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PHYTOSOMES: A NOVEL STRATEGY TO IMPROVE BIOAVAILABILITY OF ACTIVE CONSTITUENTS

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ABSTRACT

"Phyto" refers to a plant, while "some" implies a cell. The term "autosomes" describes a novel patented method that increases bioavailability and absorption by combining standardised botanical extracts or water-soluble botanical components with phospholipids to create lipid-compatible molecular complexes. Based on recent advances and research by many researchers, the transdermal method has been carefully studied to determine its potential as a delivery system for botanical ingredients. Plant-based products and extracts are increasingly being recognized for their potential as nutritional supplements in managing inflammation, toxicity, malignancies, weight loss, and various chronic diseases or conditions. However, these products often suffer from bioavailability and stability issues. After separation, plant material will not be stable and will not pass through biofilms. Through practice, these activities are reduced to a reasonable level. To improve their suitability for drug administration, phytosomes—also known as phytosome technology—increase the hydrophilicity of medications that are otherwise exceedingly lipophilic. Also, they make hydrophilic plant components more lipophilic, which improves their transport across biological systems. It has been determined that the plant body can be used for cosmetic purposes. This article not only compares liposomes and phytosomes but also highlights the latest advancements in phytosome technology, with particular emphasis on transdermal drug delivery systems and phospholipid complexes. Many commercial products, including ginkgo, milk thistle, and tea tree, contain phytopharmaceutical compounds.

KEYWORDS: Phytosome, Bioavailability, phospholipids, autosomes.

INTRODUCTION

Botanical extracts are combined with phosphatidylcholine to form phytosomes, a new drug delivery technology that improves the phytopharmacological properties of many botanical drugs. Combine the terms “phyto” and “some” (referring to plant and cell structures) to form the term “phytosome”, sometimes called “autosome” in writing.[1]

The phytosome technique was created by the Italian firm Indena s.p.A. and enhances the efficacy of phytomedicines by including phospholipid samples, which improve their absorption and utilisation.[2]

The phytosome is a new vesicular drug delivery system that boosts the bioavailability and absorption of hydrophilic phytochemicals or plant extracts, allowing them to circumvent the drawbacks and side effects of traditional remedies.[3]

STURCTURE OF PHYTOSOMES

Standardized polyphenolic plant extracts are mixed with phospholipids, primarily phosphatidylcholine (PC), to form the structure of the plant body.[4]

The polar head of phospholipids interacts with active substances to generate phytosomes. There is no involvement of the phospholipid complex's two lengthy fatty acid chains in its formation. Phospholipid head group stabilisation is really achieved by interactions with active components, rather than the other way around. A lipophilic environment may be created by allowing the two long fatty acid chains to revolve around the polar region of the molecule. When diluted with water, the plant stem forms aggregates that resemble small cells and share some properties with liposomes. Phytosome are somewhat similar to liposomes.[6]

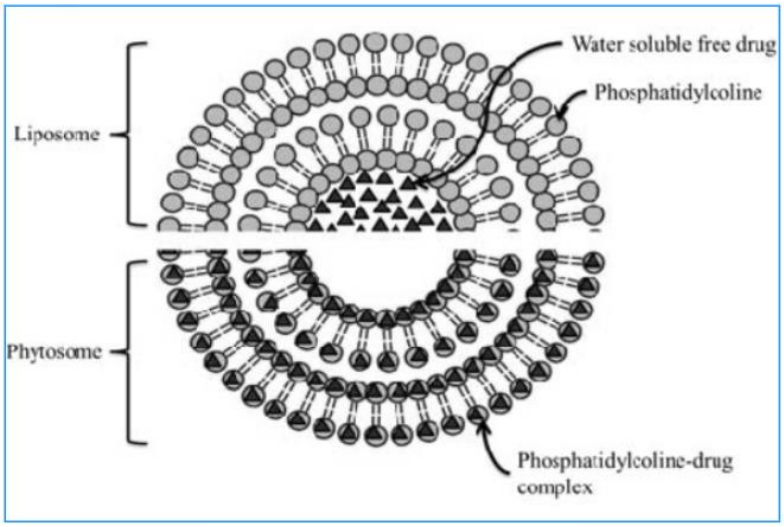

Figure 1: Structure of Phytosome.

