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Review Article

Phytosomes: A Novel Drug Delivery for Herbal Extracts

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ABSTRACT

The term "phyto" means plant while "some" means cell-like. Phytosome is novel emerging technique applied to phyto-pharmaceutical which contains phytoconstituents to herbal extract surrounds and bound by lipids. Phytosome shows better absorption, hence produces better bioavailability than the conventional herbal extracts. Because of their improved pharmacological and pharmacokinetic properties. Phytosomes are herbal formulation which has enhanced the therapeutic effects of the plant extracts and herbal lead molecule by increasing bioavailability in the target site compared to conventional herbal extracts. This is improved forms of herbal formulation which contain the bioactive phytoconstituents of herb essence enclosed and bound by a lipid. Phytosomes demonstrated improved pharmacokinetic and pharmacodynamic response than customary botanical extracts.

Keywords: Phytosomes; Bioavailability, Phospholipids, phytoconstituents.

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Introduction of phytosomes:

Phytosomes is a complex of a phospholipid and natural active ingredients. It is claimed that phytosome increases absorption of "conventional herbal extracts" or isolated active principles both topically as well as orally. Hydrophilic phytoconstituents can be complexed with clinically useful nutrients such as phospholipids to convert them into lipid soluble complexes. Such complexes can be used to prepare liposome-like vesicles called as phytosomes(1,2).

In phytosomes, the complexation of phospholipids and water soluble active plant components involve chemical bond formation and therefore more stable. The phytosomes substantially improve the bioavailability of these hydrophilic active components. Some of the phospholipids that are reported for phytosome preparation include soy phospholipids, phosphatidylcholine etc. Phytosomes can easily cross the lipid membranes and are reported to increase the bioavailability of poorly lipid soluble plant based drugs by increasing the absorption in gastrointestinal tract.

Phytosome is also called as Phytolipids delivery system which forms a bridge between the conventional delivery system and novel delivery system. The term "phyto" means plant while "some" means cell-like. The phytosomes

technology produces a little cell, whereby the plant extract or its active constituent is protected from destruction by gastric secretions and gut bacteria owing to the gastro-protective property of phosphatidylcholine. Most of the bioactive constituents of phytomedicines are water-soluble molecules (e.g. phenolics, glycosides, and flavonoids). However, water-soluble phytoconstituents are limited in their effectiveness because they are poorly absorbed when taken orally or when applied topically (3). Phytosomes are not liposomes - structurally, the two are distinctly different as shown in Fig. The phytosome is a unit of a few molecules bonded together, while the liposome is an aggregate of many phospholipid molecules that can enclose other phytoactive molecules but without specifically bonding to them. Liposomes are touted delivery vehicles, but for dietary supplements their promise has not been fulfilled. But for Indena's phytosome products numerous studies prove they are markedly better absorbed and have substantially greater clinical efficacy.(4,5) Phytosomes are advanced forms of herbal products that are better absorbed, utilized, and as a result produce better results than conventional herbal extracts. Phytosome is a complex between a natural product and natural phospholipids, like soy phospholipids. Such a complex is obtained by reaction of stoichiometric amounts of phospholipid and the substrate in an appropriate solvent. They are miscible both in water and in oil/ lipid

environments, and are well absorbed orally. Phospholipids are small lipid molecules in which the glycerol is bonded only to two fatty acids, instead of three as in triglycerides, with the remaining site occupied by a phosphate group. The phospholipids mainly employed to make phytosomes, is phosphatidylcholine, derived from soybean (*Glycine max*). The phytosome process has been applied successfully too many popular herbal extracts including Ginkgo biloba, grape seed, hawthorn, milk thistle (*Silybummarianum*), green tea (*Theasinensis*) and ginseng (*Panax ginseng*). The flavonoids and terpenoids components of these herbal extracts are able to directly bind to phosphatidylcholine. (6, 7)

Common Drug Delivery Systems used in Pharmaceutical technology:

The “Somes” the cell like formulations of novel drug delivery system. There are different types of somes like Liposomes. Liposomes are nano size artificial vesicles of spherical shape that can be produced from natural phospholipids and cholesterol.

Herbosomes: Herbosomes are purified phytochemical extracts complexed with phospholipids for a better bioavailability and enhanced biological activities.

Cubosomes: Cubosomes are nanoparticles but instead of the solid particles, cubosomes are self-assembled liquid crystalline particles of certain surfactant with proper ratio of water with a microstructure that provides unique properties of practical interest.

