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REVIEW ARTICLE

Phytosomes: An advanced drug delivery system

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ABSTRACT

Phytosomes are the advanced drug delivery. The primary goal of this research is to concentrate on phytosomes, which are widely utilised as the greatest technology in the pharmaceutical industry because to their expanded therapeutic benefit and unique adverse effects. The main objective of this review is to focus on Phytosomes which are being used large as best technology in pharmaceutical field because of expands their therapeutic effect and minimize unusual side issues. Phytosomes is a news specific technology developed to integrate standardized plant extracts into phospholipids to give a lipid soluble molecular complex with boosted bioavailability and absorption, which is termed as "phytosomes". The two words that make up phytosomes are *"Phyto"* and *"Some,"* both of which refer to plants and cells, respectively. The review's first section introduces phytosomes technology and highlights its benefits, while its second section gives an overview of preparation techniques, evaluation, and possible applications. A brand-new, unique technology called phytosomes was developed to incorporate regular plant extract into phospholipid to produce a molecular complex that is lipid soluble .It is enhanced pharmacokinetics and bioavailability. It is used for develop the pharmaceutical formulation for improve bioavailability of herbal phyto constituents. This is advanced form of herbal formulations which encompasses the bioactive phytoconstituents of herb extracts surround and fated by a lipid. The present review brief description the highpoint of phytosomes technology, preparation methods, advantages, properties, evaluation and application of phytosomes.

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INTRODUCTION

A new drug delivery system, phytosomes is a novel method of drug delivery that pushes the limits of the conventional drug delivery system. Ayurveda in our country has a great body of knowledge, but its full potential has only recently come to light. It is popular for delivering herbal medications at a predetermined rate, delivering medications to the site of action, reducing toxic effects, increasing the bioavailability of medications in phytosomal preparations, and controlling the distribution of medications by either combining medications in a carrier system or altering the molecular makeup of medications [1, 2].

Phytosome is newly introduced patented technology by Indian to develop and as similate the standardized herbal extract. The vital active components of the pharmaceutical crude extracts are shielded from destruction by gastrointestinal fluid and gut bacteria because the phytosome formulation procedure forms a tiny cell-like structure [1].

Phytosomes are more bioavailable than herbal extracts because of their increased capacity to pass lipid-rich biomembranes and eventually enter the blood. Different pharmaceutical carriers, including particulate systems, polymeric micelles, macro- and micromolecules, are used in novel drug delivery methods [3].

A unique and well-known drug delivery method is phytosomes. Increase in the bioavailability of drugs occurs in phytosomal preparations,

delivery of drugs at the site of action, decrease in toxic effects, and supervision of the bloodstream of drugs are achieved by combining the drugs in to carrier systems or by altering the structure of the drugs at looking at their cell [1].

Phytosomes are herbal medications that have been packed inside of vesicles and are accessible in Nano form. The primary component of a herbal extract is protected from microbial and digestive secretion destruction because the phytosomes give a cover-like covering all over the drug's active ingredient. The ability of phytosomes to absorb from a water-tender environment into a lipid-tender enviro of the cell membrane and ultimately enter blood circulation is efficient [4].

Phytosomes are created when a molar ratio amount of phospholipid reacts with standardised plant extract or polyphenolic components in an aprotic solvent. The development of chemical interactions between phytoconstituents and phosphatidylcholine molecules gives phytosomes a higher degree of stability. Phosphatidylcholine is not only carrier; it is also having hepato protective activity and nutritional value [5].

Water-soluble phytochemicals or conventional plant extracts are when combined with phospholipids to produce lipid-friendly structural compounds, greatly enhancing bioavailability and osmosis. Phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine or phosphatidylserine, are the phospholipids used, but phosphatidylcholine are broadly used because of their certain therapeutic value in case of alcoholic steatosis liver diseases, drug induced cirrhosis injury and hepatitis. Phospholipids are further selected as common digestive aids and as transporter for lipid miscible and water miscible nutrients. Phytosomes can easily cross the intercellular lipid layer of the skin and the lipophilic route of enterohepatic cell membranes [4].

Plant extracts with water-soluble components and phospholipids were originally created by an Italian pharmaceutical and nutraceutical company to enhance their pharmacokinetics. The invention was given the name "Phytosome." The words "phyto" and "some" denote plants or cells that are comparable to them. Phytosomes are more successfully used to increase the bioavailability of many well-known herbal extracts because they contain an H-bond between phospholipids and the phytoconstituents. They can also be produced for a variety of therapeutic purposes or as dietary supplements and also have medicinal properties [1].

Phytosomes

Phytosome is an innovative patented technology developed to integrate standardized herb extracts into phospholipids to give a lipid compatible molecular composite with improved bioavailability and absorption, which is entitled as phytosomes. Phytosomes also mentioned as Herbosomes. The term "phyto" express plant, term "some" express same like cell [1].

