Review Article

Phytosome- Valuable Phyto-Phospholipid Carriers.

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Abstract
A Phytosome is a complex between polar polyphenolics and dietary phospholipids that shows definite physicochemical and spectroscopic features. Phytosomes are superior forms of herbal products that are better absorbed, utilized and produce better results than conventional herbal extracts due to increased bioavailability. These are formulated by using natural or synthetic phospholipid along with active components. Phytosomes are complexes of phospholipid as phosphatidyl choline, phosphatidyl ethanolamine etc. with polyphenolic component. Polyphenolic component are simple flavonoids, with or without natural mixture in aprotic solvent like simple flavonoids, phosphatidyl serine with polyphenolic component. Phytosome is different from the liposome according to the physicochemical properties. Phytosomes being much better absorbed than liposomes. Phytosomes are also superior to liposomes in skin care products. Thus, this article also presents an overview of the techniques of preparation of phytosome, characterisation and their applications.

Keywords: Phospholipid complex; Phytomedicines; Planterosome.

1. Introduction
Phytomedicines are the complex mixture prepared from plant which shows better bioavailability and therapeutic effectiveness as compared to conventional herbal extracts. Phytosome are hydrophilic bioactive phytoconstituents having advanced herbal complex of active ingredient and phospholipid products that are better absorbed and utilized by the body, and consequently produce better results than conventional herbal extracts. Phytosome is a Greek word “phyto” means to plant and “some” means cell-like. Phytosome technology enhances the bioavailability of herbal extracts. It is bioactive phytoconstituent complex between polar polyphenolics and dietary phospholipids that shows definite physicochemical and spectroscopic features.

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molecule allows obtaining a higher adhesion of the product itself to the surface, it comes into contact with and a better interaction of various molecules with cell structure occurs. Phytosome is a valuable component of herbal extract which enhance the bioavailability of herbal component. This aspect is also vital important in cosmetics and pharmaceutical formulations. It mainly protects the herbal extract from destruction by the digestive secretions and gut bacteria. Phytoconstituent is water soluble and can be converted into lipid-compatible molecular complex therefore it is called phytosomes. The lipid-phase substances are employed to make phytoconstituents phospholipids from soy, mainly phosphatidyl choline (PC). PC is a natural component of lecithin and principle molecular building block of the cell membranes; miscible both in water and oil phase, and well absorbed when taken orally. PC is not merely a passive "carrier" for the bioactive phytoconstituent of the phytosomes but is itself a bioactive nutrient with documented clinical efficacy for liver disease [2]. Phytosome preparation is enough to provide reliable clinical benefits that lead to provide substantial PC intakes.

![Phosphatidylcholine](image)

**Fig. 1.** Structure and Occurrence of Phosphatidylcholine.

Phytosome enhances the absorption of lipid insoluble polar phytoconstituents through oral as well as topical route showing better bioavailability. Therefore significantly greater therapeutic benefit and also has appreciable drug entrapment. Thus phytosome formulation is helpful in the various herbal extract products to enhance the bioavailability and therapeutic benefits. Phytosome process has been applied to numerous well-liked herbal extracts, including Ginkgo biloba, Milk thistle, Green tea, Grape seed, Hawthorn, Ginseng etc. The phytoconstituents is quite well for the direct binding to PC in which, the choline head binds to phytoconstituents while the fat-soluble phosphatidyl portion comprising the body and tail then envelopes the choline-bound material. This result in a little microsphere or cell being product [3].

**Benefits of phytosome** [4, 5, 6]

1. Enhances the absorption of herbal constituent and hence the bioavailability which lead to dose reduction.
2. Enhances the absorption of lipid insoluble polar phytoconstituents through oral as well topical route
3. Shows significant drug entrapment.
4. Adds the nutritional value to the phospholipid. The phytosome by protecting the valuable components of herbal extract from destruction by digestive secretions and gut bacteria.
5. Widely used in cosmetics due to their more skin penetration and high lipid profile.
6. Liver targeting can be facilitated by improving the solubility of bile to herbal constituent.
7. PC used in preparation of phytosomes, acting as a carrier, moreover acts as a hepatoprotective giving the synergistic effect when hepatoprotective substances are employed.
8. Application of phytoconstituents in form of phytosome improves their percutaneous absorption and act as functional cosmetics.
9. Permeate the non-lipophilic botanical extract to be better absorbed in intestinal lumen.
10. Used to give liver protectant flavonoids because they were easily bioavailable.

**Properties of Phytosomes**

**Physico-Chemical properties** [7]:

1. The term phytosome is used to define a complex between a natural product and natural phospholipids that are obtained by the reaction of stoichiometric amounts of phospholipids and phytoconstituents in an appropriate solvent.
2. Spectroscopic data show that the main phospholipid-substrate interaction is due to the formation of hydrogen bonds between the polar head of the
phospholipids (that is phosphate and ammonium groups) and the polar functionalities of the substrate.

3. Phytosomes can accommodate the active principle that is anchored to the polar head of the phospholipids. Phospholipids are an integral part of the membrane.

4. In case of the catechin-distearoyl-PC complex is formation of H-bonds between the phenolic hydroxyls of the flavones moiety and the phosphate ion on the PC side.

5. For example in the case of the Catechin-distearoyl phosphatidyl choline complex, there is the formation of H-bonds between the phenolic hydroxyl ends of the flavones moiety and the phosphate ion on the phosphatidyl choline moiety.

6. Phosphatidyl choline can be deduced from the comparison of H$^1$-NMR and C$^{13}$-NMR spectra of the complex with those of the pure precursors.

