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PHYTOSOMES: A NOVEL DRUG DELIVERY FOR HERBAL EXTRACTS

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ABSTRACT: Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Our country has a vast knowledge base of Ayurveda whose potential is only being realized in the recent years.The effectiveness of any herbal medication is dependent on the delivery of effective level of the therapeutically active compound. Severe limitation exists in their bioavailability when administered orally or topically. Phytosomes are recently introduced herbal formulations that are better absorbed and as a result produce better bioavailability and actions than the conventional phyto-molecules or botanical extracts. In the recent days, most of the prevailing diseases and nutritional disorders are treated with natural medicines. Several plant extracts and phytoconstituents, 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 owing to the presence of phosphatidylcholine which likely pushes the phytoconstituent through the intestinal epithelial cell outer membrane, subsequently accessing the bloodstream phytosomes have improved pharmacokinetic and pharmacological parameter which in result can advantageously be used in the treatment of the acute and chronic liver disease of toxic metabolic or infective origin or of degenerative nature.

INTRODUCTION: Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Our country has a vast knowledge base of Ayurveda whose potential is only being realized in the recent years. However, the drug delivery system used for administering the herbal medicine to the patient is traditional and out-of-date, resulting in reduced efficacy of the drug. If the novel drug delivery technology is applied in herbal medicine, it may help in increasing the efficacy and reducing the side effects of various herbal compounds and herbs. This is the basic idea behind incorporating novel method of drug delivery in herbal medicines. Thus, it is important to integrate novel drug delivery system and Indian Ayurvedic medicines to combat more serious diseases. For a long time herbal medicines were not considered for development as novel formulations owing to lack of scientific justification and processing difficulties, such as standardization, extraction and identification of individual drug components in complex poly herbal systems.

However, modern phyto pharmaceutical research can solve the scientific needs (such as determination of pharmacokinetics, mechanism of action, site of action, accurate dose required etc.) of herbal medicines to be incorporated in novel drug delivery system, such as nanoparticles, microemulsions, phytosomes, matrix systems, solid dispersions, liposomes, solid lipid nanoparticles and so on. In the past, almost all the medicines were from the plants; the plant being man's only chemist for ages. Herbs are staging a comeback, herbal 'renaissance' is happening all over the globe and more and more people are taking note of herbal therapies to treat various kinds of ailments in place of mainstream medicine. There are three main reasons for the popularity of herbal medicines:

- There is a growing concern over the reliance and safety of drugs and surgery.
- Modern medicine is failing to effectively treat many of the most common health conditions.
- Many natural measures are being shown to produce better results than drugs or surgery without the side effects.

Also there is increasing evidence that many current drug therapies simply suppress symptoms and ignore the underlying disease processes. In contrast, many natural products appear to address the cause of many diseases and yield superior clinical results. Unfortunately, most physicians and patients are not aware that these natural alternatives exist. Some drugs have an optimum concentration range within which maximum benefit is derived, and concentrations above or below this range can be toxic or produce no therapeutic benefit at all.

On the other hand, the very slow progress in the efficacy of the treatment of severe diseases has suggested a growing need for a multidisciplinary approach to the delivery of therapeutics to targets in tissues. From this, new ideas on controlling the pharmacokinetics, pharmacodynamics, non-specific toxicity, immunogenicity, bio-recognition and efficacy of drugs were generated. These new strategies, often called drug delivery systems (DDS), are based on interdisciplinary approaches that combine polymer science, pharmaceutics, bioconjugate chemistry.

Novel drug delivery system is a novel approach to drug delivery that addresses the limitations of the traditional drug delivery systems. Modern medicine cures a particular disease by targeting exactly the affected zone inside a patient's body and transporting the drug to that area. Novel drug delivery system attempts to eliminate all the disadvantages associated with conventional drug delivery systems. There are various approaches by which novel drug delivery can be achieved.