Colloidosomes: Colloidosomes are solid microcapsules formed by the self assembly of colloidal particles at the interface of emulsion droplets which are hollow, elastic shells whose permeability and elasticity can be precisely controlled.

Ethosomes: Ethosomes are noninvasive delivery carriers that enable drugs to reach the deep skin layers and/or the systemic circulation. They contain phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water.

Aquasomes: Aquasomes are spherical 300nm particles used for drug and antigen delivery. The particle core is composed of noncrystalline calcium phosphate or ceramic diamond, and is covered by a polyhydroxyl oligomeric film. Aquasomes were prepared by self-assembling of hydroxyapatite by co-precipitation method and thereafter preliminary coated with polyhydroxyl oligomers (cellobiose and trehalose) and subsequently adsorbed with bovine serum albumin (BSA) as a model antigen. BSA-immobilized aquasomes were around 200 nm in diameter and spherical in shape and had approximately 20-30% BSA-loading efficiency.

Pharmacosomes: pharmacosomes are pure drug vesicles formed by the amphiphilic drugs. Any drug possessing a free carboxyl group or an active hydrogen atom ($-OH$, NH_2) can be esterified (with or without a spacer group) to the hydroxyl group of a lipid molecule, thus generating an amphiphilic prodrug. The amphiphilic prodrug is converted to pharmacosomes on dilution with water.

Niosomes: Niosomes are non-ionic surfactant vesicles and, as liposomes, are bilayered structures. Niosomes present low production cost, greater stability, and resultant ease of storage. Niosomes are chemically stable, can entrap both lipophilic and hydrophilic drugs either in aqueous layer or in vesicular membrane and present low toxicity because of their non-ionic nature.

Proniosomes: Proniosomes are dry formulations of surfactant-coated carrier, which can be measured out as needed and rehydrated by brief agitation in hot water.

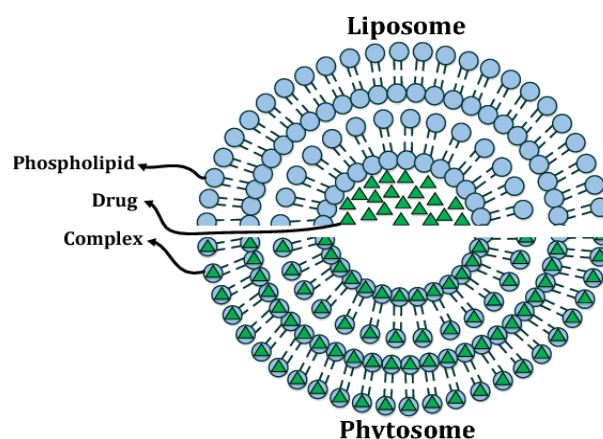


Fig no: 1 Difference between phytosomes and liposomes.
The molecular organization of phytosomes (lower segment) liposome (upper segment)

Benefits of Phytosomes (8):

1. There is a dramatic enhancement of the bioavailability of botanical extracts due to their complexation with phospholipid and improved absorption in the intestinal tract.
2. They permeate the non-lipophilic botanical extract to allow better absorption from the intestinal lumen, which is otherwise not possible.
3. The formulation of Phytosome is safe and the components have all been approved for pharmaceutical and cosmetic use.
4. They have been used to deliver liver protecting flavonoids because they can be made easily bioavailable by phytosomes. In addition to this, Phosphatidylcholine is also hepatoprotective and so provides a synergistic effect for liver protection.
5. This technology offers cost effective delivery of phytoconstituents and synergistic benefits when used as functional cosmetics to protect the skin against exogenous or endogenous hazards in normal as well as stressful environmental conditions.
6. They can be also used for enhanced permeation of drug through skin for transdermal and dermal delivery.
7. These are platform for the delivery of large and diverse group of drugs (peptides, protein molecules).
8. The vesicular system is passive, non-invasive and is available for immediate commercialization.
9. Phosphatidylcholine, an essential part of the cell membrane used in phytosome technology, acts as a carrier and also nourishes the skin.
10. There is no problem with drug entrapment during formulation preparation. Also, the entrapment efficiency is high and moreover predetermined; because the drug itself forms vesicles after conjugation with lipid.
11. They offer a better stability profile because chemical bonds are formed between the phosphatidylcholine molecules and Phytoconstituents.
12. The dose requirement is reduced due to improved absorption of the main constituent. They can also be given in smaller quantities to achieve the desired results.

