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SHORT REVIEW

Phytosomes: A Contemporary Method for Delivering Novel Herbal Drugs

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Abstract

Our country has a wealth of Ayurvedic expertise, but only recently has its full potential been recognized. Any herbal medication's efficacy depends on the medically active substance being delivered at an effective dosage. When given directly or externally, their bioavailability is severely constrained. With increased effectiveness, quality, and enhancement of active plant components, phytosome technology has evolved as a dedicated and hopeful means of delivering new drugs. Traditional herbal remedies have been used for a long time to successfully treat various types of illnesses, but their effectiveness has often been limited by the difficulty of getting the active compounds to their intended targets in the body. However, recent advances in herbal formulation technology have made it possible to create more efficient and targeted delivery systems for these compounds. This study emphasizes the special qualities of the phyto-phospholipid complex and how they are used in cutting-edge natural drug administration. The emphasis of the current review is on phytosome production and characterization methods, benefits, and significant developments.

Keywords: Herbal, Novel Drug Delivery, Phytosome, Phospholipid, Phyto-phospholipid Complex

1. Introduction

The use of plants for medicinal purposes dates back to the past when people got acquainted with the therapeutic consequences of various herb-based compounds. Plants contain a diverse array of secondary metabolites, such as flavonoids, alkaloids, terpenoids and phenolic acids, which have been found to possess medicinal properties. Several herb extracts have been subjected to chemistry and pharmacological investigations over the last century to be capable of their chemical constituents explaining and evaluating the consequences of traditional medicine. Phytosomes are a type of lipid-compatible molecular complex that is produced by using water-soluble phytoconstituents or standard plant extract to phospholipids. Indena, an established maker of pharmaceuticals and nutraceuticals, created this method of manufacturing. Phospholipids are a type of lipid that is naturally present in cell membranes. When plant extract or phytoconstituents are incorporated into phospholipids, it creates a molecular complex that is more easily absorbed by the body. This is because the phospholipids act as carriers, delivering the plant compounds directly to the cells that need them. It has been revealed that phytosomes have greatly improve the bioavailability as well as absorption of chemical substances derived from plants as well. In fact, research has demonstrated that phytosomes can improve the absorption of some compounds by up to 20 times compared to standard plant extracts. Phytosomes are commonly used in the production of dietary supplements and herbal remedies. They are used to boost natural compounds' absorption, minimise the total amount of active components required to provide the intended effect and raise their potency. Overall, phytosome technology is an innovative approach to

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improving the bioavailability of plant-based compounds, and it has the potential to enhance the effectiveness of many herbal remedies and dietary supplements[1]. To get entrance to the enterocyte cell membrane's lipid-friendly environment, the cell lining of the gut wall, phytosomes may emerge from a hydrophilic environment (for example, the gut). The phytosome's phospholipid structure parallels that of the cell membrane, permitting it to bind to the membrane and release plant compounds into the cell. Once inside the cell, the plant material can be transported to the bloodstream and their target tissues. This process enhances the bioavailability and effectiveness of the plant-based compounds, as more of the active ingredients are able to reach their intended targets[2]. Phytosomes have better pharmacological and pharmacokinetic parameters, making them useful in the therapy of chronic liver disease and infectious disorders. It is also useful in formulations for medicinal products and cosmetics, as well as a treatment for inflammation[3].

2. Structure of Phyto-phospholipid Complexes[4]

2.1 Phytosomes

Phytosomes are complexes formed between a phospholipid and phytoconstituents (active compounds derived from plants). For the formation of lipid-compatible molecular complexes referred to as phytosomes, it has recently become possible to add standard plant extract or water-soluble phytoconstituents into phospholipids (Figure 1). The interaction that occurs among the polar head of phospholipids and the structural components of plants leads to the formation of phytosomes. Phospholipids contain a phosphate group within their polar head, resulting in it being hydrophilic, hence attracted to water.

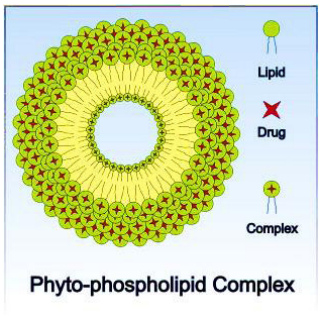


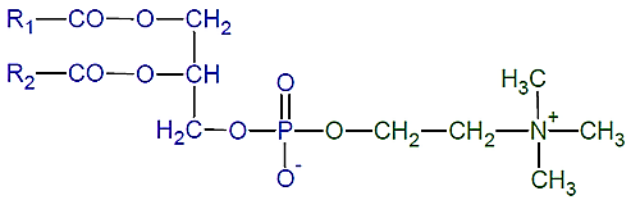
Figure 1. Structure of phyto-phospholipid complex.

