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Phytosomes as innovative delivery systems for phytochemicals: An updated review

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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 stand sophisticated herbal preparations that contain the phytoactive ingredients found in extracted from herbs and have the ability towards change the cell membranes hydrophilic to lipophilic state. They may be produced as pills, creams, gels, suspensions, and other medicinal forms. Many illnesses now have a fantastic treatment alternative in phytosomes. Their therapeutic applicability may be limited by poor bioavailability and selectivity. The great potential of the emerging nanotechnology in the delivery of bioactive phytochemicals is reviewed, with particular focus on phytosomes as an innovative lipid-based nanocarrier. Additionally, we compared phytosomes with liposomes as the gold standard of lipid-based nanocarriers for the topical delivery of phytochemicals. Finally, the advantages of phytosomes in topical applications are discussed.

Keywords: Phytosomes, nanocarriers, medicine, phytochemicals, topical application.

Introduction

Phytochemicals

These phytochemicals are plant based bioactive polyphenolic compounds produced by plants for their protection through primary & secondary metabolism. Phytochemicals are compounds in plants. (Phyto means -plantin Greek.) These substances are found in plant-based foods such as fruits, vegetables, whole grains, nuts, seeds and legumes. They give plants their color, flavor and aroma. Phytochemicals can also exhibit their influence, including acting as substrates, cofactors or inhibitors of enzymatic reactions. The antioxidant activity that has for phytochemicals is a potential property. It has ability to enhance the essential nutrients.

By demonstrating their chelating properties, they can get rid of undesirable constituents from the GIT. Numerous herbal extracts are taken from different plant species due to various medicinal benefits present in them. They also include the properties like wound healing, antimicrobial, and anti-inflammatory, relive burns & other skin diseases also. The Phytochemicals of most plant extracts are used in cosmeceutical and pharmaceutical application in the medicines. The skin is most likely infected by the change in environment and due to increase in pollution intensity. A variety of common skin conditions like acne, urticaria, pruritus, psoriasis, eczema & fungal, bacterial infections can also be treated by the medicinal herbs. Some phytochemical properties are present in food that has the nutritional and energetic properties that is why they called as pharmaceutical compounds. Phytochemicals also have the ability to search the free radicals present in human tissue. An example of the utility of phytochemicals is salicin, which is a compound found in willow tree bark. It has anti-inflammatory and analgesic activity, and is also used as a precursor to numerous conventional non-steroidal anti-inflammatory drugs (NSAIDs). Due to its widespread use and high demand, greater quantities of salicin were prepared using chemical synthesis.

The potential bioactivity of phytochemicals, there remains concerns about their quality, safety and efficacy. Phytochemicals are categorized into three major categories based on their structural elements: terpenoids, alkaloids and polyphenolic substances. Numerous flavor and aromatic molecules are terpenoids, including menthol, linalool, geraniol, and caryophyllene, while catechol's, lignin's, tannins, stilbenes, and flavonoids are phenolic compounds. Alkaloids are further divided into Pyrrolidine, Pyrrolidine-pyridine, Pyridine-piperidine, and Isoquinoline alkaloids based on their heterocyclic ring systems [3].

Phytosomes

Phytosomes is a technology developed by incorporating standardized plant extracts or water soluble phytoconstituents into phospholipids to form complexes that have the ability to increase the extracts bioactivity. Phytosomes and liposomes are encapsulation systems with wider future applications in food industry. The term PHYTO means plant while SOME means cell-light. Phytosomes technology produces a little cell, is able to better transit from a hydrophilic environment into the lipid friendly environment, and it enhance the bioactivity of phospholipids (Contain Phosphorus, a polar and non-polar part in their structure) used in phytosomes production. Phytosomes and liposomes are examples of the encapsulating system that are suitable in food and pharmacokinetic applications [5].

Encapsulation: It is a process that entraps one substance within another substance, and therefore produces particles with diameter of a few nm to few mm. Encapsulation can change liquids and other ingredients into powders, making them simpler to process and easier to use. It can also be used to improve the ―freeze and thaw ability‖ of sensitive ingredients by providing protection against moisture and cross contamination. Encapsulation in food and dosage forms used to mask unfavorable odors or taste [6].

Liposomes: liposomes are small artificial vesicles of spherical shape that can be created from cholesterol & natural non-toxic phospholipids.

