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PHYTOSOMES: NATURE'S SECRET TO ENHANCED BIOAVAILABILITY

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ABSTRACT

Background: Medicinal herbs have long been used for treating various ailments, with plant-derived compounds recognized for their therapeutic benefits and minimal side effects compared to conventional medicines. However, issues with the bioavailability of active herbal components have limited their effectiveness. Phytosomes, or herbosomes, are a drug delivery technology that enhances the absorption and bioavailability of these plant-based compounds, providing a potential solution for maximizing the medicinal efficacy of herbal ingredients. **Method:** Phytosome complexes are synthesized by combining plant extracts with phospholipids in specific molar ratios, typically 1:1, to create a more stable and bioavailable formulation. Common preparation methods include solvent evaporation, supercritical fluid extraction, and lyophilization. Each technique is optimized to improve the stability, solubility, and therapeutic action of the phytosomes. **Results and discussion:** Phytosome technology has shown significant improvements in the bioavailability of phytochemicals, such as silymarin and curcumin, enhancing their pharmacological effects. Applications of phytosomes span various therapeutic areas, including cancer treatment, rheumatism, wound healing, and respiratory conditions. Studies indicate that phytosomes improve drug stability, absorption, and targeted delivery, effectively managing complex diseases with reduced side effects. **Conclusion:** Phytosomes represent a promising advancement in natural medicine by addressing bioavailability challenges associated with herbal compounds. The improved formulation techniques and broad applications suggest a bright future for phytosome-based therapies, especially in areas where conventional treatments may have limitations. Further research and development in phytosome technology could lead to enhanced clinical outcomes and expand the use of herbal remedies in modern medicine.

INTRODUCTION

The active ingredients in medicinal herbs have been utilized to cure different illnesses. Herbal remedies are used for a variety of purposes. Therefore, herbal remedies heal far more ailments than conventional medicines without having negative side effects because modern medications cannot treat all pathologies. Some denote something that is cell-like, but "Phyto" refers to the plant.

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The Microsphere drug delivery technology known as phytosomes, sometimes called herbosomes, enhance absorption and improve the bioavailability of low soluble medications [1-3]. Because of their ability to scavenge free radicals, the flavonoids and phenolic compounds in *Tabernaemontana divaricata* have high oxidative properties. Plants are used as gum, oil, or extracts to treat various illnesses [4]. Most physiologically active plant elements are polar or water-soluble; nevertheless, limited absorption leads to restricted usage of these chemicals, ultimately lowering their bioavailability. Herbal preparations are needed to have an appropriate equilibrium between hydrophilic (for absorption) and to pass through lipid bilayer balance and lipophilic. Plant preparations are extensively utilized in both conventional and contemporary medical systems. Numerous pharmacological investigations have been conducted throughout the conventional era to examine the therapeutic use of multiple plant extracts and their components. Significant progress has been achieved in the last year to create innovative medication delivery systems (NDDS) in favor of a range of botanical extracts, the components that make them active [5]. The flavonoid aglycon diosmetin [DT] is derived from the glycoside diosmin and is present mainly in citrus fruits, legumes, olive leaves, marjoram, chrysanthemums, and other plant sources. Due to the limited amount of diosmetin extracted from natural sources, almost all of them are obtained by hydrolyzing diosmin. One of the main problems with Dt is that it is less hydrophilic and water-soluble, which causes absorption to occur lower in the GI system and restricts its usage in the food and pharmaceutical industries [6,7]. Phytosomes are a unit of a few molecules. Encompass additional Phyto active compounds and phospholipid molecules, albeit not explicitly attaching to them. The innovative paradigm for phytosomes technology is a substantial improvement in bioavailability, greater clinical benefit, and guaranteed tissue distribution, not nutrition safety. Therefore, the Phyto phospholipid compounds are more absorbed and produce more bioavailable material than free active ingredients [8]. Herbosomes are another name for phytosomes. Modern technology allows compounds with toxicity profiles to be repurposed as phytosomes, liposomes, nanoparticles, and other forms [9]. Complex chemicals called phosphatides are responsible for the development of plasma membranes. They are the fundamental components of life. Molecules known as phospholipids are present, during which two fatty acids and glycerol are attached to the area that the phospholipid group still inhabits [11].

