Review Article

Review on Phytosomes: An Innovative Method of Medication Administration

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ABSTRACT

Throughout the universe, herbal treatments have been used extensively seeing as pristine times and have been distinguish by medical experts and individuals due to their superior therapeutic value and lack of negative effects as compared to modern drugs."Some" relate to a cell, while "Phyto" implies a plant. It is often referred to as "herbosomes," a novel, patented technology in which phospholipids and absorption and bioavailability are significantly increased by the synthesis of water-soluble phytoconstituents or standardized plant extracts into lipid-compatible molecular complexes. Flavonoids from plants and other naturally hydrophilic chemicals have demonstrated promise in further biochemically and pre-clinical research for that therapy regarding about various dermal problems, forms of carcinoid, age- defying, and many other curative and defensive medical conditions. These chemicals' hydrophilic nature and distinct chemical structure present significant challenges due to their low cutaneous or gastrointestinal absorption. The utilization of phytosomes was a new formularization terminology who support to pull of those issues. Plant-derived extracts are becoming more and more popular as dietary additives for the homeostatic supervision of inflammation, toxicity, cancer, slimming, and other acute otherwise chronic deteriorating messes. In spite of, that product often have issues with bioavailability and stability. After being distinct, plant products can take place unsettled and may not be able to pass through the biomembrane. These tasks are reduced to a reasonable extent by the phytosome approach. Many items on the market, including *Ginkgo biloba, Silybum marianum*, and *Camellia sinensis*, feature phytosomal drug delivery systems. The chemical and biological characteristics of phytosomes as well as the formulation process are included in the study. The technologies used to evaluate and characterize phytosome shed light on a variety of approaches that are helpful in screening for different phytosome features.

Keywords: Phytosome; Phytoconstituent; Phospholipid; Bioavailability; Product; Vesicle; Disease.

INTRODUCTION

Traditional drug and herbal medicines has been utilize curative in favor of a long-lived use that preserve health with a various of procedure. Phytosomes is a novel technology emerged in 1989.Many plant extracts has been the subject of synthetic substance and living organisms (pharmacology) investigations during the departed centenary in an effort to determine their chemical makeup whereupon validate their medicinal value. The oodles of the bioactive constituent in phytomedicine, such as flavonoids, glycosides, also phenolic, molecules are dissolve in water. However, because they are poorly absorbed, the impact of water soluble phytoconstituents is restricted.[1]

"Some" assign to homologous a cell like, afterwards "Phyto" allude a plant. (Figure 1) Phytosomes are a novel, cutting-edge dose formulation technique that improves absorption of herbal items and drugs, producing better results than conventional herbal extracts.[2-3]

Their enhanced pharmacokinetic and pharmacological properties are beneficial not only for pharmaceutical and cosmetic formulations but also for the management of acute illnesses. Numerous prominent herbal extracts, such as Anchi ginseng (*Panax ginseng*), milk thistle in (doodh patra) India (*Silybum marianum*), grape seed, hawthorn, *ginkgo biloba*, and green tea (*The sinensis*), has been successfully processed using the phytosomal method. These plant extracts' flavonoid and terpenoid constituents can attach to phosphatidylcholine directly. Strong lipophilicity and improved topical absorption of complex compounds are two characteristics of the phytosomes that improve the structure, hydration, and enzyme balance of the skin.[4]

Phytosomes are herbal medications contained in vesicles that are sold in nanoscale form. The phytosomes shield the medication's active ingredient from being destroyed by germs and digestive secretions, which encase it in an envelope-like covering.

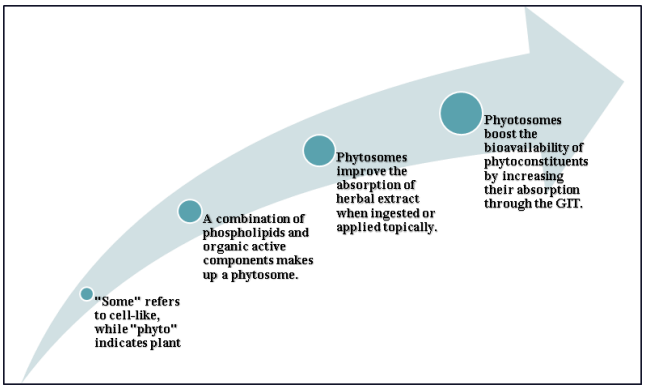

Figure 1

Phytosome can efficiently absorb from an environment that loves water to one that loves lipids in the cell

membrane before entering the bloodstream. The current study highlights the prospective uses and state-of-the-art technical developments in the area of NDDS for the advantage of herbage and orthodox flora-based therapies.

The process of creating phytosomes enhances the number of herbal compounds by facilitating better absorption, raising bioavailability, and encouraging medication transport to the tissues. They offer local application at the location of necessity. Topical cosmetic pharmaceutical hybrids designed to improve appearance by adding extra health-related properties to the ingredients are known as functional cosmetics. The correct and economical use of herbal remedies is achieved through the dual uses of phytosomes as a topical medicinal agent and cosmetics with enhanced efficiency and safety.[5]

Phosphatidylcholine, phosphatidylserine, phosphati dylethanolamine, and phosphatidylinositol are a few of the phospholipids that are utilized. However, phosphatidylcholine is most frequently utilized seemly to its potential therapeutic benefit in cases of hepatitis, drug-raised hepatic damage, alcoholic steatosis, and liver disorders.[6]

Phytosomes word formed with the help of two word. (Phyto+Somes) (Figure 2).

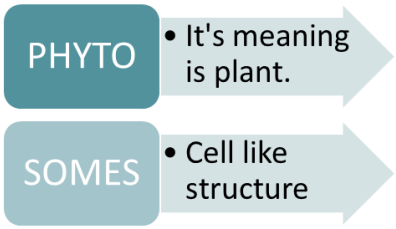

Figure 2

Bioactive polyphenolic substances present naturally in pla nts, known as phytochemicals,havebeen the subject of int ense research seemly to their probable healthandnourishi ng advantages for homosapiens.They are in charge of the plant's color, flavor, and scent in addition to providing pro tection.Scientists from all over the world have been intere sted in these compounds because of their strong bioactivi ty against many diseases, minimal cytotoxicity, and poten tial application in the manufacturing of nutritional supple ments and cosmetics.[7]

Pytosomes is a specialized style of plant distillate, this is chemically bound with phospholipids, which are natural components of cell membranes. It's peerless fabrication enhances the phytoconstituents' bioavailability and absorption, potentially improving their therapeutic efficacy. While the utilization of phytosomes in the cure of concern is an area of emerging interest, there is limited direct clinical evidence specifically focused on phytosomes for anxiety disorders.