13. Low risk profile: This technology has no large-scale drug development risk since the toxicological profiles of the phytosomal components are well documented in the scientific literatures.

14. Relatively simple to manufacture with no complicated technical investment required for the production of Phytosomes.

15. They transport from cell membrane and enter the cell membrane easily.

16. Phytosomes proves to be of significantly greater clinic benefits.

17. Facilities liver targeting by increasing the solubility in bile salts.

18. The required dose is reduced as the absorption of the active phyto constituents is improved.

19. Phytosomes improve transdermal absorption of phytoconstituents.

20. Phytosomes are widely used in cosmetic due to improved skin penetration and high lipid profile.

21. Valuable component of herbal extracts are protected from destruction by digestive ecretion and gut bacteria.

22. It assure proper delivery of drug respective tissues.

23. Phosphotidylcholine used in preparation of phytosomes; besides acting as carrier also act as hepato protective as result it improve a synergistic effects.

24. Phosphotidylcholine used in formulating phytosomes process besides actng as carrier also nourishes the skin as it is an essential part of a cell membrane.

25. Phytosomes are also superior to liposomes in skin care products.

26. phytosomes show better stability profile due to formation of chemical bonds between phosphotidylcholine molecules & phytoconstituents.

27. Phytosomes insure increased duration of action for herbal drugs.

28. Phytosomes are used in preparation of phytosomes , besides acting as carrier also act as hepatoprotective , gives synergistic effects.

Difference between phytosomes and liposomes

Table 1:-Difference between phytosomes and liposomes

Phytosomes	Liposomes
Phytosome is a unit of a molecules bounded together.	Liposome is an aggregate of many phospholipid molecules that can enclose other phytoactive molecules but without specifically bonding to them.
Phytosome process the phosphatidylcholine and the plant components actually form a 1:1 or a 2:1 molecular complex depending on the substances complexed. Involving chemical bonds. So they better absorbed and shown better bioavailability.	In liposome no chemical bond is formed. The phosphtidylcholine molecules surround the water soluble substance. There may be hundereds or even thousands of phosphtidylcholine molecules surrounding the water soluble compound.
Phytosome complex can somewhat be compared to an integral part of the lipid membrane. Where the polar functionalities of the lipophilic guest interact via hydrogen bonds with the polar head of a phospholipids (i.e. phosphate and ammonium groups). Forming a unique pattern which can be characterized by spectroscopy.	In liposomes. The active principles are dissolved in the central part of the cavity. With no possibility of molecular interaction between the surrounding lipid and hydrophilic substance.
Phytosomes act with the solvent having a reduced dielectric constant such as Acetone, Dioxane, Metyhlenechloride, Hexane and Ethyl acetate etc.	Liposomal drug complex is formed in the presence of the water or buffer solution.

PROPERTIES OF PHYTOSOMES (9):

1. Chemical properties

Phytosomes is a complex between a natural product and natural phospholipids, like soy phospholipids which is obtained by reaction of stoichiometric amounts of phospholipid and the substrate in an appropriate solvent. It is confirmed by the spectroscopic analysis that the main phospholipid-substrate interaction is due to the formation of hydrogen bonds between the polar head of phospholipids (i.e. phosphate and ammonium groups) and the polar functionalities of the substrate. Phytosomes assumes a micellar shape forming liposomal-like structures in the presence of water.

2. Biological Properties

Phytosome, as an advanced form of herbal product is better absorbed, utilized and as a result produces better results

than conventional herbal extract. The increased bioavailability of the phytosome over the non complexed botanical derivatives has been explained and verified by various pharmacokinetics and pharmacodynamic tests on experimental animal models and on human subjects(9).