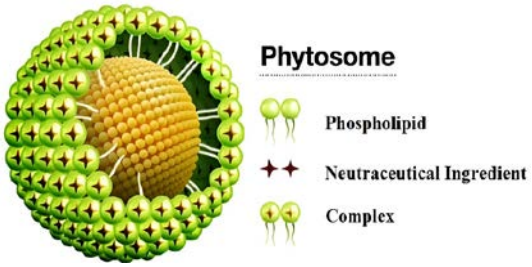

Figure 1: Structure of Phytosomes [10]

ASPECTS OF PHYTOSOMES

In the current literature, the four essential elements in favor of synthesizing plant-derived phosphatide complexes are plant-founded constituents, the function of phosphatide, the stoichiometric ratio in the, and solvents. Other substances, such as polyphenols, could also be employed as active ingredients in phytosomes, such as evodiamine and siramasin [12]. Thus, since phytosomes are not merely polyphenols, complexes formed of them might theoretically be combined with any dynamic moiety.

1. Ingredients made from plants

Phytosomes are complexes of plant extracts or phytoconstituents and phospholipids, and the plant extracts used in phytosomes are the ingredients made from plants in phytosomes.

- Plant extracts containing phytoactive components chosen by researchers are assessed for their Pharmacological action, which is demonstrated in vitro rather than in vivo. Most of these substances are polyphenolic, preferred in the water phase, and unable to cross biological barriers.
- Other substances, like rutin and curcumin, have lipophilic properties that make them insoluble in stomach contents.
- Phyto-phospholipid complexes enhance the solubilization of lipid-soluble polyphenols into the water aspect and the permeability of cell membranes with hydrophilic polyphenols since the water phase.
- Furthermore, the formation of intricate structures could protect polyphenolic compounds from oxidation, photo-decomposition, and aqueous breakdown [12,13].

2. Phosphatides

It is one of a large group of naturally occurring phospholipids that are glycerol phosphate derivatives and usually contain a nitrogenous base.

- Phosphatides, notably glycerophospholipids and sphingomyelins, are categorized according to their backbones & are found extensively inside plants & egg yolk

- Phosphorylated choline, Phosphorylated ethanolamine, Phosphorylated glycerol, Phosphorylated serine, Phosphorylated inositol, and phosphate acid are the main constituents of glycerophospholipids.
- Phosphatides made commercially are currently available for purchase. PS, PE, and PC are the primary phosphatides that form intricate water-loving head groups and two water-hating alkyl chains.
- PC is the most popular phospholipid. It is utilized to create phospholipid complexes because of its amphipathic nature, which permits mild solubilization in aqueous and lipid solution media [12].

3. Phospholipids with phytoactive ingredients in a stoichiometric ratio

Phyto-phospholipid complexes are employed by reacting a synthetic or natural phospholipid with the active constituents in a molar ratio of 0.5 to 2.0, whereas a stoichiometric ratio of 1:1 is considered to be the most efficient ratio for preparing phospholipid complexes