Table 1: Distinctive Features Of Phytosomes And Liposomes.[7,8]

Liposomes	Phytosomes
The medium containing the film or cavity contains the active ingredients.	The active component, a crucial component of the membrane, is provided by molecules that are stabilised by hydrogen bonds to the polar head of the phospholipids.
There are no chemical bond formations.	There exist chemical bond formations.
These are phospholipid-based spherical vesicles with a bilayer that surround aqueous liquids containing specific medications and nutrients.	They are combinations of phospholipids and organic active substances.
Both hydrophilic and hydrophobic compounds are delivered via liposomes.	Phytosomes primarily transport poorly soluble plant-based compounds, such as terpenes and flavanones.
Compared to phytosomes, liposomes have a lower bioavailability.	Compared to liposomes, phytosomes have superior absorption and bioavailability.

PHYTOSOMES COMPONENTS

Phospholipids are produced during the extraction process or when polyphenolic compounds such as flavonoids, terpenoids, tannins, and xanthones are combined with stoichiometric amount of phospholipid (phosphatidylcholine) in non-polar complex solvents.[9] Hydrogen bonding creates a lipid vesicle that phopholiposomes are made of: the polyphenol component of the bioactive herbal extract and the phosphate group of the phospholipid matrix in a nonpolar solvent.[10] The tail incorporates phytoconstituents bound to choline that are water-soluble because of the lipophilic portion of the phospholipid. Phytochemicals like flavonoids and terpenoids, which are water-soluble and contain polyphenolic rings, are chemically bound to phosphate and have a great affinity for it. This interaction forms the main structure of the phytosome.[11, 12, 13]

Phospholipids

Plant seeds and egg yolk are rich sources of phospholipids. Glycerophospholipids and sphingomyelins are two types of phospholipids distinguished by their backbone structures. Phoridyl choline (PC), phosphatidyl ethanolamine (PE), phosphatidyl serine (PS), phosphatidic acid (PA), phosphatidyl inositol (PI), and phosphatidyl glycerol (PG) are all glycerophospholipids.[14]

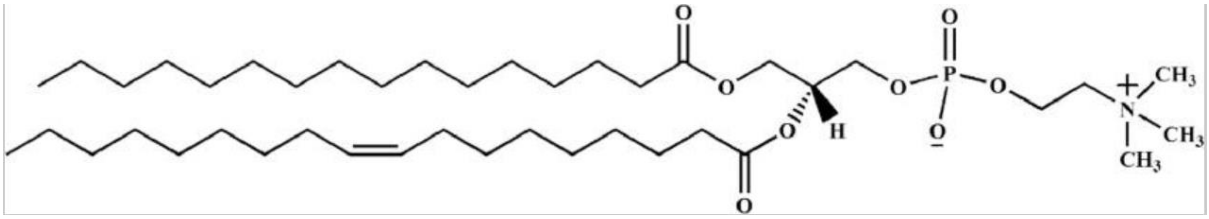

Figure: Structure of Phosphatidylcholine (PC)[15]

Phyto-active constituents

The significant in vitro pharmacological effects of botanical extract active components attract the majority of research attention, overshadowing concerns about these compounds' in vivo activities. Polyphenols make up the bulk of these active ingredients. Some physiologically significant polyphenolic compounds found in plants, such as hesperidin, prefer the aqueous phase and are unable to penetrate biofilms. On the other hand, some compounds, such as curcumin, are highly lipophilic and insoluble in gastric juice. Phospholipid complexes improve the water-permeability of hydrophilic polyphenols and the water-solubility of lipophilic polyphenols. Complex synthesis also shields polyphenols from environmental threats including oxidation, hydrolysis, and photolysis.[16] Table:2 lists a few phytosomes that are available in the market.

