



Review Article

Phytosome: A Brief Overview

Sanjay Saha*, Anupam Sarma, Pranjal Saikia, Tapash Chakrabarty

Girijananda Chowdhury Institute of Pharmaceutical Science, Department of Pharmaceutics, Azara, Guwahati- 781017, Assam (India)

Corresponding Author's Email: san.sahampharm@gmail.com

Abstract: In the recent days, most of the prevailing diseases and nutritional disorders are treated with natural medicines. Several plant extracts and phyto constituents, despite having excellent bioactivity in vitro demonstrate less or no in vivo actions due to their poor lipid solubility or improper molecular size or both, resulting in poor absorption and bioavailability. So, much work has been directed towards the development of new concept in herbal delivery system i.e., "phytosomes" which are better absorbed, utilized and as a result produce better results than conventional herbal extracts. Phytosomes often known as herbosomes. The term "phyto" means plant while "some" means cell-like. Phytosomes are little cell like structure. Phytosome is composed of phospholipids, mainly phosphatidylcholine, producing a lipid compatible molecular complex with other constituents. Phytosomal complexes were first investigated for cosmetic applications. But PHYTOSOME process was developed and patented by Indena, a leading supplier of nutraceutical ingredients like milk thistle, ginkgo biloba, grape seed, green tea, hawthorn, ginseng etc. Recently, green tea and one of its active components EGCG has received attention from major supplement brands for weight management supplements. Phytosomes are superior to liposomes due to Complex formation ratio of component and phospholipids is 2:1 and 1:1 respectively, much better absorption and stability profile. Phytosome is anti-inflammatory as well as antioxidant. In experimental animal models it improved resistance to atherosclerotic lesion development, enhanced a protective prostaglandin, and protected ventricular heart pump muscle against damage from circulatory deprivation. Development of phytosomes is at the budding stages in India and abroad. It has a lot of potential in the field of medicine, pharmaceuticals and cosmetics.

Keywords : Phytosomes, medicine, Drug Development, Phospholipids

INTRODUCTION

Phytosome is a patented process developed by Indena, to incorporate phospholipids into standardized extracts and so vastly improve their absorption and utilization. Phytosomes are advanced herbal products produced by binding individual component of herbal extract to phosphatidylcholine resulting in a product that is better absorbed and produces better results than the conventional herbal extracts. Many phytoconstituents have multiple rings and, therefore, cannot be absorbed from the intestine into the blood by simple diffusion. Also, some herbal phytomolecules are poorly miscible with oils and other lipids and often fail to pass through the small intestine because of its lipoidal nature. The effectiveness of any herbal product is dependent upon delivering an effective level of the active compounds. Phytosome has an added dimension; the proven health giving activity of the phospholipids themselves. The phytosome process has been applied to many popular herbal extracts including Ginkgo biloba, grape seed, hawthorn, olive fruits and leaves, milk thistle, green tea, ginseng, kushenin, marsupsin and curcumin. The flavonoid and terpenoid components of these herbal extracts are able to directly bind to phosphatidylcholine. Increased bioavailability of the phytosomes over the simpler, non-complexed plant extract has been demonstrated by pharmacokinetics and activity studies, conducted in animals as well as human beings. These compounds can be considered novel

entities on the basis of their physiochemical and spectroscopic characteristics. Presently phytosomes are used primarily in cosmetics to deliver water soluble substances to the skin. This technology is also useful in pharmaceutical formulations intended for treatment of oral cavity in which the contact times are very short because phospholipid allows a greater adhesion of the product itself to the surfaces it comes into contact with [1, 2, 3]

Most of the bioactive constituents of phytomedicines are flavonoids (e.g. anthocyanidins from bilberry, catechins from green tea, silymarin from milk thistle). However, many flavonoids are poorly absorbed [4]. The poor absorption of flavonoid nutrients is likely due to two factors. First, they are multiplexing molecules too large to be absorbed by simple diffusion, while they are not absorbed actively, as occurs with some vitamins and minerals. Second, flavonoid molecules typically have poor miscibility with oils and other lipids, severely limiting their ability to pass across the lipid-rich outer membranes of the enterocytes of the small intestine. Water-soluble flavonoid molecules can be converted into lipid-compatible molecular complexes, aptly called phytosomes. Phytosomes are better able to transition from a hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane and from there into the cell. Finally reaching the blood [5]. Phosphatidylcholine is not

merely a passive "carrier" for the bioactive flavonoids of the phytosomes. But is itself a bioactive nutrient with documented clinical efficacy for liver disease, including alcoholic hepatic steatosis, drug-induced liver damage, and hepatitis.⁶ Phytosomes are not liposomes; structurally, the two are distinctly different. The phytosome is a unit of several molecules bonded together, while the liposome is an aggregate of many phospholipid molecules that can enclose active phytomolecules. But without specifically bonding to them.