- To form phytosomes, phytoconstituents are often mixed using organic or synthesized phosphatides in different molar proportions of 0.5 to 2.0, while a quantitative proportion of 1:1 is more frequently used to form intricate phospholipids [example, a 1:1 combination of quercetin and lipoid S 100 was used. to produce phytosomes of quercetin]. Curcumin and SPC Lipoid® S 100 were mixed in 1:1 concentration-based ratios, making the soft capsule and Phytosome complex of curcumin phytosomal.
- Results show that the preparations have encapsulated phytosomes and are more stable. In a different study, researchers created diosgenin phytosomes, which are efficient against lung cancer cells when used in a 1:1 molar ratio. Results showed enhanced diosgenin water and greater cytotoxic activities against human cancer cells.
- Nonetheless, research has employed a variety of lipids and active ingredients in quantitative proportions. The results show that phytosomes with a 1:5 stoichiometric ratio have the greatest physical attributes and the most drug loading.
- Use the stoichiometric ratios of 1:1, 1.4:1, 2:1, 2.6:1, and 3:1 to synthesize phytosomes and conduct a comparative study. According to the results, the most efficient stoichiometric ratio was 3:1. Chrysin-loaded phytosomes were also produced to increase glucose absorption by muscle fibers.
- Researchers' data indicate that utilizing a 1:3 molar ratio was the most reliable. Consequently, using a 1 to 1 quantitative ratio directed at the Phosphatide production interactions is not required. To accomplish particular objectives, like increased medication incorporation, the active transporter quantitative chemistry components might be altered in favor of different medicines [12].

4. Diluents

It refers to substances that increase the volume or bulk of the formulation without significantly affecting its therapeutic activity.

- Scientists have previously employed various them to manufacture phospholipid Phyto complexes. Typically, aprotic solvents like halogen, hydrocarbons, cyclic ethers, and ethyl acetate Phyto phospholipid complexes have been synthesized using derivatives and methylene chloride.
- But because of their success rate, prototic solvents like methanol and ethanol have taken their location. In studies aimed at treating inflammatory diseases, rutin and phospholipids combined using methanol.
- For a more extended period of medicine retention time through skin contact, the authors created a polymeric matrix patch. The enhanced preparation revealed 31.32 and 26.56% of skin infiltration, according to the results.
- The patch's anti-inflammatory actions further proved the effectiveness in a rat-paw edema model when contrasted to typical diclofenac gel-produced chrysin-loaded phytosomes to increase muscle cells' glucose absorption. Utilizing solvent evaporation technology, phytosomes are entered in conjunction with Chrysin. It was made of phytosomes by combining soy PC or egg phospholipids [12].

COMMON PREPARATION OF PHYTOSOMES

- Natural or synthetic source of obtaining phospholipids.
- Phospholipids dissolved in organic solvents [EG: Acetone or Dioxane].
- Add herbal extract to the solution of phospholipids with constant stirring.
- Evaporate the solution using spray drier or rotary evaporator
- It forms a thin film, and rehydration of the film forms the phytosomal suspension.
- Using the precipitation technique, collect the phytosomes [13].

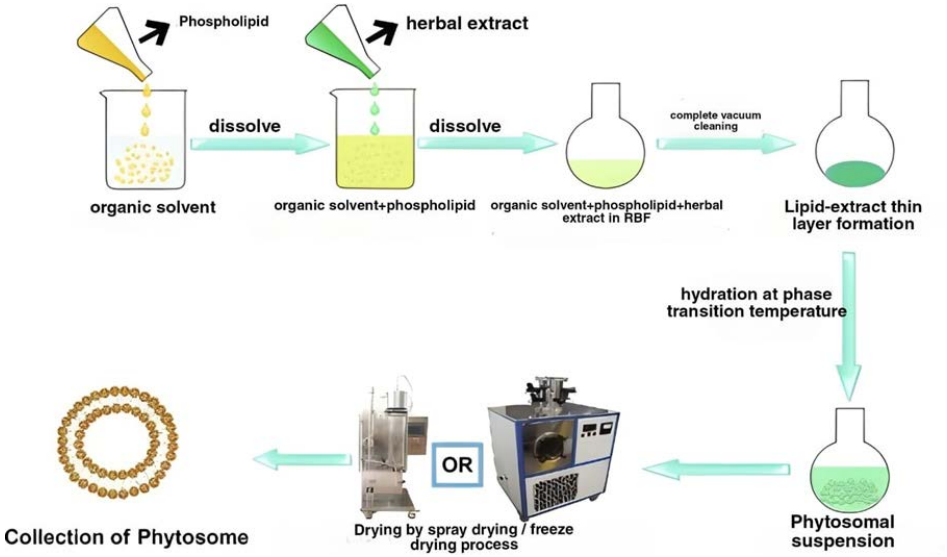

Figure 2: Common preparation of phytosomes [14]