Any herbal medication's efficacy depends on the therapeutically active component being delivered at an effective dosage. When given topically or orally, their bioavailability is severely constrained. Phytosomes are commercially available herbal preparations that absorb better than herb extracts. Numerous botanical products' compositions, biological activity, and health-promoting effects have been demonstrated by phytochemical and phyto-pharmacological sciences [2].

Effectively capable of absorbing from a lipid-tender environment of the cell membrane into a water-tender environment, phytoconstituents can eventually reach blood circulation [6].

Flavonoids, tannins, glycosidic aglycones, and other water-soluble phytoconstituents are poorly absorbed either because of their large molecular size, which prevents passive diffusion, or because of their poor lipid solubility. This severely restricts their ability to pass across the lipid-rich biological membranes, certifying subpar bioavailability [2, 6].

Phytosome Technology

The phytosome technique, created by the Italian company Indena S.P.A., significantly increases the bioavailability of specific phytomedicines by integrating phospholipids into standardised plant extract, which improves their pharmacokinetics and use. The polyphenols hardly dissolve in either lipids or water. In an effort to be demonstrated with the aid of spectroscopic analysis, the polar qualities of the lipophilic capture through hydrogen bonds and polar interaction with the charged phosphate head of phospholipids [7].

The hydrophilic choline group head attaches to the complex while the hydrophobic phosphatidyl group covers the confined section because phosphatidylcholine is a bifunctional molecule [4].

According to a precise qualitative examination, the unit phytosome is normally connected to at least one phosphatidylcholine molecule by a flavonoid molecule. A touch micro sphere or cell is created as a result. Due to the gastroprotective property of phospholipid, the phytosome drug delivery creates a contact cell that shields the herb extract or its active element from being destroyed by gastric secretions and gut bacteria [7].

Advantages of Phytosomes:

- ✓ In contrast to other nano drug delivery systems such solid lipid nanoparticles and nanostructure fattransporter, phytosomes have a straightforward formulation process [1].
- ✓ It is ensured that the medicine will reach its target tissues properly [3].
- ✓ Phytosomes have a clinical benefit that is noticeably greater [3].
- ✓ Phosphatidylcholine and phytoconstituent establish chemical bonds, which improves the stability profile of phytosomes [8].
- ✓ There is no chance of drug entrapment during the formulation process [6].
- ✓ A small dose can have the desired effects since the active ingredient is more absorbed [6].
- ✓ In the development of phytosomes, phosphatidylcholine, a component of the cell film, functions as a messenger and feeds the epidermis [9].
- ✓ Phytosomes are more effective since they are able to penetrate the skin due to the lipid layer that surrounds them [9].
- ✓ Phosphatidylcholine is not just a carrier; it also has nutritional value and hepatoprotective properties.
- ✓ It enhances lipid-insoluble phytoconstituent absorption both topically and orally [10].
- ✓ The components of Phytosome have all received approval for usage in both medicinal and cosmetic products, and the formulation is safe [11].
- ✓ Phytosome lengthens the duration of action and makes bile more soluble in herbal constituents [12].

Preparation of Phytosomes:

1) Anti-solvent Precipitation Process:

The most used method of solvent evaporation, The most popular method of solvent evaporation involves placing certain amounts of plant extract and phospholipids in a round bottom flask and heating them up in a refluxing mixture with 20 ml of dichloromethane.

For two hours, the temperature of this reaction mixture is held at no higher than 60 degrees.

After adding 5–10 mL of hexane (20 mL), the liquid was carefully condensed while being constantly stirred.

In order to acquire the precipitate, it was filtered, collected, and stored in night desiccators.

In a mortar, the dry precipitate is mush. sieved through meshes #100.

A powdered mixture containing fix amount of medication and phospholipids was maintained in an amber-colored glass bottle at room temperatures [1, 3, 6, 12- 14].

2) Solvent Evaporation Method:

The most popular method of solvent evaporation calls for precise measurements of the medication and phospholipids to be put into a flask with a circular bottom.

Organic solvent contained in flask, flushed with 20 cc of acetone at to get the highest yield and drug trapping, this reaction mixture is maintained at an ideal temperature for a set period of time (hours).

To obtain the precipitate that was filtered and collected, the mixture is concentrated with hexane to 5–10 mL.

In an amber-colored glass bottle, a dry phytosome compound was put and let to stand at room temperature [1, 3, 6, 12- 14].

3) Rotary Evaporation Technique:

The most popular method of solvent evaporation involves dosing a circular vacuum base flask with a specific quantity of medication and phospholipids.

Combined in a 30 mL water-miscible organic solvent (organic solvent) container and stirred in a rota evaporator for two hours at a temperature of but 50°C.