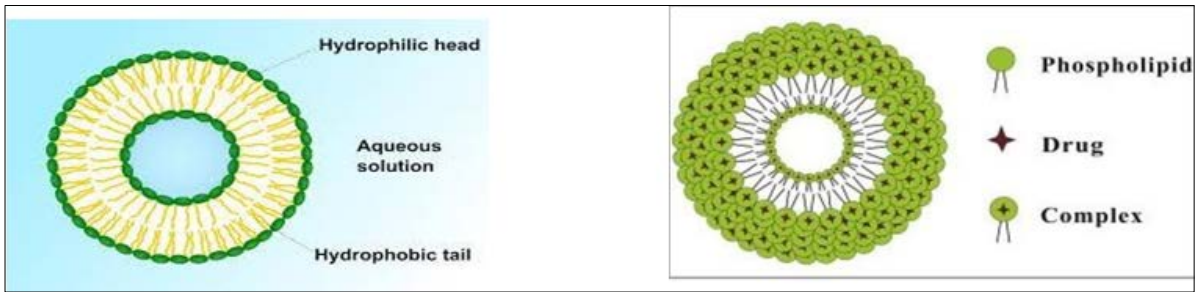


Fig: 1 Phytosomes

Liposomes also have been used in cases in which the lipophilic drug dissolves into the liposomal bilayer. To overcome the low absorption of bioactive polyphenolic phytocompounds, nanosized drug delivery systems can be utilized to enhance their penetration across biological barriers by their unique physicochemical properties, increasing the bioavailability of phytocompounds. Nanocarriers have an important function over conventional phytochemicals obtained at other scales in protecting the bioactive polyphenolic phytochemicals from oxidation and degradation, hence maintaining their long-term effects as well as improving their stability. The high surface area of nanoparticles supports the effective delivery of active ingredients into the skin in case of topical applications of phytochemicals. The mechanism of polyphenolic phytochemicals 'incorporation into nanoparticles is by the hydrogen bond (H-bond) or through hydrophobic interactions. Phytosomes are complex of phospholipids & natural active phytochemicals, bound in their structures, obtained by the reaction between phosphatidylcholine (or any hydrophilic polar head groups) & plant extracts in an aprotic solvent. Phytosomes, also called Phyto-phospholipid complexes, are the vesicular systems formed by the interaction between hydrophilic parts of phospholipids and the Phyto-active components resulting in the formation of hydrogen bonds between them. The structural difference between liposomes and phytosomes is that liposomes have their active ingredient inside the hydrophilic cavity or within the layers of membranes while in phytosomes, those components are a part of the membrane. The resulting complex helps these active ingredients to pass through the outer membrane of gastrointestinal cells and reach their functional site. The absorption of these components is greatly increased and their bioavailability becomes much greater as compared to the original component.

Principle

Phosphatidylcholine (or phosphatidylserine) is a bifunctional compound. The phosphatidyl moiety is lipophilic and the choline (serine) moiety is hydrophilic in nature. This dual solubility of the phospholipid makes it an effective emulsifier. Thus, the choline head of the molecule binds to these compounds while the lipid soluble phosphatidyl portion comprising the body and tail which then surrounds the choline bound material**.** Hence, the phytoconstituents produce a lipid compatible molecular complex with phospholipids, (also called as Phyto phospholipid complex) [7].

Structure

The active phytoconstituents and the polar head (choline moiety) combine physically and chemically to generate Guggulosomes and phytosomes, which complexes of Phyto-phospholipids in their chemical makeup. These complexes entail the anchoring of phospholipid head groups. In complexes that result in the creation of a lipophilic surface, the polar component is encapsulated by fatty acid chains. The substance that makes up a liposome is active, either in a cavity between the membrane's several layers. The substance that makes up phytosomes active is a component

of the membrane itself. Phytosomes structure contains the active ingredients of the herb surrounded by the phospholipids. The presence of the surfactant i.e. the phospholipid in the molecule which are shielded from water triggered degradation while at the same time, allows obtaining a higher adhesion of the product itself to the surface it comes into contact with and a better interaction of various molecules with cell structure. The size of phytosomes varies from 50 nm to a few hundred micrometers [8].

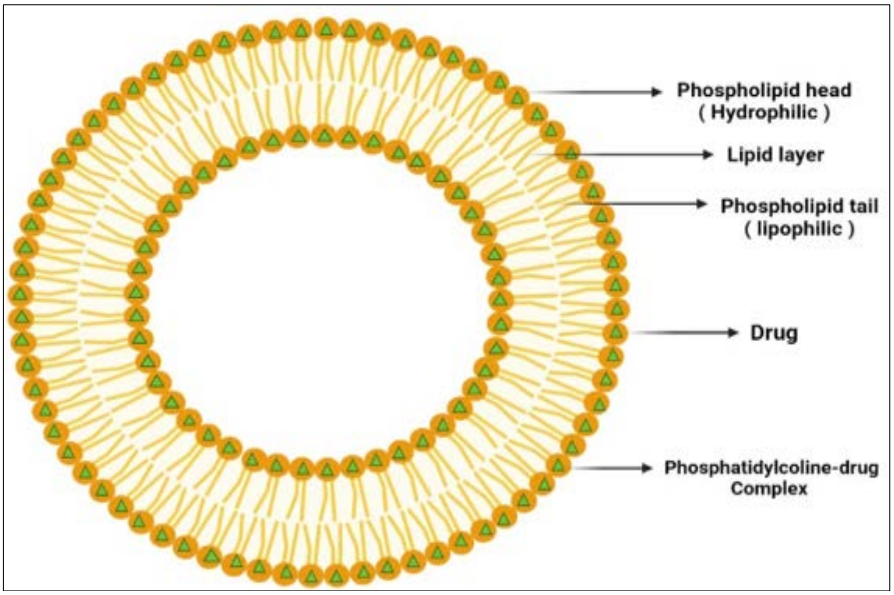


Fig 2: Structure of phytosomes

Properties of phytosomes

Chemical properties

A 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 nonpolar solvent. 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. Molecules are anchored through chemical bonds to the polar head of the phospholipids, as can be demonstrated by specific spectroscopic techniques [9].

Components of phytosomes

A phytoconstituents, the role of phospholipids and the stoichiometric ratio in the as well as solvents are the four key components listed in the current literature for the production of Phyto-phospholipid complexes. In addition to polyphenols, additional compounds may be used as the active component in phytosomes, such as 20(R)-25-methoxyl-dammarane-3, 12, 20-triol (25-OCH3-PPD), siramasin, and evodiamine. So, phytosomes are not just polyphenols, and complexes made from them could, in theory, be mixed with any active moiety.