Advantages of Herbal Medicines:

- Herbal medicines are very cheap in comparison to the conventional form of medication. It's something which every pocket can afford, unlike other forms of medication which can create a big hole in your wallet.
- Herbal medicines are known to be more productive in comparison to other forms of medication in curing certain conditions. Unless mixed with other chemical components, they are known to be all natural.
- One of the greatest benefit associated with herbal medicine is the less existence of side effects. Also, they tend to offer long lasting benefits in terms of overall wellness.
- Obesity is a growing problem which is known to have hazardous issues on an individual's health. Herbal medicine can help one deal with the problem of obesity very effectively without consuming much time and efforts.

Disadvantages of Herbal Medicines:

- In some instances, individuals switch to herbal medication without realizing that the symptoms can be linked to a different ailment. Unlike, conventional medication which involves constant monitoring of your health, herbal medicines are taken without prescription which means that in some cases, individual might be undergoing a trial and error process with their medication.
- Although herbal medicines has the potential to cure many ailments, the curing period is usually longer in comparison to conventional

medication. One needs to have immense patience while undergoing herbal treatment.

- Herbal medicines can cause allergic reactions in some cases. Before resorting to herbal medication you need to ensure that you are not allergic to the particular herb that you will be consuming. Conventional medication can also cause allergic reactions, but they are usually taken upon prescriptions which is why the chances of allergic reactions are less.

- The government does not approve of any kind of herbal medication. It's usually consumed upon the person's own risk, and when it comes to branded herbal supplements one can't expect any kind of quality assurance

Phytosomes: The effectiveness of any herbal medication is dependent on the delivery of effective level of the therapeutically active compound. Severe limitation exists in their bioavailability when administered orally or topically. Phytosomes are recently introduced herbal formulations that are better absorbed than extracts. The term "phyto" means plant, while "some" means cell-like. Over the past century; phytochemical and phyto-pharmacological sciences established the compositions, biological activities and health promoting benefits of numerous botanical products. Most of the biologically active constituents of plants are polar or water soluble molecules. However, water soluble phytoconstituents (like flavonoids, tannins, glycosidic aglycones etc) are poorly absorbed either due to their large molecular size which cannot absorb by passive diffusion, or due to their poor lipid solubility; severely limiting their ability to pass across the lipid-rich biological membranes, resulting poor bioavailability [1].

Phytomedicines, complex chemical mixtures prepared from plants, have been used for health maintenance since ancient times. But many phytomedicines are limited in their effectiveness because they are poorly absorbed when taken by mouth. The Phytosome® technology, developed by Indena S.p.A. of Italy, markedly enhances the bioavailability of select phytomedicines, by incorporating phospholipids into standardized extracts and so vastly improve their absorption and utilization [2].

Over the past century, chemical and pharmacologic science established the compositions, biological activities and health giving benefits of numerous plant extracts. But often when individual components were separated from the whole there was loss of activity the natural ingredient synergy became lost [3].

Standardization was developed to solve this problem. As standardized extracts became established, poor bioavailability often limited their clinical utility. Then, it was discovered that complexation with certain other clinically useful nutrients substantially improved the bioavailability of such extracts. The nutrients so helpful for enhancing the absorption of other nutrients are the phospholipids. Phospholipids are complex molecules that are used in all known life forms to make cell membranes. They are cell membrane building blocks, making up the matrix into which fit a large variety of proteins that are enzymes, transport proteins, receptors, and other biological energy converters. In humans and other higher animals the phospholipids are also employed as natural digestive aids and as carriers for both fat-miscible and water miscible nutrients [4].

Increased bioavailability of the phytosomes over the simpler, non complex plant extracts has been demonstrated by pharmacokinetic (tissue distribution) and activity studies, conducted in animals as well as in humans. Phytosomes has an added dimension the proven health giving activity of the phospholipids themselves. Phytosome is also often known as Herbosomes [5]. Phytosomes exhibit better pharmacokinetic and pharmacodynamic profile than conventional herbal extracts. Molecular layer consisting of PC and other phospholipids provides a continuous matrix into which the proteins insert (**figure 1**).