After adding an antisolvent such n-hexane and swirling continuously, a thin layer is produced. Obtain the filtered and collected precipitate.

The dried precipitate phytosome complex was maintained at ambient temperature in an amber-colored glass bottle [1, 3, 6, 12, 14].

4) Ether Injection Technique

In this method, an organic solvent is used to dissolve the drug's lipid complex. This combination is gradually added to a heated aqueous medium, where it forms vesicles.

Amphiphiles' phase turns on the concentration. Amphiphiles can create a monomer state both when the concentration is greater and when it is lower. There are numerous possible structures, including those of the round, cylindrical, disc, cubic, and hexagonal types [1, 15].

5) Dehydration-Rehydration Technique:

The phospholipid and bioactive ingredient are dissolved in organic solvent.

A rotavap evaporator is then used to completely terminate the organic solvent and the aqueous component under pressure and condensed temperature.

A thin layer containing a fused compound of phospholipid and bioactive compound would be formed in the round vaccum base flask.

The mono layer is countered with water to remove the solvents completely. Then the mono layer is re hydrated with water to form micelles.

The lipoid thin layer upon frostbite with the water forms micelles that are probe sonicated to accomplished micelle size [1, 16].

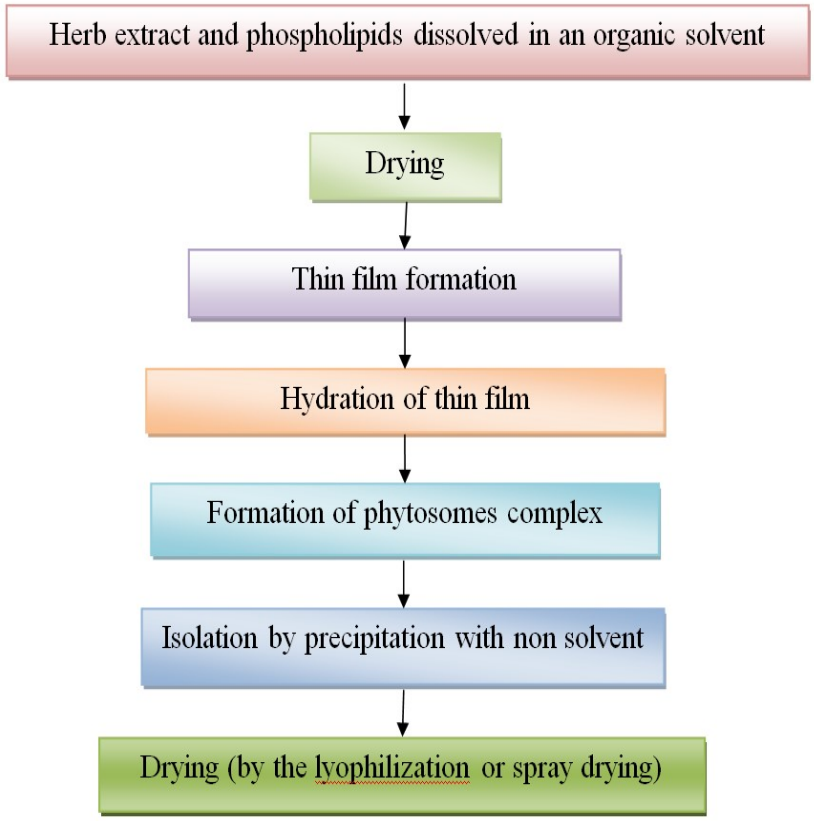

Figure 3: General method of preparation of phytosomes [1, 3, 14]

Evaluation of Phytosomes [1, 3, 6, 7, 12, 13, 15-27]

A. Visualization: Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) can measure the size and form of phytosomes (scanning electron microscopy).

1) Transmission Electron Microscope Analysis

The size of phytosomal vesicles was demonstrated using a transmission electron microscope and a 1000-fold amplification. Swung the chemical in water and examined it with a transmission electron microscope.

2) SEM Analysis

The size and appearance of the particle were assessed using SEM. Brass fragments were coated with gold in an ion sputter after being dried and placed on a compound hand-held microscope. 100 random scans of the building.

B. Zeta Potential Land Vesicle Size:

The zeta potential and particle size as they can be determined utilising a robotic computer inspection system using photon correlation spectroscopy and dynamic light scattering (DLS).

C. Entrapment Efficiency:

The Ultracentrifugation technique can be used to determine the effectiveness of drug trapping by phytosomes.

D. Transition Temperature:

The differential scanning calorimeter can determine the vesicular lipid systems' transition temperature.

E. Surface Tension Activity Measurement:

In a Du Nouy ring tensiometer, the surface tension activity of the medication in aqueous solution is measured using the ring method.

