Preparation of Phytosomes by using herbal extract

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Abstract: The distribution of an effective level of the therapeutically active component is a prerequisite for the success of any herbal medicine. However, there is a serious restriction on their bioavailability when given Nowadays, the majority of prevalent illnesses and nutritional deficiencies are treated topically or through oral administration. Phytosomes represent a recent advancement in herbal formulations, demonstrating enhanced absorption, increased bioavailability, and improved efficacy in comparison to conventional phyto molecules or botanical extracts.By binding the standardized plant extract or any of its constituents to phospholipids—primarily phosphatidylcholine—a lipid-compatible molecular complex known as a phytosome is created. The pharmacokinetic and pharmacodynamic profiles of phytosomes are superior than those of traditional herbal extracts. This study highlights the latest developments and uses of several standardized plant extract phytosomes.

Keywords: Herbal extracts; Bioavailability; Phytosomes; Herbal Drug delivery

1.INTRODUCTION

Since ancient times Preparations involving plants or their components have been extensively utilized in popular medicine, and most people on the planet currently use Herbal medicine[1]. By increasing the delivery of herbal ingredients to tissue, phytosomes improve their absorption and bioavailability, lowering their dosage and minimizing their adverse effects.Additionally, they shield the active herbal element from being destroyed by the stomach acids and bacteria in the intestines. A reputable pharmaceutical and nutraceutical manufacturer invented the patented technology known as "Phytosome," which combines standardized Plant extracts or aqueous solutions phytoconstituents with phospholipids to create lipid-compatible molecular complexes known as "phytosomes," which significantly increase the absorption and bioavailability of the phospholipids [2] . Because phytosomes have better pharmacokinetic and pharmacological properties, they can be beneficially used to treat liver diseases, both acute and chronic, that are caused by toxic metabolism, infectious agents, or degenerative processes. In addition, it can be used into medicinal and cosmetic formulations for its anti-inflammatory properties [3]. The improved microsphere or cell forms of herbal products known as phytosomes have recently been created. These forms are better absorbed than traditional herbal extracts and generate better pharmacokinetic and pharmacodynamic profiles. Herbosomes is another name for these. "Phyto" refers to a plant, while "some" denotes a cell-like structure[4]. The incompatibility of flavonoid molecules with oils and other lipids usually hinders their ability to flow through the lipid-rich outer membranes of the small intestine's enterocytes. It is possible to transform soluble flavonoid molecules into lipid-compatible molecular complexes, which are suitably named phytosomes [5].

2.Phytosome:

The distribution of an effective level of the therapeutically active component is a prerequisite for the success of any herbal medicine. When applied topically or orally, their bioavailability is severely limited. Herbal compositions called phytosomes, which are more readily absorbed than extracts, were recently introduced. "Some" refers to something resembling a cell, and "phyto" indicates a plant. Throughout the last hundred years, the fields of phytochemical and phyto-pharmacological studies have determined the chemical compositions, biological properties, and health-promoting advantages of various plant-based products. Polar or watersoluble molecules make up the majority of the components of plants that are physiologically active. However, the high molecular size of Water-soluble

phytoconstituents, including flavonoids, tannins, glycosidic aglycones, etc. prevents them from being absorbed by passive diffusion, and their poor lipid solubility severely limits their capacity to traverse the lipid-rich biological membranes, resulting poor bioavailability [6-7]. Convectional delivery systems and new delivery systems are connected through the phytosome, also known as the phytolipid delivery system. Indena has developed a patented technique that allows phospholipids to be combined with Standardized plant extracts or water-soluble phytoconstituents are utilized to form lipid-compatible molecular complexes, enhancing absorption and bioavailability.Upon forming reversible complexes with phospholipids, certain phytoconstituents, including flavonoids, terpenes, and saponins, exhibit longer-lasting and more potent anti-inflammatory and vasokinetic effects compared to when the same amount of the drug is administered in free form. The primary cause of this is the complexation of phospholipids with active substances. [8-9].

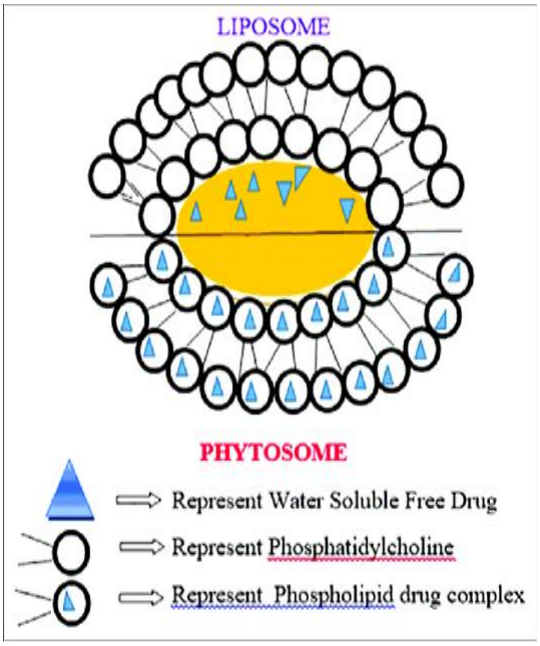

Fig 1.1

3.Properties of phytosomes:

a. Physico Chemical properties: Phytosomes are created through the combination of a natural substance and natural phospholipids, such as those found in soy. This results in a formation where the natural substance and soy phospholipids are intricately linked. When stoichiometric concentrations of phospholipids and the substrate react in the right solvent, a complex like this is produced. Based on spectroscopic evidence, it has been demonstrated that the primary mechanism of phospholipid-substrate interaction is the hydrogen bond creation between the polar functionalities of the substrate and the phospholipid's polar head, which includes phosphate and ammonium groups. Phytosomes take on a micellar shape and form liposomal-like structures when they are handled with water. Whereas the active principle in phytosomes is attached to the polar head of phospholipids and forms an essential component of the lipid bilayer, the active principle in liposomes is dissolved in the internal pocket or floats in the layer membrane. For instance, in the catechin distearoylphosphatidylcholine complex, the phosphate ion on the phosphatidylcholine moiety and the phenolic hydroxyl terminals of the flavones moiety form H-bonds. By comparing the complex's 1 H-NMR and 13 C-NMR spectra with those of the pure precursors, phosphatidyl choline can be inferred. The fatty chain signals hardly change at all. Based on this information, it may be extrapolated that the active principle is wrapped in excessively long aliphatic chains, creating a lipophilic envelope that protects the polar head of the phospholipid and flavonoid molecules and allows the complex to dissolve in low polarity liquids. [10]. The complex formed by natural phospholipid and phytoconstituents is known as a phytosome. It is created by reacting the right amount of phospholipid with the main constituents in a certain solvent. b. The formation of hydrogen bonds between the polar head of the phospholipid and the polar functionality of the main constituents is what causes the interaction between the phospholipid and substrate. c. Upon exposure to a hydrophilic environment, phytosomes exhibit a structure akin to that of liposomes, with the main difference being that the primary constituent of a liposome interacts within the internal pocket, whereas the primary active constituent of a phytosome is encased in the polar head of phospholipid and becomes an integral component of the membrane[11-12].

b.Biological Properties:

When taken orally, phytosome enhances both the overall bioavailability and the active ingredient's absorption. When compared to traditional herbal extracts, these advanced herbal medicines are more effective. In terms of pharmacokinetics, phytosome performs better than conventional herbal

medications[11-12]. Phytosomes are sophisticated herbal preparations that outperform traditional herbal extracts in terms of absorption, utilization, and overall effectiveness. Pharmacokinetic investigations or pharmacodynamic tests in experimental animals and human subjects have revealed the higher bioavailability of the phytosome over the non-complexed botanical derivatives[13].

3.MECHANISM OF PHYTOSOME TECHNOLOGY

The primary process used in phytosome technology is the complexation of polyphenols with phospholipid in a 1:1 or 1:2 ratio, which forms a phytosomal complex with a lipid layer around the components [14]. Chemical bonds hold molecules to the polar choline head of the phospholipid. According to precise chemical analysis, a flavonoid or polyphenol molecule connected to at least one phosphatidylcholine molecule often makes up the unit phytosome. A tiny microsphere or cell is created as a result[15]. Phospholipid complexes may be taken up from the GIT by enterocyte-based transport, and as the figure illustrates, drugs can be transported to the systemic circulation through the intestinal lymphatic system, which has a vast network all throughout the body. The ability to avoid first-pass metabolism and use lymphatic transport for tailored medication administration is its main benefit. [16].