The yielding of phospholipid compounds that have the phospholipids head group attached is rendered possible by the binding of phospholipids with active ingredients; yet, the complex fails to grow in accordance with both of those long fatty acid chains.

These complexes were able to develop a lipophilic surface due to the two prolonged chains of fatty acids of the phospholipids. These complexes may combine into agglomerates that resemble tiny cells and have a connection to liposomes when diluted in water. However, there are some differences between the two:

- Liposomes can be made in a range of sizes and can be unilamellar (a single lipid bilayer) or multilamellar (multiple lipid bilayers). Phyto-phospholipid complexes, on the other hand, tend to form smaller agglomerates that are not as well-defined in structure as liposomes.
- Liposomes can encapsulate both lipophilic and hydrophilic molecules, while phyto-phospholipid complexes are typically used to encapsulate lipophilic molecules.
- Liposomes have gone through major studies for use in drugs systems for administration, while phyto-phospholipid complexes are a relatively new technology with fewer studies published on their use.
- Overall, phyto-phospholipid complexes have some similarities to liposomes but are a distinct technology with their own unique properties and applications; Figure 2 exhibits the variation between complexes and liposomes.

Numerous studies have shown that phytosome results have much higher clinical potency and greater uptake than niosomes, as well as companies have



Note: Where R1 and R2 are the carbon chains such as fatty acids.

Figure 2. Structure of Phospholipid.

successfully used this technology in a variety of standardized flavonoid formulations. The chart below summarizes the key distinctions between liposomes and phytosomes (Table 1, Figure 3).