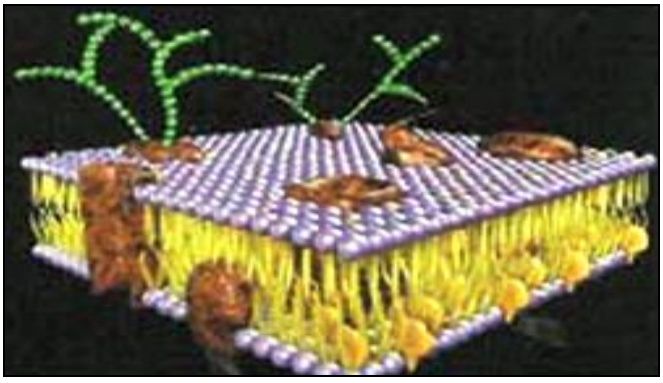

FIGURE 1: CELL MEMBRANES ARE LARGELY LIPID PHASE

Advantages and Disadvantages:

- Phytosomes enhances the absorption of lipid insoluble polar phytoconstituents through oral as well as topical route showing better bioavailability, hence significantly greater therapeutic benefit.
- As the absorption of active constituent(s) is increased, so its dose requirement is reduced.
- Phosphatidylcholine used in preparation of phytosomes, besides acting as a carrier also acts as a hepatoprotective.
- In case of phytosomes. Chemical bonds are formed between phosphatidylcholine molecule and phytoconstituent, so they show better stability profile than liposome.
- Application of phytoconstituents in form of phytosome improve their percutaneous absorption and act as functional cosmetics.

Disadvantage:

- Phytoconstituent from phytosomes are rapidly eliminated.

Mechanism of Phytosome Technology [6]**:** Phytosomes results from the reaction of a stoichiometric amount of the phospholipid (phosphatidylcholine) with the standardized extract or polyphenolic constituents (like simple flavonoids) in an aprotic solvent [7]. 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 which then envelopes the choline bound material.

Hence, the phytomolecules (**figure 2**) produce a lipid soluble 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 [8, 9]. Precise chemical analysis indicates the unit phytosome is usually a flavonoid molecule linked with at least one phosphatidylcholine molecule.

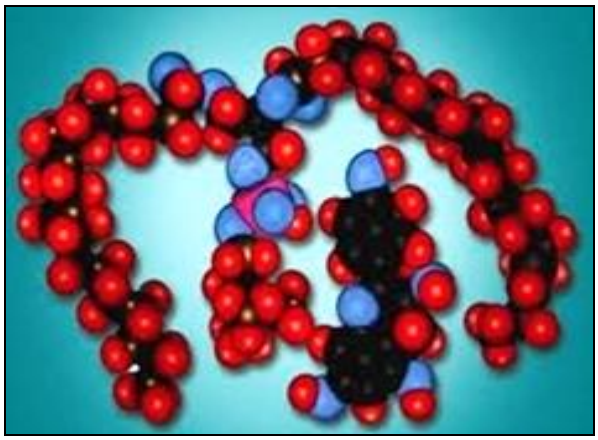

FIGURE 2: A FLAVONOID MOLECULE IS ENVELOPED BY A PHOSPHOLIPID MOLECULE

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 the gastro protective property of phosphatidylcholine [10].

Difference between liposome and 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 herbosome 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 (hydrogen 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 (cosmetic) products [11].

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 [12, 13]. 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 (cosmetic) products.

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, phytosome's host their polyphenolic guest, generally little soluble both in water and in lipids, at their surface where the polar functionalities of the lipophilic guest interact via hydrogen bonds and polar interactions with the charged phosphate head of phospholipids, forming a unique arrangement that can be evidenced by spectroscopy. The phytosome formulation also increases the absorption of active ingredients when topically applied on the skin, and improves systemic bioavailability when administered orally. In water medium, a phytosome will assume a micellar shape, forming a spherical structure, overall similar to a liposome, but with a different guest localization [14].