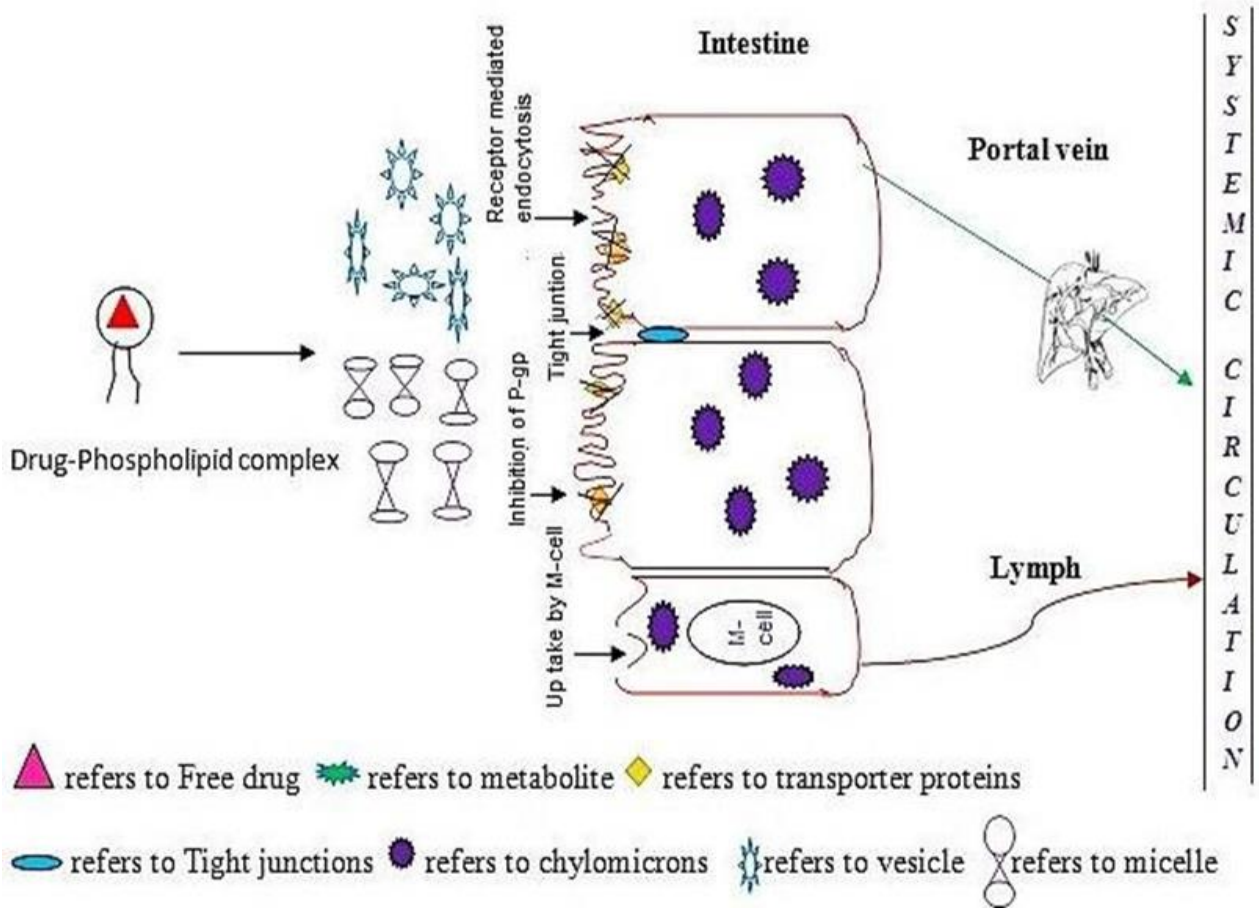

Fig :2

4.METHOD OF PREPARATION

1.Solvent evaporation technique using a rotary evaporator:

The solvent evaporation technique is the most often used and well-liked preparation method. This procedure involved solubilizing the phospholipid in an organic solvent and utilizing a rotatory evaporator to evaporate the medicament or extract. Liu and colleagues used the solvent evaporation approach to produce the evodiamine-phospholipid complex for improving the systemic availability [17]. In a recent study by X. Chen, Glycyrrhizinate phytosome was prepared for nasal vaccination using the solvent

evaporation technique. Tetrahydrofuran was used as the solvent for the complex formation, and the complex formed shows good drug-loading capacity, and increased solubility in n-octanol[18]. Likewise, Alotaibi et al. examined the hepatoprotective potential of sylymarin phytosome and sylymarin by itself. The phytosomes were synthesized using solvent evaporation, resulting in an approximately six-fold increase in oral bioavailability when compared to pure silymarin. Collectively, these findings highlight the role that phytosomes play in improving the solubility and oral availability, which eventually results in positive therapeutic benefits. [19]. The steps involved in preparing phytosomes are depicted in Figure. The soy extract and phosphatidylcholine, which are dissolved in ethanol and refluxed for two hours under vacuum using rotavapor at 30 °C, 120 rpm, are used to produce the nanosized soy phytosome-based thermogel. The zeta potential values (–51 ± 7.06 mV) and drug release (77.16% within 2 hours) indicate the stability profile and release properties of the phytosomes in comparison to the crude extract. Either soy phosphatidylcholine (SPC) or egg phospholipid (EPL) is used as the phospholipid source by the chrysin-loaded phytosomes. The phytosome generated by EPL has a homogeneous size distribution (polydispersity index: 0.30), with an average size and zeta potential of 117 nm and –31 mV, respectively. More stable was the phytosome generated by EPL, with a ratio of of 1:3. The average particlesize and zeta potential of phytosomes (1:3) prepared using SPC show 134 ± 0.1 and –33 ± 4.1 mV, respectively [20].