7. Such evidence inferred that the too long aliphatic chains are wrapped around the active principle, producing a lipophilic envelope. This shields the polar head of the

8. Phospholipid and flavonoid molecule and enables the complex to dissolve in low polarity solvents $^{[8, 9]}$.

Method of Preparation
Phytosomes are prepared by process in which the standardized extract or active ingredient of herbal is bind to the phospholipids. They are prepared by two methods that are Solvent Evaporation and Mechanical Dispersion. Steps of preparation of phytosome are shown in fig.1.

1. Solvent Evaporation method $^{[11]}$
It is the most common technique used for the preparation of phytosomes. The most preferable ratio of phospholipids to flavonoids is 1:1 or 1:2 $^{[13]}$. Phospholipids are selected from a group of soy lecithin or from bovine or swine brain or dermis in which the acyl group may be same or different and mostly derived from palmitic, stearic, oleic, and linoleic acids. Phytoconstituents are selected from a group consisting of kaempferol, quercetin, quercetin-

3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoside, diosmine, 3-rhamnoside, (+) catechin, (-) epicatechin, vitexine, apigenin-7-glucoside, luteolin, ginkgometine, luteolinguoside and isoginkgometine. The starting material of the components like flavonoids are insoluble in ethyl ether, chloroform, benzene but it extremely soluble in these solvents after the formation of phytosomes. Due to this chemical and physical property change is due to the formation of a true stable complex $^{[14]}$.

2. Mechanical Dispersion method
It is used for the preparation of marsupsin-phospholipid complexes. Phospholipids is dissolved in a suitable solvent and active ingredient is added drop by drop while sonicking the solution. $^{[15]}$ Curcumin phospholipids complexes are prepared by adding the phospholipids to the ethanol solution of the hydroalcoholic extract of turmeric rhizomes, under reflux and with stirring. Prepared complex called phytosome can be isolated by precipitation with nonsolvent, lyophilization, spray drying or vacuum drying. $^{[16, 17, 18]}$

How Phytosome Differ From a Liposome?
Liposome a microscopic spherical particle formed by a lipid bilayer enclosing an aqueous compartment. Phytosome is a complex of a natural active ingredient and a phospholipid. In liposomes, the active principles are water soluble and are hosted in the inner cavity, with little, if any, interaction taking place between the hydrophilic principle and the surrounding lipid core. Conversely, Phytosomes host their polyphenolic guest, generally little soluble both in water and in lipids, at their surface (Figure 2), where the polar functionalities of the lipophilic guest interact via hydrogen bonds and polar interactions with the charged phosphate head of phospholipids which forming a unique arrangement that can be evidenced by spectroscopy$^{[1-7]}$.

The Phytosome formulation also increases the absorption of active ingredients when topically applied on the skin $^{[19-17]}$, and improves systemic bioavailability when administered orally. In water medium, phytosome a micellar shape, spherical structure, overall which is similar to a liposome, but a different localization.
Liposomes are used primarily in cosmetics to deliver water-soluble substances to the topical. A liposome is formed by mixing a water-soluble substance with PC. No chemical bond is formed; PC molecules surround the water-soluble substance. It’s may be hundreds or even thousands of PC molecules surrounding the water-soluble compound. Similarly the phytosome process the PC and the individual plant components actually form a 1:1 or a 2:1 complex depending on the substance. The difference results in Phytosomes being much better absorbed than liposomes. Phytosomes are superior to liposomes in skin care products [7, 8].

Characterization of Phytosomes

Different evaluation techniques used for phytosomes

Different evaluation techniques used for phytosome were classified as,

1. Physicochemical evaluations
2. Spectroscopic evaluations
3. Biological Evaluation
4. 1. Physicochemical evaluation:
   The Physicochemical evaluation of phytosomes is as given in table No. 1.

2. Spectroscopic evaluations

The formation of the complex can be confirmed by 1H-NMR, 13C-NMR, IR spectroscopy by comparing the spectrum of the complex with the spectrum of the individual components and their mechanical mixtures. Also there are useful tool for the control of the stability of phytosomes when micro-dispersed in water or when incorporated in very simple cosmetic gels. From a practical point of view, the stability can be confirmed by comparing the spectrum of the complex in solid form (phytosomes) with the spectrum of its micro dispersion in water after lyophilization, at different times. In the case of simple formulations, it is necessary to subtract the spectrum of the excipients (blank) from the spectrum of the cosmetic form at different times, comparing the remaining spectrum of the complex itself [22, 23].

1. Biological Evaluation

The selection of models for in-vitro and in-vivo evaluations is based on the expected therapeutic activity of biologically active phytoconstituents present in the phytosomes 24. For example, in vitro antihepatotoxic activity is done by evaluating the antioxidant and free radical scavenging activity of the phytosomes. For assessing antihepatotoxic activity in-vivo, the effect of prepared phytosomes on animals against thioacetamide, paracetamol or alcohol induced hepatotoxicity can be examined. The in vivo safety evaluation of glycyrrhetinic acid Phytosome® ointment, a commercial product, involves the skin sensitization and tolerability studies 25.

Conclusion

The use of the herbal extract is limited due to their poor absorption and poor bioavailability after oral administration. So that phytosome is novel approach are help for the improve the absorption and the bioavability. It improves the stability of the herbal extract. Phospholipids based drug delivery system have been found promising for better and effective delivery of drug and providing much appropriate systematic drug delivery. Phytosomes are superior to liposomes due to much better absorption and stability profile.

References

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