However, several herbal extracts with anxiolytic properties have been studied in various forms, including traditional herbal preparations and standardized extracts. Some of these herbs include passionflower (Passiflora incarnata), ashwagandha (Withania somnifera), kava (Piper methysticum), and valerian (Valeriana officinalis), among others. These herbages have been traditionally used for their calming and anxiolytic effects.[8]

When considering the main use of phytosomes in the cure of anxiety, it's vital to observe that the enhanced bioavailability and improved delivery of phytoconstituents to target tissues could potentially lead to more effective therapeutic outcomes. As with any treatment approach, it's crucial to consult with a qualified healthcare professional before using phytosome formulations or any herbal supplements for the management of anxiety. Individual responses to herbal treatments can vary, and interactions with other medications or existing health conditions should be carefully considered.[9]

Phytochemicals parts (figure 3) can be classified into three primary types based on their structural components: terpenoids, alkaloids, and polyphenolic substances.Trepeniods are a class of compounds that contain tannins, lignins, catechols, stilbenes, and flavonoids; phenolic components include menthol, linalool, geraniol, and caryophyllene. Based on their heterocyclic ring structures, alkaloids are further classified as isoquinoline, pyrrolidine, pyrrolidine-pyridine, and piperidine alkaloids.[10]

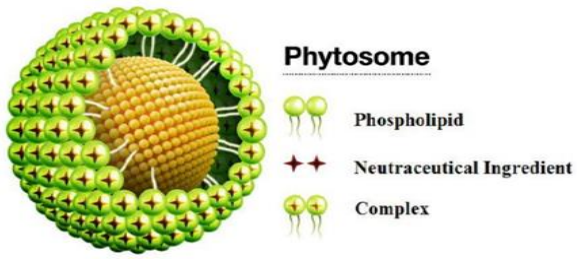

Figure 3

These days, increasing pollution levels and changing environmental conditions increase the risk of skin illnesses. Consequently, herbal medications have gained popularity in both developed and developing countries because of their significant biological efficacy, higher safety margin, and lower cost when compared to synthetic treatments.[11]

Since many herbal extracts derived from various plant species have medical benefits such as antimicrobial and anti-inflammatory properties, the capacity to promote wound healing and blood clotting, and the ability to treat burns and other skin diseases, they have been investigated for their potential to treat skin conditions.[12-13]

Medicinal herbs are an effective way to cure a number of common skin ailments, such as psoriasis, urticarial, eczema, acne, and other bacterial and fungal skin illnesses.[16-17]. With its high molecular weight and consequently limited solubility and poor skin absorption.[14]

PROPERTIES OF PHYTOSOMES

The combination of a natural substance and a natural phospholipid is called a phytosome. Phytosome increase

the absorption through the formation of miscelles.Lipophilic substances with a set melting point are called phytosomes. Upon being exposed to water, phytosomes acquire the shape of aggregating structures.

They can become an essential component of the membrane by allowing for the active principle associated with the phospholipid polar head.

For example: in catechindistearoyal phospholipid complex, H-bonds are formed.

These are advanced herbal products that work better in terms of absorption, application, and outcomes than conventional botanical herbal extracts. Surveys on the pharmacokinetics furthermore pharmacodynamics of phytosomes in both human and animal subjects have demonstrated that phytosomes have a higher bioavailability than simple botanical derivatives. They are easily soluble in non-polar solvents, have a definite melting point, and are only slightly soluble in lipids. These materials are lipophilic. After being dissolved in water, they take on a micellar form and develop structures that are somewhat similar to liposomes.

The physical-chemical attributes

As was previously mentioned, a standardized plant extract is used as the substrate in a reaction with a stoichiometric amount of phospholipid to create phytosomes. The interaction within the phospholipid and the substrate is caused by an H- bond that is composed between the polar functions of the substrate and the polar head, which are the phosphate and ammonium groups, according to spectroscopic data. A phytosome can range in size from 50 nm to several hundred µm. Phytosomes take on a liposome-like micellar structure when they come into contact with water.[15]

A phytosome is made up of a natural material and naturally occurring phospholipids, like soy phospholipids. Such a complex is created when a selected polyphenol (such simple flavonoids) combines with phospholipid at stoichiometric quantities in a nonpolar solvent.

These compounds are lipophilic in nature, readily soluble in nonpolar solvents, and moderately soluble in lipids, in contrast to the hydrophilic moiety. Additionally, their melting points are different. When phytosomes come into contact with water, they form a micellar aggregate and acquire liposome-like features.[17-18]

The biological attributes

Pharmacokinetic studies and pharmacodynamics testing in both human subjects and experimental animals have shown that phytosomes are novel sophisticatedfor as much better immersed and utilized than conventional plant extracts or non-complexed essence, producing more biologically active and better results. Due to their size, permeability of the membrane, and percentage of entrapment, and the precise combination, quantity, and purity of the components they use, phytosomes are able to exhibit certain behaviours in mechanical or biological systems.[16]

Liposomes and phytosomes are not the same thing, which are entrapped hydrophilic drug molecules in gaps or cavities between membranes. These days, liposomes are mostly employed for beauty applications and can entrap several hundred phospholipid molecules. (Figure 4) Rather, the phytosomes entail the interplay between one to four phospholipid molecules and the chemically linked phytoconstituents. Studies have demonstrated that phytosomes exhibit superior membrane permeability and stability when compared to liposomes.[19-20]

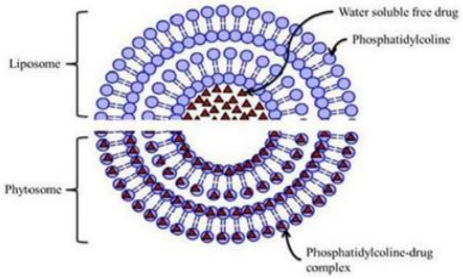

Figure 4

ADVANTAGE OF PHYTOSOMES

They increase bioavailability due to phospholipid complex, thus improve therapeutic effect. They are required in fewer doses due to high bioavailability. They improve gastrointestinal absorption. They show high stability. They are preferred over liposomes in cosmetics because of their strong lipophilicity, which results in great penetrability. Their clinical benefits are higher. Additionally, phytosomes work better in skin care products than liposomes. There is no difficulty in drug snare while formulating Phytsomes.Due to the drug's conjugation with lipids to produce vesicles, entrapment efficiency is high and almost entirely predefined. It is evident that the medication's bioavailability has improved.

The dose required has been reduced due to the principal ingredient's maximum absorption. Using Phytosomes to modify herbal therapy does not have to jeopardize the nutritional safety of the herbal extracts. It assures that the right tissue will receive the drug. Important components of an herbal extract are contained in phytosomes, which are microscopic cells they are shielded from gut bacteria and digestive fluids that would otherwise destroy them.