Phospholipids

Phospholipids are small lipid molecules where glycerol is bonded to two fatty acids, while the third hydroxyl, normally one of the two primary methylenes, bears a phosphate group bound to a biogenic amino or to an amino acid. Phospholipids are a class of lipids and are a major component of all cell membrane. In humans and other higher animals the phospholipids are also employed as natural digestive aids and as carriers for both fatmiscible and water miscible nutrients. They are miscible both in water and in lipid environments, and are well absorbed orally. Phospholipids from soybean, (Glycine max) mainly

phosphatidylcholine is a lipophilic agent that readily complex polyphenolics and widely employed to make phytosomes. Phosphatidylcholine, the major molecular

building block of cell membranes is a compound miscible in both water and in oil/lipid environments. (10,11)

Table 2 :-Phospholipids

Natural phospholipids	Synthetic phospholipids
PC - Phosphatidyl choline	DOPC - Dioleoyl Phosphatidylcholine
PE- Phosphatidyl ethanolamine	DOPE - Dioleoyl phosphatidyl ethanolamine
PS - Phosphatidyl serine	DSPC - Distearoyl phosphatidyl choline
	DSPE - Distearoyl phosphatidyl ethanolamine
	DLPC - Dilauryl phosphatidyl choline

COMPLEXING AGENTS IN PHYTOSOMES:

Phospholipids are lipids containing phosphorous and a polar portion and non polar portion in their structure. Phospholipids are abundant in egg yolk & plant seeds. phospholipids can be depend on backbone is divided into two types.

1. Glycerophospholipids
2. Sphingomyelins

1. Glycerophospholipids

- 1) Phosphatidylcholine (PC) or Lecithin
- 2) Phosphatidylethanolamine (PE) Cephalin
- 3) Phosphatidylserine (PS)
- 4) Phosphatidic acids (PA) or Phosphatidate
- 5) Phosphatidylinositol (PI)
- 6) Phosphatidylglycerol (PG)
- 7) Cardiolipin (CL)

PC, PE & PS are major phospholipids used to prepare complexes that are composed of hydrophilic head group & two hydrophobic hydrocarbon chains. PC is most frequently used to prepare phospholipid complexes. Benefits of PC is Amphipathic property gives solubility in water and lipid media. It exhibits robust biocompatibility & low toxicity. PC is essential components of cell membranes. PC molecules exhibits Hepatoprotective activity & clinical effects is shown treatment of liver disease, Hepatitis, Fatty liver & Hepatocirrhosis. Phyto-phospholipid complex can not only improve solubility of lipophilic polyphenols in aqueous phase but also membrane penetrability of hydrophilic ones from aqueous phase.

PC is an important substrate of synthesis of the neurotransmitter acetylcholine, and having the function of nourishing the brain and improving intelligence .

PE is a playing an important role in membrane fusion .

PS is a improving function of nerve cells, regulating the conduction of nerve impulse, and enhancing the memory function of brain . The common feature of apoptosis . The main acidic phospholipids of membranes of platelets, and involved in the clotting process .

PI is the precursor of second messenger, which plays a very important role in the process of transmission of messages in neural system .

CL is a phospholipid of unusual structure is localized almost exclusively to inner mitochondrial membrane, is particularly rich in unsaturated fatty acids. This phospholipid plays an important role in mitochondrial bioenergetics by affecting the activity of key proteins of mitochondrial inner membrane .

SM is along with cholesterol, constituting the key components of the stable, detergent-resistant nanodomains in membranes, called functional lipid rafts which have been identified as the important membrane structure of signal transduction, protein transport and sorting of membrane components .

Solvents:

- Aprotic solvents
- Aromatic hydrocarbons
- Halogen derivatives
- Methylene chloride
- Ethyl acetate
- Cyclic ethers

Structure of phosphotidylcholine (PC)

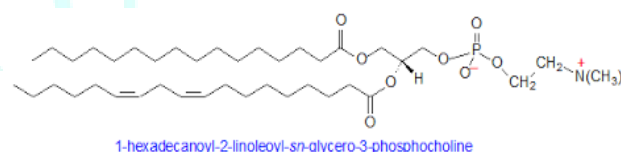


Fig 2:-Structure of phosphotidylcholine (PC)

PC is a phospholipids attached to choline particle. phospholipids contains fatty acids, glycerol ,and phosphorous.the phosphorous part of phospholipids substance –the lecithin –is made up of PC. PC is chemical contained in eggs, soyabean mustard , sunflower & 0other foods. PC are used for treating hepatitis, eczema, gall bladder disease, circulation problems, high cholesterol and premenstrual syndrome; for improve effectiveness of kidney dialysis; for boosting the immune system & for preventing aging. healthcare providers sometimes gives the phosphotidylcholine intravenously (IV) for chest pain , fat globules in the blood (fat embolism), high cholesterol , liver disease & fatty plaque deposits in arteries. PC is injected under the skin (subcutaneously) for treating non-cancerous fatty tumors (lipomas), excess fat around eyelids & yellowish cholesterol deposits just under surface of skin (xanthelasma). Phosphatidylcholines (PC) are a class of phospholipids that incorporate choline as a headgroup. They are a major component of biological membranes and