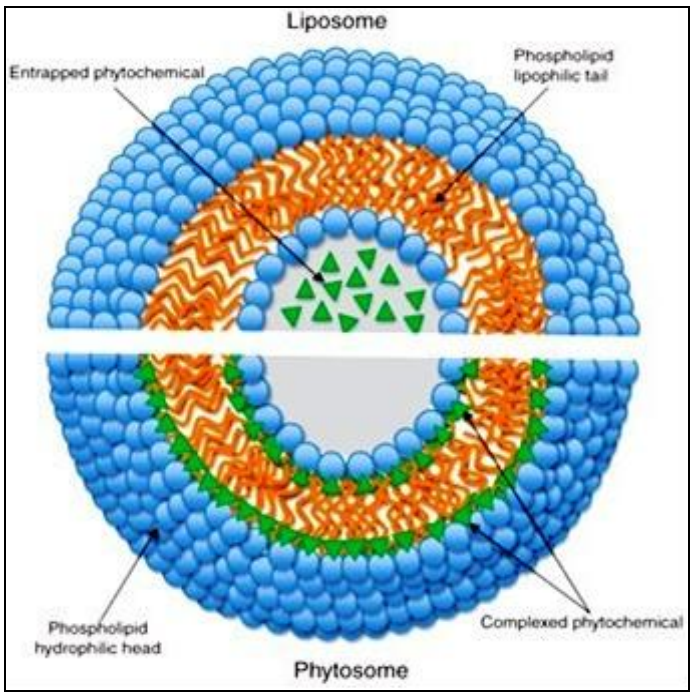

FIGURE 3: DIFFERENCE BETWEEN LIPOSOME AND PHYTOSOME

Preparation Methods:

- Phytosomes are novel complexes which are prepared by reacting from 3-2 moles but preferably with one mole of a natural or synthetic phospholipid, such as phosphatidylcholine, phosphatidylethanol amine or phosphatidyiserine with one mole of component for example- flavolignanans, either alone or in the natural mixture in aprotic solvent such as dioxane or acetone from which complex can be isolated by precipitation with non solvent such as aliphatic hydrocarbons or lyophilization or by spray drying. In the complex formation of phytosomes the ratio between these two moieties is in the range from 0.5-2.0 moles. The most preferable ratio of phospholipid to flavonoids is 1:1.

- **Naringenin-phosphatidylcholine phytosome**: Naringenin–PC complex was prepared by taking naringenin with an equimolar concentration of phosphatidylcholine (PC). The equimolar concentration of PC and naringenin were placed in a 100 mL round bottom flask and refluxed in dichloromethane for 3hrs. On concentrating the solution to 5–10 mL, 30 mL of n-hexane was added to get the complex as a precipitate followed by filtration. The precipitate was collected and placed in vacuum desiccators [15, 16].

- **Silybin- Phospholipid Complex Preparation:** The required amounts of drug and phospholipids were placed in a 100 ml round-bottom flask and dissolved in anhydrous ethanol. After ethanol was evaporated off under vacuum at 40C, the dried residues were gathered and placed in desiccators overnight, then crushed in the mortar and sieved with a 100 mesh. The resultant silybin–phospholipid complex was transferred into a glass bottle, flushed with nitrogen and stored in the room temperature [17].