Benefits regarding phytosomes over traditional dosage forms: Phospholipids' complexation with plant extracts increases bioavailability significantly.[19]

They allow for improved absorption from the intestinal lumen by penetrating the non-lipophilic plant extract, which would not be feasible otherwise.[20]

All of the ingredients in the phytosome formulation are safe and have been authorized for usage in medical and cosmetic settings.

DISADVANTAGE OF PHYTOSOMES

- Stability Problem.
- Phytoconstituents from phytosome are rapidly eliminated.
- When administered orally and tropically they limit their bioavailability.

Figure 5

A comparison of phytosome and liposome (Table 1)

Numerous studies on phytosomes have demonstrated their superior therapeutic efficacy over liposomes in terms of absorption, bioavailability, and quality of life. (Figure 6) Comparing different phytosomes.[9]

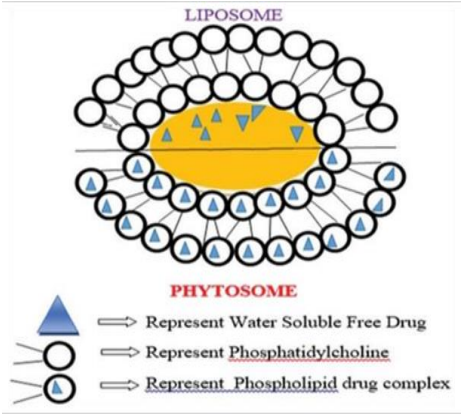

Figure 6:

Table 1: Comparison between Phytosome and Liposome

Sr. No.	Properties	Phytosome	Liposome	References
1.	Bonding	Associated with few molecules (mainly with Phospholipid and polyphenol extract)	Number of molecules and even they are not connected well	**21**
2.	Oral drug delivery	Best for oral delivery	Connected well poor oral bioavailability.	**22**
3.	Phospholipid ratio	Preferably 1:1, 1:2 ratio is preferred for its preparation.	Up to ten times more lipids are used than the main active ingredients.	**23**

Methods of Preparations

Using precise weighing, 10 millilitres of chloroform are mixed with cholesterol and phosphatidylcholine in a round-bottom flask. The flask is then sonicated for 10 minutes in a bath sonicator. A rotating evaporator is used to extract the organic solvent at 45–50°C.

A thin layer of phospholipid mixture is created when the solvent is completely removed, and it is hydrated with the plant's methanolic extract in a rotary evaporator (at 37–40°C for an hour).

The mixture of plant extract and lipid is hydrated, and then it is sonicated for 20 minutes in an ice bath to dissipate heat. After harvesting, the phytosomes are placed in an amber-colored bottle and kept in the freezer between 2 and 8°C.

COMMON STAGES FOR PREPARATION OF PHYTOSOMES (Figure 7)

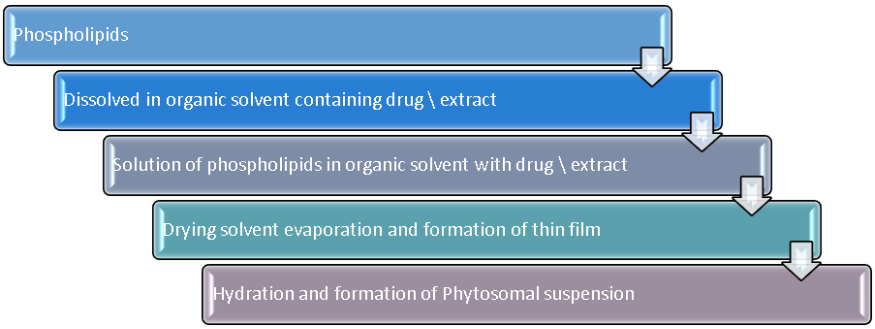

Figure 7

Table 2: Commercially Available Phytosomal Product

Sr. No.	Trade name	Chief constituents	Origin	Shot	Utilization
1.	Centella phytosomes	Triterpine	*Centella asiatica*	-	Cicatrizing, trophodermic
2.	Ginselect phytosomes	Ginsenosides	*Gingko biloba*	120 mg	Adaptogenic
3.	Greenselect phytosomes	Polyphenols	*Camellia sinensis*	-	Free radical scavenging activity
4.	Leucoselect	Polyphenols	*Vitis vinifera*	300 mg	Antioxidant
5.	Meriva	Curcuminoids	*Curcuma longa*	200-300 mg	Anti-inflammatory
6.	Silymarin	Silymarin	*Silybum marianum*	-	Antihepatotoxic
8.	Crataegus phytosomes	exin-2'-Orhamonoside	*Crataegus Mexicana*	-	Antioxidant

General method of preparation

Another method, to make phytosomes, a precise amount of phospholipid—soy lecithin—is added along with plant extracts in an aprotic solvent. The primary component of soy lecithin is phosphatidylcholine, which serves two purposes. While the phosphatidyl component is a lipid soluble substance connected to the choline bound complex, the choline part is attached to the hydrophilic primary active ingredients. It causes a lipid complex to develop that is more stable and bioavailable. Another method of creating phytosomes is to react, in a ratio of 0.5 to 2.0, phospholipid, synthetic or natural, containing standardized plant extract. A 1:1 ratio is typically favoured, though. To eliminate the new complex from the process, it can be lyophilized, spray-dried, or precipitated using a non-solvent (often an aliphatic hydrocarbon). The reaction can be carried out in an aprotic solvent, such as acetone, methylene chloride, or dioxane alone, or in a natural combination.

Using a thin layer rotary evaporator vacuum approach, phytosome vesicles were created. In a 250 ml round-bottom flask, the phytosomal complex have being combined accompanised by anhydrous ethanol. A rotary evaporator has the flask attached to it. At roughly 60°C, the solvent will evaporate and form a thin coating around the flask. Phosphate buffer (7.4) is used to hydrate the film, and as the lipid layer separates, vesicle suspension is formed in the phosphate buffer. 60% amplitude probe sonication was applied to the phytosomal suspension. For a whole day, the phytosomal suspension will be kept refrigerated prior to characterisation. The reflux approach is one way to prepare phytosomes. A 100 mL round-bottom flask containing phospholipid and polyphenolic extract has being refluxed in DCM for one hour at a temperature not to exceed 40°C. After evaporating the clear solution, 15 mL of n-hexane was added as far as hasty formed. After being extracted, the precipitate was put in a desiccator.[24]

It is recommended to weigh phospholipid and cholesterol exactly into a round-bottom flask, dissolve them in 10 mL of chloroform, and then use a bath sonicator to sonicate the mixture for 10 minutes. It is possible to remove organic solvent by exposing it to a rotating evaporator at 40°C with reduced pressure. In a rotary evaporator, a thin layer that has been completely solvent-freed is hydrated with the drug's polyphenolic extract. The phospholipid mixture was sonicated in an ice bath to release heat. The prepared phytosomes were stored in an amber-colored vial.[25-26]

Various phytosome technology methods

The decreased bioavailability and absorption of polyphenolic components can be attributed to two main factors. These primary components are made up of many ringed molecules that are present in sufficient amounts for the diffusion mechanism to absorb them. The second factor is that flavonoid molecules, which are the primary constituents of polyphenols, are poorly soluble in lipids. These are the barriers that stop them from passing through biological membranes and being absorbed.[27]

Differential scanning calorimetry

Phospholipid complex medicine, polyphenolic extract medication, and phosphatidylcholine were physically mixed and heated in an aluminium cell at a pace of 50–250°C per minute in a nitrogen atmosphere.