Milk Thistle: The First Phytosomes:

The first commercial phytosome preparation was based on the flavonoid silybin, the major constituent of silymarin. A flavonol complex extracted from the milk thistle fruit (*Silybum marianum*, family Asteraceae/Compositae). This phytosome preparation was initially christened IDB 1016 or Silipide [7, 8, 9] and subsequently recast as Siliphos* Phytosome™. [7] Silybinphosphatidylcholine is clinically validated for its antioxidant, anti-inflammatory, and liver detoxification benefits [10].

Advantages of Phytosomes:

The phytosome technology has revolutionized the nutraceutical industry by serving the following benefits: [11 12 13 14]

1. Phytosomes produces a little cell where the valuable components of herbal extracts are protected from destruction by digestive secretions and gut bacteria.
2. It assures proper delivery of drug to the respective tissues.

Properties of Phytosomes:



Fig-Phytosome

Chemical Properties:

Phytosomes is a complex between a natural product and natural phospholipids, like soy phospholipids. Such a complex results from the reaction of stoichiometric amounts of phospholipid with the selected polyphenol (like simple flavonoids) in a

3. The nutrient safety of the herbal extracts need not be compromised by conveying the herbal drug as means of phytosomes.
4. Dose requirement has been reduced due to the maximum absorption of chief constituents.
5. Marked enhancement in the bioavailability of drug occurs.
6. Entrapment efficiency is high and more over predetermined because drug itself is in conjugation with lipids in forming vesicles.
7. There is no problem in drug entrapment while formulating phytosomes.
8. Phytosomes shows better stability profile due to the formation of chemical bonds between phosphatidylcholine molecules and the phytoconstituents.
9. Phosphatidylcholine used in formulating phytosome process besides acting as a carrier also nourishes the skin as it is an essential part of a cell membrane.
10. Phytosomes are also superior to liposomes in skin care products.
11. Phytosomes proves to be of significantly greater clinical benefit.
12. Phosphatidylcholine used in preparation of phytosomes, besides acting as a carrier also acts as a hepatoprotective as a result it imparts a synergistic effect when hepatoprotective substances are employed.
13. Their low solubility in aqueous media allows the formation of stable emulsions or creams.
14. Facilitates the liver targeting by increasing the solubility in bile salt.

nonpolar solvent. [15] On the basis of their physicochemical and spectroscopic data, it has been shown 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 functional groups of

the substrate. They are lipophilic substances with a clear melting point, freely soluble in nonpolar solvents (in which the hydrophilic moiety was not), and moderately soluble in fats. When treated with water, phytosomes assume a micellar shape forming liposomal-like structures. In liposomes the active principle is dissolved in an internal pocket or floats in the layer membrane, while in phytosomes the active principle is anchored to the polar head of phospholipids, becoming an integral part of the membrane. [16, 17, 18]

Biological properties:

Phytosomes are advanced forms of herbal products that are better absorbed, utilized and as a result produce better results than conventional herbal extracts. The increased bioavailability of the phytosome over the non complexed botanical derivatives has been demonstrated by pharmacokinetic studies or by pharmacodynamics tests in experimental animals and in human subjects [19].

Bioavailability of Phytosomes:

It is evident from many research studies that phytosomes have an improved absorption and bioavailability when compared to the conventional means. Most of the research studies are focused on *Silybum marianum* (milk thistle), the fruit of which contains a water-soluble phytoconstituent (flavonoids) which is known to have a hepatoprotective effect. But these flavonoids are poorly absorbed. The chief and most potent constituent of milk thistle is Silybin. A brief summary of some of the research studies is given as:

- According to Crema *et al.*, 1990, when single oral doses of Silybin directly bound to phosphatidylcholine (Silybin phytosome) are fed, its absorption was approximately seven times more than the absorption from regular milk thistle extract containing 70-80% silymarin content).
- A research study was conducted by (Yanyu *et al.*, 2006) in which he prepared silymarin phytosome and has shown its pharmacokinetics in rats. The phytosome was administered to rats orally. The results showed that the bioavailability and biological effects of Silybin was increased remarkably.
- Some of the studies have reported the better results produced by consuming ginkgo phytosome than the conventional ginkgo extract. A bioavailability study was conducted on healthy human volunteers in which it was found that the levels of flavonoids and terpenes (GBE constituents) peaked after 3 hours and persisted longer last for 5 hours.