PREPARATION TECHNIQUES

1. Solvent Evaporation Method

- A marsupsin-phospholipid complex is created using a liquid antisolvent precipitation technique that involves mechanical dispersion. In the solvent evaporation method, the drug and phospholipids are mixed in a flask with a solvent system (e.g., tetrahydrofuran and ethanol). A 1:1 ratio of drug to phospholipid is often considered optimal for forming complexes, as shown in many studies.
- The oxymatrine-phospholipid complex is made by mixing the drug and phospholipid in various ratios (1:4, 1:2, 1:6, 1:3) and evaporating the solvents through mechanical agitation. The best complex was achieved with a 3:1 ratio at 60ºC for 3 hours.
- In another study, an embelin-PC complex was made with molar ratios ranging from 1:0.5 to 1:3, and the best formulation had a drug concentration of 80 g/l and a 0.9:1 phospholipid to drug ratio (w/w). The drug content in this complex was 45.78%, and the total formulation reached 100%.
- Researchers now often use aprotic solvents like methylene chloride, ethyl acetate, and dioxane, and experiment with phospholipids from various sources in their formulations.

2. Supercritical Fluid Extraction

Supercritical fluids effectively create large particles (5–2000 nm). Complexes of puerarin and phospholipids were made using three traditional methods: lyophilization, solvent evaporation, and micronization. Supercritical fluids are also used to improve the solubility of poorly soluble drugs (SEDS). In the GAS method, separate solutions of the drug and phospholipid are exposed to a supercritical anti-solvent before pressure is applied. This process resulted in a 93% yield.

3. Lyophilization

- Both synthetic and natural phospholipids, along with phytoconstituents, are dissolved in different solvents. The phospholipid mixture is then added to a solution containing the phytoconstituents and stirred until a complex form. This complex is then separated using lyophilization.
- The phospholipids used in phytosome preparation contain acyl groups, which can be from phosphorylcholine, phosphatidylserine, or phosphatidylethanolamine, and are usually derived from fatty acids like stearic, oleic, palmitic, and linoleic acid.
- Of the techniques mentioned for phytosome preparation, the **solvent evaporation method** is the most widely used because it is highly effective in forming phospholipid complexes [12].

TECHNOLOGICAL ADVANCES IN PHYTOSOMES

In recent years, we have seen a significant breakthrough in discovering new medications, predominantly in the form of innovative medication delivery systems that expand pharmaceuticals' drug action and absorbance. A significant development in nutritional complementary products and botanical medicine is phytosomes technology. It summarizes

current developments in Phytosome technology, along with citations to pertinent research and publications [15].

1. Increased Bioavailability

The purpose of phytosomes is to enhance the body's absorption of phytochemicals. This is accomplished by the phytochemicals and phospholipids forming a combination that improves the solubility and stability of the substance. Recent studies have indicated that phytosomes greatly increase the bioavailability of certain botanical extracts. Researchers studied silymarin, which was employed as a silybin phospholipid complex to increase silybin distribution [16,17].

2. Improved Formulation Techniques

The manufacture of Phytosome complexes is now more scalable and efficient because of advancements in formulation processes. Various techniques such as microencapsulation, surgery, radiation therapy, chemotherapy, spray drying, and others have been developed to enhance the stability and release characteristics of Phytosome formulations [18].

3. Environmental Impact and Sustainability

A recent study has also examined the sustainability of phytosome technology, including reducing waste in production processes and utilizing environmentally benign sources of phospholipids [19].