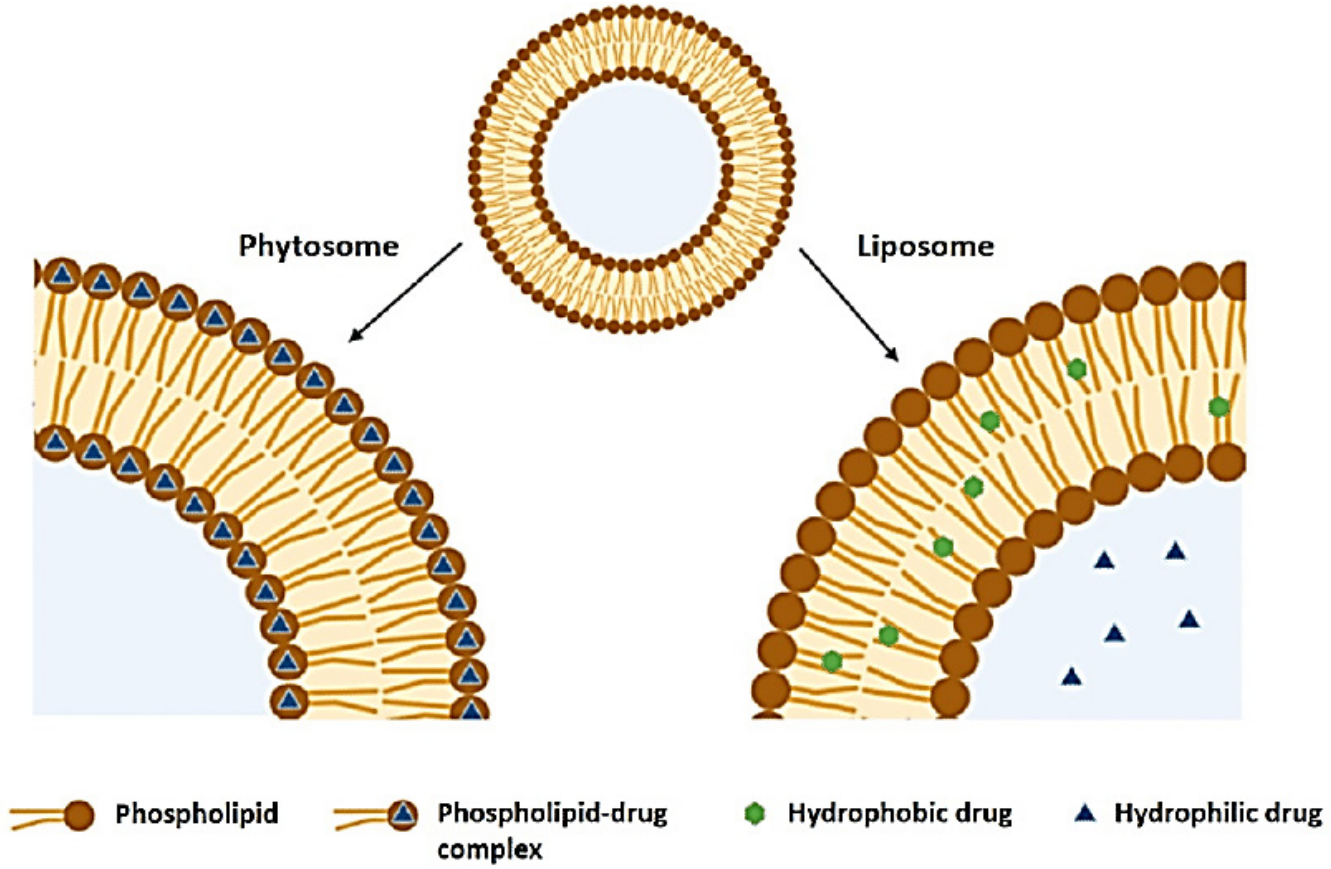


Figure 3. Difference between phytosome and liposome.

Table 1. The major difference between phytosomes and liposomes is as follows[5-12]

Liposomes	Phytosomes
These chemical components become dispersed in the membrane layer or cavity medium.	Chemical connections between this substance's active chemical components and the polar head of the phospholipid hold it in place.
There are currently no generating chemical bonds.	Chemical interactions occur.
The bilayer of the lipids membrane or the aqueous inside of the vesicles all contain the components that are active.	H-bonds hold the bioactive molecules close to the polar tip of the phospholipids.
The water-soluble molecule is bound in this by a number of phosphatidylcholine molecules.	In phytosome, phosphatidylcholine and plant compound form a 2:1 or 1:1 complex depending on the substances.
Formed in the presence of a buffer solution or water.	Act with solvents such as acetone, 1,4-dioxane, ethyl acetate and acetone.
The bioavailability of liposomes is less than phytosomes.	Phytosomes have higher bioavailability and are significantly more easily absorbed than liposomes.
Phospholipid content is considerably greater.	Contents of phospholipids are less high.
Skin absorption has decreased.	Raised more skin absorption
Substantially decreased stability.	Enhanced stability.

3. Phytosome Complex Components

3.1 Principle of Phytosome Technology[13]

The substance called phosphatidylcholine, also referred to as phosphatidylserine, has a pair of functions. The choline (serine) portion is hydrophilic, whereas the phosphatidyl moiety is lipophilic. Because of its double absorption, phospholipids act as potent emulsifiers. Thus, the phosphatidylcholine molecule's choline head makes bonds in these elements, and the lipid-soluble phosphatidyl a part, comprising the tail and body, covers the choline-bound component. As a result, as confirmed, the phytoconstituents and phospholipids develop a molecular molecule that is ideal for lipids (also known as a phyto-phospholipid complex).

3.2 Phospholipids[14]

Phospholipid methods of delivery made in industry nowadays play an integral part and have become more prevalent. To do this, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine and sphingomyelin are the essential components. The primary active component in all of this is phospholipid, which is formed by a glycerol unit attached to a phosphate group, with two fatty acids completing the association. Phosphatidylcholine, a phospholipid with an essential function in biological membranes and hepatoprotective characteristics, is the most significant phospholipid applied in phytosome synthesis.

Nowadays industrially produced phospholipid delivery systems, such as phytosomes, have gained popularity due to their potential benefits in various applications. Phytosomes are specifically designed to enhance the efficacy and bioavailability of bioactive compounds, particularly plant extracts.

Phospholipids play a crucial role in these delivery systems, and phosphatidylcholine is one of the most prominent phospholipids working. A glycerol unit is attached to two fatty acids to form the phospholipid phosphatidylcholine, and a phosphate group makes the link between them. It is an essential component in human memories and is present in many natural sources, especially soy and chicken eggs.

Phosphatidylcholine has several important functions in the body. It acts as a building block for cell membranes, providing structural integrity and fluidity. Additionally, it plays a role in lipid metabolism, transport, and signalling processes. In the context of phytosomes, phosphatidylcholine acts as a carrier molecule for bioactive compounds, facilitating their absorption and delivery to target tissues.

Furthermore, phosphatidylcholine has been studied for its hepatoprotective properties. it has been shown to support liver health and protect against liver damage in various conditions. This makes it a valuable component in phytosome formulations aimed at improving liver function and protecting the liver from toxic substances.

Overall, phospholipids, particularly phosphatidylcholine, are key ingredients in industrially produced phospholipid delivery systems like phytosomes. They play a vital role in enhancing the delivery and bioavailability of bioactive compounds and offer additional benefits such as hepatoprotective effects.

3.3 Phyto-active Constituents[15]

Instead of focusing on in vivo activities, researchers normally employ significant in vitro pharmacological effects to figure out the active substances of plant extracts. A great deal of these compounds are polyphenols. Hesperidin is one of the physiologically active polyphenolic substances from plants that favour the aqueous phase and is unable to cross biological membranes. Others, rutin and curcumin, have strong lipophilic and cannot break down in aqueous gastrointestinal secretions.

