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Open Access REVIEW

Properties, preparation methods and applications of Phytosomes: A Review

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ABSTRACT

Phytosome is produced by the reaction of mostly in stoichiometric amounts of phospholipid standardized herbal phosphatidylcholine in an aprotic extract. The aim of the present review was based on the properties, preparation methods and applications of Phytosomes. The composition of phytosomes is complicated and includes both natural phytoconstituents and phospholipids, such as the phosphatidylcholine-rich phospholipids found in soy. These complexes are produced when phospholipids in stoichiometric proportions react with phytoconstituents in an aprotic solvent. They increase bioavailability due to phospholipid complex, thus improve therapeutic effect. They are required in fewer doses due to high bioavailability. Because of their superior pharmacokinetic and pharmacological properties, phytosomes can be used to treat liver issues resulting from either infection or metabolism. Additionally, they possess UV, lipolytic, vasokinetic, anti-oedema, cicatrising, trophodermic, nutraceutical, antioxidant, cardioprotective, and anti-wrinkle qualities. New formulations known as phytosomes contain hydrophilic flavonoids and other related chemicals with enhanced skin or gastrointestinal tract bioavailability. They offer several distinct advantages over other conventional formulations. Phytosome production is a simple technique that might be swiftly scaled up for commercial use.

Keywords: Phytosome, soya lecithin, phospholipids, topical drug delivery system.

INTRODUCTION

Phytosome is produced by the reaction of mostly in stoichiometric amounts of phospholipid standardized herbal phosphatidylcholine in an aprotic extract. Phosphatidylcholine is a bifunctional solvent. Phosphatidyl moiety of a molecule being lipophilic by nature, the head of the choline moiety and the bifunctional compound which is the bifunctional compound's tail being naturally hydrophilic. The moiety of choline phosphatidylcholine is linked to the of the whereas the hydrophilic phytoconstituents are phosphatidyl part that is lipid soluble next envelops the complex with the choline bound. As a phyto-phospholipid complex is created as a result. improved in terms of lipid solubility [1].

The phytosome is one of the most powerful delivery systems for improving bioavail ability and the health benefits of common plant constituents. The phytosome is a liposome-like structure made from phospholipids constructing a bilayer membrane. The phytoconstituents can be embedded in the membrane by forming H-bonds at the head group of phospholipids [2][3].

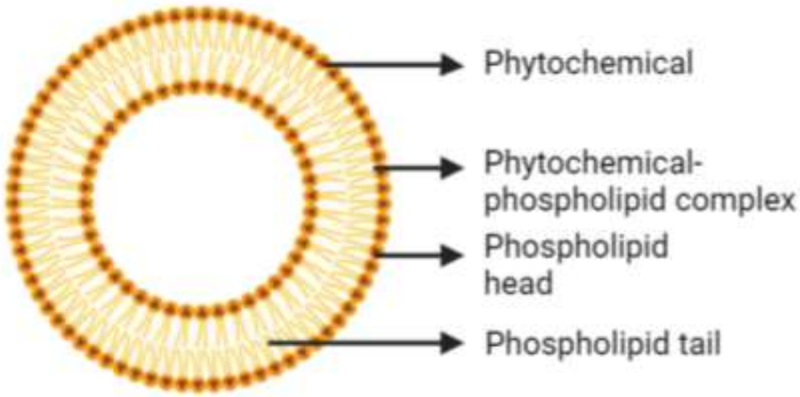

Fig 1. Structure of Phytosome

Properties of phytosomes

The composition of phytosomes is complicated and includes both natural phytoconstituents and phospholipids, such as the phosphatidylcholine-rich phospholipids found in soy. These complexes are produced when phospholipids in stoichiometric proportions react with phytoconstituents in an aprotic solvent [4].

1. The active component that is tethered to the polar head of the phospholipids and eventually turns into a structural component of the membrane can be accommodated by phytosomes.
2. Phytosomes are an improved herbal medicine delivery system that offers superior results than standard dosage forms in terms of absorption and utilization. Pharmacokinetic research and testing in both human volunteers and experimental animals have shown that the bioavailability has risen.
3. Lipophilic compounds with a known melting point, widely soluble in non-polar solvents, and only moderately soluble in fats are phytosomes.
4. After being exposed to water, phytosomes take on a micellar shape and create structures that resemble liposomes but vary fundamentally from them.