Table 2: Therapeutic Applications Of Different Phytosomes In The Market.[17, 18, 19, 20, 21]

S.no.	Trade name	Phytoconstituents complex	Indication
1.	Ginkgoselect® phytosome	Ginkgo flavono glycosides from Ginkgo biloba	Shields the vascular lining and brain.
2.	Silybin phytosome	Silybin from silymarin	Protects the skin and liver from free radical damage.
3.	Glycyrrhiza phytosome	18-beta glycyrrhetinic acid	Anti-inflammatory activity
4.	Sabalselect® phytosome	An extract of saw palmet to berries through supercritical CO_2 (carbondioxide) extraction	It helps keep the prostate functioning normally.
5.	PA2 phytosome horse Chestnut bark	Proanthocyanidin A2 from	Anti-wrinkles, UV protectant
6.	Zanthalene phytosome	Zanthalene from zanthoxylum bungeanum	Soothing, anti-irritant, anti-itching
7.	Centella phytosome	Terpenes	Vein and skin disorders
8.	Hawthorn phytosome™	Flavonoids from Crataegus sp.	Nutraceutical, cardio-protective and antihypertensive

Solvents

A wide range of solvents have been investigated and shown to be effective. When the yield of phospholipid complexes is high enough, ethanol is a safe and effective solvent that leaves minimal residue and does little harm. Some liposomal complexes work by allowing the plant body to interact with a low dielectric solvent in the presence of water or in the absence of solution.[17]

Stoichiometric ratio of active constituents and phospholipids

Phospholipid complexes are usually made by reacting active substances with either synthetic or natural phospholipids in a molar ratio ranging from half to two.22 Nevertheless, it is believed that a 1:1 stoichiometric ratio is optimal for the synthesis of phospholipid compounds.23 As an example, a quercetin-phospholipid complex is formed when Lipoid S 100 and quercetin are mixed in a 1:1 molar ratio.24 But scientists have used a wide range of phospholipid to active component stoichiometric ratios. Consider the silymarin-phospholipid complexes that Mariana et al. made using various ratios, such as 1:5, 1:10, and 1:15. The researchers found that the complex with a 1:5 ratio had the best physical properties and the largest loading capacity at 12.18% ± 0.30%. Oxymatrine-phospholipid complexes were made at stoichiometric ratios of 1:1, 1.4:1, 2:1, 2.6:1, and 3:1 in a different investigation by Yue et al. They found that the 3:1 ratio yielded the best results.[26] Hence, it's evident that a 1:1 stoichiometric ratio may not be universally optimal for phospholipid compound formation. Depending on specific objectives, such as maximizing drug loading, it may be necessary to explore varying stoichiometric ratios of phospholipids and active ingredients across different drug classes.[15]

ADVANTAGE OF PHYTOSOMES[27]

The following benefits of phytosomes, which are promising little spheres, are making them more and more popular for the delivery of phytoconstituents.

- Phospholipid, or phosphatidylcholine, is one of the important phytosome constituents that serves as a carrier and offers health benefits like hepatoprotective action.
- There is an increase in the efficacy due to the improved absorption of hydrophilic active components.
- Phytosomes have better stability.
- Because of the lipid layer around the phytoconstituent, phytosomes can penetrate skin and increase efficacy.
- Phytosomes improve liver targeting by making bile more soluble in phytoconstituents derived from herbal sources.[28]
- Bile becomes more soluble in herbal ingredients when phytosomes are present.[29]
- Increased time period of action.[30,31,32]
- Because these carriers increase drug absorption, the use of herbal supplements may reduce dosage requirements.
- The stabilisation process involves the establishment of chemical interactions between plant material and active chemicals, such as phosphatidylcholine molecules.
- Using phytosomes to administer drugs transdermally is safe.