One study shows that some patients suffering from Reynaud's disease and intermittent circulation were fed with ginkgo phytosome which was shown to produce a

30-60% greater improvement compared to regular standardized GBE (*Ginkgo biloba* extract). [20]

Phytosome Technology:

The flavonoid and terpenoid constituents of plant extracts lend themselves quite well for the direct binding to phosphatidylcholine. Phytosomes results from the reaction of a stoichiometric amount of the phospholipid (phosphatidylcholine) with the standardized extract or polyphenolic constituents (like simple flavonoids) in a non-polar solvent [21]. Phosphatidylcholine is a bifunctional compound, the phosphatidyl moiety being lipophilic and the choline moiety being hydrophilic in nature. Specifically the choline head of the phosphatidylcholine molecule binds to these compounds while the lipid soluble phosphatidyl portion comprising the body and tail which then envelopes the choline bound material. Hence, the phytoconstituents produce a lipid compatible molecular complex with phospholipids, also called as phyto-phospholipid complex. Molecules are anchored through chemical bonds to the polar choline head of the phospholipids, as can be demonstrated by specific spectroscopic techniques [22, 23]. Precise chemical analysis indicates the unit phytosome is usually a flavonoid molecule linked with at least one phosphatidylcholine molecule. The result is a little micro sphere or cell is produced. The term "phyto" means plant while "some" means cell-like. The phytosome 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 Likewise phytosomes, a liposome is formed by mixing a water soluble substance with phosphatidylcholine in definite ratio under specific conditions. Here, no chemical bond is formed; the phosphatidylcholine molecules surround the water soluble substance. There may be hundreds or even thousands of phosphatidylcholine molecules surrounding the water-soluble compound. In contrast, with the phytosome process the phosphatidylcholine and the plant components actually form a 1:1 or a 2:1 molecular complex depending on the substance(s) complexed, involving chemical bonds. This difference results in phytosome being much better absorbed than liposomes showing better bioavailability. Phytosomes have also been found superior to liposomes in topical and skin care products [26].

Method of Preparation:

Phytosomes are prepared by reacting 3–2 moles (preferably with one mole) of a natural or synthetic phospholipid, such as phosphatidylcholine, phosphatidyl- ethanolamine or phosphatidylserine, with one mole of phytoconstituents either alone or in the natural mixture in an aprotic solvent, such as dioxane or acetone, in a 1:2 or 1:1 ratio. ²⁵ The optimum ratio of phospholipid to phytoconstituent is 1:1. The complex thus formed can be isolated by precipitation with an aliphatic hydrocarbon or lyophilization or spray drying. [26].

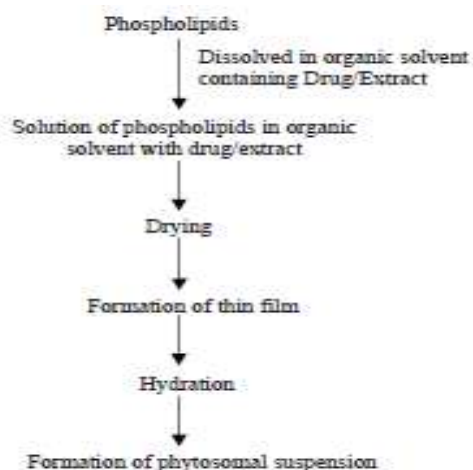


Figure: Common stages for preparation of phytosome

Some liposomal drug complexes operate in the presence of water or buffer solution where the phytosomes interact with a solvent with a reduced dielectric constant. The common stages for the preparation of phytosomes²⁷ are charted in Fig. 2. Mareno and Lampertico [25], Jiang *et al* [28], Maiti *et al* [29] have described the methods used for phytosome preparation. Jiang, *et al.* (2001) have optimized the preparation conditions using a uniform design and step regression and have prepared Herba Epimedii total flavonoid phytosomes (EFP) by means of solvent evaporation and investigated the cumulative dissolution of different ratios of EFP-PVP precipitates by means of dissolution release. The optimized preparation conditions are as follows: solvent-tetrahydrofuran, lecithin to PVP ratio— 2.5, temperature—40°C and reaction time-3 hrs. The oil/water apparent partition coefficient of icariin was enhanced more than 4-fold by phospholipid. The cumulative dissolution of Herba Epimedii flavonoids of the EFP-PVP precipitate was significantly higher than that of its physical mixture and a Herba epimedii extract tablet [28]. Yanyu *et al* (2006) prepared a silybin-phospholipid complex using ethanol as a reaction medium. Silybin and phospholipids were resolved into the medium, after the organic solvent was removed under vacuum condition, and a silybin-phospholipid complex was formed [30].