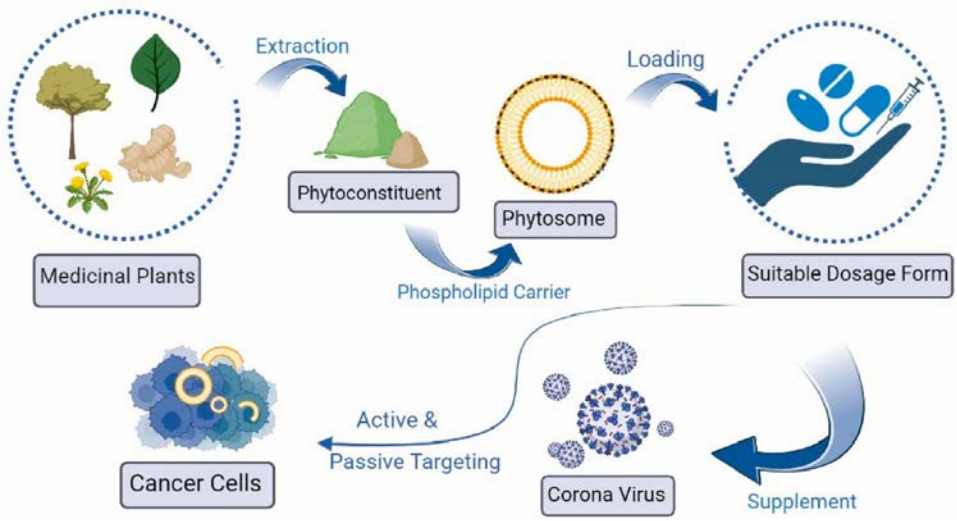

Figure 3: Advancement in phytosomes drug delivery system [15]

STRUCTURAL VERIFICATION OF PHYTOPHOSPHOLIPID COMPLEXES

1. Ultraviolet Spectra (UV)

It is possible to use samples with different UV absorbances to ascertain each one's structural characteristics. Most investigations have not demonstrated any changes in the UV absorbance qualities of the components, either during or after complexation. Chemicals do not change in color when combined with phosphatides [20].

2. Differential Scanning calorimetry (DSC)

The transition temperature, melting points, appearance of new advancements, vanishing of existing advancements, and variation in the related advanced area can all be used to identify interactions. The characteristic advancement of Phyto-phospholipid complexes frequently diverges considerably from that of a physical combination. The active component is believed to be provided by strong contacts that stop the two phospholipids' fatty chains from rotating freely. The polar portion of phospholipids carries out this function. The rutin and PC advancements disappeared from the DSC thermogram, which displays distinct peaks smaller than the physical mixture [21].

3. Fourier Transform Infrared Spectroscopy (FTIR)

FTIR is a functional structural analysis technique that generates various functional groups with distinct bond numbers, positions, shapes, and intensity characteristics. The creation of the latter can be confirmed by comparing the intricate phospholipid spectra with the Phyto-phospholipid complexes. of tangible combinations. Different research may reveal different outcomes. Kalita and Das made phyto-phospholipid compounds made of rutin. A physical mixture's FTIR of pure rutin was

superimposable with that of rutin and Phyto-phospholipid complexes. Mazumder et al. used the FTIR of the phytosome to create sinigrin-phytosome complexes. distinct peaks from those of phospholipids, sinigrin, and their mechanical mixes were displayed by complex [22].

4. Diffraction of X-rays

X-ray diffraction is currently a valuable method for analyzing the microstructure of certain non-crystalline substances along with crystalline materials. Phyto-phosphatide complexes, PCs, active ingredients, or the physical combinations of these components typically execute X-ray diffraction. X-ray diffraction of a physical combination of an active ingredient exhibits firm crystalline peaks, suggesting a high crystal shape. However, Phyto-phospholipid complexes with active constituents lack crystalline peaks, indicating that the Components in phospholipid complexes take on an amorphous or molecular shape [22].

