International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 27-07-2024, Accepted: 26-08-2024, Published: 10-09-2024
Volume 9, Issue 3, 2024, Page No. 63-67

Phytosomes pharmaceutical delivery system: A comprehensive review

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Abstract
The unique "Phytosome" pharmaceutical delivery system, which overcomes problems with traditional drug administration methods, is the subject of this study's investigation. The goal is to get more knowledge about the advantages, possibilities, workings, elements, and characteristics of phytosomes as well as methods for assessing the transportation of medications that are placed into them. The study also covers advances in phytosome technology and approaches for creating phytosomal-loaded medicine delivery. According to the study's findings, the phytosome is superior to conventional herbal extracts in a number of ways, including improved stability, hepatoprotection, skin penetration, and systematic targeting. The therapeutic efficacy of the phytosome is significantly different from that of the standard B. *monnieri* extract. This study offers chances to improve operations and address issues related to the traditional kind of herbal medicine distribution system, which has significant implications for the pharmaceutical and herbal medicine industries.

Keywords: Technological developments, phytosomes, phospholipids, solubility, biological accessibility, drug transport, bioavailability, and botanical extracts

Introduction

"Phytosome" is a novel medicine delivery device that addresses issues with conventional drug administration techniques. "Some" means "like a cell," and "phyto" means "plant." To create phytosomes, which are lipid-compatible molecular assemblies that significantly increase the absorbance and biological accessibility of phospholipids, standardized plant-based chemicals that are soluble in water must be added [1].

The inventor of this phytosome method is indena. Phytosomes are herbal preparations that contain a single component of the herbal extract bound to phosphatidycholine and polymer. This product outperforms conventional herbal extracts in terms of effectiveness [2].

The phytosome method has also been used to process many well-knownbotanical extracts, encompassing ginkgo biloba, ginseng, greentea, hawthorn, milkthistle and grapeseed. Because of their flavonoid and terpenoid components, these plant extracts are excellent candidates to phosphatidylcholine directly for binding. Certain components of herbal extracts can bind to phosphatidylcholine to form phytosomes. This procedure yields a more absorbable dose form with more potency than conventional herbal extracts [3].

Phytosome application in herbal medicine is highly advantageous. These include delivering the medication to the intended site of action, reducing harmful effects, controlling the drug's distribution by carrier system insertion, or altering the drug's molecular structure. Additionally, it is making medications more bioavailable [4].

Many of the main ingredients in herbal medicine, such as glycosides and flavonoids, are readily soluble in water. Nevertheless, the effectiveness of these ingredients is limited since they may be hydrophobic or only partially soluble, which results in reduced therapeutic benefit when administered topically. Many attempts have been made to increase the medicine's bioavailability by forming it into a specificmetabolic system; liposomes, phytosomes are two viable choices. When compared to traditional herbal extracts, the formulation development process using these methodologies may result in better bioavailability of herbal medications [5].

For herbal medications, phytosomes and naoemulsios offer a number of benefits, such as increased solubility and bioavailability, protection against toxicity, enhanced dispersion of tissue macrophages, stability, consistent delivery, and resistance to chemical and physical deterioration. As a result, there is a great deal of potential for improving the activity and solving issues related to the standard kind of herbal medication delivery system [6].

Advantages of phytosomes

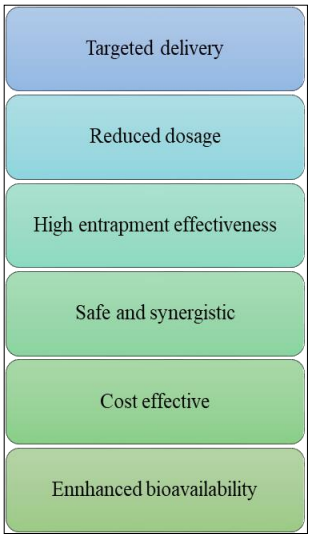

Fig 1: Advantages of phytosomes [7, 8]

Prospects of phytosomes [9]

The improved capacity of phytosomes to transition from an aqueous condition to the lipid-friendly atmosphere of the enterocyte cell membrane and then inside the cell allows for systemic targeting**.**

1. Although phytosomes have a strong lipid profile and may penetrate the skin with ease, they are frequently used in cosmetic goods.
2. Phytosomes facilitate liver targeting by making bile more soluble in herbal ingredients.
3. They boost dermal and oral uptake of theplant substances insoluble in lipids, hence raising their biological accessibility and in turn, their therapeutic efficacy.
4. Because the plant extract and the phosphatidylcholine molecule form chemical bonds, phytosomes have an additional steady profile.
5. The intended effects can be obtained with a small dosage once the assimilation of the active ingredients rises.