Plant-Based Ingredients

Researcher-selected Phyto-active components extracts from plants are evaluated for their pharmacological action shown *in vitro* as opposed to their effects *in vivo*. Most in these chemicals are polyphenols, some of those are seen in polyphenolic components have a preference considering the aqueous phase and are unable to pass via membranes in living things. Others, such by way of rutin and curcumin, alternatively, there are lipophilic characteristics then are not soluble in fluids in the stomach that are aqueous. Both the solubilization that are lipophilic polyphenols the phase of water as well as cell membrane permeability with hydrophilic polyphenols since the water phase are improved by Phyto-phospholipid complexes. Additionally, the creation of complexes may shield polyphenols from photolysis, oxidation, and hydrolysis.

Phospholipids

Phospholipids stand widely distributed inside of a plant, an egg yolk, they are, and classified based on their backbones, specifically sphingomyelins and glycerophospholipids. The primary components of glycerophospholipids are Phosphorylcholine, Phosphoryl ethanolamine, Phosphoryl glycerol, Phosphoryl serine, Phosphoryl inositol, and Phosphoric Acid (PI). Currently, commercially produced phospholipids may be found on the market. The main phospholipids involved in the production of complexes with a hydrophilic head group, two hydrophobic hydrocarbon chains, and are PS, PE, and PC. Due to its amphipathic character, which allows for mild solubilization in aqueous and lipid solutions media, PC is the most preferred phospholipid among them and is used in the creation of phospholipid complexes. PC is also an important a component of cell membranes helps explain why it works well with living things and doesn't harm them.

Solvents

A number have been used in the past used by scientists for the synthesis of phospholipid Phyto complexes. In most cases, aprotic solvents such as ethyl acetate, hydrocarbons, cyclic ethers, halogen derivatives, and methylene chloride have all been used towards synthesize complexes of Phyto phospholipids. However, owing to their success rate, ethanol and methanol are examples of prototic solvents have taken their place. In research to treat inflammatory disorders, the combination of rutin and phospholipids created using methanol. The authors developed a polymeric matrix patch for a better medication retention period over the skin. Results indicated that the improved preparation exhibits 31.32 and 26.56% of the skin penetration, then the patch's anti-inflammatory impact demonstrated its efficiency in a rat-paw oedema model when compared to standard diclofenac gel. In order to improve the absorption of glucose in muscle cells, developed chrysinloaded phytosomes. Solvent evaporation technology is used as a way to create phytosomes that are loaded with chrysin. It was phytosomes created through integrating phospholipids from eggs or soy PC [10].

Methods of preparation

The unique compound known as a Phytosome is made up of lipids and plant extracts. A technique known as phytosomal phospholipid binding was developed to bind the standardized extract of the herb's active components to phospholipids like PC either phosphatidyl ethanolamine or phosphatidyl serine via a polar end. A phospholipid that is either natural or synthetic and 3-2 moles of an herbal extract are combined to form a Phyto some. The reaction takes place using an aprotic solvent like the complex is derived from dioxane or acetone may be separated by precipitation combined with non-solvents like Lithium-based hydrocarbons, lyophilization, or by spraying. These two moieties are arranged in a ratio between 0.5 and 2.0 moles during the complicated development of phytosomes. Phospholipids and flavonoids should be used in a 1:1 ratio. illustrates the step-by-step method of Phyto some preparation. The steps below make up the general technique of making phytosomes.