Scanning electron microscopy (SEM)

The particle's appearance and size were assessed using SEM. For an electron microscope, a dry sample was placed on an ion sputter-coated brass stub. Scanning the complex with a 100 arbitrary speed.

Transition electron microscopy (TEM)

By a 1000 magnification, the size of phytosomal vesicles was measured by TEM.

Drug entrapment and loading capacity

The drug phytosome complex was separated from the untrapped drug by centrifuging it for 90 minutes at 4°C at 10,000 rpm. UV spectroscopy can be used to measure the amount of free drug present.

The calculation for drug entrapment % is:

Weight of total drug – Entrapment efficiency % = $weight\ of\ free\ drug/weight\ of\ total\ drug \times 100$

Fourier transform infrared spectroscopy (FTIR) analysis

FTIR research verifies the phospholipid medication's structural integrity and chemical stability. To make pellets, the phytosomal medication will be crushed under 600

kg/cm2 of pressure using potassium bromide. We'll survey the 4000-400 cm−1 ranges.[28-29]

Size analysis and zeta potential

The particle and zeta sizes of the phytosomal complex are measured using the Malvern Zetasizer. An argon laser is used in both the particle size analysis and the zeta sizer.[30-31]

In vitro and in vivo evaluations

The qualities of the medication, its primary phytoconstituents, which are coated in a phospholipid layer, and the justification for the choice of the specific animal model for testing have an impact on both the in vitro and in vivo evaluations.[32-33]

Measurement of surface tension activity

The drug's surface tension activity in an aqueous solution can be measured using the ring method in a Du Nouy ring tensiometer.[34-35]

Drug content

A suitable spectroscopic method or a modified high performance liquid chromatographic method can be used to quantify the drug's quantity.[36]

Spectroscopic evaluations

The following spectroscopic techniques are employed to verify the complex's formation.

I.H-NMR

The NMR spectra of (+)-catechin and its stoichiometric combination with distearoylphosphatidylcholine have been studied by Bombardelli et al.38 Nonpolar solvents dramatically change the 1 H-NMR signal from the atoms involved in the complex's formation, and the signals specific to each individual molecule are not summated.[37]

II.13C-NMR

The lack of all flavonoid carbons is evident in the 13C-NMR spectra of (+)-catechin and its stoichiometric combination with distearoylphosphatidylcholine, especially when recorded in C6D6 at ambient temperature.

ASSESSMENT OF PHYTOSOMES

The evaluation of phytosomes involves assessing their physicochemical properties, as well as their pharmacokinetic and pharmacodynamic characteristics. Here are some common methods used to evaluate phytosomes.

Particle Size Analysis

Phytosome particle size can be assessed using microscopy, dynamic light scattering, or laser diffraction. This aids in comprehending the stability and physical properties of the phytosome formulation.

Morphological Characterization

The appearance and structure of phytosomes can be observed at the microscopic level using scanning electron microscopy (SEM) and transmission electron microscopy (TEM).

Fourier Transform Infrared Spectroscopy (FTIR)

By studying the interaction between the plant extract and phospholipids in the phytosome formulation, FTIR analysis can be used to learn more about the chemical composition and bonding of the two components.

Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA)

DSC and TGA can be used in order to assess the thermal behavior, stability, and phase transitions of phytosomes, which are important for understanding their physical properties.

***In vitro* Dissolution Studies**

Dissolution studies can be conducted to evaluate the release profile of the active constituents from phytosomes, providing insights into their dissolution behavior and potential for improved bioavailability.

Pharmacokinetic Studies

The pharmacokinetic profile of phytosomes, which includes the active components' absorption, distribution, metabolism, and excretion in relation to conventional herbal extracts, can be evaluated by in vivo investigations.

Pharmacodynamics Studies

Pharmacodynamic evaluations involve studying the biological effects and therapeutic efficacy of phytosome formulations in relevant animal models or clinical trials.

Stability Studies

Accelerated stability testing can be conducted to evaluate the physical and chemical stability of phytosomes under different storage conditions, including temperature, humidity, and light exposure.

Bioavailability Studies

Comparative bioavailability studies can be performed to determine the extent of absorption and systemic availability of the active constituents from phytosomes compared to conventional herbal extracts.

APPLICATIONS

Over the past century, research in the domains of phytochemistry and phytopharmacology has identified the chemical makeup, biological characteristics, and health benefits of several plant-based products.

The majority of the compounds that make up plants' physiologically active constituents are polar or soluble in water. Water soluble phytoconstituents, like tannins, terpenoids, and flavonoids, are poorly absorbed because of their large molecular size, which inhibits passive diffusion, or their poor lipid solubility, which severely limits their ability to cross lipid-rich biological membranes and results in poor bioavailability. The process of isolating and purifying

the constituent components of an extract frequently results in the loss of the natural component synergy, which can cause the purified constituent's unique bioactivity to be lost partially or completely.[29]

It has been noted that complexing these extracts and their individual components with a few other clinically beneficial nutrients significantly increases their bioavailability. Among the nutrients that are very helpful for enhancing absorption are phospholipids.