DISADVANTAGES OF PHYTOSOMES

Although the phytosome has many benefits, it also has some deadly effects. Phospholipids, such as lecithin, have been shown to promote the growth of breast cancer cells (MCF-7).[33] Leaking botanical ingredients from "some" parts of the plant's body is bad because it reduces the amount of medicine needed, which is a sign of the plant's instability. [34]

Phytosomes containing dosage forms

When it comes to phospholipid complex formulations, whether applied topically or taken orally, a better grasp of the time needed for dissolution and the form's dissolution is crucial for optimising bioavailability. Some examples of phytosome-containing dosage forms are provided below.[35]

1. **Soft gelatin capsules:** For this purpose, Indena recommends the use of vegetable or semi-synthetic oil in suspension form with a particle size of 100% < 200 µm.
2. **Hard gelatin capsules:** Hard gelatin is generally filled into size 0 capsule, quantity not exceeding 300 mg without the use of a pre-compression technique.
3. **Tablets:** The best way to produce tablets with larger unitary doses is through dry granulation. We avoid wet granulation since it negatively affects the phospholipid complex.
4. **Topical dosage forms:** To maximize the benefits of the phospholipid complex, the emulsion is employed in this process.

PREPARATION TECHNIQUES FOR PHYTOSOMES

a) Phytosome vesicles are produced using the thin-layer rotary evaporator absorption method. Mix plant stem complex and absolute ethanol in a 250 ml round-bottom flask. A bottle is connected to the rotating evaporator area. At approximately 60°C the solvent evaporates and forms a thin layer around the flask. Phosphate buffer (7.4) is used to hydrate the membrane, and when the lipid layer is separated, a vesicle suspension is formed in the phosphate buffer. Use a 60% amplitude ultrasonic probe to correct the plant removal. Before habituation, the phytosomal suspension will be stored in the refrigerator for a day.[36]

b) React equal amounts of soy lecithin or phospholipid with polyphenolic extract and 5 ml of dichloromethane (DCM) and stir until the mixture evaporates. After the DCM was evaporated, 5 mL of n-hexane was added to the thin film with stirring and placed in a fume hood to ensure that all of the solvent disappeared. After complete removal of n-hexane, the films were sonicated and hydrated to form the required phytosome complex.[37]

c) The phospholipid and polyphenolic extract should be weighed precisely. Reflux 30 mL of DCM with 100 mL of the mixture in a 100 ml round-bottom flask set at 60°C for three hours. Then reduce to 5–10 ml and stir constantly to ensure precipitation. The precipitate was collected and placed in a vacuum desiccator overnight. When dry, filter the precipitate through a #100 mesh sieve and place in a closed amber container.[38]

d) The reflux method can be used in the construction of phytosome. Reflux the 100 mL round-bottom flask containing the phospholipid and polyphenol extract in DCM for one hour at a temperature not exceeding 40°C. After evaporating the clear liquid, add 15 mL of n-hexane to precipitate. After extraction, the sediment is placed in a desiccator.[39]

e) Once the phospholipids and cholesterol have been weighed into a round-bottom flask, dissolve them in 10 mL of chloroform, and then sonicate the mixture using a sonicator bath for 10 minutes. The organic solvent can be removed by placing it in a 40°C low power rotating evaporator. A completely solvent-freed thin layer in the evaporator area is hydrated with the polyphenolic extract of the drug. The phospholipid mixture is sonicated in an ice bath to dissipate the heat. Store the prepared phytosome in amber-colored bottles.[40]

CONCLUSION

Denaturation and bioavailability are perennially significant concerns for herbal products. There are a ton of cutting-edge methods available in NDDS form.

Despite these methods, the most effective novel options for herbal medications to solve this kind of issue is phytosomes. The pharmacotherapeutics and pharmacokinetics of herbal medications have been enhanced by this method. This type of delivery technology is also used in the cosmeceutical and nutraceutical fields to increase skin permeability and therapeutic impact. The phospholipids used to make phytosome have their own benefits in the body, and the process of making phytosomes is simple and repeatable.

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