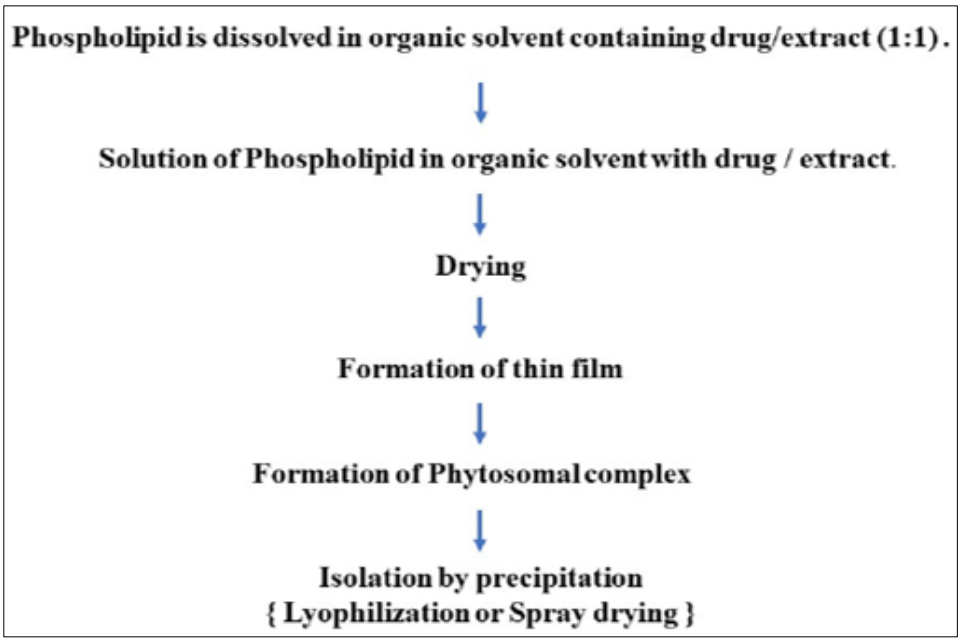


Fig 3: Schematic representation of Phytosomal preparation

Solvent evaporation technique

A There is a marsupsin-phospholipid complex created by means of a precipitation of liquid antisolvent technique that is mechanically dispersion orientated. The medication and the phospholipids are typically combined in a flask with an appropriate solvent/solvent system when using the solvent evaporation procedure (i.e., tetrahydrofuran and ethanol). A 1:1 stoichiometric ratio has been deemed the best for forming complexes in the majority of research studies. Until all of the solvents had evaporated, both solutions were mechanically agitated made the oxymatrine-phospholipid complex using ratios of 1, 4, 2, 6, and 3 between the medication and the phospholipid. The complex was then improved using a composite design approach. The most productive complex was created using a 3:1 ratio at 60ºC for three hours. In molar ratios ranging from 1:0.5 to 1:3, created an embelin-PC complex. The best formulation was created with a drug 80 g/l concentration, together with a phospholipid to ratio of 0.9 drugs (w/w). It was determined that the medication content in the complex was 45.78%, and combined percentage of the final it was formulated 100%. Aprotic solvents, such as methylene chloride, ethyl acetate, dioxane, etc., have greatly supplanted them. Researchers have employed phospholipids from several sources Along with the solvent system in their experiments.

Super-critical fluids being used (SCF)

Supercritical liquids are a powerful tool for particle preparation in large sizes (5-2000 nm). Complexes of puerarin and phospholipids were created using 3 different traditional techniques, such as lyophilization, solvent evaporation, and micronized puerarin. Supercritical fluids have been utilized to enhance the solubility characteristics of poorly soluble medication candidates (SEDS). In the GAS method, separate phospholipid and medication solutions were each given a supercritical anti-solvent up prior to the ultimate pressure being applied. The resulting technique produced a 93% yield.

Lyophilization process

Each synthetic and natural phospholipids then phytoconstituents were melted in various solvents, and then a mixture that contains phospholipid was additional to another solution including phytoconstituents, which was then stirred until complex formation occurred. The developed complex is separated through lyophilization. The phospholipids utilized in the process of phytosomes contain acyl group that can be the phosphorylcholine and phosphatidylserine might be the same or distinct and phosphatidylethanolamine are primarily derived from stearic, oleic, palmitic, and linoleic acids. The active principle of phytosomes becomes a structural component.

Gas anti-solvent method (GAS)

In the gas anti-solvent method, the drug and phospholipid solutions were each individually mixed with a supercritical anti-solvent till the desired the ultimate pressure was obtained. After that, the vessel for the reaction was left in place aimed at 3 hours at a constant pressure of 10 mPa and a temperature of 38 °C.

Enhancing dispersion using supercritical fluids

The phospholipid complex was synthesized using supercritical procedures. The supercritical antisolvent, the liquid solution, and the SEDS process was all infused into the precipitation unit. A 0.1 mm diameter nozzle was used to introduce carbon dioxide gas into the mixture of drugs and puerarin. The final procedure generated a 93% yield complex.

Anti-solvent precipitation technique

Numerous studies in addition to the conventional a precipitate of anti-solvent method, including n-hexane by way of the antisolvent, toward precipitate out the pharmaceutical compound of phospholipids the organic solvent. Research is based on a patented procedure for producing a combination of Phyto phospholipids with andrographolide employing the anti-solvent is n-hexane, while dichloromethane serves as the reaction media for this product's ultimate precipitation. As a result, subsequently removed by evaporation, and the residue is typically dried in a vacuum. Anhydrous co-solvent lyophilization was used in a more recent study to create a rutin-phospholipid complex methanol was used to dissolve both the medication and the phospholipids, although at separate rates containers. Mechanical stirring was used to combine the two solutions until all of the solvents had evaporated. As opposed to the crystalline rutin, the rutin-phospholipid complex was shown by photomicrography to be in an amorphous form. When the ratio of medicine to phospholipids was 1:3, the results were much better.

