectives:

- To Study the Phytosomes and their role in bioavailability enhancement
- To Explain Technological Advances in Phytosomes
- To Common Stages in the Preparation of Phytosome
- To explain some Characterization of Phytosomes

Research Methodology

The current study employs an exploratory research design to investigate phytosomes and their function in enhancing the bioavailability of herbal constituents. The research relies solely on secondary data gathered from a variety of published sources, which include peer-reviewed journals, research articles, books, conference papers, and reputable scientific websites. A systematic review and analysis of pertinent literature regarding phytosome technology, formulation methods, characterization techniques, technological advancements, and applications in drug delivery was conducted. The information collected was critically assessed and synthesized to gain insights into the effectiveness of phytosomes in enhancing the solubility, absorption, and therapeutic efficacy of phytoconstituents. This qualitative review-based methodology offers a thorough understanding of the current advancements and future possibilities of phytosomal drug delivery systems. This approach provides a comprehensive overview of the existing knowledge and developments within the realm of phytosomal drug delivery systems.

Result and Discussion:

Cell membranes are constructed by complex molecules called phospholipids. Phospholipids are lipid molecules in which the phosphate group takes up the remaining space after the glycerol is joined to two fatty acids. Phosphatidylcholine, derived from soybeans (glycine max), is the most widely utilized phospholipid. Phytosomes are created by reacting 1-2 mol of phospholipids, such as phosphatidylcholine, phosphatidylethanolamine, or phosphatidylserine, with 1 mol of a bioactive component, such as terpenoids or flavonoids, in an aprotic solvent (dioxane, acetone, methylene chloride, ethyl acetate). Herbal extracts containing flavonoid and terpenoid components are frequently made because they are made to directly bond with the phosphatidylcholine moiety. Hydrophilic bioactive phytoconstituents of herbs (phosphatidylcholine) are surrounded and secured by phospholipid-containing phytosomes. It is made up of lipid bilayers (fig. 1). [8]

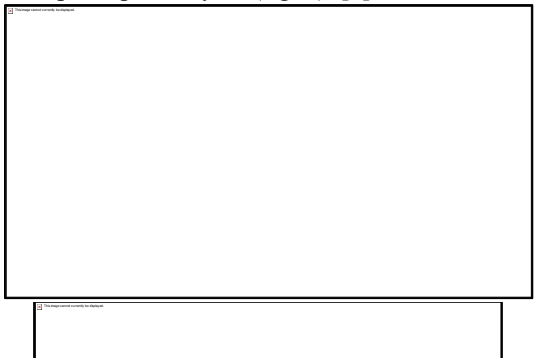

Figure 1: Structure of phytosome

Technological Advances in Phytosomes

We have witnessed a major advancement in the discovery of new drugs in recent years, mostly in the form of novel drug delivery methods that increase the drug action and absorption of pharmaceuticals. Phytosome technology is a major advancement in botanical medicine and nutritional supplements. It provides an overview of recent advancements in phytosome technology and includes references to relevant studies and publications.

1. Increased Bioavailability

Phytosomes are used to improve the body's absorption of phytochemicals. This is achieved by the phytochemicals and phospholipids combining to increase the substance's stability and solubility. Phytosomes significantly boost the bioavailability of some plant extracts, according to recent research. In order to improve silybin distribution, researchers looked at silymarin, which was used as a silybin phospholipid complex.

2. Improved Formulation Techniques

Thanks to improvements in formulation techniques, the production of phytosome complexes is now more efficient and scalable. To improve the stability and release properties of phytosome formulations, a number of methods have been devised, including microencapsulation, surgery, radiation therapy, chemotherapy, spray drying, and others.

3. Environmental Impact and Sustainability

A recent study also looked at the sustainability of phytosome technology, which includes using phospholipids from environmentally safe sources and cutting waste in production procedures. [9]