can be easily obtained from a variety of readily available sources, such as egg yolk or soybeans, from which they are mechanically or chemically extracted using hexane. They are also a member of the lecithin group of yellow-brownish fatty substances occurring in animal and plant tissues. Dipalmitoyl phosphatidylcholine (a.k.a. lecithin) is a major component of pulmonary surfactant and is often used in the L/S ratio to calculate fetal lung maturity. While phosphatidylcholines are found in all plant and animal cells, they are absent in the membranes of most bacteria, including *Escherichia coli*. Purified phosphatidylcholine is produced commercially.

Uses of phosphotidylcholine:

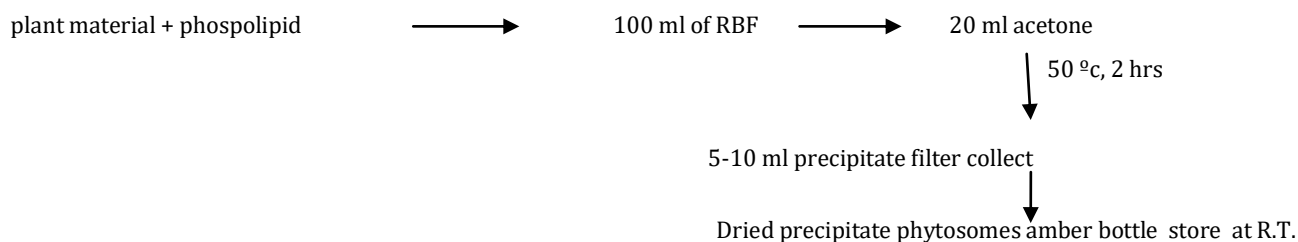
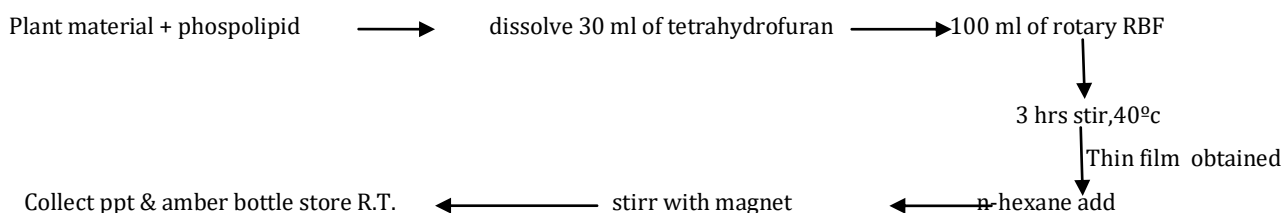
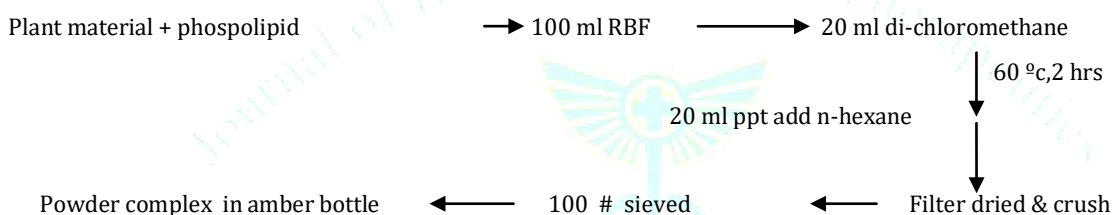
- Inflammatory bowel disease (ulcerative colitis).** Research suggests that taking various types of phosphatidylcholine daily for up to 3 months improves symptoms in people with ulcerative colitis.
- Hepatitis A.** Taking phosphatidylcholine by mouth does not seem to improve liver function in people with hepatitis A.
- Infant development.** Taking phosphatidylcholine during pregnancy does not seem to improve the brain development of the infant.
- Improving a medical procedure called peritoneal dialysis.** Taking phosphatidylcholine by mouth does not seem to improve a medical procedure called peritoneal dialysis.
- A movement disorder called tardive dyskinesia.** Taking phosphatidylcholine by mouth does not seem to improve a movement disorder called tardive dyskinesia.
- Acne.** Early research suggests that applying a cream containing 4% niacinamide and phosphatidylcholine to the skin seems to improve acne in some people.
- Liver disease caused by alcohol.** Early research suggests that taking phosphatidylcholine daily for 24 months does not increase survival in people with liver disease caused by drinking alcohol.
- Reducing fat deposits.** Early research suggests that injections of phosphatidylcholine under the skin may make fatty deposits on the chin, thigh, hips, abdomen, back, neck, and elsewhere look smaller to some people. Improvements appear to last for 2-3 years or longer. In one study, 80% of patients reported improvements in facial fat that lasted for up to 3 years. However, these results have been questioned because the studies were not well designed.
- Declining brain function caused by liver disease.** Research suggests that taking phosphatidylcholine daily for 6-8 weeks does not improve declining brain function in people with liver disease or liver failure.
- Hepatitis B.** Studies regarding hepatitis B show conflicting results. It is not clear if phosphatidylcholine is beneficial.
- Hepatitis C.** Early research suggests that taking phosphatidylcholine by mouth, together with interferon, seems to improve liver function in people with hepatitis C.
- Inability to break down cholesterol in the body.** Early research suggests that taking phosphatidylcholine does not reduce cholesterol levels in the body of people who are unable to break down cholesterol
- Treating non-cancerous fatty tumors (lipomas).** There is one report that injecting a phosphatidylcholine solution directly into a lipoma can shrink the tumor by about 35%. However, this treatment might cause an unwanted reaction in the lipoma.
- Liver disease not related to alcohol use (nonalcoholic fatty liver disease; NAFLD).** Early research suggests that taking a product containing phosphatidylcholine, along with vitamin E, and silybin, a chemical in milk thistle might improve liver function in people with the liver disease known as NAFLD.
- Memory loss.** There is early evidence that taking a single 25 mg dose of phosphatidylcholine can improve some measures of memory in healthy college students.
- Eyelid fat.** There is some evidence that injecting a phosphatidylcholine solution reduces bulging lower eyelid fat pads in some people.
- Anxiety.**
- Eczema.**
- Gallbladder disease.**
- Manic-depressive illness.**
- Circulation disorders of the arms and legs.**
- Weight loss.**
- Premenstrual syndrome (PMS).**
- Alzheimer's disease.**
- Depressed immunity.**
- Preventing aging.**