Using patented technology, a well-known pharmaceutical and nutraceutical manufacturer created phytosomes, which are lipid-compartible molecular complexes that greatly increase phospholipid absorption and bioavailability. Complex substances called phospho-lipids are necessary for the construction of cell membranes in all known life forms.Humans and other higher animals use phospholipids as natural digestive aids and as carriers of both fat- and water-soluble nutrients. They are readily absorbed when taken orally and are annexable in lipid and water environments. Phytosomes are more accessible than conventional herbal extracts since they can more easily cross the lipoidal bio barrier and eventually reach the systemic circulation.[38-39]

- **Clinical applications of Phytosomes**

The Role of Phytosomes in the Nervous System

(A) The Phytosomes in Cognitive Impairment and Neuronal Damage

Numerous investigations assess the phytosome's bioavailability in relation to comparable unformulated products using animal models, with an emphasis on the active components' tissue distribution. The phytosome formulation had the best performance as an MAO inhibitor and radical scavenger using an in vitro transwell model of the blood-brain barrier, making it a good model to boost the extract's antidepressant-like effects.[40-41]

(B) The Phytosomes in Migraine

Phytosomes in Migraine Disorders the same research team examined the effectiveness of administering 60 mg of Ginkgo biloba terpenes phytosome, 11 mg of coenzyme Q10, and 8.7 mg of vitamin B2 twice a day to fifty individuals suffering from migraine with aura in two different trials. [42-44]

The Phytosomes in the Gastrointestinal System

(A)The Phytosomes and Gut Microbiota

Lecithin-curcuminoid formulation and unformulated curcuminoids are two different curcumin-based products whose effects on human colonic metabolism were studied in a recent study. Following the fermentation of both extracts in an in vitro fecal model, curcuminoid content was measured, potential curcuminoid breakdown was evaluated, and the primary metabolites involved in the fermentation of human feces were identified using mass spectrometry. The outcomes shown that curcuminoid catabolites were more frequently observed following the fermentation of curcuminoids prepared with lecithin.[45-47]

(B)The Phytosomes against Bowel Inflammation

The 43 patients voluntarily selected to either receive one 250 mg tablet daily or no supplements for a period of four weeks. The supplementation group saw reduced levels of rectal involvement, anaemia, malaise, watery stools, blood in stools, cramps and diffuse intestinal pain, as well as a decrease in white blood cell count. Additionally, there was less of a need for additional medications and medical testing.[48-49]

The Phytosomes Effect in the Genitourinary System

(A)The Phytosomes and Breast Cancer

In the first research, as part of a 4-week treatment regimen before to surgery, 12 patients with early-stage breast cancer received 44.9 mg of epigallocatechin-3-gallate. The treatment plan included taking 300 mg of a commercial lecithin formulation with green tea catechins every day.[50]

The Phytosomes Role in Prostate Diseases

The effects of phytosomes loaded with silibinin on prostate cancer were assessed in three different investigations. In the first in vivo investigation, male TRAMP mice with a palpable prostate tumor were fed a meal containing 0.5% or 1% w/w phytosomes. Following 11 weeks, the diet reduced the prostate's weight and tumors by up to 60% in a dose-dependent manner.[51-52]

A pair of clinical trials were carried out to assess the effects on human subjects. Thirteen patients with prostate cancer participated in the first pharmacokinetic Phase I research. The daily oral dosage of phytosome was raised from 2.5 g to 20 g.[53-54]

The Phytosomes in Female Reproductive System Conditions

The effects of a 2 g (4 × 500 mg daily) curcumin phytosome supplement were assessed over the course of two weeks in six endometrial cancer patients who were not receiving concomitant cancer treatments. Supplementation resulted in a decrease in leukocyte MHC expression, monocyte counts, and CD8 + T cell ICOS protein levels. There were no other significant changes observed in inflammatory indicators, such as the range of immune cell types, T cell activity, or levels of the protein cyclooxygenase-2 (COX-2).[55-56]

The Phytosomes in Urinary Tract Dysfunctions

The biological effects of phytosomes on the urinary system were assessed in two clinical trials. In the first trial, urine was evaluated for its capacity to prevent the growth of Candida albicans after 13 healthy subjects were given cranberry extract phytosome or the corresponding standardised extract to drink. For a week, the subjects took two cranberry phytosome or cranberry extract capsules daily, and their poop was measured at various intervals.[57-58]

The Phytosomes as Modulators of the Immune System

An in vivo investigation that used 50 mg/kg of Wistar rats for seven days prevented liver damage and inflammation brought on by paracetamol.[59]

In a different study, grape seed extract—which contains a high concentration of epigallocatechin 3-O-gallate—was evaluated for its immunomodulatory qualities in its phytosomal form.

An evaluation of serum cytokines demonstrated that a one-month treatment of elderly individuals with grape seed phytosomes (300 mg/die) affected their immunological response. Specifically, the treatment increased the synthesis of INFγ and IL-2, suggesting a possible role in the Th1/Th2 balance.[60]

The Phytosomes Effect in Wound Healing

A. Mazumder et al. examined Sinigrin's capacity to heal wounds in HaCaT cells both as a phytosome complex and as an isolated substance in 2016. Sinigrin is a well-known glucosinolate present in plants in the Brassicaceae family.[61]

Only 65.63% of the wound could be healed by the ethanolic extract alone; in contrast, the phytosomes showed around 90.40% recovery.[29]As was previously mentioned, the Demir et al. 2014 study showed that the created vesicles also showed improved wound.[62]

In comparison to sinigrin alone, a complex comprising sinigrin and phytosome showed positive benefits on wound healing in HaCaT cells. [63]

The Phytosomes Role in the Respiratory System Diseases

(A) The Phytosomes in Asthma and Bronchitis

The usual treatment for those with mild to severe persistent asthma is a combination of betaagonists and corticosteroids, which was utilized in a multicentre research with thirty-two asthmatic volunteers. The 500 mg of Boswellia serrata that the patients were randomly assigned to receive.[64]

(B) The Phytosomes Role in Lung Cancer

Using the mammary gland tumor cell line (ENU1564), the anticancer effects of curcumin with phosphatidylcholine injected into the mammary fat of athymic nude mice were assessed.

We used free curcumin to assess the phytosome's effects. The curcumin phytosome significantly decreased lung metastases and the production of MMP-9, a protein associated to tumor invasion and metastasis, including breast cancer, while having no effect on the tumor's size. This was related to the results of the same study on how grape seed phytosomes affected lung cancer cells' in vitro activities. Both Ki-67 and the grading of bronchial histology showed a significant reduction after therapy in bronchial samples.[65]

The Phytosome Role in Hepato-Protective

It has been discovered that Ginkgo biloba leaf extracts (family: Ginkgoaceae) exhibit strong CNS, antioxidant, hepatoprotective, anti-diabetic, and cardio protective properties. The results of the investigation showed that 200 mg/kg of G. biloba phytosomes considerably reduced the cardiac necrosis caused by isoproterenol. The cardio protective properties of phytosomes were further validated by histopathological study of the myocardium. Its reduction in myocardial necrosis (as seen by lower AST, LDH, and CPK release as well as histoarchitectural changes) and increase in endogenous antioxidants are responsible for its cardio protective impact.[66-67]