Formulation of Phytosome:

Phytosome® complexes can be formulated both orally and topically. In order to obtain the best performances of this technological innovation both in terms of formulating manageability and enhanced bioavailability (as appropriate disintegration and dissolution time of oral forms, for instance)

Soft gelatin capsules: Soft gelatin capsules represent an ideal solution to formulate Phytosome® complexes. The Phytosome® complex can be dispersed in oily vehicles to obtain suspensions to be filled in soft gelatin

capsules. Vegetable or semi-synthetic oils can be used to this purpose. Indena recommend a granulometry of 100% <200 µm to best perform capsule production. According to Indena experience, not all the Phytosome® complexes behave in the same way when dispersed in oily vehicles and when the oily suspension is filled in the soft gelatin capsules; for this reasons preliminary feasibility trials should be performed to select the most suitable vehicle.

Hard gelatin capsules: The Phytosome® complex can be formulated in hard gelatin capsules as well. A direct volumetric filling process (without precompression) can be applied, even if the apparently low density of the Phytosome® complex seems to limit the maximum amount of powder that can be filled into a capsule (usually not more than 300 mg for a size 0 capsule). With a piston tamp capsule filling process, however, it is possible to increase the amount of powder which can be filled in a capsule, but precompression might affect the disintegration time. Indena recommend to carefully monitor the related parameters during product/ process development. A preliminary dry granulation process is advisable define the best manufacturing process.

Tablets: Dry granulation represents the ideal manufacturing process to obtain tablets with higher unitary doses and with suitable technological and biopharmaceutical properties. However, due to the limited flowability, potential stickiness and low apparent density of the Phytosome® complex, a direct compression process can be applied only for low unitary doses; note that whenever a direct compression process is applied, the Phytosome® complex should be diluted with 60-70% of excipients to optimize its technological properties and to obtain tablets with appropriate technological and biopharmaceutical characteristics. On the other hand, wet granulation should be avoided due to the negative effect of water and heat (granulation/ drying) on the stability of the phospholipid complex.

Topical dosage forms: The Phytosome® complex can be formulated topically as well. The ideal process to incorporate the Phytosome® complex in emulsion is to disperse the phospholipidic complex in a small amount of the lipidic phase and add it to the already created emulsion at low temperatures (not higher than 40°C). The Phytosome® complexes are dispersible in the main lipidic solvents employed in topical formulations. In case of formulations containing a limited amount of lipids, the Phytosome® complex might also be dispersed into the watery phase, and again added to the final formulation at temperature lower than 40°C.

SOME PATENTED TECHNOLOGIES RELATED TO PHYTOSOMES:

There are a number of innovative processes and formulation research studies in the field of phytosomes carried out by a number of academic scientist as well as by industrial laboratories. Some patents for phytosomes and other related technologies along with their applications and innovations are listed in Table 1.

Table 1: Some patented technologies related to phytosome.

Title of patent	Innovation	Patent No.	Reference
Phospholipid complexes of olive fruits or leaves extracts having improved bioavailability	Phospholipids complexes of olive fruits or leaves extracts or compositions containing it having improved bioavailability.	EP/1844785	[31]
Compositions comprising <i>Ginkgo biloba</i> derivatives for the treatment of asthmatic and allergic conditions	Compositions containing fractions deriving from <i>Ginkgo biloba</i> , useful for the treatment of asthmatic and allergic conditions	EP1813280	[32]
Fatty acid monoesters of sorbityl furfural and compositions for cosmetic and dermatological use	Fatty acid monoesters of sorbityl furfural selected from two diff series of compounds in which side chain is a linear or branched C3 -C19 alkyl radical optionally containing at least one ethylenic unsaturation	EP1690862	[33]
Cosmetic and dermatological composition for the treatment of aging or photodamaged skin	Composition for topical treatment of the skin comprises a substance that stimulates collagen synthesis and a substance that enhances the interaction between extracellular matrix and fibroblasts Cosmetic or dermatological composition for topical treatment	EP1640041	[34]
Treatment of skin, and wound repair, with thymosin beta 4	Compositions and methods for treatment of skin utilizing thymosin β 4.	US/2007/0015698	[35]
Soluble isoflavone compositions	Isoflavone compositions exhibiting improved solubility (<i>e.g.</i> , light transmittance), taste, color, and texture characteristics, and methods for making the same.	WO/2004/045541	[36]
An anti-oxidant preparation based on plant extracts for the treatment of circulation and adiposity problems	Preparation based on plant extracts which has an anti-oxidant effect and is particularly useful in treatment of circulation problems such as phlebitis, varicose veins, arteriosclerosis, haemorrhoids and high blood pressure	EP1214084	[37]
Complexes of saponins with phospholipids and pharmaceutical and cosmetic compositions containing them	Complexes of saponins with natural or synthetic phospholipids have high lipophilia and improved bioavailability and are suitable for use as active principle in pharmaceutical, dermatologic and cosmetic compositions	EP0283713	[38]