Diagram of phytosomes

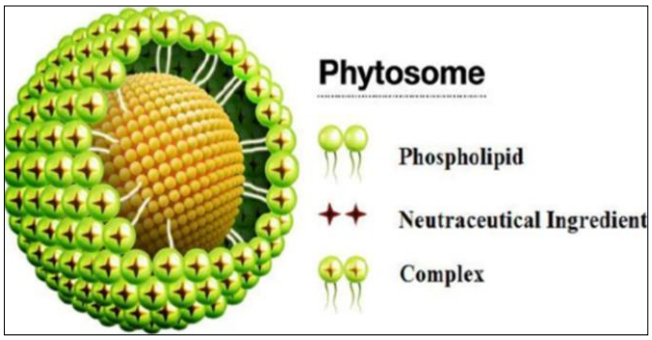

Fig 2: Shows the structure of phytosomes [5]

Table 1: Qualities of the Phytosomes [10, 11, 12, 13]

Phytosomes	Phytoconstituents	Indications
Silybin	Silybin from silybummarianem	Hepatoprotective.
Greentea	Epigallocatechin from theasinesis	Neutraceutical, antioxidant, anti-cancer.
Grapeseed	Procyanidins from vitisvixifera	Neutraceutical, anti-cardio protective.
Centella	Terpenes	Skin and vein conditions.
Milk thistle	Silymarin's Silybin	Reduces abnormal blood vessel, improve capillary tone.
Oliveoil	Olea europaea oil's polyphenols	Anti-inflammatory.
Ginseng	Panax ginseng's ginsenosides	Neutraceutical.
Hawthorn	Crataegus leaf flavanoids	Neutraceutical, immunomodulator.
Palmetto	Fattyacids,alcohols	Non-cancerous prostate enlargement
Ginkgo	Ginkgo biloba contains flavanoids	Protects the vascular linings, the brain, and aging skin.
Bilberry	Which provides anthocyanos ides	Antioxidant.
Echinacea	Echinacosides from Echinacea augustifolia	Immunomodulator.

Methods and materials

Procedures for preparing phytosomal-loaded drug delivery

Standard processes and a variety of approaches are available for the preparation of medication delivery using phytosomes.

General method of preparation

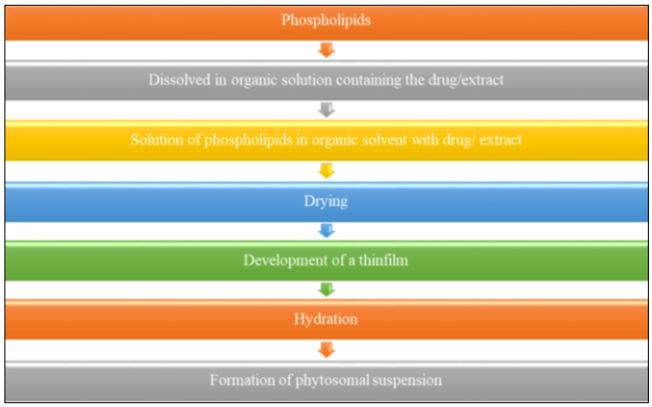

Fig 2: General preparation of Phytosomes [8]

1. Method of solvent evaporation

A flask with a spherical bottom can have the exact amount of drug, polymer, and phospholipids put to it. It can then be refluxed for two hours at 50 to 60 degrees Celsius with a designated solvent. The precipitate can be created by concentrating the mixture to 5–10 ml, after which it can becleared and deposited. The amber-colored glass vial containing the dried precipitate phytosome can be kept at room temperature [2].