Andrographolide (AN), which is derived from Andrographis paniculata Linn, has been traditionally used to treat a variety of conditions, such as fever, inflammation, tonsillitis, pharyngitis, laryngitis, pneumonia, tuberculosis, pyelonephritis, and hepatic impairment. When compared to its phytosome dose, the drugs equimolar dose exhibits lower absorption and higher serum levels of SGOT and SGPT, suggesting its hepatoprotective properties.[68]

The Phytosome Role in Enhancing Bioavailability

Anti-inflammatory, anti-tumor, anti-nociceptive, anti-obesity, and thermoregulatory activities are only a few of its many pharmacological properties. Evodiamine is a quinoline alkaloid found in Evodia rutaecarpa. Evodiamine exhibits potential as an anti-tumor agent since it slows proliferation, causes apoptosis, and decreases invasion and metastasis in a variety of tumor cells. Evodiamine phytosomes were found to have improved absorption, a longer half-life, a greater in vitro dissolution rate, and a higher bioavailability. An extended duration of action and increased bioavailability were noted as a consequence of the drug's protracted release from the phytosome. Furthermore, by avoiding the liver and preventing the medication from coming into direct touch with the enzymes involved in hepatic metabolism, these phytosomes may lessen the first-pass metabolism of evodiomine. Evodiamine's bioavailability was 1772.35 µg h-1 L-1, while its half-life was 1.33 hours.[69-71]

Limitations of Phytosome

Despite offering several benefits as a medicine delivery technology, phytosomes are not widely available. Yamila B. Gándola et al. (2014) report that lecithin, in particular, is a phospholipid that can promote proliferation in the MCF-7 breast cancer cell line.30 The phytoconstituents leaching off the "some" may be a serious phytosome drawback, as it lowers the intended medication concentration and highlights the fragile nature of these constituents.[72]

CONCLUSION

Appropriate formulations and delivery systems are needed to maximize the distribution of the beneficial components in plant products, especially those that contain flavonoids and other phenolic compounds. Hydrophilic flavonoids and other similar compounds with improved skin or

gastrointestinal tract bioavailability are found in new formulations called phytosomes. Compared to other traditional formulations, they provide a number of clear advantages. The process of creating phytosomes is easy to understand and may be quickly expanded to a commercial scale.

For this kind of innovative formulation, the analytical methods and characterisation techniques are well-established. Several patents have already been awarded for innovative phytosomal compositions, processes, and applications. The utilization of phytosome technology has significant potential to boost formulation technique.

Phytosomes are new substances made up of phospholipid-containing lipophilic complexes of parts of several plants, such as ginseng, S. marianum, and G. Biloba. The process of preparing phytosomes is non-convectional.

Compared to the individual component, there is a noticeable increase in the absorption of phytosome in the gastrointestinal system, which raises the plasma level. The component to phospholipid complex formation ratios are 1:1 and 2:1, respectively. Phytosomes have many applications in cosmetology and are utilized as a medication.

There is still much to learn about phytosomes in terms of potential medicinal uses. Between the traditional distribution system and the innovative delivery mechanism, phytosomes provide a link. Phytosomes are a sophisticated herbal extract type that exhibits superior absorption properties compared to traditional herbal extracts.

Phytosomes can be utilized to treat liver problems originating from either metabolism or infection since they possess superior pharmacokinetic and pharmacological qualities. They also have lipolytic, vasokinetic, anti-oedema, cicatrizing, trophodermic, neutraceutical, antioxidant, cardioprotective, anti-wrinkles, and UV properties.

Researchers wishing to investigate vesicular drug delivery systems that include effective drugs on target without metabolizing will find the information gathered here helpful. It is important to investigate the use of phytosome technology in the cure of varied skin-related terms as well as neurological, cardiovascular, and autoimmune diseases. To create phytosomes that are extremely target-specific, more research can be done. An effort was made to look into the ongoing phytosome research. and their potential uses in wound healing, antioxidant, and anti-cancer activity, transdermal, enhancing bioavailability, hepato protective, anti-oxidant, cancer (nervous system, pancreatic, breast, skin and also in lung cancer), Asthma and bronchitis, immune system, UTI, Prostate disease, also used in a Migraine etc. Phytosome technology is more significant than free medication delivery since it is an effective drug delivery technique.

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REFERENCES

1. Manach.C, Scalbert. A, MorandC. Polyphenols: food sources and bioavailability. Am. J. Clin. Nutr., 2004;79: 727-747

2. Dubey.D, Shrivastava.S, Kapoor.S, et al. Phytosome: a novel dosage structure, http://www.pharmainfo.net/reviews/ Phytosome novel dosage-structure, 2007.

3. Gupta.A, Ashawal M.S, Saraf.S, Phytosomes: a novel approach towards functional cosmetics. J. Plant Science, 2007;644-649.

4. Mascarella.S, Therapeutic & antilipoperoxidant effect of silybin phosphatidylcholine complex in chronic liver disease. Cur. Ther. Res. 1993;53:98-102.

5. Kalita B., Das K.M., Sharma K.A., "Novel Phytosome formulation making herbal extract more effective" J Pharm Technol 2013;6 (11):1295-99.

6. Jadhav I.A., Wadhave A.A., Arsul V.A., Sawarkar H.S., "Phytosome a novel approach in herbal drug" Int J Pharm Anal, 2014;2(5):478-83.

7. Jasemi, S.V.; Khazaei, H.; Aneva, I.Y.; Farzaei, M.H.; Echeverría, J. Medicinal Plants and Phytochemicals for the Treatment of Pulmonary Hypertension. Front. Pharmacol. 2020;11:18-25.

8. Oveissi, V.; Ram, M.; Bahramsoltani, R.; Ebrahimi, F.; Rahimi, R.; Naseri, R.; Belwal, T.; Devkota, H.P.; Abbasabadi, Z.; Farzaei, M.H. Medicinal plants and their isolated phytochemicals for the management of chemotherapy-induced neuropathy: Therapeutic targets and clinical perspective. DARU J. Pharm. Sci. 2019;27:389–406.

9. Kooti, W.; Servatyari, K.; Behzadifar, M.; Asadi-Samani, M.; Sadeghi, F.; Nouri, B.; Marzouni, H.Z. Effective Medicinal Plant in Cancer Treatment, Part 2: Review Study. J. Evid.-Based Integr. Med. 2017;22:982–995.

10. O'Hagan, D. Pyrrole, pyrrolidine, pyridine, piperidine and tropane alkaloids (1998 to 1999). Nat. Prod. Rep. 2000; 17:435–446.

11. Ekor, M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Front. Pharmacol. 2014;4:177.

12. Bahramsoltani, Farzaei.R, Rahimi M.H, R. Medicinal plants and their natural components as future drugs for the treatment of burn wounds: An integrative review. Arch. Dermatol. Res. 2014;306:601–617.