Advantage of Phytosomes [5][6][7]

- They increase bioavailability due to phospholipid complex, thus improve therapeutic effect. They are required in fewer doses due to high bioavailability.
- They improve gastrointestinal absorption.
- They show high stability.
- They are preferred over liposomes in cosmetics because of their strong lipophilicity, which results in great penetrability.
- Their clinical benefits are higher. Additionally, phytosomes work better in skin care products than liposomes.
- There is no difficulty in drug snare while formulating Phytosomes. Due to the drug's conjugation with lipids to produce vesicles, entrapment efficiency is high and almost entirely predefined.
- It is evident that the medication's bioavailability has improved.
- The dose required has been reduced due to the principal ingredient's maximum absorption.
- It assures that the right tissue will receive the drug. Important components of an herbal extract are contained in phytosomes, which are microscopic cells they are shielded from gut bacteria and digestive fluids that would otherwise destroy them.
- Benefits regarding phytosomes over traditional dosage forms: Phospholipids' complexation with plant extracts increases bioavailability significantly.
- They allow for improved absorption from the intestinal lumen by penetrating the non-lipophilic plant extract, which would not be feasible otherwise.

Disadvantage of Phytosomes [8]

- Stability Problem.
- Phytoconstituents from phytosome are rapidly eliminated.
- When administered orally and tropically they limit their bioavailability

Application of phytosomes

1. Silymarin phytosome

In order to study the pharmacokinetics in rats, researchers produced the phytosome of silymarin. Due to the silybin-phospholipid combination's outstanding improvement in its lipophilic property, which in turn boosted silybin's biological function, the bioavailability of silybin in rats was significantly raised after oral administration of the complex in the study. Silymarin phytosome has superior anti-hepatotoxic action compared to silymarin alone and can be extremely effective in preventing the harmful effects of aflatoxin B1 on the performance of broiler chicks [9].

Silymarin was complexed with phospholipids in a silymarin phytosome. Phytosomes outperformed single ingredients and had a more sustained effect. A human investigation was carried out by Barzaghi et al. to evaluate the silybin absorption when it was directly linked to phosphatidylcholine.

2. Green tea phytosome

Green tea leaves are distinguished by the presence of the polyphenol epigallocatechin 3-O-gallate. Essential element These substances are effective modulators of several metabolic processes connected to the loss of homeostasis in serious chronic degenerative illnesses like atherosclerosis and cancer. Additionally, green tea provides us with a variety of health benefits, including antioxidant, anticarcinogenic, antimutagenic, hypocholesterolemic, cardiovascular protection. Despite these positive effects, polyphenols from green tea extract still have problems [10].

Due to the issue of low bioavailability. The oral bioavailability of green tea polyphenols is significantly increased by their complexation with phospholipids. When comparing the plasma concentration of total flavonoids across the study's six-hour duration. It was prepared both phytosomally and non-phytosomally. Total Radical trapping Antioxidant Parameter, or TRAP, was used to measure antioxidant capacity. The maximum antioxidant impact resulted in a 20% improvement and it revealed that the phytosome formulation had roughly twice as much of an overall antioxidant impact.

3. Quercetin-phospholipid based phytosome

By using a straightforward and repeatable procedure, Maiti et al. created the quercetin phospholipid phytosomal complex. They also demonstrated that formulation had superior therapeutic action to non-phytosomal (conventional) preparation in the treatment of carbon tetrachloride-induced liver injury in rats.

4. Grape seed phytosomes

Proanthocyanidins/procyanidins from the grape seed extract (Vitis vinifera) are oligomeric polyphenols with different molecular sizes that are complexed with phospholipids to form grape seed phytosome [11].

5. Curcumin phytosomes

In two distinct experiments, Maiti et al. created the flavonoid phytosomes of naringenin (from grape, Vitis vinifera) and curcumin (from turmeric, Curcuma longa linn). In all dose levels examined, the complex's antioxidant activity was noticeably greater than that of pure curcumin. The generated phytosome of naringenin produced stronger antioxidant activity in the other study than the free compound with a longer duration of action, which may be related to a slowing down of the molecule's quick removal from the body [12].

6. *G. biloba* leaves phytosomes

As per researches, biloba phytosome yielded superior outcomes. In comparison to the standard plant extract. The level of GBE ingredients (flavonoids and terpenes) from the phytosomal form peaked after 3 hours and lasted longer for at least 5 hours after oral administration, according to a bioavailability study with healthy human volunteer administration. It was discovered that the plasma terpene concentration produced by the phytosomal GBE was 2-4 times higher than that of the phytosome-free GBE. Peripheral vascular problems and cerebral insufficiency are its main symptoms, and it can also improve diminished cerebral blood flow. It is the perfect ginkgo product, even for long-term use, because to its enhanced oral bioavailability and acceptable tolerability treatment. Studies utilising ginkgo phytosomes have demonstrated to induce 30–60% higher improvements in peripheral vascular diseases patients enhancement in comparison to the common standardised GBE [13].

Studies on gingko phytosome were also carried out, and they produced superior outcome compared to the traditional form. For the investigations, ginkgo phytosome was given for five days in guinea pigs, in which three distinct agonists (histamine, PAF, and acetylcholine) were used to cause bronchoconstriction. At the greatest peak, the bronchospastic inhibition was assessed expressed as differences from the baseline values. The results showed that ginkgo phytosome has increased efficacy over conventional forms in that it cannot only prevent direct bronchial constriction but also tends to lessen TXA2-mediated bronchoconstriction (histamine & PAF).