2.Salting out method or anti-solvent precipitation process:

The antisolvent procedure is a quick and simple way to get ultrafine drug particles, which are needed for oral dosage forms to dissolve and absorb. For the preparation of medications with ultrafine active ingredients, the anti-solvent precipitation method works well. After the medication is dissolved in the solvent, it is mixed with the antisolvent—a solvent in which the drug is not soluble.As the solution and antisolvent are combined, the medication precipitates. The requirement that the phytoconstituent be soluble in the solvent is a drawback of this approach. The solvent used in the antisolvent precipitation method was either acetone or DMSO [21]. Here, a specified amount of phospholipids and herbal extract are allowed to reflux for two to three hours at a temperature not more than fifty degrees Celsius in 20 milliliters of typical organic solvents. It is then reduced to a minimal volume, and after vacuum filtration, it is stored in airtight amber-colored glass bottles. Next, an anti-solvent such as n-hexane is added to help the complex form as precipitates[22].

3. Mechanical dispersion process:

Here, the phospholipid remains in touch with the drug's aqueous phase after dissolving in an organic solvent. To create the encapsulated product, phosphatidylcholine is dissolved in an organic solvent, such as diethyl ether, and then slowly injected into the phytoconstituents' prepared aqueous solution. The removal of the organic layer that follows causes the phytosome complex to develop [23]. The process of mechanical dispersion is involved in the synthesis of the gymnemic acid phosphatidylcholine complex. Gymnemic acid that has been created in an ethanol in water (1:1) combination is added drop by drop to 100g of phosphatidylcholine that has been dissolved in 1 liter of ethanol. This mixture is then refluxed at 60°C in a mechanical stirrer to prepare the phytosome. The mixture was then vacuum-concentrated and vacuum-dried for 68 hours at 40 °C. Since pure gymnemic acid was insoluble in low polar solvents like n-octanol and chloroform, the produced compound was soluble in these solvents. The generated complex exhibits a faster rate of release in vitro. X-ray diffraction confirms that the complex generated is phyto-phospholipid complex due to its amorphous nature[24].

4. lyophilization methods:

The process of lyophilization In DMSO, DSN was completely dissolved. After adding the obtained DSN solution (2.5% weight/volume) to the solution of SPC dissolved in 1.5% weight/volume of t-butylalcohal, the mixture was stirred for three hours using a magnetic stirrer until complex formation occurred. After that, the complex was separated using lyophilization. The resulting DSN:SPC involute (yield 90.4%, weight/weight) was stored in a desiccator over P2O5 at 4°C until testing after the samples were abstracted from the freeze drier. The impact of several formulation parameters, such as SPC type (Lipoid® S100, Lipoid® S75, and Lipoid® S PC-3), drug phospholipid ratios (1:1, 1:2, and 1:4), and co-solvent types of chemicals (methanol, ethanol, chloroform, acetone, and TBA), was evaluated for the culled developing approach. Usually, non-traditional techniques are used to build phytosome complexes.

The reaction between an equal amalgamation of natural or synthetic phospholipid and active ingredients or herbal extract in acrostic organic solvents forms modernistic herbal complexes. [25-26]. Common stages in formulation of phytosomes Various methods of preparation are as follows:

a.Anti-solvent precipitation process:A specified quantity of phospholipids and herbal extract are refluxed with 20 milliliters of organic solvents, such as acetone, for two to three hours under experimental settings below 50°C. After reducing the reaction mixture's volume to a minimum of 10 milliliters and adding a low-polarity solvent, such as n-hexane, while stirring, precipitates are produced. In desiccators, filtered precipitates are kept. The dried precipitates are ground into a powder and placed in a dark amber glass bottle to be kept at room temperature[27].

b. Rotary evaporation process: In a round-bottom glass container, a specified weight of herbal extract and phospholipids were combined with 30 ml of water miscible organic solvent, such as acetone, and stirred for two hours at a temperature of no more than 50°C in a rota evaporator. Antisolvents such as n-hexane are frequently added to thin films that are produced through continuous swirling with a stirrer[28]. The precipitate of the produced phytosomes is frequently kept at a regulated temperature and humidity in amber-colored glass containers. Drop by drop, phospholipids dissolved in ether are injected into a solution containing the phytoconstituents to be encapsulated. Following solvent abstraction, it causes the production of cellular vesicles, which results in the formation of involutes[29].

5. Characterization and evaluation of phytosomes: The performance of phytosomes in physical and biological systems is influenced by various factors including physical size, membrane permeability, proportion of entrapped solutes, chemical composition, as well as the quality and quantity of the initial components. Consequently, the characterization of phytosomes can be conducted based on their physical characteristics, such as shape, size, distribution, percentage of captured drug, entrapped volume, percentage of drug released, and chemical composition[30].