13. Dawid Pac, R. Medicinal plants used in treatment of inflammatory skin diseases. Adv. Dermatol. Allergol. 2013;3:170–177.

14. Manach.C, Scalbert.A, Morand.C, Rémésy.C, Jiménez.L, Polyphenols: Food sources and bioavailability. Am. J. Clin. Nutr. 2004;79:727–747.

15.Franceschi F, Giori A, "(Indena S.p.A.). Phospholipid complexes of olive fruits or leaves extract having improved bioavailability" Patent app. WO2007118631, 2007.

16.Manach C., Scalbert A., Morand C., "Polyphenols, food sources and bioavailability" The American Journal of clinical Nutrition, 2004;79:727-47.

17. Semalty.A, Semalty.M, Rawat.M.S.M, 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.biology-online.org/articles/phytosomes-short-review., 2008.

19. Bombardelli.E, Phytosome: a new cosmetic delivery system. Boll. Chim. Farm., 1991;130:431-438.

20. Bombardelli.E, Spelta.M, Phospholipid-polyphenol complexes: a new concept in skin care ingredients. Cosm. & Toil., 1991;106:69-76

21. Franceschi F., Giori A., "(Indena S.p.A.). Phospholipid complexes of olive fruits or leaves extract having improved bioavailability" Patent app. WO2007118631, 2007.

22. Manach C., Scalbert A., Morand C., "Polyphenols, food sources and bioavailability" The American Journal of clinical Nutrition, 2004;79:727-47.

23. Jain N., Gupta P.B., Thakur N., Jain R., Banweer J., "Phytosome a novel drug delivery system for herbal medicine" Int J Pharm Sci Drug Res, 2010;2(4):224-32.

24. Kareparamban A.J., Nikam H.P., Jadhav P.A., Kadam J.V., "Phytosome a novel revolution in herbal drugs" Int J Res Pharm Chem 2012:2(2):300-9.

25. Dhase S.A., Saboo S.S., "Preparation and evaluation of phytosome containing methanolic extract of leaves of Aegle marmelos (Bael)" Int J Pharm Technol Res, 2015;8(6):232-3.

26. Amin T., Bhat S., "A review on phytosome technology as a novel approach to improve the bioavailability of nutraceuticals" Int J Online Adv Res Technology, 2012;1:1-15

27. Kidd P.M., "Bioavailability and activity of Phytosome complexes from botanical polyphenols, The silymarin, curcumin, green tea, and grape seed extracts" Altern Med Rev, 2009;14(3):226-46.

28. Bombardelli E., Mustich G., "Bilobalide Phospholipid Complex their Uses and Formulation Containing them" U.S Patent No. EPO 275005, 1991.

29. Middleton E., Kandaswami C., "The impact of plant flavonoids on mammalian biology: implications for immunity, inflammation, and cancer" In Harborne JB, editor, The Flavonoids, Advances in Research Since 1986. 1st Ed, 1994, London, Chapman and Hall, 1994;619-652.

30. Yanyu.X, Yunmei.S, Zhipeng.C, et al. The preparation of silybin phospholipid complex and the study on its pharmacokinetics in rats. Int. J. Pharm., 2006;307: 77-82.

31. Jain.N.K, Liposomes as drug carriers, controlled and novel drug delivery, 1st edition, CBS publisher, 2005;321-326.

32. Maghraby GMM El, Williams A.C, Barry B.W, Oestradiol skin delivery from ultradeformable liposomes: refinement of surfactant concentration. Int. J. Pharm., 2000;196: 63-74.

33. Fry D.W, White J.C, Goldman I.D, Rapid secretion of low molecular weight solutes from liposomes without dilution. Anal. Biochem., 1978;90: 809-815.

34. Liposomes: A Practical Approach, Preparation of liposomes and size determination, New RRC (Ed.), Oxford University Press, 1990, 36-39.

35. Cevc.G, Schatzlein.A, Blume.G, Transdermal drug carriers: basic properties, optimization and transfer efficiency in case of epicutaneously applied peptides. J. Control. Release, 1995;36:3-16.

36. Berge BAI.V, SwartzendruberVAB, Geest.J, Development of an optimal protocol for the ultrastructural examination of skin by transmission electron microscopy. J. Microsc., 1997;187: 125-133.

37. Dayan.N, Touitou.E, Carrier for skin delivery of trihexyphenidyl HCl: ethosomes vs liposomes. Biomaterials, 2002;21:1879-1885.

38. Murray D.Phytosomes-Increase the Absorption of Herbal Extract [online].2008[cited 2008 Sep 28]. Available from: URL: www.doctormurray.com/article/silibin.htm.

39. Pandey S., Patel K., "Phytosomes, Technical Revolution in Phytomedicine" International Journal of Pharm Tech Research, 2010;2(1):627-63.

40. Mancini S, Nardo L, Gregori M, et al. Functionalized liposomes and phytosomes loading Annona muricata L. aqueous extract: potential nanoshuttles for brain-delivery of phenolic compounds. Phytomedicine. 2018;42:233–244. doi:10.1016/j.phymed.2018.03.053

41. Naik SR, Pilgaonkar VW, Panda VS. Neuropharmacological evaluation of Ginkgo biloba phytosomes in rodents. Phytother Res. 2006;20(10):901–905. doi:10.1002/ptr.1973

42. Ahmad H, Arya A, Agrawal S, et al. Rutin phospholipid complexes confer neuro-protection in ischemic-stroke rats. RSC Adv. 2016;6 (99):96445–96454. doi: 10.1039/C6RA17874J

43. Ahmad H, Arya A, Agrawal S, et al. Phospholipid complexation of NMITLI118RT+: way to a prudent therapeutic approach for beneficial outcomes in ischemic stroke in rats. Drug Deliv. 2016;23(9):3606–3618. doi:10.1080/10717544.2016.1212950

44. D'Andrea G, Bussone G, Allais G, et al. Efficacy of Ginkgolide B in the prophylaxis of migraine with aura. Neurol Sci. 2009;30(S1):S121–S124. doi:10.1007/s10072-009-0074-2

45. Williams B, Watanabe CMH, Schultz PG, et al. Age-related effects of Ginkgo biloba extract on synaptic plasticity and excitability. Neurobiol Aging. 2004;25(7):955–962. doi:10.1016/j. neurobiolaging.2003.10.008

46. Allais G, D'Andrea G, Maggio M, et al. The efficacy of ginkgolide B in the acute treatment of migraine aura: an open preliminary trial. Neurol Sci. 2013;34(S1):S161–S163. doi:10.1007/ s10072-013-1413-x

47. Bresciani L, Favari C, Calani L, et al. The effect of formulation of curcuminoids on their metabolism by human colonic microbiota. Molecules. 2020;25(4):940-9. doi:10.3390/molecules25040940

48. Solda C, Sperti C, Romeo B, et al. Use of meriva as complementary therapy of locally advanced or metastatic pancreatic cancer (PC) with gemcitabine (GEM). J Clin Oncol. 2016;34(15_suppl): e15696–e15696. doi:10.1200/JCO.2016.34.15_suppl.e15696

49. Pellegrini L, Milano E, Franceschi F, et al. Managing ulcerative colitis in remission phase: usefulness of Casperome (R), an innovative lecithin-based delivery system of Boswellia serrata extract. Eur Rev Med Pharmacol Sci. 2016;20 (12):2695–2700.