5. Nuclear magnetic resonance imaging (NMR)

The characterization of the complexes' structures is greatly supported by the 1H and 13C NMR techniques. As previously noted, hydrogen bonds, rather than chemical bonds, are responsible for the interactions between polyphenols and phospholipids. Based on NMR findings, Angelico et al. established that certain polar phenolic functional groups of silybin A and phosphatides can form hydrogen bonds. The hydrophobic regions of lipids may serve to enclose the core choline-bioactive elements of these complexes, as indicated by the spectra of various Phyto-phosphatide complexes [22].

APPLICATION

1. Cancer treatment

- The main obstacles to creating novel treatments were safety, efficacy, and specificity. In contrast to conventional medicines, pure components are derived from natural sources or intentionally made goods, which might provide protection over an extended period but are frequently accompanied by adverse effects [23].
- In modern times, the number of new tumor cases and tumor-related deaths is rising, and in the ensuing years, it is predicted that the number of tumor diagnoses will increase. As a result, there is a growing need to develop stronger anticancer drugs from conventional sources to maximize their therapeutic potential [24].
- In recent years, new anti-cancer drugs have been developed, especially innovative medication delivery methods that enhance pharmaceutical drug action and absorbance and their capacity to precisely deliver therapeutic doses to carcinoma cells with minimal cytotoxicity and wholesome tissues [15].

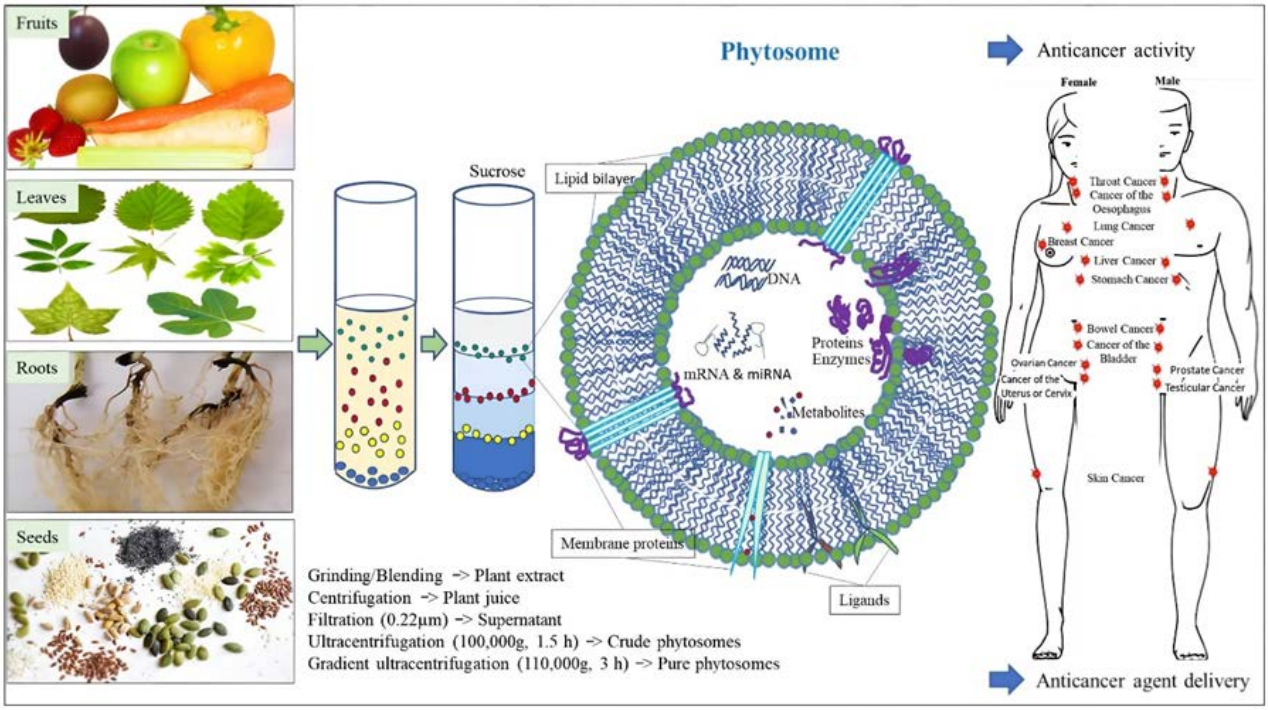

Figure 4: Anti-cancer activity [25]