Phytosomes can form complexes with hydrophilic polyphenols, creating structures that can easily interact with and penetrate cellular membranes. The phospholipid component of the phytosome can help facilitate the transport of hydrophilic polyphenols across biological barriers, increasing their bioavailability and potential therapeutic effects.

Therefore, by utilizing phyto-phospholipid compounds like pyrosomes, both lipophilic and hydrophilic polyphenols can be effectively delivered and absorbed in the body, overcoming their inherent solubility and membrane permeability limitations. This can lead to improved therapeutic outcomes and enhanced utilization of the beneficial properties of polyphenolic compounds found in plants.

Furthermore, complex formation can shield polyphenols from external variables such as oxidation, photolysis, and hydrolysis.

3.4 Solvents[15-20]

Indeed, the choice of solvent is an important consideration in the formation of these complexes and can significantly impact their properties and characteristics.

The formation of phyto-phospholipid complexes has traditionally been done using aprotic solvents such as aromatic, halogen derivatives, hydrocarbon, methylene chloride, ethyl acetate, or cyclic ethers. These solvents offer good solubility for both the phytochemicals and phospholipids, facilitating the formation of complexes. However, they may have drawbacks such as toxicity, environmental concerns, or residual solvent issues.

There has been an upsurge in recent years in the use of protic solvents like ethanol and methanol for making phospholipid complexes. Protic solvents are desirable because they are less dangerous, less harmful to the environment, and simple to get rid of. Ethanol, since it is less harmful, environmentally friendly, and simple to eliminate. Ethanol, in particular, has gained popularity as a solvent for forming phyto-phospholipid complexes. It can effectively solubilize both the phytochemicals and phospholipids and can be removed under controlled conditions, leaving minimal residue and causing less harm.

In the context of liposomal drug compounds or phytosomes that interact with a solvent with a lower dielectric constant, buffer solution or water is often used. These solvents provide an environment suitable for the interaction and formation of the complexes, and their use aligns with the physiological conditions in which these compounds may be administered.

Furthermore, the Supercritical Fluid (SCF) method, particularly the Supercritical Anti-Solvent (SAS) process, has emerged as an optimistic for producing submicronic and micronic particles with size distribution and controlled size. SCF technology utilizes supercritical fluids, which are substances above their critical temperature and pressure, to manipulate the formation and characteristics of the complexes. This approach offers advantages such as mild processing conditions, solvent-free nature, and the ability to control particle size and morphology.

Overall, the selection of a solvent in the development of phyto-phospholipid complexes depends on various factors including toxicity, solubility, environmental impact, ease of removal, and the desired properties of the final product. Researchers consider these factors to select the most suitable solvent that meets their specific requirements and ensures the successful formation of high-quality complexes (Table 2).

4. Stoichiometric Relationship between Phospholipids and Active Ingredients[21-25]

A natural or synthetic phospholipid has frequently reacted with its active constituents in a molar ratio that varies from 0.5 to 2.0 resulting in the phyto-phospholipid molecule. On the other hand, it has been proposed that the best stoichiometric ratio for making phospholipid complexes is 1:1. For instance, quercetin-phospholipid molecules are generated by merging Lipid S-100 and quercetin in a 1:1 molar ratio.

Table 2. Recipients in phytosomes development

Chemical	Example	Uses	References
Solvents	Acetone, methylene chloride, dioxane	As an Aprotic solvent	26
Non-solvents	n-hexane or aliphatic hydrocarbons	Complex precipitation	26
Phospholipid	Distearylphosphatidylcholine, egg phosphatidyl choline, soyaphosphatidylcholine, phosphatidyl choline, dipalmitoylphosphatidylcholine	Cellular vesicles generating component	27, 28
Alcohols	Methanol, ethanol	solvent	29-31
Buffering agents	7 % v/v ethanol tris buffer (pH 6.5) and Saline phosphate buffer (pH 6.5)	Hydrating medium	30, 31
Colour and Dyes	DHPE-rhodamine, fluorescein	Study with cono-focused scanning laser microscopy	32, 33

However, unique stoichiometric ratios of active components and phospholipids have been used, with Maryana *et al.*, producing silymarin-phospholipid complexes with stoichiometric ratios of 1:15, 1:10, and 1:5 and identifying those complex structures with a stoichiometric ratio of 1:5 had the greatest physical characteristics and the maximum loading capacity of 0.30% 12.18%. As a result, a stoichiometric number of 1:1 is not always optimum for phospholipid complex formulation. For various kinds of pharmaceuticals, we should try with varying stoichiometric ratios of active components and phospholipids for different objectives, such as maximum drug loading.