2. Sphingomyelin (SM)

All SM of biological sources are D-erythro configuration. SM are important component of animal cell membranes. PC & SM are very similar in molecular structure they have some differences. The backbone of SM is sphingosine. The backbone of PC is glycerol.

Table 3:-Sphingomyelin (SM)

S. N.	Phosphotidylcholine (PC)	Sphingomyelin (SM)
1)	The backbone of PC is Glycerol.	The backbone of SM are Sphingosine.
2)	Each PC molecule average contains 1.1-1.5 cis -double bonds.	Each SM molecule average contains 0.1-0.35 cis -double bonds in amide linked acyl chains.
3)	Saturation of hydrophobic regions of PC is less than that of SM.	Saturation of hydrophobic regions of SM is higher than that of PC.
4)	The PC are symmetric molecules.	The SM are asymmetric molecules.
5)	The typical contain moderate length (16-18) of acyl chains and length of two chains are approximately equal.	The typical acyl length of naturally occurring SM are usually more than 20, while the paraffin residue of Sphingosine are relatively shorter.

Method of preparation: (12,13,14)**solvent evaporation method-****Rotary evaporation method -****Anti-solvent precipitation technique-****CHARACTERIZATION TECHNIQUES OF PHYTOSOME (15,16,17)**

3.1 Visualization: Visualization of phytosomes can be done using transmission electron microscopy (TEM) and by scanning electron microscopy (SEM). (18).

SEM was used to determine the size of the particle and its appearance. Dry sample was placed on electron microscope brass stub coated with gold in an ion sputter. Random scanning of the complex at 100.

3.2 Particle size and zeta potential: The particle size and zeta potential can be determined by dynamic light scattering (DLS) using a computerized inspection system and photon correlation spectroscopy (PCS) (19). Size analysis and zeta potential Malvern Zeta sizer is used to check the particle size and zeta size of phytosomal complex. Argon laser is used for this particle size and zeta sizer characterization.