Figure 2: Advancement in phytosomes drug delivery system

Common Stages in the Preparation of Phytosome

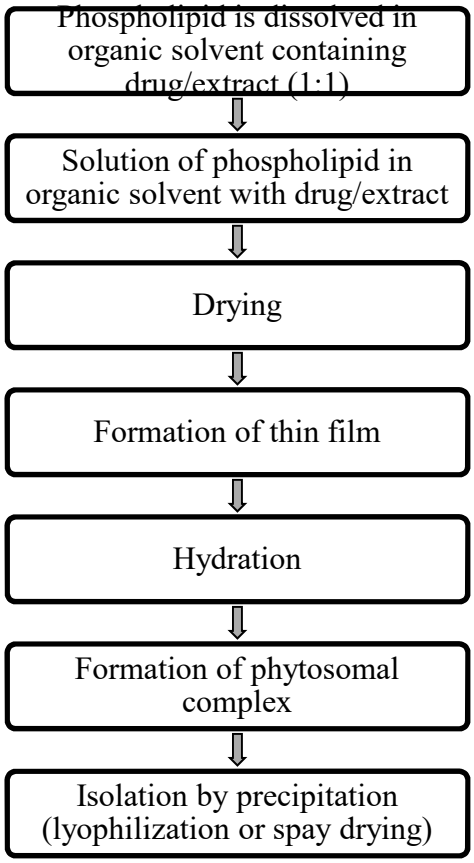

Figure 3: Preparation of Phytosome

Preparation Techniques:

One mole of phytoconstituent and two to three moles of phospholipid can react to form phytosomes, also referred to as phyto-phospholipid complexes. The reaction can be conducted in organic solvents or in aprotic solvents, such as dioxane, methylene chloride, and phyto-phospholipid complexes that are separated by lyophilization or non-solvent precipitation. Figure 3 illustrates the general steps involved in phytosome preparation.

As seen in (Fig. 4), common methods used to prepare phytosomes include solvent evaporation, anti-solvent precipitation, and co-solvent lyophilization.

Solvent evaporation:

In a round-bottom flask, phospholipids and phytoconstituents are combined with an organic solvent such ethanol. The solution is magnetically stirred for a few hours, then a rotary evaporator is used to evaporate the solvent under vacuum at 40 degrees Celsius. A thin layer forms on the flask wall following the evaporation of the solvent. The phytosomal dispersion is obtained by dispersing a thin film in distilled water.

Precipitation of anti-solvents:

The standardized phytoconstituent and phospholipids are placed in a round-bottom flask in the proper amount and dissolved in an aprotic solvent, such as acetone or dioxane. For complex formation, the solution is refluxed and agitated for a full night at a temperature not to exceed 600C. Precipitation is used to separate the complex from non-solvents such n-hexane. The precipitate was allowed to settle before being filtered and vacuum-dried at 400 degrees Celsius.

Co-solvent lyophilization:

Co-solvent lyophilization involves dissolving the phospholipid and phytoconstituent in distinct solvents. Additionally, both solutions are combined by either gentle agitation or constant stirring until a clear combination is formed. The complexes that are separated by cosolvent lyophilization of a transparent mixture under vacuum for a few hours are gathered and kept. [10-11]

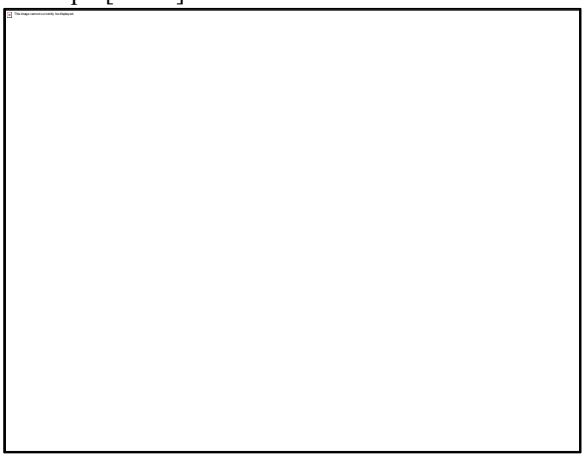

Figure 4: Common methods used to prepare phytosomes

Table 1: Phytosomes Preparation Using Varied Techniques [12]

S. No.	Herbal drug	Methods utilized	Characterization techniques	Inferences
1.	Mangiferin	Solvent evaporation and	DSC, TGA, FTIR,	Enhanced biopharmaceutical