Rotary evaporation technique

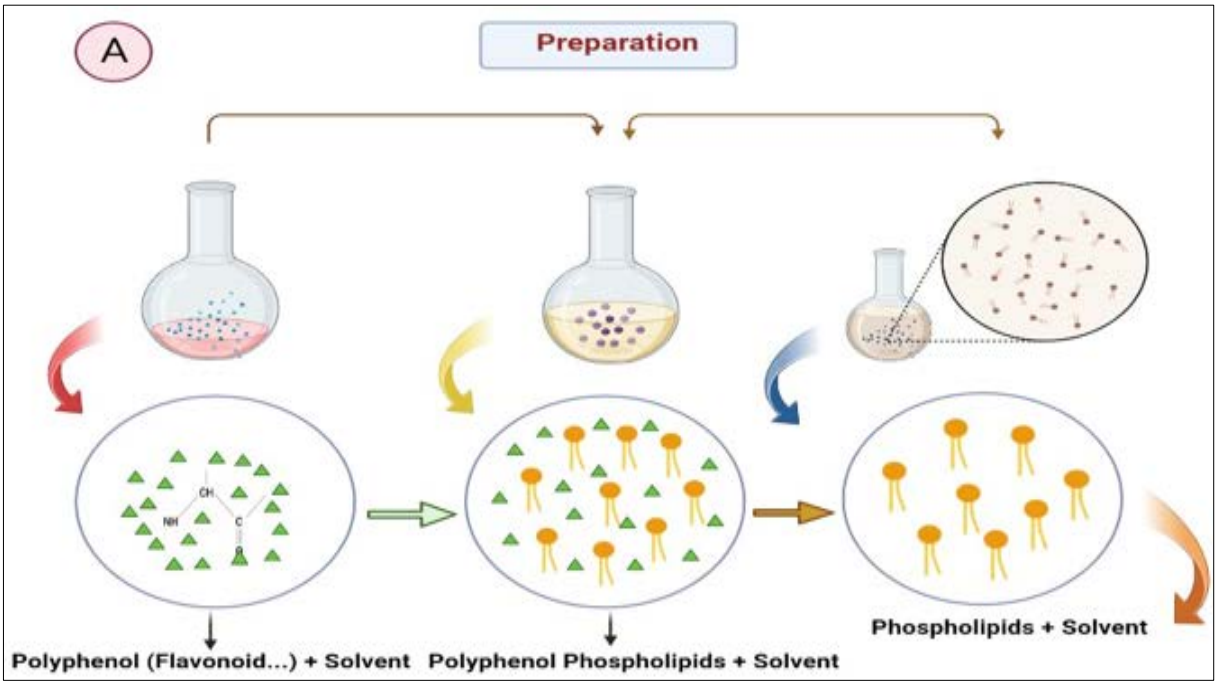
Thirty milliliters of tetrahydrofuran were used to dissolve the specified amount of plant material and phospholipid in a rotating circular bottom flask. The mixture was then agitated for three hours at a temperature below 40 degrees Celsius. Sample was in a thin film, and assembled, the addition of n-hexane, and the mixture was using a magnetic stirrer, the mixture was continually swirled. In a glass container that is amber in color, the precipitate was removed and put down at ambient temperature.

Salting out

The extract and PC are dissolved in ethanol before being stirred together. The process of precipitation creation involves adding n-hexane to the mixture to create a precipitate Phytosome.

Thin layer hydration

Cholesterol was dissolved in dichloromethane, whereas fraction, PC, and were all dissolved in methanol. Once the solvent has entirely vaporized, with a thin dry layer has developed on the bottom of the container, the mixture is gently evaporated at 45°C using a rotary evaporator. The resulting thin film of lipid is then pumped combined with nitrogen gas kept prior to by one night at room temperature receiving hydration treatment. On a rotary evaporator set at 45°C, aquabidest was used to hydrate the film layer. Using sonification and a homogenizer, the technique to calculate particle size was also optimized [11-12].



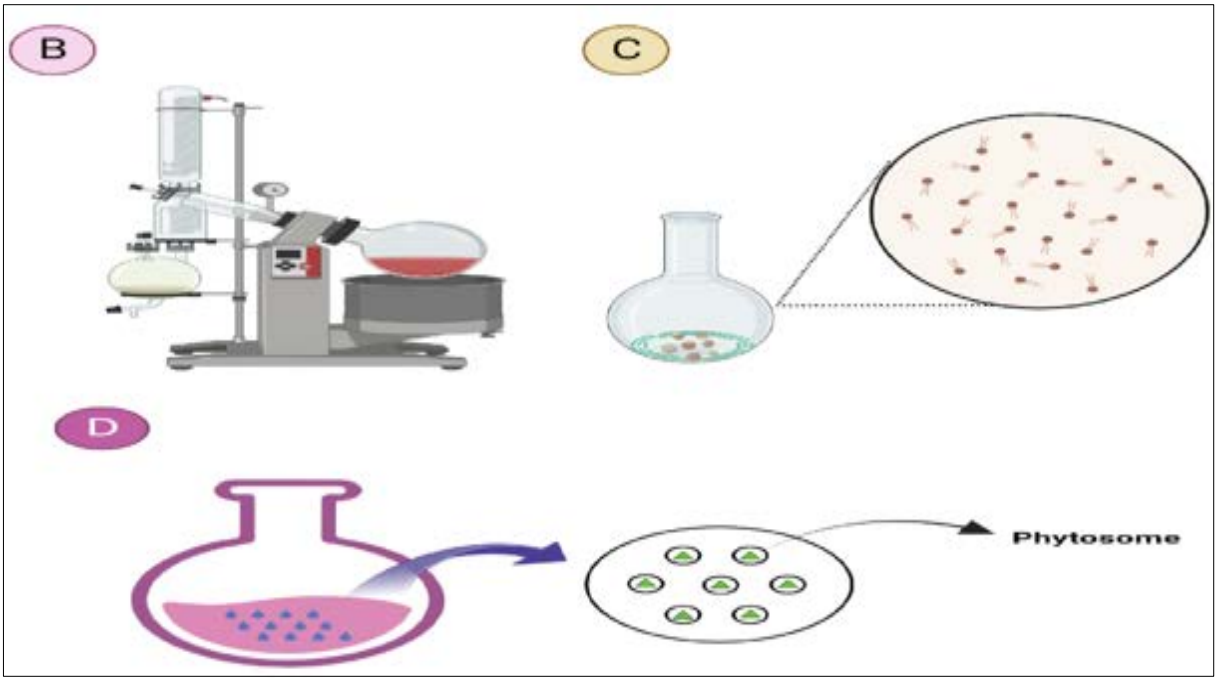


Fig 4: Thin-film hydration technique. A-Preparation, B- Refluxing and concentration under reduced pressure C- drying and thin layer formation D-Hydration and size reduction