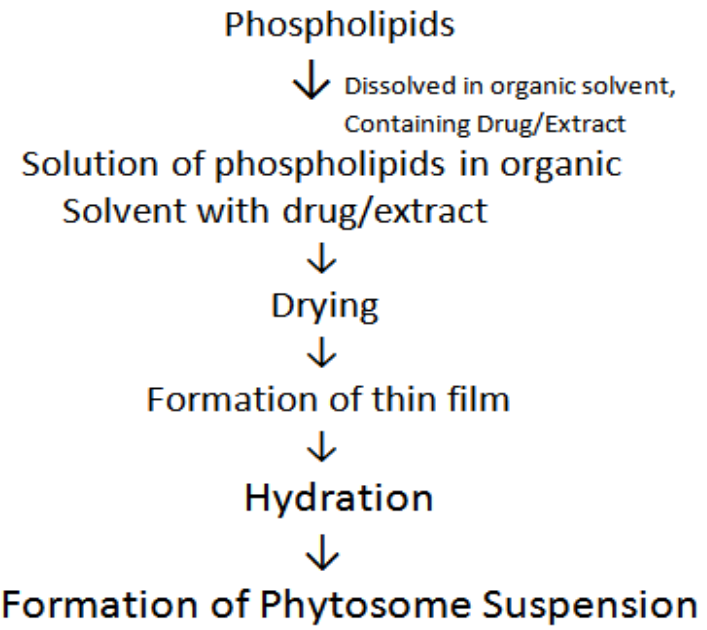

FIGURE 4: MAIN STEPS IN PREPARATION OF PHYTOSOMES

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

1. Phytosomes can accommodate the active principle that is anchored to the polar head of the phospholipids, becoming an integral part of the membrane. For example, in case of the catechindistearoyl PC complex, there is formation of H-bonds between the phenolic hydroxyls of the flavones moiety and the phosphate ion on the PC side [18].

2. Phosphotidylcholine: Study of comparisons of nuclear magnetic resonance of the complex with those of the pure precursors indicates that the signals of the fatty chain are almost unchanged. Such evidences inferred that the two long aliphatic chains are wrapped around the active principle, producing a lipophilic envelope that shields the polar head of the phospholipid and the catechin [19].

3. Phytosomes are advanced forms of herbal products that are better absorbed, utilized and, as a result, produce better results than conventional botanical herbal extracts. The increased bioavailability of the phytosome over the non-complexed botanical derivatives has been demonstrated by pharmacokinetic studies or by pharmacodynamic tests in experimental animals and in human subjects [20].

4. Phytosomes are lipophilic substances with a definite melting point, freely soluble in non-polar solvents, and moderately soluble in fats [21].

5. When treated with water, they assume a micellar shape, forming structures that resemble liposomes exhibiting fundamental differences [22].

Evaluation of Phytosomes [23, 24, 25, 26]:

I. **Characterization technique:**

1. **Visualization:** Visualization of phytosomes can be achieved using transmission electron microscopy (TEM) and by scanning electron microscopy (SEM).

2. **Vesicle 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).

3. **Entrapment efficiency:** The entrapment efficiency of a drug by phytosomes can be measured by the ultracentrifugation technique [23].

4. **Transition temperature:** The transition temperature of the vesicular lipid systems can be determined by differential scanning calorimeter [24].

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.

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 [25].

7. **Drug content**: The amount of drug can be quantified by a modified high performance liquid chromatographic method or by a suitable spectroscopic method.

II. **Spectroscopic evaluations:** To confirm the formation of a complex or to study the reciprocal interaction between the phytoconstituent and the phospholipids, the following spectroscopic methods are used.

1. **^{1}HNMR:** The NMR spectra of (+)-catechin and its stoichio-metric complex with distearoylphosphatidyl choline have been studied by Bombardelli *et al*., [26]. In non polar solvents, there is a marked change of the ^{1}H-NMR signal originating from the atoms 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-(CH3)3 of choline undergoes an uplift shift. Heating the sample to 60˚ results in the appearance of some new broad bands, which correspond mainly to the resonance of the flavonoid moiety.

2. **^{13}CNMR:** In the ^{13}C-NMR spectrum of (+)-catechin and its stoichiometric complex with distearoyl phosphatidylcholine, particularly when recorded in C6D6 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 signals belonging to the flavonoid moieties reappear, although they are still very broad and partially overlapping.

3. **FTIR:** The formation of the complex can be also be confirmed 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 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 microdispersion in water after lyophilization, at different times. In the case of simple formulations, it is necessary to subtract the spectrum of the cosmetic form at different times, comparing the remaining spectrum of the complex itself.

III. ***In vitro* and *in vivo* evaluations:** Models of *in-vitro* and *in-vivo* evaluations are selected on the basis of the expected therapeutic activity of biologically active phytoconstituents present in the phytosomes. [27, 28]. For example, *in-vitro* antihepatotoxic activity can be assessed by the antioxidant and free radical scavenging activity of the phytosomes [29]. For assessing antihepatotoxic activity in-vivo, the effect of prepared phytosomes on animals against thioacetamide paracetamolor, alcohol- induced hepatoxicity can be examined [30, 31]. Skin sensitization and tolerability studies of glycyrrhetinic acid-Phytosome® ointment, a commercial product, describe the in vivo safety evaluation methodology [32].