2. Treatment for rheumatism

- Rheumatism is a chronic immune-mediated swelling disease marked by excruciating joint swelling, inflammation of the synovial membranes of the joints, and harm to the bones and cartilage linked to progressive articular damage, comorbidity, and loss of function.
- One of the current DMARDs on the market is leflunomide (LEF). Moreover, curcumin (CUR) has many biochemical benefits, including anti-inflammation, anti-diabetic, analgesic, and anticarcinogenic properties.
- A combination technique involves using phytosomes co-encapsulated with leflunomide and curcumin to enhance the clinical results of rheumatism treatment.
- The best phytosomes loaded with turmeric extract and leflunomide showed excellent stability, spherical morphology, increased pharmaceutical entrapment, and a prolonged release pattern of encapsulated drugs.
- The particle size in phytosomes was around 760 nm, and the zeta potential value was -55.7. Compared with the free medications and their physical mixes, oral treatment of the curcumin/leflunomide phytosomes in arthritic rats reduced paw swelling and inflammatory markers [26].

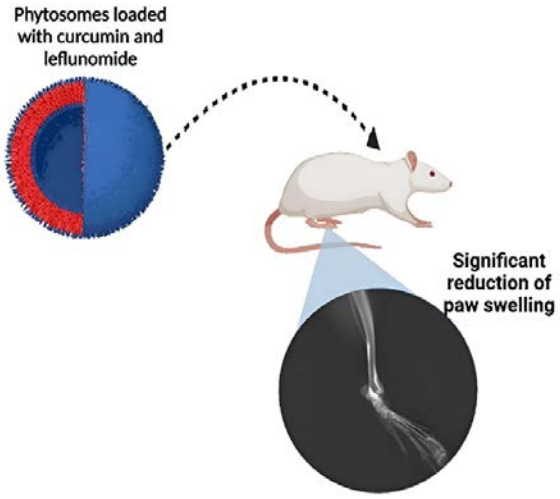

Figure 5: Treatment using phytosomes led to a marked reduction in the symptoms of rheumatism [26]

3. To treat wound healing

- Crocetin, an aglycon apocarotenoid dicarboxylic acid, is formed by hydrolyzing crocetin into ester with dextrose molecules.
- It is accountable for the color of the saffron threads or saffron crocus flowers (Iridaceae).
- Apocarotenoid crocin, a key element in the orange tubular flower cup of Nyctanthes arbor-tristis flowers, was initially shown to be the primary coloring agent of saffron stigma.
- When crocin is present, saffron stigma shows good wound healing ability.
- Crocetin is isolated from the tubular calyx of N. arborists, and stability is increased by captivating it in sacs.
- Then, the activity of tissue regeneration is assessed. Crocetin was extracted by treating the ethanolic extract of N. arbor-tristis' tubular calyx with sodium bicarbonate and then regenerating the compound with hydrochloric acid.
- The process of lipid film hydration was used to create the phytosomes. The gel with phytosomes identical to 1% w/w crocetin was then applied to Wister albino rats' incision and excision wounds to assess its ability to promote wound healing.
- Entrapment into phytosomes was observed to increase the stability of crocetin. The research showed that two categories of injuries showed good wound healing potential when treated with gel infused with crocetin phytosomes.
- In the excision trauma model, the epithelization period significantly ($P<0.001$) decreased from 26 to 9 days in contrast to the control group and shattering strength in the repaired skin significantly ($P<0.001$) increased from 328.8 to 857.0 grams [27].