Biological functions

Evidence of Phytosomes' Function in the Nervous System

The Role of Phytosomes in Neuronal Damage and Cognitive Impairment

In animal models, the bioavailability of phytosomes compared to similar unformulated products has been examined. Following the injection of a specific hydrophosome, discovered a higher concentration of Boswellia acids in Boswellia serrata. Looked into silymarin's capacity to prevent ethanol-induced brain damage in unborn rats. Gamma-glutamyl transpeptidase was one of the antioxidant enzymes with typically higher activity in the phytasome formulation group. Reduced pentobarbitone-induced sleep duration and reduced effects of chlorpromazine in Wistar rats were observed Curcumin phytosomes from the hippocampus and cerebellum of rats have been shown to reduce neuroinflammation and the number of activated microglia. A second study assessed the antioxidant activity in the rat brain for four weeks following either acute (7 days) or sub chronic (14 days) therapy.

Phytosomes' impact on neuropathy

Studied the clinical efficacy of curcumin phytosomes (500 mg), lipoic acid (300 mg), and B vitamins in patients with carpal tunnel syndrome awaiting surgical intervention (3 months, n = 180). Patients who received supplements twice daily before and after surgery for three months had fewer night problems at 40 days and were less likely to have a positive Phalen's test three months later. A comparable formulation based on piperine, curcumin phytosomes, and/or lipoic acid decreased pain (66%) in all combinations in neuropathic patients after 8 weeks. While lipoic acid alone did not provide statistically significant benefits, supplementation reduced the usage of conventional medication (i.e., dexibuprofen) by 40%.

The Role of Phytosomes in the Digestive System

The Role of Phytosomes in Pancreatic Cancer

In a prospective Phase II experiment, the synergistic effects of gemcitabine and the curcumin phytosome were examined in advanced pancreatic cancer. A total of 44 patients with locally advanced or metastatic pancreatic cancer were recruited and were given gemcitabine (10 mg/m2/min, infusion over 100 min on days 1, 8, and 15 every 28 days) along with 4 capsules each containing 500 mg of doxorubicin (2000 mg/die). In this trial, the response rate served as the main goal, while progression-free survival, overall survival, quality of life, and tolerability served as the secondary endpoints. The study's findings imply that the use of curcumin phytosomes in combination with gemcitabine may be beneficial for the treatment of pancreatic cancer.

Phytosomes' effectiveness in treating bowel cancer

Athymic nude mice were used to compare *in vivo* the protective effects of oral silibinin and silybinphytosome against the development of the human colorectal HT29 xenograft. The silybin-phytosome dose of 100 mg/kg demonstrated effectiveness in lowering tumour weight and volume that was comparable to silibinin 200 mg/kg.Oxaliplatin and curcumin phytosomes were combined to study the efficacy of the treatment in colorectal tumor-bearing animals and oxaliplatin-resistant cell lines *in vitro*. This combination enhanced the antiproliferative ability of oxaliplatin *in vitro* when compared to oxaliplatin alone and a control. Additionally, in the HCT116 nude mice xenograft model, a favourable impact was shown, with a decrease in tumour growth, a reduction in the pharmacodynamic markers Ki-67 and Notch-1, and an increase in cleaved caspase-3.

The Function of Phytosomes in Diseases of the Respiratory System

The Role of Phytosomes in Asthma and Bronchitis

In healthy participants with mild-to-moderate asthmatic episodes and rhinitis, a pilot study examined the benefits of quercetin phytosomes in addition to standard management (SM). Subjects took one or two QFIT tablets per day

(control group) in addition to or instead of SM. After 30 days, the quercetin phytosome + SM group outperformed the control group in terms of avoiding and minimizing daytime and nighttime symptoms, maintaining a higher peak expiratory flow, reducing variability, and having a favorable safety profile. A combination of corticosteroids and beta-agonists, the conventional treatment for individuals with moderate or severe persistent asthma, were given to 32 asthmatic volunteers who were recruited in a multicenter research study. Boswellia serrata phytosomes at 500 mg/day were administered randomly to the individuals for 4 weeks, or no further therapy was given. In comparison to patients who only received conventional medication, participants in the phytosome group required fewer inhalations. Only mild to severe side effects, like not being able to sleep or feeling sick, were reported with phytosome therapy, which was well liked. To increase naringenin's pulmonary bioavailability, and developed a new phytosome. DipalmitoylPC (DPPC), one of the major lipids found in pulmonary surfactant, was successfully employed to administer naringenin. Rats with acute lung damage were used to study the pharmacodynamics of naringenin-loaded DPPC phytosomes for dry powder inhalation (NPDPIs, 10 mg/rat, containing roughly 3 mg naringenin) and to investigate the relevant mechanisms of action. Direct administration of these phytosomes into the lungs of rats showed protection against lung damage.