A.Different characterization techniques used for phytosomes:

- Visualization: Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) are both effective methods for visualizing phytosomes. [31].
- Vesicle size and Zeta potential: By employing a computerized inspection system and photon correlation spectroscopy (PCS), dynamic light scattering (DLS) can be utilized for the assessment of particle size and zeta potential[32].
- Entrapment efficiency: The ultracentrifugation method can be used to determine how well a medicine is entrapped by phytosomes[33].
- Transition temperature: Differential scanning calorimetry can be used to find the vesicular lipid systems' transition temperature[34].
- Surface tension activity measurement: The ring method employed in a Du Nouy ring tensiometer allows for the evaluation of the surface tension activity of the drug in an aqueous solution[12].
- Vesicle stability: Vesicles' stability can be ascertained by evaluating their size and structure over time. DLS measures the mean size, and TEM tracks structural alterations[36].
- Determination of %yield: yield: % yield of phytosome complex was determined by the following formula:
    - (%) Yield= (Practical yield)/(Theoretical yield)*100
- Determination of drug content: To ascertain the drug content, a 100 mg compound is dissolved in 10 milliliters of methanol. Following an appropriate dilution, the drug content was ascertained using a UV Spectrophotometer set to measure absorbance at 269 nm. [37].

B.Spectroscopic evaluations: The interaction between the phytoconstituent molecule and the phospholipid molecule is crucial and can be assessed using the following spectroscopic methods:

1. 1H-NMR:

The relationship between the phospholipid and phytoconstituent can be ascertained in a number of instances using their NMR spectra. According to NMR analysis, the 1H-NMR signal of those specific atoms involved in the complex formation shows a noticeable shift. [38-39].

2. 13C-NMR:

The majority of the resonances maintain their original sharp line shape of fatty acid chains, which correspond to the glycerol and choline component of the lipid (between 60 and 80 ppm), while some of the signals

are displaced and others are expanded. All of the flavonoid moieties' signals resurface after heating to 60˚, albeit they are still somewhat broad and partially overlap [40].

3. Ultraviolet spectra:

Samples with varying UV wave-length absorption reflection can be utilized to assess their own structural characteristics. The majority of investigations have not shown any variations between the constituents' UV absorption properties before and after complexation. When Xu et al. created luteolin-phospholipid complexes, they discovered that the luteolin's distinctive peaks persisted [41].

4.Fouier Transform Infrared: Comparing the spectra of the complex with those of its individual components and their mechanical mixtures, IR spectroscopy serves as a valuable tool in determining the synthesis of the complex. FTIR spectroscopy is also beneficial for monitoring the stability of phytosomes when dispersed in water or incorporated into highly alkaline cosmetic gels. In practical terms, confirming the stability of the complex involves comparing its solid form spectrum (phytosomes) with the time-series spectrum of its microdispersion in water post-lyophilization. In the case of uncomplicated formulations, the spectrum of the cosmetic form needs to be subtracted from the spectrum of the excipients (blank) at different time intervals, revealing the residual spectrum of the complex itself.

C.In vitro and in vivo evaluations:

Based on the anticipated therapeutic action of the biologically active phytoconstituents found in the phytosomes, models of in-vitro and in-vivo evaluations are chosen[42]. For example, the antioxidant and free radical scavenging abilities of phytosomes can be employed to assess the in-vitro antihepatotoxic effectivenessThe effect of produced phytosomes on animals against thioacetamide-, paracetamolor alcohol-induced hepatoxicity can be investigated for evaluating antihepatotoxic activity in-vivo[43-44]. The in vivo safety assessment methodology for the glycyrrhetinic acid-Phytosome® ointment, a commercially available product, is outlined in studies on skin sensitization and tolerance. [45].

6.Advantages of Phytosomes:

1.Enhanced Bioavailability: Phytosomes improve the bioavailability of herbal extracts by increasing their absorption and transportation to the target tissues. By binding the herbal constituents to phospholipids, phytosomes improve their solubility and compatibility with lipids, allowing for better absorption and utilization by the body.

2.Increased Stability: Phytosomes protect the active compounds in herbal extracts from degradation and oxidative damage, thereby increasing their stability and shelf life. The phospholipid coating provides a protective layer around the active constituents, ensuring and potency.

3.Targeted Delivery: Phytosomes can be designed to specifically target certain tissues or cells in the body, thereby enhancing their therapeutic effects. By modifying the composition or properties of the phytosome, it is possible to achieve targeted delivery and improve the efficacy of herbal medicine.

4.Reduced Dosage: Due to the improved bioavailability and targeted delivery, phytosomes allow for the use of lower dosages of herbal extracts while still maintaining therapeutic effects. This not only reduces the risk of side effects but also makes herbal medicine more cost-effective.

5.Improvedetics: Phytosomes exhibit favorable pharmacokinetic profiles, with enhanced absorption and distribution of active compounds. This leads to a quicker onset of action and prolonged duration of effect, improving the overall effectiveness of herbal medicine.

6.Versatility: Phytosomes can be formulated with a wide range of herbal extracts, allowing for the development of innovative herbal combinations and formulations. This versatility expands the possibilities for creating customized herbal medicines to suit individual needs.

7.Enhanced Absorption:Phytosomes enhance the absorption of herbal extracts by improving their solubility and permeability. The phospholipid structure of phytosomes allows them to easily merge with the cell membrane, facilitating the transport of active compounds into the bloodstream. This increased absorption ensures that a larger amount of the herbal extract reaches its target site, maximizing its therapeutic potential.