Evaluation of Phytosomes:

Various spectroscopic and in-vitro and in-vivo evaluations are applied on phytosomes. The following are the characterization techniques used for phytosomes in characterizing its physical attributes-

1. **Entrapment efficiency:** The entrapment efficiency of a phytosomal formulation can be determined by subjecting the formulation to ultracentrifugation technique. [39]

2. Transition temperature: The transition temperature of vesicular lipid system can be determined by differential scanning calorimetry [40 41].
3. **Vesicle size and Zeta potential:** The particle size and zeta potential of phytosomes can be determined by dynamic light scattering which uses a computerized inspection system and photon correlation spectroscopy [42, 43].
4. **Surface tension activity measurement:** The surface tension activity of drug in aqueous solution can be measured by ring method Du Nouy ring tensiometer [44].
5. **Spectroscopic evaluation:** The spectroscopic evaluations are widely employed in order to confirm the formation of complex between phytoconstituents and the phospholipid moiety as well as to study the corresponding interaction between the two.

The widely employed methods are listed below-

¹H NMR: The complex formation between the active phytoconstituents and the phosphatidylcholine molecule can be estimated by this method. Bombardelli studied the NMR spectra of phytosome complex in nonpolar solvents. There is a marked change in ¹H NMR signal originating from atoms involved in the formation of complex, without any summation of the signal peculiar to individual molecules. The signals from protons belonging to the phytoconstituents are broadened. In phospholipids there is broadening of signals while the singlet corresponding to the N-(CH₃)₃ of choline undergoes an upfield shift [43 45].

¹³C NMR: In the ¹³C NMR of the phytoconstituents and the stoichiometric complex with the phosphatidylcholine when recorded in C₆D₆ at room temperature all the phytoconstituents carbons were invisible. The signals corresponding to the glycerol and choline portion are broadened and some are shifted, while most of the resonance of the fatty acids chains retain their original sharp line shape [43 45].

FTIR: The spectroscopic evaluation of the formed complex can be confirmed by FTIR simply by comparing the spectrum of the complex and the individual components and that of the mechanical mixtures. FTIR can also be considered as a valuable tool in confirming the stability of the phytosomal complex. The stability can be confirmed by comparing the spectrum of the complex in solid form with that of the spectrum of micro-dispersion in water after lyophilization at different times [43, 45].

In-vivo studies are performed on Beagle dogs, rodents, wistar rats to compare pharmacokinetics parameters between pure extracts and its phospholipid complex [46,47].

APPLICATION:

To examine the various advantages of phytosomes, especially their ability to enhance the bioavailability of polar phytoconstituents, various therapeutic applications of phytosomes have been explored. The details of the type of phytosomes, active constituents, the daily dose and specific indications are given in Table- 2.

Table 2: Therapeutic applications of different phytosomes with their dose. [48, 49, 50, 51]

Phytosomes	Phytoconstituent complexed with PC	Daily dosage	Indication
<i>Leucoselect</i> ® phytosome	Procyanidolic oligomers (PCOs) from grape seeds	50–100 mg	Systemic antioxidant, specific. Best choice for most people under age of fifty. Also specific for the eyes, lungs, diabetes, varicose veins, and protection against heart disease.
<i>Greenselect</i> ® phytosome	Epigallocatechin 3- <i>O</i> -gallate from <i>camelia sinensis</i> (Green tea)	50–100 mg	Systemic antioxidant. Best choice for protection against cancer and damage to cholesterol
<i>Ginkgoselect</i> ® phytosome	24 % ginkgo flavono glycosides from <i>Ginkgo biloba</i>	120 mg	Best choice for most people over the age of 50. Protects brain and vascular lining [52]
Silybin phytosome	Silybin from silymarin (milk thistle)	120 mg	Best choice if the liver or skin needs additional antioxidant protection
<i>Siliphos</i> ™ milk thistle phytosome	Silybin from silymarin	150 mg	Good choice for liver or skin support [53]
Hawthorn phytosome	Flavonoids	100 mg	Best choice in heart disease
<i>Panax ginseng</i> phytosome	37.5% ginsenosides from roots of <i>Panax ginseng</i>	150 mg	As a Food Product
Glycyrrhiza phytosome	18-beta glycyrrhetic acid	–	Anti-inflammatory Activity [54]