F. Vesicle Stability:

Analyzing the evolution of vesicle size and structure provides insight into the stability of vesicles. Differential light scattering (DLS) is used to determine the average size, and transmission electron microscopy is used to track structural changes (TEM).

G. Drug Content:

A customised high-performance liquid chromatographic method or an appropriate spectroscopic method can be used to quantify the amount of medication.

Properties of Phytosomes [11, 13]

Physical Properties

- ✓ Phytosomes include lipophilic compounds with distinct melting points.
- ✓ The size of a phytosome intermediate might vary from 50 nm to a sporadic hundred μm.
- ✓ It is easily soluble in non-polar solvents, but it is insoluble in water and only moderately soluble in lipids.
- ✓ miscellar shape like liposomal compositon are for medicine when Phytosome are handle with water.

Chemical Properties

- ✓ Spectroscopic analysis data supports the development of a hydrogen bond between the polar functions of the material and the polar head of phospholipids (phosphate and ammonium groups).
- ✓ From the13CNMR and 1HNMR data, it can be inferred that the fatty chain gives unmovable signals both in the complex andin free phospholipid, which indicates that long aliphatic chains are wrapped around the active principle, producing lipophilic cover.

Application of Phytosomes:

1) Enhancing Bioavailability:

Numerous studies have been conducted that demonstrate enhanced phytosome efficiency and administration when compared to the standard method. The majority of phytosomal are directed at Silybum marianum, a top source of flavonoids that protect the liver (family: Steraceae), Its fruit contains flavonoids that have been shown to have hepatoprotective effects and to treat conditions like cirrhosis, lipid infiltration of the liver, and hepatitis. Silymarin primarily contains three flavonoids out of which bysilybin overrule, defeatsilydianin, silychristin also Silybinis.the one which is most potent as it shields the liver by conserving glutathione in parenchymal cells [1, 6].

2) Cancer Treatment:

The chemical compound like flavonoids, anthocyanins flavones, isocatechins isoflavones, coumarins, lignins, catechins, of medicinal plants mainly possess antioxidant properties that bring on their antitumour capability. Some herb based complexes are poisonous at excessive concentrations and make certain side [1].

3) Phytosome of Green Tea

Green tea leaves *(Theasinensis)* is characterized by presence of a polyphenolic compound epigallocatechin 3-O-gallate as the solution constituent. These compounds powerful modifier of some more biochemical steps joined to break the homeostasis in main chronic degenerative disease such as antitumor and coronary artery stroke.

Green tea also supplies us with a number of helpful activities such as hypocholesterolemic, antioxidant, antimutagenic, cardioprotective effects, anticarcinogenic, the complexation of polyphenols derived from green tea with phospholipids strongly improves the oral bioavailability [28].

4) Phytosomes of Curcumin

The phytosomes of turmeric yellow (flavonoid from turmeric, *Curcumalonga linn*) and naringenin (flavonoid from *Vitis vinifear,* grape) in two different studies, the high activity of antioxidant was seen when compared to the clarified turmeric yellow in all dose quantity trials.

Another study found that the naringenin phytosome produced better antioxidant activity than the free compound with a longer duration of action, which may be related to a slower rate of the molecule's quick removal from the body [28, 29].

5) Phytosomes of *Gingko Biloba* Leaves

Studies have shown that ginkgo phytosome (prepared from standardized extract of *Ginkgobiloba* leaves) produced improved results associated to the conservative standardized extract from plant (GBE, 6% terpene lactones 24% and ginkgo flavonoid glycoside). Its main indications are cerebral insufficiency and peripheral vascular disorders and it can also ameliorate reduced cerebral circulations. Its good tolerability and enhanced oral bioavailability make it the idealized ginkgo product even for long period treatment [15, 16, 28-30].

6) Phytosomes of Coated Tablet

An oral formulation of coated tablets containing significantly absorbable green tea extract for analyzing rotund subjects [n=100] of both genders on a hypocaloric diet which results into the total absence of harmful effects and thus emerge to be effectual and safe aid for losing the weight [2].

7) Phytosomes of Hesperetin Phytosomes

Hesperetin and hydrogenated phosphatidylcholine can be combined to create a new hesperetin phytosome. The compound was estimated for antioxidant activity, which interconnect that the phytosomes had sophisticated relative bioavailability than that of active drug unit [2, 3].

CONCLUSION

Phytosmes are advanced drug delivery system. Phytosomes are a new type of bioactive components that can be absorbed more effectively through the skin and when consumed. A new, patented method called phytosome assimilates standardised herbal plant extracts into phospholipids to produce structural compounds that are compatible with lipids and have better bioavailability and absorption. The process for making phytosomes is straightforward and accessible. Many areas of phytosome are to be discovered in upcoming in the prospect of pharmaceutical application.

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