8.Specific Targeting: Phytosomes can be engineered to target specific tissues or organs in the body. By modifying the composition or surface characteristics of the phytosome, it is possible to achieve targeted delivery. This targeting can help concentrate the herbal extract in the desired location, thus enhancing its

therapeutic effects and reducing potential side effects in non-target tissues.

9.Protection and Stability: Phytosomes provide a protective shield around of herbal extracts, rendering them more stable and less prone to degradation. This increased stability helps maintain the potency of extract over time and ensures a longer shelf life for phytosome-based herbal formulations.

10.Improved Solubility: Many active compounds in herbal extracts are poorly soluble in water, which can limit their absorption and effectiveness. Phytosomes, by incorporating these compounds into a lipid-based carrier, enhance their solubility. This improved solubility allows for better dispersion of the herbal extract in the body, leading to increased absorption and bioavailability.

11.Combination Formulations: Phytosomes can be formulated with multiple herbal extracts, allowing for the creation of combination formulations that offer synergistic effects. This flexibility enables the development of tailored phytosome-based products that address specific health or individual needs.

12.Reduced Side Effects: Due to the increased bioavailability and targeted delivery, phytosomes can enable the use of lower dosages of herbal extracts. This reduction in dosage helps minimize the risk of potential side effects while still maintaining therapeutic efficacy.

7.Disadvantages:

1) Sometimes people move to herbal medicine without realizing that the symptoms may be related to another illness. Herbal medicines are taken without a prescription, in contrast to conventional medication, which requires ongoing health monitoring. As a result, individuals may occasionally be going through a trial-and-error phase when taking herbal medicines.

2) Herbal medications can treat a wide range of illnesses, but their healing times are typically longer than those of conventional treatments. When receiving herbal treatment, one must be extremely patient.

3) In certain instances, herbal medications may result in allergic reactions. Make sure you are not allergic to the specific herb you will be taking before turning to herbal medicine. Allergy reactions can also occur with conventional medications, but these are less common because conventional medications are typically taken as prescribed.

4) Herbal medicine of any kind is not approved by the government. It's often used at the consumer's own risk, and there is no guarantee of quality for branded herbal supplements.

8.Application:

A.Experimental Biomedical Applications of Phytosomes: Phytosomes, the unconventional form of delivery of herbal drugs, aid the absorption through the biomembrane quickly and produce better results than the conventional dosage forms; further confirmed by Studies involving pharmacokinetic and pharmacodynamic assessments in animals are crucial for understanding the effects of drugs and humans trials.

a.Phytosome for liver protection:

It's difficult to target the medication to the right place at the right time. But the phytosome complex will make the bile salts more soluble, which will help the liver target the active component straight into the hepatic cell. In addition to its hepatoprotective properties, phosphatidylcholine liquefies fat, aiding in the treatment of fatty liver disease. Phosphatidylcholine derived from soy phospholipids is hepatoprotective and heals drug and alcohol addiction-related liver damage[48]. Because of andrographolide (AN), the medicinal plant Andrographis paniculata has liver-protecting properties. But the systemic availability was what prevented its intended delivery. For example, to improve systemic absorption, Jain and collaborator created a phytosome filled with andrographolide and soya-phosphatidylcholine. The bioavailability of the AN-loaded phytosome is higher than that of the unloaded AN. The results of the in vivo investigation show that, in comparison to plain AN, there is a higher protective percentage on liver tissue along with elevated serum SGOT and SGPT levels[49] . Giudice and colleagues looked into the value of herbal therapy for liver illness in a trial that was carried out on dogs. For 30 days, the silymarin phytosome, choline chloride, l-cystine, artichokes, and vitamin E (Epacare pet) were combined with pasta as a dietary supplement. The active ingredient in this case is sylymarin phytosome, which increases silymarin's bioavailability and enhances its therapeutic efficacy as a liver protectant.Lastly, in healthy dogs, the feed supplementation has a therapeutic advantage on the liver enzymes and free radical scavenging action. [50]. Milk thistle (Silybum marianum) is a liver-protectant that is mostly recommended to treat gall bladder problems, nonalcoholic fatty liver disease,

hepatocarcinoma, and hepatitis C. El-Gazayerly and colleagues compared the effects of silymarin phytosomes to extract on liver protection and free radical scavenging in rats with hepatotoxicity induced by carbon tetrachloride. Phosphatidylcholine, a surfactant that increases the solubility of numerous components in the milk thistle extract, has been found to reduce the concentration of SGPT generated by carbon tetrachloride induction in the phytosomes derived from silymarin. In addition to its application in hepatoprotection, silymarin is often used as a renal protectant, for example in the treatment of renal toxicity caused by vincristine, acetaminophen, cisplatin, and cyclosporine. Likewise, when scientists contrasted the canine silybin-phosphatidylcholine complex with a commercially accessible, standardized extract of silymarin, they discovered that the phytosome complex administration markedly improved the bioavailability in dogs for the treatment of liver dysfunction [51]. A study found that phytosomal curcumin has shown chemopreventive effects on hepatocellular carcinoma development in vivo (transgenic mouse model)[52] Ginkgo biloba, An essential herb in traditional Chinese medicine, it is frequently used for its powerful effects on the central nervous system, including enhanced memory, increased mental alertness, and decreased mental weariness. It is also prescribed for its cardioprotective, anti-asthmatic, and antidiabetic properties. In the meantime, Ginkgo biloba phytosomes (GBP) have been shown to have hepatoprotective and antioxidant properties when applied to mouse liver damage caused by carbon tetrachloride (Naik and Panda, 2007). Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), and glutathione reductase (G.R.) levels are elevated in rats given GBP after they have been exposed to carbon tetrachloride-induced liver damage. It is also observed that the phytosome aids in the restoration of the enzyme levels[53].