Applications of phytosomes [33, 34, 35, 36, 37]: Different phytosome products have demonstrated significant therapeutic effects when compared with the conventional herbal extracts .

TABLE 1: COMMERCIAL PHYTOSOMES PREPARATION [19, 39, 40, 41, 42]

Phytosomes Phosphatidyicholine	Phytoconstituent complexed	Indication	Dose
Silybin Phytosome	Silybin from silymarin marium	Nutraceutical, antioxidant for Liver and skin	120mg
Ginkgo Phytosome	24%ginkgo flavonoids from *Ginkgo biloba*	Protect brain and vascular lining	120mg
Olive oil Phytosome	Polyphenols from Europaea oil	Antioxidant, antiinflammatory, Anti-hyperlipidemic	-
Grape seed phytosome	Procynid ins from *Vitis vinifera*	Nutraceutical, systemic antioxidant	50-100mg
Haw thorn Phytosome	Flavonoids from carteagus sp.	Nutraceutical, cardio protective, Anti hypertensive	100mg
Centella Phytosome	Terpenes	Vein and skin disorders	-
Ecdhinacea Phytosome	Echinacoside from *Echinacea augustifolia*	Nutraceutical, immunomodulator	-

Recent research on *Silybum marianum*: Recent research shows enhanced absorption and bioavailability with phytosomes compared with the conventional delivery systems.

- Most of the herbosome studies are focused on ***Silybum marianum*** (Milk thistle), which contains premier liver protectant flavonoids. Silymarin primarily contains three flavonoids of the subclass flavonol (having a fully saturated C-ring).

Silybin predominates, followed by silydianin and silychristin. Silybin is actually a flavonolignan, probably within the plant by the combination of a flavonol with a coniferyl alcohol. Silybin is the most potent of the three, 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 [38].

The antioxidant capacity of Silymarin substantially boosts the liver's resistance to toxic chemicals the fruit of the Milk thistle plant contains flavonoids known for hepatoprotective effects, a standardized extract from *Silybum marinum* is an excellent liver protectant but is poorly absorbed orally. Silybin protects the liver by conserving glutathione in the parenchymal cells, while PC helps to repair and replace cell membranes. These constituents are likely to offer the synergistic benefit of sparing liver cells from destruction. In its native form within the Milk thistle fruit, Silybin occurs primarily complexed with sugars, as a flavonyl glycoside or flavonolignan. Silybin has been extensively researched and found to have impressive bioactivity, although limited by poor bioavailability.

- Tedesco *et al.,* [39] reported that the Silymarin phytosomes show better anti-hepatotoxic activity than Silymarin alone and can provide protection against the toxic effects of Aflatoxin B1 on the performance of Broiler chicks. Busby *et al.* reported that the use of a Silymarin phytosome showed a better fetoprotectant activity from ethanol-induced behavioral deficits than uncomplexed Silymarin Grange *et al*.conducted a series of studies on the Silymarin phytosome containing a standardized extract from the seeds of *Silybum marinum* administered orally to animals and found that it could protect the fetus from maternally ingested ethanol.

- Yanyu *et al*., [40] prepared the Silymarin phytosome and studied its pharmacokinetics in rats. In the study, the bioavailability of Silybin in rats was increased remarkably after oral administration of the prepared Silybin-phospholipid complex due to an impressive improvement of the lipophilic property of the Silybin-phospholipid complex and improvement of the biological effect of SilybinBarzaghi *et al*. conducted a human study designed to assess the absorption of Silybin when directly bound to PC. The plasma Silybin levels were determined after administration of a single oral dose of Silybin phytosome and a similar amount of Silybin from Milk thistle to healthy volunteers. The results indicated that the absorption of Silybin from the Silybin phytosome is approximately seven-times greater compared with the absorption of Silybin from the regular Milk thistle extract (70-80% Silymarin content).