3.3 Drug entrapment efficiency: The entrapment efficiency of a drug by phytosomes can be measured by the ultracentrifugation technique (20). Drug entrapment and loading capacity Drug phytosomal complex was centrifuged at 10000 rpm for 90 minutes at 4°C to separate phytosome from the untrapped drug. The concentration of free drug can be measured by doing ultraviolet spectroscopy. The percentage drug entrapment can be calculated as given formula:

$$\text{Entrapment efficiency \%} = \frac{\text{Weight of total drug} - \text{weight of free drug}}{\text{Weight of total drug}} \times 100$$

3.4 Transition temperature: The transition temperature of the phytosomes can be determined by differential scanning calorimetry (21).

3.5 Surface tension activity measurement: The surface tension activity of the drug in aqueous solution can be measured by the ring method in a Du Nouy ring tensiometer (22).

3.6 Vesicle stability: The stability of vesicles can be determined by assessing the size and structure of the vesicles over time. The mean size is measured by DLS and structural changes are monitored by TEM (23).

3.7 Drug content: The amount of drug can be quantified by a modified high performance liquid chromatographic method or by a suitable spectroscopic method (24).

3.8 spectroscopic evaluations

To confirm the formation of a complex and interaction between the phytoconstituent and the phospholipids, the following spectroscopic methods are used (25).

a) ¹H NMR

The NMR spectra of (+) catechin and its stoichiometric complex with distearoyl phosphatidylcholine have been studied by *Bombardelli et al* (26). In nonpolar solvents, there is a marked change of the ¹H NMR signal originating from the atoms that is involved in the formation of the complex, without any summation of the signal peculiar to the individual molecules. The signals from the protons belonging to the flavonoids are to be broadened that the proton cannot

be relieved. In phospholipids, there is broadening of all the signals while the singlet corresponding to the $N(CH_3)_3$ of choline undergoes an up field shift. By heating the sample to 60, the 1H NMR shows the appearance of some new broad bands, which correspond mainly to the resonance of the flavonoid moiety.

b) ^{13}C NMR

In the ^{13}C NMR spectrum of (+) catechin and its stoichiometric complex with distearoyl phosphatidylcholine, particularly when recorded in C_6D_6 at room temperature, all the flavonoid carbons are clearly invisible. The signals corresponding to the glycerol and choline portion of the lipid (between 60–80 ppm) are broadened and some are shifted, while most of the resonances of the fatty acid chains retain their original sharp line shape. After heating to 60, all the very broad and partially overlapping signals belonging to the flavonoid moieties reappear.

c) FTIR

The formation of the complex can also be analysed by IR spectroscopy by comparing the spectrum of the complex with the spectrum of the individual components and their mechanical mixtures. FTIR spectroscopy is also a useful tool for the control of the stability of phytosomes when microdispersed in water or when incorporated in very simple cosmetic gels. FTIR analysis will be done for checking the structure as well as chemical stability of drug, phospholipid. The phytosomal drug will be crushed with potassium bromide to obtain pellets at 600 kg/cm² pressure. Scanning will be done between the ranges of 4000–400 cm⁻¹.

d) Differential scanning calorimeter

Drug polyphenolic extract, phosphatidylcholine, a physical mixture of drug extract and Phosphatidylcholine, and drug-phospholipid complex were placed in an aluminum cell and heated to a temperature of 50–250°C/minutes from 0 to 400°C in the atmosphere of nitrogen.

CONCLUSION

This review is an attempt to present a concise profile of phytosomes as a delivery system. Phytosomes are advanced form of herbal extracts that are absorbed better than conventional herbal extracts. The article thus reviews the benefits, physical characteristics chemical properties and method of preparation of phytosomes. The formulation methodology for phytosomes is simple and can be easily upgraded to a commercial scale.