b. Phytosome for cancer treatment.

Alhakamy and a colleague investigated the use of quercetin phytosome functionalized by scorpion venom in the treatment of breast cancer. The findings indicate that the phytosome has higher mRNA expression of caspase-9, Bax, Bcl-2, and p53.54] Its anti-inflammatory, antibacterial, antiangiogenic, liver-protective, and anticancer qualities make taxifolin a pharmacologically active component. However, due to its hydrophilic nature, its application was restricted. In this work, phospholipids and taxifolin-rich ethyl acetate were mixed, and the resulting phytosomes were tested ex vivo against MCF-7 cell lines.The phytosomes exhibit reduced IC50 value and increased cytotoxic action. [55]. Aloe vera extract loaded phytosome has antitumor activity against the MCF-7 cellline[56]. Alkamy and colleagues investigated the importance of Icarrin phytosomes against ovarian cancer cells (OVCAR-3 cells). Icariin is a flavonol glycoside with pleiotropic pharmacological properties and cytotoxic effects against ovarian cancer cells. According to the study, apoptosis, increased permeability through the cells, and the intracellular generation of reactive oxygen species were all linked to cytotoxicity. [57]. Celastrol, also known as tripterine, is obtained from the medicinal plant *Trypterygium wilfordii*, having a range of medicinal uses, such as antioxidant, neuroprotective, and anti-inflammatory properties. Researchers discovered that it may have an impact on cancer, particularly human prostate cancer, A549 cells from non-small-cell lung cancer, MCF-7 cells from breast cancer, and pancreatic cancer.Celastrol's bioavailability problems led to the formulation of phytosomes, which improved the drug's absorption problems. In vivo pharmacokinetic investigations were carried out in rabbits in good health, verifying the enhanced oral availability through complexation, which is useful for anticancer drugs[58]. Diosgeninis a steroidal sapogenin that primarily serves as an intermediary in the synthesis of steroidal hormones. It has cytotoxic effects.In addition, the scientists altered the structure of diosgenin to produce novel derivatives with improved cytotoxic properties. Using MTT assays, they examined the antiproliferative properties of FZU-0021-194-P2 (P2) against human lung cancer A549 and PC9 cell lines, human cervical cancer HeLa cell line, and human hepatoma HepG2 cell line. The antiproliferative properties are formulated and tested using its phytosomes (P2P). Similarly, P2P was discovered to have a particle size of 53.6 ± 0.3 nm, which prevented the growth of cancer cells, suggesting that it is a good choice for lung cancer that is not small-cell[59].

c. Phytosome for wound healing

In live cells, metallic nanoparticles like gold nanoparticles (AuNPs) typically promote wound healing and have antioxidant properties. Demir and

colleagues used a 3:1:1 ratio (phosphatidylcholine: cholesterol: calendula extract) to construct and characterize AuNP and Calendula officinalis-loaded phytosome. According to the results of the in vitro scratch test for wound healing effects, the produced complex demonstrated good wound healing activity [60]. Since ancient times, scholars have identified a fundamental glucosinolate in plants from the Brassicaceae family. (the family that makes mustard) is sinigrin.It is unknown if sinigrin has any benefits on wound healing despite having a wide range of biological functions, including antibacterial, anticancer, and anti-inflammatory properties. According to one research, the sinigrin phytosome's ability to heal wounds utilizing HaCaT cells was discovered. The sinigrin-complex showed up at 79% wound healing activity after 42 hours, but the sinigrin by itself only reached 50%. [61].

d. Phytosome as anti-asthmatic

Airways are systematically destroyed in the process of managing asthma attacks. For mild-to-severe chronic asthma, long-acting beta-agonists and corticosteroids (inhaler therapy) are the typical treatments, which have significant side effects and are expensive. In this multicenter trial, 32 individuals with asthma have been recruited. The typical treatment regimen, which consists of inhaled corticosteroids and beta-agonists, is combined with a supplemental intervention of 500 mg/day of Boswellia phytosome (Casperome). The subjects receive treatment for four weeks. The research was done by Pierro and Vincentiis. The therapy lowers the quantity of desired inhalations related to using the prescribed medication alone [62].

e. Phytosome as antioxidant.