2. Method of rota evaporation

Thirty milliliters of tetrahydrofuran have been incorporated into a rotating circular-bottom flask together with the prescribed amount of plant material and phospholipid. After then, that mixture is stirred three hours of time at a specific temperature not to go over forty degrees Celsius.Once the substance had thinned outusing a magnetic stirrer, n-hexane was added and continuously mixed. After being collected, the precipitate was put in the shade of amber glass container and let to stand at room temperature [14].

3. Ether injection method

The method involves dissolving the medication lipid complex in an organic solvent. Vesicles are created by gradually injecting this combination into a hot aqueous agent. Amphiphiles' condition is dependent on concentration. Amphiphiles introduce a monomer state at lower concentrations; however, when concentrations rise, a range of structures, including spherical, cylindrical, disc, cubic, and hexagonal forms, may emerge [15].

4. Anti-solvent precipitation method

A spherical-bottom flask containing the prescribed amount of medication, phospholipids, and polymer can be filled and allowed to reflux with a particular solvent for two hours at a temperature not to exceed 60 degrees Celsius. The combination can be reduced to 5–10 milliliters. The precipitate can be obtained by slowly adding N-hexane and stirring continuously. After that, it can be gathered, filtered,

and kept in vacuum desicators for the night. After being crushedwithin a mortar, the dried precipitate is screened. Through # hundred meshes. The transparent glass with an amber shade vial containing the dried precipitate phytosome can be kept at room temperature [2].

5. Film formation method

In a circular-bottom flask, transparent mixture wasallowed to evaporate under vacuum for one hour at 50°C. In the desiccatorsthe thin coating was created and then stored under ambienttemperaturefor the night.For thirty minutes, precipitate was hydrated with water in a circular-bottomed flask spinning at 210 rpm [16].

6. Co-Precipitation Method

Using a supercritical fluid or a non-solvent, phyto-constituents and phospholipids are precipitated simultaneously from a shared solvent in the co-precipitation process. This method improves the homogeneity of the complexes by distributing the phytochemicals uniformlythroughout the lipid matrix. Because the co-precipitation approach operates under very mild circumstances, it is ideal for thermally labile phyto-constituents and offers good scalability [17].

7. Dehydration-rehydration method

A solvent that is organic is employed to dissolvethe phospholipid and the bioactive ingredient. A rotary vacuum evaporator is then used to entirely remove the organic solvent and the aqueous content at a lower temperature and pressure. In the round bottom flask, a thin layer comprising a conjugated combination of phospholipid and bioactive chemical would form. To totally eliminate the solvents, water is added to the mono layer. In order to create micelles, the mono layer is then rehydrated with water. After being exposed to water, the phospholipid thin layer forms micelles, which are subsequently probe-sonicated to reach the appropriate micelle size [18].

Characters of phytosomes

1. Mechanico-chemical characteristics

The sizes of phytosomes vary from 50 nm to several hundred µm [19].

A proper quantity of lecithin is reacted with a measured plant substance as the substrate to create phytosomes. The ammonium and phosphate group, or polar head, and the polar functions of the substrate, according to spectroscopic data, form a hydrogen bond that results in the phopspholipid-substrate interaction [19].

Upon coming into contact with water, phytosomes adopt a micellar shape akin to that of a liposome. These newly acquired liposomal structures are visible via photon correlation spectroscopy (PCS) in phytosomes [19].

When it comes to phytosome solubility, the structures are typically insoluble in water, somewhat unstable in alcohol, readilyable to dissolve in aprotic liquids, and moderately soluble in lipids. However, after complexing with phospholipids, certain lipophilic phytoconstituents, including turmeric, have shown improved water permeability when incorporated into phytosomes [19].

2. Biological properities

Research on the pharmacokinetics and pharmacodynamics of phytosomes on humans and experimental animals has shown that these novel complexes are more readily absorbed and used than traditionalextracts from botanicals or crude extracts. Consequently, phytosomes yield more bioavailability and favorable results [20].