		nanoprecipitation method	Power-XRD, H1-NMR, solubility studies, *in vitro* dissolution, oral bioavailability, and *in vivo* antioxidant studies.	and *in vivo* antioxidant potential.
2.	Rhein	Solvent evaporation, lyophilization and co-solvent evaporation method	FTIR, DSC, XRPD, solubility study, particle size, zeta-potential, TEM, *in-vitro* drug release, *in-vivo* characterization	Targeted different skin disorders through non-invasive topical application.
3.	Naringenin	Solvent evaporation and freeze - drying method	SEM, TEM, particle size and zeta potential, XRD, DLS, DSC	Developed sustained released dry powder inhaler for acute lung injury.
4.	Glycine max (L.) Merrill	Solvent evaporation, co-solvency, salting out	Particle size, entrapment efficiency, zeta potential, drug release, FTIR	Investigated for anti-obesity action
5.	Woodfordiafruticosa	Ethanol and reflux method	Percentage yield, entrapment efficiency, FTIR, particle size, zeta potential	Improved solubility and increased anti-oxidant activity
6.	Sinigrin	Solvent evaporation and anti-solvent method	Particle size, zeta potential, complex efficiency, TEM, DSC, FTIR	Enhanced cytotoxic effect and wound healing efficacy
7.	Diosmin	Solvent evaporation, salting out and lyophilization method	DSC, FTIR, drug content, solubility studies, TEM, *in-vitro* release studies *in vitro* self-phytosomal stability, *ex-vivo* intestinal permeation studies.	Increased dissolution and permeation
8.	Puerarin	Solvent evaporation and freeze-drying method	SEM, XRPD, DSC, IR, solubility and dissolution studies	Enhanced solubility and *in vitro* dissolution rate

Characterization of Phytosomes

1. Morphological Study

Phospholipids, amphiphilic molecules with one positive headgroup and two neutral tail groups, make up the majority of phytosomes. Furthermore, rubiadin became more soluble when combined with phospholipids to create a complex component. These TEM results revealed that phytosome formulation PC2 was more spherical than phytosome formulations PC1 and PC3. (Figure 5).

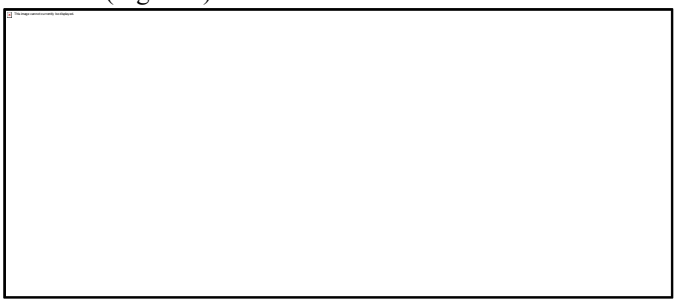

Figure 5. Photographs of PC2 formulations showing the (a) morphology of the phytosome

vesicles by TEM, and (b) particle size distribution of PC2 formulation.

2. ζ Potential, PDI, and Particle Size Distribution

The particle size distributions are reported in Table 1. The mean particle diameter for formulations PC1, PC2, and PC3 was 805.2 ± 1.4, 289.1 ± 0.21, and 721.5 ± 0.28 nm, respectively. The homogeneity of a particle in the dispersion is shown by the PDI. The PC2 formulation had the lowest PDI value of 0.127, which best demonstrated particle size uniformity (Figure 5). The stability of the ζ potential (range: + 30 to −30 mV) was assessed, and the values of the different formulations PC1, PC2, and PC3 were −5.85 ± 0.14 mV, −6.92 ± 0.10 mV, and −7.12 ± 0.23 mV, respectively.

Table 2. Mean Diameter (Dmean) of Particle Size, Polydisparity Index (PDI), ζ Potential, and % Entrapment Efficiency of Phytosome Formulationsa

Formulation	Size Dmean (nm)	PDI	ζ potential	% entrapment efficiency
PC1	805±1.4	0.285±0.03	-5.85±0.14	48.78±0.52
PC2	289.1±0.21	0.127±0.01	-6.92±0.10	84.32±0.22
PC3	721.5±0.28	0.207±0.02	-7.12±0.23	44.61±0.40

[a]All of the values are presented as the mean ± standard deviation (n = 3).

3. Entrapment Efficiency

While PC1 and PC3 formulations captured 48.78 and 44.61% of rubiadin, respectively, PC2 formulation entrapped 84.32% (Table 2). Because PC2 has the highest entrapment efficiency, it has been selected for more analysis. [13]

Conclusion:

Phytosomal delivery systems provide better bioavailability, stability, and therapeutic results while successfully addressing the pharmacokinetic issues of herbal medications. By resolving the bioavailability issues with herbal substances, phytosomes provide a promising development in natural medicine. Phytosome-based medicines appear to have a promising future because to their better formulation techniques and wide range of applications, particularly in regions where traditional treatments may be limited. Expanding the use of herbal treatments in modern medicine and improving clinical results could result from more study and development in phytosome technology. Phytosome technology has shown promise in overcoming bioavailability issues, leading to safer and more potent cancer treatment options. The potential of phytosome-based formulations as a novel strategy to anticancer therapy is highlighted in this study, encouraging additional development in preclinical, in vitro, and prospectiveclinical applications.

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