5. Properties of Phytosomes[34,35]

Following are some of the important properties of phytosomes.

5.1 Physical Chemical

- The process of creating phytosomes involves reacting a phospholipid in an amount that is stoichiometric with the plant extract. The phospholipids used are typically derived from natural sources such as soybeans or sunflower lecithin. These phospholipids consist of a polar head, which contains a phosphate group and an ammonium group, and two hydrophobic tails.
- Phytosomes are in different sizes vary from 100 µm to 50 nm.
- The method termed Photon Correlation Spectroscopy (PCS) is used for evaluating the size and movement of particles in a solution. It can be employed to study the structure of liposomes and micelles, including those formed by phytosomes. By measuring the fluctuations in the intensity of light scattered by the particles, PCS can provide information about their size, distribution, and behaviour.
- When PCS is applied to phytosomes treated with water, it can reveal the presence of liposomal structures formed by the phytosomes. The characteristic fluctuations in light scattering patterns obtained through PCS analysis can confirm the formation of micelles structures similar to liposomes, indicating the self-assembly of phytosomes in an aqueous environment.
- Overall, the interaction of phytosomes with water can lead to the formation of liposomal structures, and PCS can be used as a technique to confirm and study the characteristics of these structures.
- According to the C13 NMR and H1 NMR data, the chain of fatty acids provides unaltered Long aliphatic chains that have been bound around the lipophilic group, which is one of the signals in both the free complex and the phospholipid.
- These compounds are volatile in alcohol and insoluble in water. They are very soluble in aprotic solvents and readily soluble in lipids.

5.2 Biological Properties

Phytosomes are unique complexes that are more absorbed and administered than standard herbal extracts or non-complex extracts, raising bioavailability and giving superior effects. Examples of this are pharmacodynamics studies on humans and laboratory animals as well as pharmacokinetic studies.

6. Advantages of Phytosomes[36,37]

- The bioavailability of plant preparations can be greatly increased by complexing them with phospholipids through the process of phytosomes. Phytosomes are a useful strategy in the field of herbal medicine and nutraceuticals because of their elevated bioavailability, a property that contributes to faster absorption, boosted therapeutic efficacy, and maybe even lower essential dosages.
- By accessing the non-lipophilic plant extract, they raise intestinal lumen intake.
- The Phytosome formulation has been proven safe and both therapeutic and cosmetic purposes for every material has been approved.
- Considering that phytosomes are capable of rendering liver-protective flavonoids easily accessed, they have been utilized to transport such substances. Phosphatidylcholine also acts as hepatoprotective, which has an advantageous impact on protecting the liver.
- The approach allows the delivery of phytoconstituents at an affordable cost and offers a wide

range of advantages when applied as functional cosmetics that protect the dermis from exogenous or native dangers under both normal and stressed circumstances.
- They can also be utilized to enhance the transdermal and dermal absorption of medications through the epidermis.
- These serve as transportation hubs for a variety of medications. (Protein molecules and peptides).
- The vesicular device is non-intrusive, passive, and immediately available for commercialization.
- Phosphatidylcholine, an important component of the cell membrane used in phytosome information, functions as a carrier and dermal nutrition.
- Drug trapping is not an issue during formulation production.
- As the drug makes spheres after linking with lipid, trapping efficacy is also high and predictable.
- Due to the chemical connections that develop between the molecules of phytoconstituents and the phosphatidylcholine, they have a better stable profile.
- The required dosage is reduced as a result of improved main component absorption. To get the desired results, they can also be taken in lesser amounts.
- Relatively simple to make, requiring little complicated technological investment in Phytosome production.

7. Disadvantage

- The phytoconstituent is quickly removed from the phytosome.

8. Advances in Phytosome Technology

- The main constituent of *Bacopa monnieri* known as bacopaside has antiamnesic properties. Making phytosomes from bacopaside and testing them on rats in vivo are the objectives of this study. The molecule created by phospholipid has a significantly different therapeutic effect from the crude *B. monnieri* extract[38].
- The creation of berberine phospholipid combination solid dispersion, which increases the compound's ability to flow and disintegrate rate for commercial application while boosting its solubility, is shown through additional inquiry[39].
- Further research indicates that sinigrin phytosome can be developed. When compared to sinigrin alone, the research's findings have significance for its in vitro wound healing potential[40].
- On the basis of one study, broiler chicks were significantly protected from B1 aflatoxin and silymarin phytosomes had a higher antihepatotoxic activity than silymarin alone[41].
- The conventional *S. marianum* seed extract's phytosomes have a significant negative effect on the growing baby from maternal alcohol usage when taken orally[42].
- One clinical study showed that giving silybin phytosome to 232 chronic hepatitis patients at a dosage of 120 mg either two or three times up to 120 days greatly affected the resumption of liver function[42].
- Grapefruit seed in ischemia-induced heart damage and atherosclerosis prevention, phytosomes are also essential. Procyanidins and proanthocyanidins are the main components that trigger this[43].
- *Camellia sinensis* or green tea extract has better oral bioavailability when integrated in phytosomes when compared to uncomplexed green tea extract. Green tea's primary active component is epigallocatechin 3-o-gallate[44-46].
- Following a clinical experiment, it was shown that green tea's caffeine-free phytosomes substantially enhanced antioxidant and anti-obesity actions. It lowers LDL cholesterol as well[37-49].
- Liver damage induced on by carbon tetra chloride in rats is better cured by quercetin phytosomal complex[50].