Phytosome in preventing bronchospasm brought by by allergens. Additionally, studies have demonstrated that ginkgo phytosome is more effective than the traditional standardized extract in preventing ischemia in isolated rat hearts. The results presented above clearly provide an indication of the advantage that phytosome has over traditional treatments, demonstrating its value for herbal phytoconstituents. Topical therapies were anointed, wrapped, rubbed or applied on to skin to treat skin conditions in ancient Egypt, according to the Ebers P., which dates to 1550BC [14].

C. Galen launched the compounding of herbal treatments to Western medicine & developed a cold cream formula (Galen's Cerate) that was akin to those that are currently on the market. The Persian physician Ibn Sina asserted that topical medications have two states: the soft component that penetrates the skin & hard part that does not mentioned in his book The Canon of Medicine. As a result, Avicenna supplied the first known mechanistic approach in topical and transdermal distribution, which still supports our present knowledge and pharmaceutical development [15].

Effective medication administration entails delivering medicines to the site of action in the shortest time possible. The term topical delivery refers to a module for treating local ailments that involves applying a formulation to the skin, eyes, nose, and vaginal area. When a medicine is applied to the topical areas, it avoids pre-systemic metabolism, pH of stomach- disturbances and fluctuations in plasma conc. that occur often when a drug is delivered orally [16].

The following are some of the other benefits linked with the topical drug delivery system [17]-

- Patient acceptance and cooperation
- Easy to apply
- Painless
- BA of drugs is being improved
- Physiological and pharmacological responses are improved
- Drug exposure to non-infectious tissue/sites with little systemic toxicity

Preparation methods for phytosomes

1. Plant extracts are combined with a certain quantity of phospholipid, soy lecithin, in an aprotic solvent. Phosphatidylcholine, the main ingredient in soy lecithin, has two functions. The choline portion is linked to the hydrophilic principal active ingredients, whereas the phosphatidyl component is a lipid-soluble material related to the choline bound complex. It results in the formation of a more stable and bioavailable lipid complex. Another way to produce phytosomes is to react synthetic or natural phospholipids with standardised plant extract in a ratio of 0.5 to 2.0. However, a 1:1 ratio is usually preferred. The new complex can be precipitated using a non-solvent (often an aliphatic hydrocarbon), lyophilised, or spray-dried to remove it from the process. Acetone, methylene chloride, or dioxane are examples of aprotic solvents that can be used alone or in a natural combination to conduct the reaction [18].
2. Phytosome vesicles were produced using a thin layer rotary evaporator vacuum technique. The phytosomal complex was mixed with anhydrous ethanol in a 250 ml round-bottom flask. The flask is connected to a rotary evaporator. The solvent will evaporate and create a thin layer surrounding the flask at about 60°C. The film is hydrated with phosphate buffer (7.4), and vesicle suspension forms in the buffer as the lipid layer separates. The phytosomal suspension was subjected to 60% amplitude probe sonication. Before characterisation, the phytosomal suspension will be refrigerated for an entire day. One method for preparing phytosomes is the reflux approach. Phospholipid and polyphenolic extract were refluxed in DCM for an hour at a temperature not to exceed 40°C in a 100 ml round-bottom flask. Following the clear solution's evaporation, 15 millilitres of n-hexane were added till hasty was formed. The precipitate was placed in a desiccator upon extraction [19].
3. Phospholipid and cholesterol should be precisely weighed into a round-bottom flask, dissolved in 10 millilitres of chloroform, and then sonicated for 10 minutes using a bath sonicator. Organic solvent can be eliminated by subjecting it to a spinning evaporator at 40°C under low pressure. The drug's

polyphenolic extract is used to hydrate a thin layer that has been fully solvent-free in a rotary evaporator. Heat was released by sonicating the phospholipid mixture in an ice bath. An amber-colored container was used to hold the produced phytosomes [20].

CONCLUSION

To optimise the distribution of the beneficial components in plant products, particularly those that contain flavonoids and other phenolic compounds, appropriate formulations and delivery systems are required. New formulations known as phytosomes contain hydrophilic flavonoids and other related chemicals with enhanced skin or gastrointestinal tract bioavailability. They offer several distinct advantages over other conventional formulations. Phytosome production is a simple technique that might be swiftly scaled up for commercial use. The analytical and characterisation procedures are well-established for this type of novel formulation. Numerous patents for novel phytosomal formulations, procedures, and uses have already been granted. The application of phytosome technology has great promise for improving formulation process. Free medicine is not as important as phytosome technology.

CONFLICT OF INTEREST

Authors declare for none conflict of interest.

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