50. Lazzeroni M, Guerrieri-Gonzaga A, Gandini S, et al. A Presurgical Study of lecithin formulation of green tea extract in women with early breast cancer. Cancer Prev Res. 2017;10(6):363–369. doi:10.1158/1940-6207.CAPR-16-0298

51. Singh RP, Raina K, Sharma G, et al. Silibinin inhibits established prostate tumor growth, progression, invasion, and metastasis and suppresses tumor angiogenesis and epithelial-mesenchymal transition in transgenic adenocarcinoma of the mouse prostate model mice. Clin Cancer Res. 2008;14(23):7773–7780. doi:10.1158/ 1078-0432.CCR-08-1309

52. Flaig TW, Gustafson DL, Su L-J, et al. A phase I and pharmacokinetic study of silybin-phytosome in prostate cancer patients. Invest New Drugs. 2006;25(2):139–146. doi:10.1007/s10637-006-9019-2

53. Flaig TW, Glodé M, Gustafson D, et al. A study of high-dose oral silybin-phytosome followed by prostatectomy in patients with localized prostate cancer. Prostate. 2010;70(8):848–855. doi:10.1002/pros.21118

54. Ledda A, Belcaro G, Dugall M, et al. Meriva (R), a lecithinized curcumin delivery system, in the control of benign prostatic hyperplasia: a pilot, product evaluation registry study. Panminerva Med. 2012;54(1):17–22.

55. Tuyaerts S, Rombauts K, Everaert T, et al. A phase 2 study to assess the immunomodulatory capacity of a lecithin-based delivery system of curcumin in endometrial cancer. Front Nutr. 2019;5:44-49. doi:10.3389/fnut.2018.00138

56. Wang B, Li F, Pan N, et al. Effect of ice structuring protein on the quality of quick-frozen patties subjected to multiple freeze-thaw cycles. Meat Sci. 2021;172:108335. doi:10.1016/j.meatsci.2020.108335

57. Baron G, Altomare A, Regazzoni L, et al. Profiling Vaccinium macrocarpon components and metabolites in human urine and the urine ex-vivo effect on Candida albicans adhesion and biofilmformation. Biochem Pharmacol. 2020;173:113726.

58. Ledda A, Belcaro G, Feragalli B, et al. Temporary kidney dysfunction: supplementation with Meriva (R) in initial, transient kidney micro-macro albuminuria. Panminerva Med. 2019;61 (4):444–448.

59. Ram P, Vivek K, Kumar SP. Nanotechnology in sustainable agriculture: present concerns and future aspects. Afr J Biotechnol. 2014;13(6):705–713. doi:10.5897/AJBX2013.13554

60. Magrone T, Pugliese V, Fontana S, et al. Human use of leucoselect (R) phytosome (R) with special reference to inflammatory-allergic pathologies in frail elderly patients. Curr Pharm Des. 2014;20(6):1011–1019. doi:10.2174/13816128206140220144411

61. Mazumder A., Dwivedi A., Du Preez J. L. & Du Plessis J., In vitro wound healing and cytotoxic effects of sinigrinphytosome complex, Int. J. Pharm., 2016;498:283-9.

62. Demir.B, Barlas F.B, Guler.E, Gumus P. Z, Can.M, Yavuz.M, Coskunolbef. H and Timur.S, Gold nanoparticle loaded phytosomal systems: synthesis, characterization and in vitro investigations, RSC Adv., 2014;4:34687.

63. Mazumder A, Dwivedi A, Du Preez JL, et al. In vitro wound healing and cytotoxic effects of sinigrin–phytosome complex. International Journal of Pharmacy. 2016;498 (1–2):283–293. doi:10.1016/j.ijpharm.2015.12.027

64. Ibrahim A, El-Meligy A, Fetaih H, et al. Effect of curcumin and meriva on the lung metastasis of murine mammary gland adenocarcinoma. In Vivo. 2010;24 (4):401–408

65. Mao JT, Lu Q-Y, Xue B, et al. A pilot study of a grape seed procyanidin extract for lung cancer chemoprevention. Cancer Prev Res. 2019;12(8):557–565. doi:10.1158/1940-6207.CAPR19-0053

66. Panda V. S. & Naik S. R., Cardioprotective activity of Ginkgo biloba Phytosomes in isoproterenol-induced myocardial necrosis in rats: A biochemical and histoarchitectural evaluation, Exp. Toxicol. Pathol., 2008; 60:397–404.

67. Naik S. R. & Panda V. S., Hepatoprotective effect of Ginkgoselect Phytosome in rifampicin induced liver injurym in rats : Evidence of antioxidant activity, Fitoterapia, 2008;79:439–445.

68. Jain P. K., Khurana N., Pounikar Y., Gajbhiye A. & Kharya M. D., Enhancement of absorption and hepatoprotective potential through soya-phosphatidylcholine-andrographolide vesicular system, J. Liposome Res., 2013; 23(2):110–8.

69. Qunyou Tan, Shan Liu, Xueliang Chen, Mingjun Wu, Hong Wang, Huafeng Yin, Dan He, Huarong Xiong, and Jingqing Zhang, Design and evaluation of a novel evodiaminephospholipid complex for improved oral bioavailability, AAPS Pharmaceutical Science & Technology, 2012;13(2):534–547.

70. Franceschi, Federico, Giori, A., Phospholipid compleses of olive fruits or leaves extracts having improved bioavailability, 2006;1:1–8.

71. Bombardelli, Patri, P. Complexes of saponins with phosphlipids and pharmaceutical and cosmetic compositions containing them. IJWAR, 1988;9:41-48.

72. Yamila B. Gándola, Sebastián E. Pérez, Pablo E. Irene,Ana I. Sotelo, Johanna G. Miquet, Gerardo R. Corradi, AdrianaM. Carlucci, and Lorena Gonzalez. Mitogenic effects of phosphatidylcholine nanoparticles on MCF-7 breast cancer cells. Biomed Res. Int. 2014;6:33-39.

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