<i>Mirtoselect</i> [®] phytosome	Anthocyanosides from an extract of Bilberry	–	These improve capillary tone, reduce abnormal blood vessel permeability & are potent antioxidants. They hold great potential for the management of retinal blood vessel problems and venous insufficiency.
<i>Sabalselect</i> [®] phytosome	An extract of saw palmetto berries through supercritical CO ₂ (carbon dioxide) extraction	–	It delivers fatty acids, alcohols and sterols that benefit prostate health. Also beneficial for non-cancerous prostate enlargement
<i>Polinacea</i> TM phytosome	Echinacosides and a unique high-molecular weight Polysaccharide from <i>Echinacea angustifolia</i>	–	It enhances immune function in response to a toxic challenge
<i>Oleaselect</i> TM phytosome	Polyphenols from olive oil	–	As potent antioxidants, inhibit harmful oxidation of LDL cholesterol, and also have anti-inflammatory activity.
<i>Lymphaselect</i> TM phytosome	A standardized extract of <i>melilotus officinalis</i>	–	Indicated for venous disorders, including chronic venous insufficiency of the lower limbs.

Most of the phytosomal studies are focused to *Silybum marianum* which contains premier liver-protectant flavonoids. The fruit of the milk thistle plant (*S. marianum*, Family *Steraceae*) contains flavonoids known for hepatoprotective effects. Silymarin has been shown to have positive effects in treating liver diseases of various kinds, including hepatitis, cirrhosis, fatty infiltration of the liver (chemical and alcohol induced fatty liver) and inflammation of the bile duct. The antioxidant capacity of silymarin substantially boosts the liver's resistance to toxic insults while PC helps repair and replace cell membranes [55].

Francesco *et al.*, (2009) studied on a recently developed oral formulation in the form of coated tablets (Monoselectm *Camellia*[®]) (MonCam) containing highly bioavailable green tea extract (GreenSelect[®] Phytosome) was tested in obese subjects (n=100) of both genders on a hypocaloric diet. Fifty subjects were assigned to the green tea extract plus hypocaloric diet, while the other 50 subjects followed the hypocaloric diet only. After 90 days of treatment, significant weight loss and decreased body mass index (BMI) were observed in the group taking the herbal extract (14 kg loss in the green tea group compared to a 5 kg loss in the diet-only group); waistline was reduced only in male subjects [55].

Maiti *et al.* developed the quercetinphospholipid phytosomal complex by a simple and reproducible method and also showed that the formulation exerted better therapeutic efficacy as compared to the non-phytosomal conventional preparation in rat liver injury induced by carbon tetrachloride [56].

Green tea leaves (*Theasinensis*) is characterized by presence of a polyphenolic compound epigallocatechin 3-O-gallate as the key component.

These compounds are potent modulators of several biochemical process linked to the breakdown of homeostasis in major chronic-degenerative diseases such as cancer and atherosclerosis. Green tea also furnishes us with a number of beneficial activities such as antioxidant, anticarcinogenic, antimutagenic, hypocholesterolemic, cardioprotective effects. In spite of such beneficial activities furnished by polyphenols from green tea extract the polyphenols suffer from the problem of poor bioavailability. The complexation of polyphenols derived from green tea with phospholipids strongly improves the oral bioavailability.

Conclusion:

The poor absorption and the poor bioavailability associated with the polar phytoconstituents limits its use. These hindrances can be tackled by formulating an appropriate drug delivery system. Phospholipid based drug delivery system have been found promising for better and effective delivery of drug and can enhance the rate and extent of drug absorption across the lipoidal biomembrane. Phytosome are one of the phospholipid based drug delivery system with a better absorption and stability profile as compared to other phospholipid based drug delivery system like liposome. Presently phytosomes are used primarily in cosmetics to deliver water soluble substances to the skin. The technology can effectively deliver the product by topical and oral route. Technology is having a lot of commercial application. Phytosomes enables pharmaceutical manufacturers to provide new pharmaceutical products using water soluble drugs and provides new developments in medical industry.

References:

1. Bombardelli E, Curri SB, Della LR, Complexes between phospholipids and vegetal

- derivatives of biological interest, *Fitoterapia*, 90 (suppl.1), 1989, 1-9.
2. Parris K, Kathleen H, A review of the bioavailability and clinical efficacy of milk thistle phytosome: a silybinphosphatidylcholine complex, *Altern Med Rev*, 10(3), 2005, 193-203.
 3. Gupta A, Ashawat MS, Saraf S, Phytosome: A novel approach towards functional cosmetics, *J Plant sci*, 2(6), 2007, 644-649.
 4. Maiach C, Scalbert A, Morand C, et al. Polyphenols: food sources and bioavailability. *Am J Clin Nutr* 2004; 79:121-141.
 5. Bombardelli E, Curri SB, Delia Loggia R, et al. Complexes between phospholipids and vegetal derivatives of biological interest. *Fitoterapia* 1989; 60:1-9.
 6. Kidd PM. Phosphatidylcholine (Monograph). In: Czap K, Miller AL, Head KA. et al. eds. *Alternative Medicine Review Monograph*.^ Voionie One. Dover. ID: Thorne Research, Inc.: OO2:3K)-315.
 7. www.indena.com/pdf/ephytasome.pdf [Accessed June 20, 2009]
 8. Malandrino S, P'ihcri G. UB-1016. *Drum Euture* 1990; 15:226-227.
 9. Barzaghi N, Crema F, Gatti G, et al. Pharmacokinetic studies on IdB 1016. a silyliin-phosphariJylcholine complex, in healthy human subjects. *Eur J Drug Metab PiwmKicDfcmci* 1990; 15:333-338.
 10. Kidd P, Head K. A review of the bioavailability and clinical efficacy of milk thistle phytosome: 3 silybinphosphatidylcholine complex (Siliphos'), *Altern Med R* (T 2005; 10:193-203.
 11. Sharma S, Sikarwar M: Phytosome: A review, *Plant indica* 2005; 1(2): 1-3.
 12. Bombardelli E: Phytosome: New cosmetic delivery, *Boll chim farm* 1991; 130(11): 431-438.
 13. Sharma S., Roy RK. Phytosomes: An Emerging Technology; *International Journal of Pharma Research and Development*; Vol 2(5); 2010; p no: 2
 14. Manthena S., Srinivas P. Sadanandam; Phytosome in herbal drug delivery; *Journal of natural Pharmaceutils*; Vol 1(1); 2010; p no 16
 15. Bombardelli E, Curri SB., Loggia Della R., et al. Complexes between phospholipids and vegetal derivatives of biological interest. *Fitoterapia*. 1989, 60: 1-9.
 16. Dubey D., Shrivastava S., Kapoor S., et al. Phytosome: a novel dosage structure, <http://www.pharmainfo.net/reviews/phytosome-novel-dosage-structure>, 2007.
 17. Semalty A., Semalty M., Rawat MSM. The phytophospholipid complexes- phytosomes: a potential therapeutic approach for herbal hepatoprotective drug delivery. *Pharmacognosy Reviews*, 2007, 1: 369-374.
 18. Vasanti S. Phytosomes: A short review. Available at <http://www.biologyonline.org/articles/phytosomes-short-review.html>. 2008.
 19. Franco PG., Bombardelli, Ezio. Complex compounds of bioflavonoids with phospholipids, their preparation and uses and pharmaceutical and cosmetic compositions containing them, U.S. Patent No-EPO 275005, 1998.
 20. Amin T, Bhat SV. A Review on Phytosome Technology as a Novel Approach to Improve The Bioavailability of Nutraceuticals; *International Journal of Advancements in Research & Technology*, Volume 1(3); 2012; page no: 3
 21. Bombardelli E, Curri SB, Loggia Della R, Del NP, Tubaro A, Gariboldi P. Complexes between phospholipids and vegetal derivatives of biological interest. *Fitoterapia* 1989; 60:1-9.
 22. Bombardelli E. Phytosome: new cosmetic delivery system. *Boll Chim Farm* 1991; 130 (11): 431-38.
 23. Bombardelli E, Spelta M. Phospholipid-polyphenol complexes: A new concept in skin care ingredients. *Cosm & Toil* 1991; 106 (3): 69-76.
 24. Phytosomes: A technical revolution in phytomedicine. Available at: <http://www.indena.com> Accessed- Oct. 2, 2008.
 25. C. Marena, M. Lampertico. Preliminary clinical development of silybin: A new complex of silybin in toxic liver disorders. *Planta Med.*, 1991, 57: A124-A125.
 26. S. Mascarella. Therapeutic & antiliperoxidant effects of silybin-phosphatidylcholine complex in chronic liver disease. *Curr. Ther. Res.*, 1993, 53: 98-102.
 27. N. K. Jain. Liposomes as drug carriers, controlled and novel drug delivery, 1st edition, CBS publisher, 2005, 308.
 28. Y. N. Jiang, Z. P. Yu, Z. M. Yan, et al. Preparation of herba epimedii flavanoid and their pharmaceuticals. *Zhongguo Zhong Yao*, 2001, 26: 105-108.
 29. K. Maiti, K. Mukherjee, A. Gantait, et al. Enhanced therapeutic potential of naringenin-phospholipid complex in rats. *J. Pharm. Pharmacol.*, 2006, 58: 1227-1233.
 30. X. Yanyu, S. Yunmei, C. Zhipeng, et al. The preparation of silybin-phospholipid complex and the study on its pharmacokinetics in rats. *Int. J. Pharm.*, 2006, 307: 77-82.
 31. Franceschi F., Giori A. A phospholipid complex of olive fruits or leaves extracts having improved bioavailability. EP1844785, 2007.
 32. Di Pierro F. Compositions comprising Ginkgo biloba derivatives for the treatment of