9. Some Commercial Registered Phytosome Products

There have been multiple attempts made to market Phytosome, and some of them are given in Table 3 with their commercial formulations and intended medicinal applications.

Table 3. Commercial registered phytosome products

Sr. No.	Name of Plant Drug	Botanical Source	Chemical Constituent	Marketed Product	Use	References
1.	European Chestnut	*Aesculus hippocastanum*	Saponins	Escin β sitosterol Phytosome™	Vasoactive properties and Anti-oedema	51
2.	*Ammi visnaga*	*Ammi visnaga*	Visnadine	Visnadex™	To strengthen microcirculation	51
3.	*Madukparni*	*Centella asiatica*	Madecassic acid	Centella triterpenoid Phytosome™	skin disorder and anti-ulcer	51
4.	Mayblossom	*Crategus oxyacanthoides*	Quercitin and hesperin	Hawthorn Phytosome™	Antihypertensive, Nutraceutical and cardioprotective	51
5.	Maidenhair Tree	*Gingko biloba*	Gingko flavonoids and Ginkgolides	Phytosome™ Gingko	Antiageing, anti-asthmatic	51
6.	Soya bean	*Glycine max*	Genistein and daidzein	Soyselect Phytosome™	Cardioprotective and increase immunity	51
7.	Sweet wood	*Glycyrrhiza glabra*	Glycyrrhetinic acid	Glycyrrhetinic acid Phytosome™	As a dermatitis and anti-inflammatory	51
8.	*Panax ginseng*	*Panax ginseng*	Ginsenosides	Ginseng Phytosome™	Immunomodulatory and nutraceutical	51
9.	Broomcorm millet	*Panicum miliaceum*	Mineral salts, vitamins and amino acids, unsaturated fatty acids,	Millet Phytosome™	Use as anti-stress	51
10.	*Ruscus aculeatus*	*Ruscus aculeatus*	Ruscogenin, neoruscogenin	Ruscogenin Phytosome™	Anti-aging, Sunscreen agent, and anti-inflammatory	51
11.	Yellow Sandal-wood	*Santalum album*	Ethyl ximenynate and ximenynic acid	Ximilene Phytosome™	Improve circulation	51
12.	Jambu	*Syzygium cumini*	Tannins	Madeglucyl Phytosome™	Antihyperglycemic	51
13.	Whortleberry	*Vaccinium angustifolium*	Anthocyanosidestocotrienol complex	VitaBlue Phytosome™	Improves vision, memory enhancer and anti-oxidant	51
14.	Tumbara	*Zanthoxylum bungeanum*	Hydroxy-a-sanshool	Zanthalene Phytosome™	Anti-reddening	51
15.	Bitter orange tree	*Citrus aurantium*	Naringenin	Naringenin Phytosome™	Antioxidant	51,52
16.	Gourd	*Cucurbita pepo*	Steroids, carotenoids and tocopherols	Cucurbita Phytosome™	Benign prostatic hyperplasia and Anti-inflammatory,	51,53
17.	Manna ash	*Fraxinus ornus*	Esculoside (Esculin)	Esculoside Phytosome™	Anticellulite and vasoactive	51,54
18.	Draksh	*Vitis vinifera*	Resveratrol	Biovin and leucoselec	Cardioprotective	51,54

Table 3. Continued...