There are several health advantages of ginkgo biloba. When examining the impact of its phytosome on antioxidant properties in the rat model, the findings were encouraging. The phytosome's ability to scavenge free radicals and protect the liver was the cause of its effects[63].Many medicinal plants in the Apiaceae family contain umbelliferone, which is particularly useful after exposure to ultraviolet light due to its ability to scavenge free radicals. Nevertheless, problems with permeability, solubility, and antioxidant effects—including photoprotective effects—reduce their effectiveness. This study measured the amount of antioxidant enzymes in rat skin and produced umbelliferone-loaded phytosomes to investigate the in vitro antioxidant effects.The results indicate that the phytosome complex exhibits superior ex vivo permeability and an outstanding antioxidant profile compared to its drug alone [64].

f.Phytosome as a cardiac protectant: The phytosome Ginkgo biloba Demonstrated protective effects against isoproterenol (ISO)-induced damage. cardiotoxicity. Its antioxidant properties have also been studied in rats. To induce myocardial infarction, 85 mg/kg of ISO was administered. Phytosome is administered daily at oral doses of 100 mg/kg and 200 mg/kg body weight. By lowering blood marker enzymes and Inhibiting lipid peroxidation while increasing the levels of reduced glutathione, superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase.the phytosome demonstrated substantial cardioprotection[65].

g.Industrial Applications of Phytosomes:

A phytosome, an improved liposome, is created by combining phospholipids with plant extracts such as glycosides, flavonoids, and terpenoids in the right proportion. It is frequently employed in herbal cosmetics because of its superior penetration through the epidermis and high lipid content, which serves as a herbal carrier and skin nourishment agent.Additionally, because of their quick absorption, it seems that less of a dose is required, and when phosphatidylcholine and phytoconstituents form chemical bonds, their stability pattern gets stronger. A topical preparation of the Ginkgo biloba terpenes phytosome is a commercial product with anti-inflammatory and calming properties. [66].

Phytosomes	Phytoconstituent complexed with pc	Daily dosage	Indication
Leucoselect® phytosome	Procyanidolic oligomers (PCOs) from grape seeds	50–100mg	Systemic antioxidant, specific. Best choice for most people under age of fifty. Also specific for the eyes, lungs, diabetes, varicose veins, and protection against heart disease.
Greenselect® phytosome	Epigallocatechin 3-O-gallate from camelia sinensis (Green tea)	50–100mg	Systemic antioxidant. Best choice for protection against cancer and damage to cholesterol.
Ginkgoselect® phytosome	24 % ginkgo flavono glycosides From Ginkgo biloba	120mg	Best choice for most people over the age of 50. Protects brain and vascular lining.
Silybin phytosome	Silybin from silymarin (milk thistle)	120mg	Best choice if the liver or skin needs additional antioxidant protection.
Siliphos™ milk thistle phytosome	Silybin from silymarin	150mg	Good choice for liver or skin support.
Hawthorn phytosome	Flavonoids	100mg	Best choice in heart disease.
Panax ginseng phytosome	37.5% ginsenosides from roots of Panax ginseng	150mg	As a Food Product.
Glycyrrhiza phytosome	18-beta glycyrrhetinic acid	-	Anti-inflammatory Activity.
Mirtoselect® phytosome	Anthocyanosides from an extract of Bilberry	-	These improve capillary tone, reduce abnormal blood vessel permeability & are potent antioxidants. They hold great potential for the management of retinal blood vessel problems and venous insufficiency.
Sabalselect® phytosome	An extract of saw palmet to Berries through supercritical CO_2 (carbon dioxide) extraction	-	It delivers fatty acids, alcohols and sterols that benefit prostate health. Also beneficial for non-cancerous prostate enlargement
Polinacea™ phytosome	Echinacosides and a unique high-molecular weight Polysaccharide from Echinacea angustifolia	-	It enhances immune function in response to a toxic challenge.
Oleaselect™ phytosome	Polyphenols from olive oil	-	As potent antioxidants, inhibit harmful oxidation of LDL cholesterol, and also have anti-inflammatory activity.
Lymphaselect™ phytosome	A standardized extract of melilotus officinalis	-	Indicated for venous disorders, including chronic venous insufficiency of the lower limbs.

Table 1.1

9.CONCLUSION

Making phytosomes is an easy and repeatable process. A plant will be chosen for plant extract in order to isolate its flavonoids and use phytosomes to treat a serious illness. The method demonstrates synergistic benefits as functional cosmetics and cost-effective phytoconstituent delivery. Aside from that, the body benefits from the phospholipids employed in them. Researchers interested in investigating a vesicular drug delivery system that delivers an effective medication to the target place without requiring metabolism will find the information obtained here valuable. The phytosome formulation process is straightforward and easily applied on a commercial basis. Additionally helpful in cosmetology is phytosome. Phytosome technology holds promising prospects for its application in formulation technology and utilizing hydrophilic plant chemicals.

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