- asthmatic and allergic conditions. EP1813280, 2007. V. Bertelli. Fatty acid monoesters of sorbityl furfural and compositions for cosmetic and dermatological use. EP1690862, 2006.
33. Bertelli V. Fatty acid monoesters of sorbityl furfural and compositions for cosmetic and dermatological use. EP1690862, 2006.
34. Doering T., Traeger A., Waldmann-Laue M., et al. Cosmetic and dermatological composition for the treatment of aging or photodamaged skin. EP1640041, 2006.
35. Kleinman HK., Goldstein AL et al. Treatment of skin, and wound repair, with thymosin beta 4. U. S. Patent No-20070015698, 2007.
36. Khare AB. Soluble isoflavone compositions. WO/2004/ 045541, 2004
37. Merizzi G. An anti-oxidant preparation based on plant extracts for the treatment of circulation and adiposity problems. EP1214084, 2002.
38. Bombardelli E., Patri GF. Pozzi R. Complexes of saponins with phospholipids and pharmaceutical and cosmetic compositions containing them. EP0283713, 1988.
39. GMM Maghraby E, Williams AC, Barry BW: Oestriodiol Skin Delivery from Ultra deformable Liposomes: Refinement of Surfactant Concentration, Int J.Pharm 2000; 196: 63-74.
40. Fry DW, White JC, Goldman ID: Rapid Secretion of Low Molecular Weight Solute from Liposomes Without Dilution, Anal.Biochem 1978; 90: 809-815.
41. Cevc G, Schatzlein A: Transdermal Drug Carriers: Basic Properties, Optimization and Transfer Efficiency in Case of Epicutaneously Applied Peptides, J. Control Release 1995; 36: 3-16.
42. Dayan N, Touitou E: Carrier for Skin Delivery of Trihexyphenidyl HCl: Ethosomes v/s Liposomes, Biomaterials 2002; 21: 1879-1885.
43. Gabetta B, Zini GF, Pifferi G: Spectroscopic Studies on Idb-1016 A New Flavanolignan Complex, Plant Med 1989; 55: 615.
44. BAIV Berge, VAB Wartzendruber, Geest J: Development of an Optimal Protocol for Ultrastructural Examination of Skin by TEM, J.Micros 1997; 187: 125-133.
45. Malandrino S, Pifferi G: Idb-1016 Silybin Phosphatidylcholine Complex, Drugs Future 1990; 15: 226-227.
46. Qingguo M, Er G, Ruqin W. The study on puerarin phytosomes preparation and its 1. 1H-NMR and TLC, J.Weifang.Med.Coll, 23(1), 2001, 4-5.
47. Mauri P, Simonetti P, Gardana C. Liquid chromatography/atmospheric pressure chemical ionization mass spectrometry of terpene lactones in plasma of volunteers dosed with Ginkgo biloba L. extracts, Rapid Commun Mass Spectrom., 15(12), 2001, 929-934.
48. Murray MT. Phytosomes: Herbal Support – Increase the Absorption of Herbal Extracts, Available at www.doctormurray.com/articles/silybin.htm, 2004.
49. Kidd PM. Phytosomes: highly bioavailable plant extracts. Available at <http://www.indena.com>.
50. Vitamedics. Phytosome products. Available at <http://www.vitamedics.com>.
51. Joshi A., Chaturvedi S., Kumar V., et al. Phytosomes-a revolution in herbal drugs. Pharma Review, Kongposh Publications, December, 2007–January, 2008.
52. Naik SR., Pilgaonkar VW., et al. Evaluation of antioxidant activity of Ginkgo biloba phytosomes in rat brain. Phytotherapy Research, 2006, 20: 1013-1016.
53. Murray MT. Siliphos: Nature's Potent Liver Remedy, Available at <http://www.doctormurray.com/articles/silybin.htm>.
54. Bombardelli E., Curri SB., Della Loggia R., et al. Antiinflammatory activity of 18-beta glycyrrhetic acid in phytosome form. Fitoterapia, 1989, 60: 29-37.
55. Jain N., Gupta BP., Thakur N, Jain R, Banweer J, Jain DK., Jain S. Phytosome: A Novel Drug Delivery System for Herbal Medicine; International Journal of Pharmaceutical Sciences and Drug Research; Vol. 2(4); 2010; pp 224-228
56. Maiti K, Mukherjee K, Gantait A, Ahamed HN, Saha BP, Mukherjee PK: Enhanced Therapeutic Benefit of Quercetin-Phospholipid Complex in Carbon Tetrachloride Induced Acute Liver Injury in Rats: A Comparative Study, Iran J Pharmacol Ther 2005;4: 84-90.