REFERENCES

- Awasthi R, Kulkarni GT, Pawar VK. Phytosomes: an approach to increase bioavailability of plant extracts. *Int J Pharm Pharm Sci*. 2011; 3(2): 1-3.
- Chauhan NS, Gowthamarajan K, Gopalakrishna B. Phytosomes: potential phyto-phospholipid carriers for herbal drug delivery. *J Pharm Res*. 2009; 2(7): 1267-70.
- Manach C, Scalbert A, Morand C. Polyphenols: Food Sources and Bioavailability. *Am J Clin Nutr*. 2004; 79:72747.
- Kidd P.M., Phosphatidylcholine (Monograph). In: K. Czap, A.L. Miller, K.A. Head, et al, eds. *Alternative Medicine Review Monographs Volume One*. Dover, ID: Thorne Research, Inc. 2002; 310-315.
- Kidd P.M., Glutathione (Monograph). In: K. Czap, A.L. Miller, K.A. Head, et al, eds. *Alternative Medicine Review Monographs Volume One*. Dover, ID: Thorne Research, Inc.. 2002;184-192.
- Bhattacharya S, Phytosomes: Emerging Strategy in Delivery of Herbal Drugs and Nutraceuticals. *Pharma Times* 2009; 41(3):8-12.
- Citernesi U, Sciacchitano M. Phospholipids/active ingredient complexes, *Cosm & Toil*; 1995;110(11): 57-68.
- Pawar, H.A. Bhangale, B.D., Phytosome as a Novel Biomedicine: A Microencapsulated Drug Delivery System. *J Bioanal Biomed*. 2015; 7 (1):06-12.
- Bombardelli E, Mustich G. Bilobalide?phospholipid complex, their uses and formulation containing them. 1991.U. S. Patent No. EPO 275005,
- Citernesi, U. Sciacchitano, M., Phospholipids/active ingredient complexes. *Cosm & Toil*. 1995;110 (11):57-68.
- Kidd, P.M., Phosphatidylcholine: a superior protectant against liver damage. *Alter Med Rev*. 1996; 1 (2):58-74.
- Priyanka Rathore, Gaurav Swami. Planterosomes: A potential phyto-phospholipid carriers for the bioavailability enhancement of herbal extracts. *International Journal of pharmaceutical sciences and research*. 2012; 3(3):737-755.
- Singh RP, Parpani S, Narke R, Chavan R. Phytosome: Recent advance research for novel drug delivery system. *Asian Journal of Pharmaceutical Research and Development*. 2014; 2(3):15-29.
- Rani B, Vandana, Nagpal M, Arora S. phytosomes: potential carriers for herbal drugs. *Ijrrpas*. 2013; 2(3):566-577.
- Maryana W, Rahma A, Mudhakir D, Rachmawati H. Phytosome containing silymarin for oral administration: Formulation and physical evaluation. *J Biomed Sci Eng* 2015; 25:56.
- Singh RP, Gangadharappa VH, Mruthunjaya K. Phytosome loaded novel herbal drug delivery system: A review. *Int Res J Pharm* 2016; 7(6):15-21.
- Nagpal N, Arora M, Swami G, Rageeb, Kapoor R. Designing of a phytosome dosage form with Tecomella undulata as a novel drug delivery for better utilization. *Pak J Pharm Sci* 2016; 29(4):1231-5.
- Comoglio A., Tomasi A., Malandrino S., et al. Scavenging effect of silipide?A new silybinphospholipid complex, on ethanolderived free radicals. *Biochem. Pharmacol.*, 1995;50: 1313-1316.
- Delgi U., Urbino S. D. Tolerability and cutaneous sensitization study in healthy volunteers after topical application of the product glycyrrhetic acid? Phytosome® ointment. Unpublished data submitted by CTFA, 2004; 36:2.
- Pandey S, Patel K. Phytosomes: Technical revolution in phytomedicine. *Int J Pharma Tech Res* 2010; 2:627-31.
- Jain N et. al. Phytosome: A Novel Drug Delivery System for Herbal Medicine. *International Journal of Pharmaceutical Sciences and Drug Research* 2010; 2(4): 224-228.
- Battacharya S. Phytosomes: Emerging strategy in delivery of herbal drugs and nutraceuticals. *Pharm Times* 2009; 41:3.
- Chauhan NS, Gowtham R, Gopalakrishna B. Phytosomes: A potential Phyto?phospholipid carriers for herbal drug delivery. *J Pharm Res* 2009; 2:1267-70.
- Bhattachrya S. Phytosomes: The new technology for enhancement of bioavailability of botanicals and nutraceuticals. *Int J Health Res* 2009; 2:225.
- Hikino H, Kiso Y, Wagner H, Fiebig M. Antihepatotoxic actions of flavonolignans from Silybum maritimum fruits. *Planta Med* 1984; 50:248-50.
- Valenzuela A, Aspilaga M, Vial S, Guerra R. Selectivity of Silymarin on the increase of the glutathione content on different tissues of the rat. *Planta Med* 1989; 55:420-2.