Techniques for assessing phytosome-loaded drug delivery

Distinctive scanning method

An aluminum crimp cell can holdthe medication specimen, loaded phytosome, phospholipids, polymer, and physical combination**.** The cell can then be heated with a speed of 10ºC/min between 0 and 400ºC in anitrogen-filled environment. Instrumentation can be used to measure the temperatures at which peak transitions start [22].

Particle size

A Zetasizer ZEN 3600 can be used to measurethe loaded phytosome's average diameter and zeta potential at a constant 90-degree scattering angle at 25 degrees Celsius [22].

Optical Microscopy Study

Under a microscope, phytosomes were seen in Cippon, Japan. On a glass slide, a single drop of the suspension of diluted extract-loaded nanoparticles was applied. After using a filter paper to remove any remaining solution, the slide was let to dry. Optical microscopy was then used to investigate the sample [23].

Entrapment efficiency

Phytosome loading can be diluted one-fold with 10 ml of solvent and centrifuged for 30 minutes at -4ºC and 18,000 rpm using a cooling centrifuge apparatus. It is possible to quantify the amount of free medication in the separated supernatant using UV/Vis spectroscopy. By increasing the amount to 10 ml and diluting 0.1 ml of the phytosome-loaded solution in fuel, the total dosage can be ascertained.

Entrapment efficiency (%) = Total amount of drug – amount of free drug× 100 / Total amount of drug.

Ftir spectroscopic examination

Data from the FTIR spectrum may be used to determine the morphology and chemical resistance of materials containing drugs, phytosomes, phospholipids, and polymers.Pellets can be produced by compressing samples with bromine potassium under 660 kg/cm2 of pressure. One can do spectrum scanning in the region of 4000-400 cm-1 [24].

Scaning electron microscopy

A scanning electron microscope has been utilized to evaluate the morphology and size of the particles.A ion splutter was used to cover an iron tube of an electron microscope with a dried sample, and the complicated substance was examined at 50-100 [5].

Transition electron microscopy

Using a 1000 magnification, for measuring the diameter of the phytosomal particulates, TEM was used [5].

***In-vitro* and *in-vivo* assessments**

The drug's qualities, its primary phytoconstituents enclosed by a phospholipid membrane, and the reason that specific animal model was chosen for its assessment will all play a role in both *in vitro* and *in vivo* evaluations [5].

Technological improvement in phytosome

- The widely recognized active component of *bacopa monnieri* plants, bacopaside, has the ability to prevent amnesia.The purpose of this work is to produce phytosome using bacopaside and evaluate it in practice with rats. The phospholipid-prepared compound's therapeutic effectiveness differs noticeably from that of the basic B. *monnieri* extract [26].
- An additional investigation also demonstrates the creation of a solid dispersion of berberine phospholipid complex, which improves the compound's solubility and speeds up its dissolution rate and flow capacity for industrial uses [24].
- According to a different study, sinigrin phytosome preparation has occurred. Comparing the study's outcome to sinigrin alone, it is noteworthy that the *in vitro* wound healing ability was investigated [26].
- When taken orallyphytosomes from a purified S. marianum seeds extract are having a significant impact on the fetus from alcohol use by the woman who gives birth [27].
- The phytosome from grape seeds is also very important in preventing atherosclerosis and ischemia-induced cardiac damage. Proanthocyanidins/procyanidins are the primary ingredients predominantly accountable for action [28].
- Additional studies revealed that green tea phytosomes devoid of caffeine also significantly impacted antioxidant and anti-obesity properties. It affects low-density lipoprotein as well [29].
- Rat liver damage caused by carbon tetra chloride shows that quercetin phytosomal complex has superior medicinal benefits [30].

Conclusion

By combining with phospholipids to create complexes, phytosomes are a new drug delivery mechanism that increases the bioavailability and effectiveness of substances obtained from plants. Studies have demonstrated that phytosomes have several benefits over traditional herbal extracts, including enhanced stability, hepatoprotection, skin penetration, and systematic targeting. Phytosomes have been used in a number of therapeutic domains, including musculoskeletal, central and peripheral neurological systems, immunological, gastrointestinal, genitourinary, respiratory, and integumentary systems. Pharmaceutical applications for phytosomes appear to have a bright future since they can more safely and effectively convey the advantages of natural substances.

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