Ginkgoselect Phytosome vs *Ginkgo biloba* Extract: The pharmacokinetic profile of Ginkgo selectR Phytosome has been defined in experimental animals [41, 42] and in human volunteers. Its bioavailability has been compared to GBE. Fifteen healthy volunteers were randomly divided into two groups and administered respectively with GinkgoselectR and GinkgoselectR Phytosome, providing both 9.6 mg of total terpene lactones. The subjects switched formulations after a week of wash out. Blood samples were collected at 30, 60, 120, 180, 240, 300 and 400 min after ingestion. Terpene lactones detection was performed by means of liquid chromatography/atmospheric pressure chemical ionization mass spectrometry (LC/APCI-ITMS). Ginkgolides A, B and bilobalide were absorbed to a higher extent (about three-fold) after administration of GinkgoselectR Phytosome (**figure 5**).

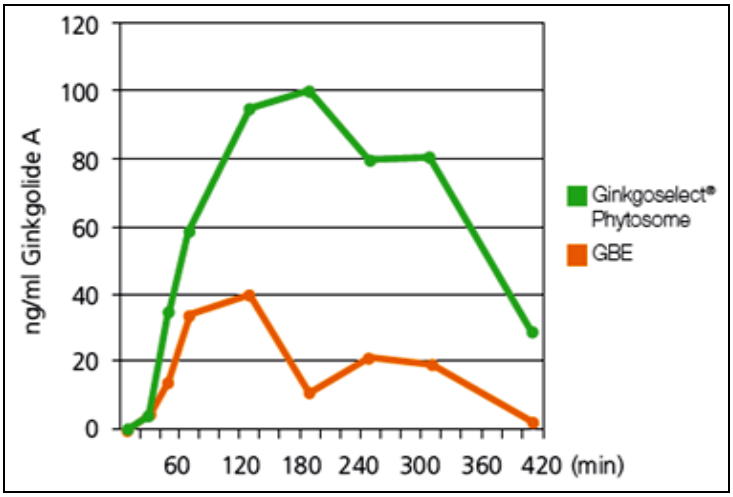

FIGURE 5: GINKGOSELECT PHYTOSOME VS GINKGO BILOBA EXTRACT

18-ß Glycyrrhetic acid Phytosome vs 18-ß Glycyrrhetic acid: Finally as an example, an activity comparison between the Phytosome and non Phytosome form by topical application is reported as well [43]. The inflammatory response of the 18β-Glycyrrhetic Acid Phytosome were assessed in the experimental model of Croton oil-induced oedema reduction. At the same dose (0.16 µM), the action of the 18β-Glycyrrhetic Acid Phytosome was found to be greater and to last longer than that of 18β-glycyrrhetic acid alone.

This means that the Phytosome not only increases the active ingredient tolerability and absorption, but also improves its efficacy (**figure 6**).

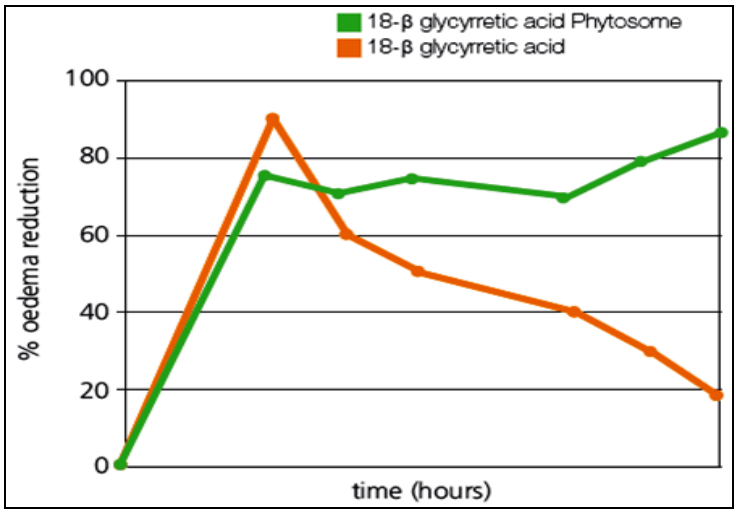

FIGURE 6: 18β GLYCYRRHETIC ACID PHYTOSOME VS 18β GLYCYRRHETIC ACID

Herbal Drugs used for the management of periodental disease:

1. ***Acacia Catechu* Wild** [44, 45]**:** *Acacia catechu* Wild. (Fam. Mimosae, Hindi- Khair, English- Citchtree, Sanskrit- Khadira) is widely used in Ayurveda for many diseases and mainly for skindiseases. *A. catechu* commonly known as Black khair and commercially used to obtain Kattha inNorth India. It found widely distributed in Jammu, Punjab, Himachal Pradesh, U.P., M.P.,Bihar, A.P. and Maharashtra. *A. catechu* is used as mouthwash for mouth, gum and throat diseaselike gingivitis, stomatitis. Kattha is cooling, digestive, astringent, bleeding piles, uterinehemorrhages, leucorrhoea, atonics dyspepsia, chronic bronchitis, etc. the decoction of bark mixed with milk is taken to cure and cough.

2. ***Aloe Vera* Miller** [46, 47]**:** *Aloe vera* is *Aloe barbadensis* Miller. (Fam. Liliaceae). It is shrubby or arborescent, perennial, xerophytic, pea-green colour plant. It grows mainly in the dry region of Africa, Asia,Europe and America. In India it is found in Rajasthan, A.P., Gujarat, Maharashtra and Tamilnadu. The species is frequently used in herbal medicine and cosmetics. Many scientific studies for the use of extracts of *Aloe vera* have been undertaken. (48-49) Traditionally, Aloe was used topically to heal wounds, skin diseases and orally as a luxative. Itis also used in conditions including diabetes, asthma, epilepsy and osteoarthritis. *Aloe vera* gel used in lotions and sunblocks. FDA has approved as a natural food flavoring agent

3. ***Ocimum Sanctum* L. (Tulsi)** [48, 49]**:** In Ayurveda, Tulsi (*Ocimum sanctum* L.) has been well documented for its therapeutic potentials and described as Dashemani Shwasaharni (antiasthmatic) and antikaphic drugs (Kaphaghna). Although, the traditional medical practitioners in India have been widely using this medicinal plant for management of various disease conditions from ancient time 16. Tulsi is used to control diabetes17. Paste of leaves is found effective in the treatment ofringworm and other skin diseases 18. It is recommended as antidote for dog bite, scorpionbite and insect bite in traditional system of medicine. The seed are mucilaginous and demulcent and given in disorders of the genitourinary system. The leaves have also been shown to possess good anti-stress and analgesic activity.

4. ***Curcuma Longa* (Turmeric)** [50, 51]**:** Turmeric commonly known as Haldi and has been used for thousands of years as a dye, a flavoring and a medicinal herb. It is a rhizomatous herbaceous perennial plant of family Zingiberaceae. It is native to tropical South Asia and needs temperatures between 20°C and 30°C. Haldi is a perennial plant with orange, oblong tubers 2 or 3 inches in length and one inch in diameter, pointed or tapering at on end. When dried, it is made into a yellow powder with a bitter, slightly acrid, yet sweet taste. In India, it has been used traditionally as a remedy

for stomach and liver ailments, as well as topically to heal sores. Ancient Indian medicine has touted turmeric as an herb with the ability to provide glow and luster to the skin as well as vigor and vitality to the entire body

CONCLUSION: This review is an attempt to present a concise profile of phytosomes as a delivery system. Herbosomes are novel formulations which offer improved bioavailability of hydrophilic favonoids and other similar compounds through the skin or gastrointestinal tract. They have many distinctive advantages over other conventional formulations. The formulation methodology for phytosome is simple and can be easily upgraded to a commercial scale.

The characterization methodologies and analytical techniques are well established for this type of novel formulation. Many patents are already approved for innovative formulations, processes and applications of phytosomes. As far as the potential of phytosome technology is concerned, it has a great future for use in formulation technology and applications of hydrophilic plant compounds.

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