Sr. No.	Name of Plant Drug	Botanical Source	Chemical Constituent	Marketed Product	Use	References
19.	Chai ki patti	*Camellia sinensis*	Epigallocatechin	Green tea Phytosome™	Anticancer	51,57
20.	Silver cluster	*Terminalia serica*	Sericoside	Sericoside	Anti-aging, skin restructuring	51,64
21.	Melilotus	*Melilotus officinalis*	Terpenoids and flavanoids	Lymphaselect™	Thrombophlebitis and anti-inflammatory	54
22.	Dwarf olive	*Olea europaea*	Tyrosol	Oleaselect Phytosome™	Anti-inflammatory,	54
23.	Cabbage palmetto	*Serenoa repens*	Phytosterols	Phytosterols	Noncancerous prostate Enlargement	54
24.	European blueberry	*Vaccinum myrtillus*	Anthocyanosides	Mirtoselect Phytosome™	Antioxidants, vasoprotective and antiinflammatory	54,49
25.	Silymarin	*Silybium maranium*	Silybin, silycristin, isosilbin	Silybin Phytosome™	Hepatitis, cirrhosis, inflammation, and hepatoprotective	55,65
26.	*Haldi*	*Curcuma longa*	Curcuminoids	Curcumin Phytosome™	Anti-inflammatory, anticancer and osteoarthritis	55,56
27.	Purple coneflower	*Echniacea angustifolia*	Echinacosides and insulin	Echinacea Phytosome™	Immunomodulatory and nutraceutical	58
28.	Pine	*Pinus maritime*	Procyanidins	Pycnogenol Phytosome™	Antiwrinkle	59
29.	Japanese arrowroot	*Radix puerariae*	Puerarin	Puerarin and phospholipid complex	Cardiovascular diseases and anti-inflammatory	60,61
30.	*Chirata*	*Swertia alternifolia*	Xanthones 26	Swertia Phytosome™	Decreasing blood sugar level	62,63

10. Methods for the Preparation of Phytosome Complexes[64-68]

10.1 Different Methods of Preparation

Phytosome compounds are typically built using unconventional techniques. Modernistic herbal complexes are produced in aprotic organic solvents by the reaction of an equimolar combination of medicinal compounds or plant extract and natural or combined phospholipids. The following are some needed methods.

10.2 Anti-solvent Precipitation Process

Under exact testing conditions at temperatures below 50°C, a specified quantity of phospholipids and an herbal extract are reacted with 20 ml of an organic solvent, such as acetone for 2-3 hours. A low polarity solvent, such as n-hexane, has been added to the reaction mixture while it is being stirred frequently, and precipitates are generated. The reaction mixture becomes concentrated to a minimum amount of 10 milliliters. Desiccators are used for preserving filtered precipitates. Pulverized desiccated precipitates are kept at room temperature in a dark amber glass container with a powdery complex.

10.3 Rotary Evaporation Process

In a round-bottomed glass container, 30 cc of a water-miscible organic liquid, such as acetone, was added. Phospholipids followed, and the mixture was stirred

constantly for two hours at a temperature under 50°C in a rota evaporator. An antisolvent, such as n-hexane, can be used to remove the thin layer that forms after continual stirring with an agitator. The resulting phytosome precipitate can be preserved in an amber-colored glass container with monitored humidity and temperature.

10.4 Solvent Ether-Injection Process

This approach uses an aqueous phase interaction among lipids dissolved in organic fluid and plant preparations. The plant substances to be encapsulated are dissolved in an aqueous solution and incorporated using phospholipids in diethyl ether, drop by drop. Cellular vesicles emerge when the fluid is withdrawn, which results in the development of complexes. Concentration has an impact on the shape of phytosomes; at low amounts, monomer amphiphiles are created; at higher concentrations, a number of structures with various morphologies, including spheres, cylinders, discs, and hexagonal or cubic vesicles, may develop. Techniques that are innovative: Supercritical fluids, which include the gas solvent approach, are among the novel techniques for phospholipid Complexation.

10.5 Complexation Rate (Yield) of the Phytosomes[69]

For order screening, the amount produced of active components combined with phospholipids is an essential indicator. The total amount of the active ingredient when mixed with phospholipids is denoted by the weight variations between the unbound particles and the first active ingredient. The formula is as follows:

$$\text{Yield (\%)} = [(a - b)/a] \times 100\%$$

Where "a" is the weight or content of the initial active constituent, "b" is the weight or content of the free active constituent, and "(a – b)" is the weight or content of the phospholipid complexes.

The yield can also be determined by UV spectrophotometry or High-Performance Liquid Chromatography (HPLC) according to the distinctive properties of the ingredients that are active. The choice of solvent, temperature, duration, medicine concentration, and stoichiometric ratio of the medicines to phospholipids are the primary factors that affect the production of phospholipid complexes.

11. Characterization of Phytosome Structure[70-72]

11.1 Partition Coefficient and Solubility

The capacity to dissolve in organic solvents or water, as well as the water/n-octanol partition parameter (P), must be measured in order to define active components, active ingredient phyto-phospholipid complexes, and physical mixtures. Active components frequently possess lower lipophilicity and hydrophilicity than phyto-phospholipid complexes, which typically have higher lipophilicity. Rahila proved that n-octanol and water are more soluble in complex embelin than in embelin and its physical combination drugs.