Role of Phytosomes in Lung Cancer

In a mammary gland tumour cell line (ENU1564) that was injected into the mammary fat of athymic nude mice, curcumin combined with PC was assessed as an anticancer agent. Free curcumin and the phytosome's impact were compared. However, curcumin phytosomes dramatically reduced lung metastasis and the production of MMP-9, a protein linked to tumour invasion and development, including breast cancer both drugs had no effect on tumour volume. In participants taking part in a lung cancer chemoprevention experiment, assessed the biological effects of oral administration of grape seed phytosome. Premalignant and malignant cells of the human lung were studied for phytosomes' effects on prostacyclin and 15-HETE eicosanoid pathways. The findings of this research suggest the use of phytosomes as an anti-neoplastic and chemopreventive drug against lung cancer.

The Role of Phytosomes in Wound Healing

In the treatment of persistent diabetic ulcers in patients with diabetic foot ulcers, a combination of Ginkgo biloba, lipoic acid, and grape seed phytosomes combined with cutting-edge drugs proved helpful 251 in NHDF cells, phytosomes containing Moringa oleifera aqueous leaf extract were shown to be non-toxic up to 3.0 mg/mL. Comparing the formulation at 1 mg/mL to the extract at the same concentration, the formulation had the fastest gap closing time (94.8% after 24 hours). On the other hand, smaller dosages as well as higher doses (1.25 and 1.50 mg/mL) failed to produce results that were statistically significant 252 The effects of combining Calendula officinalis with gold nanoparticle (AuNP) in phytosomal systems were examined in a second *in vitro* experiment using NHDF cells.

Characterization techniques of Phytosome

The following spectroscopic techniques are used to evaluate how drug and Phytosome interact**.**

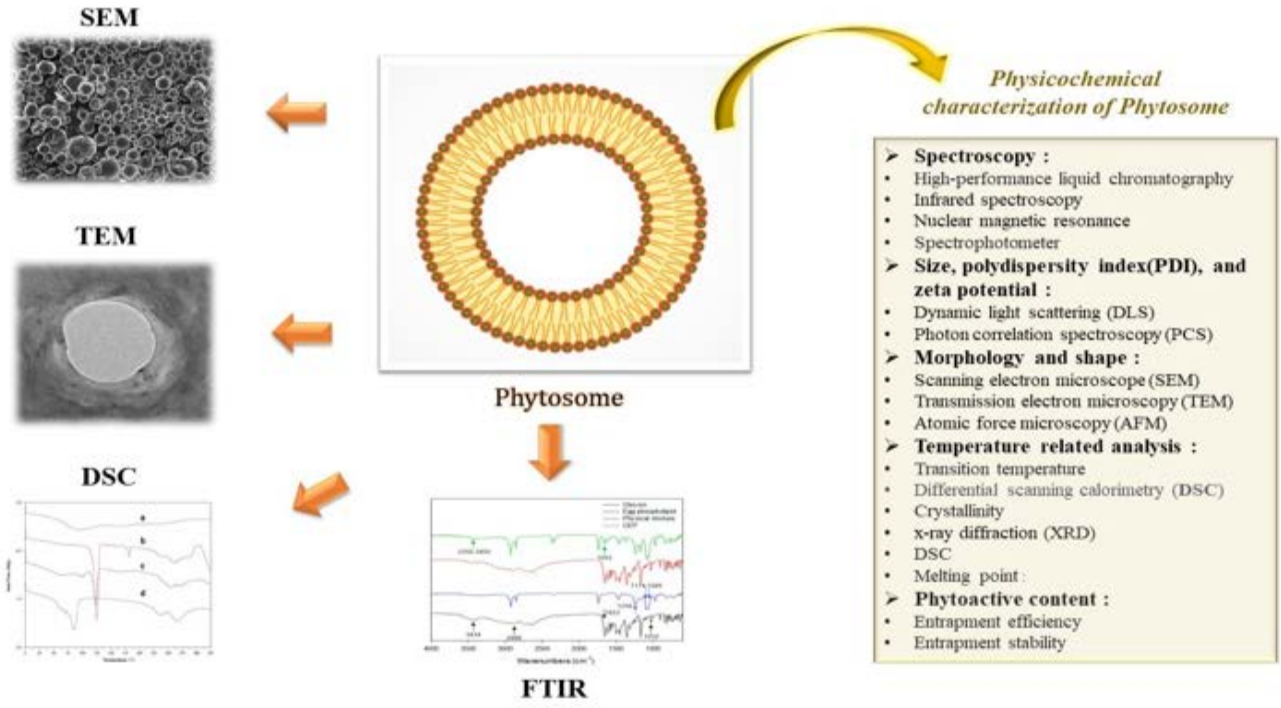


Fig 5: Various characterization parameters of phytosomes

Phytosomes and other lipid-based nanocarriers

Table 1: Different lipid-based drug delivery methods

Properties	Phytosomes	Liposomes	Transferosomes
Structure	Lipid bilayer vesicles made up of several phospholipid types that may chemically bind to phytochemicals	Cationic, anionic, and neutral lipids make up the lipid bilayer vesicles, which are made up of a greater variety of lipids.	Phospholipids, an edge activator (such as a surfactant or bile salt ranging from 10 to 25%), a little amount of ethanol, and water as a carrier make up lipid bilayer vesicles.
Encapsulation	By forming an H-bond with the phospholipids' polar tip, the bioactive molecules are anchored there.	The lipid bilayer membrane or the aqueous interior of the vesicles both contain the active components.	The aqueous core of the vesicles' active components or the membrane's lipid bilayer contain the active components.
Preparation	In reality, a 1:1 or 2:1 molecule complex with chemical bonds is formed by the PC and the phytochemicals.	The loaded elements were added to the lipid thin film after the lipid compositions were independently mixed to create the complex, which formed without the formation of any chemical linkages.	The loaded components were introduced to the lipid thin film after the lipid compositions were mixed separately to create the complex without forming any chemical linkages.
Hydration buffer	Utilize aprotic solvents including ethyl acetate, 1,4-dioxane, hexane, acetone, and metyhlenechloride.	A water or buffer solution was present when it was formed.	When a saline or buffer solution is present to form
Skin absorption	increased skin absorption	Decreased skin absorption	Decreased skin absorption and very stable.
Stability	High stability	reduced stability	

Applications

Over the last century, research in phytopharmacological sciences has uncovered information on the chemical make-up, biological functions, and conducive to health properties of plant-based product [129] water-soluble plant components such as the absorption of flavonoids, terpenoids and tannins is low. Phospholipids are the vitamins and minerals that are most beneficial for improving absorption numerous uses of phytosomes.

Silymarin Phytosomes

Silybum marianum, often known as has the best antioxidants that preserve the liver, is the subject of majority of phytosomal research. The Silymarin phytosome was created by investigated the pharmacokinetics in rats. Due to a striking the lipophilic has improved characteristics of silybin phospholipid advanced biological system that is complicated action with silybin, Rats have much higher bioavailability of silybin than raised following complicated medication taken orally in the tests. Phytosomes of silymarin have stronger antihepatotoxic action compared to silymarin alone and can protect the young broiler chickens from detrimental ramifications for aflatoxin B1.

Curcumin Phytosomes

In two distinct experiments, phytosomes containing the flavonoids naringenin and curcumin, which come from the grapefruit, Vitis vinifera. The complex's antioxidant activity was noticeably greater than that of pure curcumin at every tested dosage level. In the second trial, isozyme of naringenin generated stronger a higher level of antioxidant activity compared to the free compound longeraction's time frame, perhaps because the molecule was not being removed from the body as quickly. Curcumin is a safe antioxidant and anti-inflammatory compound with a wide range of pharmacological actions that have been shown in clinical trials to be effective against a wide range of disorders. It has been suggested that one barrier to obtaining the full therapeutic effect from curcumin administration is its limited oral bioavailability.

Quercetin-phospholipid Phytosomal complex

In rat liver damage caused by carbon tetrachloride, produced a quercetin phospholipid phytosome complex produced by a straightforward then repeatable approach. They similarly demonstrated because of the formulation displayed superior beneficial effectiveness to the substance.

Phytosomes of grape seed

The oligomeric polyphenols (proanthocyanidins found in grapes procyanidine from extract from grape seeds; Vitis vinifera) in grape seed phytosomes are complex with phospholipids and have different molecular sizes. They increase capability for all antioxidants, activation of physiological plasma defenses, and defense against cardiac damage brought on by ischemia and reperfusion.

Phytosomes of green tea

The primary component that distinguishes green tea leaves (Theasinensis) is an antioxidant called epigallocatechin 3-O-gallate molecule. These substances stand effective the modulators of number procedure of biochemical connected towards the breakdown in of homeostasis serious long-term degenerative illnesses, including cardiovascular disease and cancer. Additionally, a cup of green tea offers U's a variety of advantageous properties, including antioxidant, anticarcinogenic, and antimutagenic benefits [15].

Table 2: Pharmaceutical Use of Active Constituents of Phytosomes in Marketed Products

Sr. No	Commercial Products	Active Constituent	Pharmaceutical Use
1	Green Tea Phytosome	Epigallocatechin	Antioxidant Effect Improved Health and Wellbeing
2	Grape Seed Phytosome	Procyanidins	Natural Antioxidant protection
3	Milk Thistle Phytosome	Silybin	Antioxidant and Stimulate The Formation of New Liver Cell
4	Ginseng Phytosome	Ginsenosides	Provide adaptogenic function and resistance to stress, Nutraceutical
5	Silybin Phytosome	Silybin	Food product, Antioxidant for Liver and Skin
6	CentellaPhytosome	Terpenes	Treat Vein and skin Disorder
7	Gin select Phytosome	Panax Ginseng	Skin Tightener, Tonic
8	Bilberry Phytosome	Anthocyanosides	Potent Antioxidants, Reduce Abnormal Blood Vessel
9	Olive Oil Phytosome	Polyphenols	Anti-inflammatory, Anti hyperlipidemic
10	Palmetto Berries Phytosome	Fatty Acid, Sterols	Non-cancerous prostate enlargement

Conclusion and Future prospects

Phospholipids exhibit affinity for active components via hydrogen bond interactions. The four most popular vesicular drug delivery systems are ethosomes, niosomes, liposomes, and phytosomes denaturation and bioavailability in herbal products are perennially major concerns. The most effective and innovative methods to use herbs medications in order to deal with these problems are liposomes then phytosomes. Bioactive polyphenolic phytocompounds may more easily overcome biological barriers due to phytosomes and nanoengineered drug delivery vehicles. Many phytochemicals have been formulated successfully as phytosomes, and there are likely to be other phytochemicals that can benefit from phytosomes formulations. Future research might consider using phytosomes with other phytochemicals or the incorporation of drug and phytochemicals in the same nano-vesicle to produce synergistic effects.

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