11.2 Zeta Potential and Particle Size

Zeta potential and particle size are key complex properties related to stability and homogeneity. Phospholipid complexes typically have particle sizes between 50 nm and 100 m. Mazumder discovered sinigrin phytosome complexes, which had an average particle size of 153 39 nm. and a zeta potential of 10.09 0.98 Mv.

11.3 Scanning Electron Microscopy (SEM) and Transmission Electron Microscopy (TEM)

SEM has greatly improved our understanding of the surface shape and solid-state properties of complexes. The examination of the aggregation and diffusion of nanomaterials, as well as measurement of nanoparticle size, is frequently carried out using TEM. SEM may be utilised for observing highly crystalline forms of active chemicals; however, the structured crystals disappear following complexation. When dispersed in distilled water with moderate agitation, phyto-phospholipid complexes have small vesicle-like structures, according to TEM.

12. Verification of Phytosome Complexes' Structures

12.1 Ultraviolet Spectra (UV-spectra)

Samples can be used to explain their own structural properties by changing their UV wavelength region absorption. A majority of research efforts have not discovered any variations in the components' UV absorption characteristics prior to and after

complexation. These distinctive luteolin peaks remained present in the luteolin-phospholipid complexes created by Xu *et al*[73]. Consequently, we conclude that phospholipid complexation has no effect on composite chromophores.

12.2 Differential Scanning Calorimetry (DSC)

Transition temperatures, the development of additional peaks, the disappearance of previous peaks, melting points, and fluctuations in relative peak area may all be used to determine interactions in DSC. Phyto-phospholipid complexes frequently show peaks that are radically different from those of a physical combination. The active components have been shown to be vulnerable to strong interactions with both of the fatty chains of phospholipids as well, and the polar portion of phospholipids further prevents free rotation. Rutin-containing phyto-phospholipid complexes were formed by Das and Kalita, and the Rutin and PC peaks disappeared[74]. Their DSC thermogram showed two distinct peaks that were smaller compared to the rest of the physical mixture as a result.

12.3 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR is a successful approach of investigating structures because it generates a range of functional groups with different location, band number, intensity, and shape characteristics. By comparing the phospholipid complex spectroscopy to that of physical combinations, it is essential to verify the growth of phyto-phospholipid complexes. Different results from independent studies are possible. In reality, rutin-based phyto-phospholipid molecules were made by Das and Kalita. A physical amalgamation of Rutin and phyto-phospholipid molecules produced an FTIR that was identical to that of pure Rutin[75]. Sinigrin-phytosome complexes have been developed by Mazumder *et al*., and the FTIR of the complex exhibited variances from phospholipids, sinigrin, and their mechanical mixes[76].

12.4 X-ray Diffraction

The microstructure of both some amorphous materials and some crystal materials may currently be explored well using X-ray diffraction. Active components, referred to as phyto-phospholipid complexes, PCs, and their physical combinations often get subjected to X-ray diffraction. Strong crystalline peaks can be observed in the X-ray diffraction pattern of a dynamic element and physical combination, which suggests a high crystal form. On the contrary, active component phyto-phospholipid compounds lack a crystalline peak, indicating that the components take on a molecular or amorphous structure when combined with phospholipids. This might be responsible for the greater lipophilicity and hydrophilicity of phyto-phospholipid compounds compared to their active components[77].

12.5 Nuclear Magnetic Resonance (NMR)

The structures of the compounds may be identified via the 13C and 1H NMR techniques. As previously noted, interactions among polyphenols and phospholipids are carried out by hydrogen bonds rather than molecular bonds. Based on NMR details, Angelico *et al*., came to the conclusion that silybin[78]. Phospholipid and polar phenolic functional groups can form hydrogen bonds. The spectra for multiple phyto-phospholipid complexes demonstrate that the lipids' hydrophobic side can function to cover the core choline-bioactive regions of a complex[79].

13. Conclusion

The phyto-phospholipid complex method has developed as an advanced edge element in determining herbal extract systemic absorption. The inappropriate doubts about plant-based medications have been successfully addressed with this technique. More active biomarkers can go to the designed site of action through aiming for specified lipid permeation at greater concentrations with raised and stable therapeutic levels in plasma. These novel complexes, on the other hand, have the potential to be dependable options for better medication dosage treatment. As previously stated, phytomedicines have long been used to treat the world and are now widely accepted. Initially used in makeup, phytosome complexes are now extensively used in treatments such as anti-inflammatory, cardioprotective, antioxidant, antitumor, anticancer, and liver protection. A new composition tool termed the function of herbals is described by phytosomes in contemporary medicine targeting efforts.

14. References

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