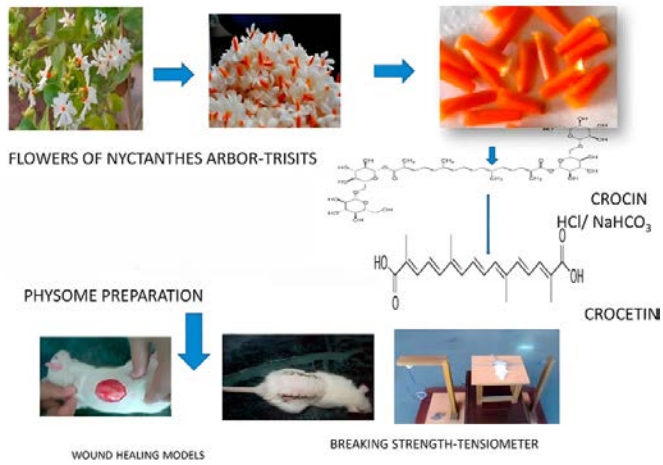

Figure 6: Treatment using phytosomes led to a notable improvement in the symptoms associated with wound healing [27]

4. To treat respiratory conditions

- A significant part of respiratory disease treatment involves phytosomes.

- Following this, phytosomal ginger extract conjugating with deacetylated chitin has been utilized for the In vivo and In vitro therapy of respiratory infections.
- The phytosomal formulation displayed a notable controlled released profile and enhanced gastrointestinal uptake of gingerol in vivo.
- Tested against Gram-positive and Gram-negative bacteria that cause lung infections, the drug action measures demonstrated significant anti-inflammatory and long-lasting antibacterial efficacy and a new Phytosome that increased naringenin's pulmonary bioavailability.
- Rats with acute pulmonary injury were used to evaluate the pharmacodynamics and associated processes of phytosomes packed with naringenin through dry powder aerosol.
- Rats that inhaled these phytosomes directly experienced relief from lung damage. The findings demonstrated that Natriuretic Peptide Downstream Pathway Inhibitors (NPDPIs) reduced fluid exudation and the release of cytokines, including Cell adhesion molecule-1 (ICAM-1) and Prostaglandin-endoperoxide synthase-2 (COX-2). Cell adhesion molecule-1 (ICAM-1) and Prostaglandin-endoperoxide synthase-2 (COX-2).
- The anti-oxidative stress benefits of phytosomes on rats were enhanced upon loading them with naringenin. Additionally, investigations from clinical trials have verified that phytosomes can be used to treat respiratory conditions.
- Studies involving clinical trials have also validated the potential of phytosomes for treating respiratory ailments. In this instance, modest studies were conducted to explore the impact of quercetin Phytosome upon healthy individuals who suffered from mild to moderate asthma attacks and rhinitis.
- When avoiding and treating symptoms throughout the day and at night, maintaining a more outstanding maximum expiratory flow rate and reducing its variation while maintaining a strong safety assessment, quercetin Phytosome outperformed the placebo group [28].

SOME COMMERCIAL PHYTOSOME PRODUCTS AND THEIR MEDICINAL USES

1. SILYBIN PHYTOSOME^{TM}: Hepatitis, Cirrhosis, Food Products
2. NARINGENIN PHYTOSOME^{TM}: Anti-Oxidant activity
3. SERICOSIDE: Anti-wrinkle
4. LEUCOSELECT PHYTOSOME^{TM}: UV Protectant
5. ESCULOSIDE PHYTOSOME$^{TM:}$ Anticellulite
6. HAWTHORN PHYTOSOME^{TM}: Nutraceutical, Cardioprotective
7. MILLET PHYTOSOME^{TM}: Antistress, Anti-wrinkle, Anti-allergic
8.ZANTHALENE PHYTOSOME^{TM}: Soothing and Anti-reddening
9. SWERTIA PHYTOSOME$^{TM:}$ Antidiabetic
10. MADEGLUCYL PHYTOSOME^{TM}: Anti-hyperglycemic, Anti-inflammatory [29].

DEVELOPMENT OF PHYTOSOME FORMULATION

Phytosome intricates can be transformed into various oral and topical dosage forms. This innovative approach enables the creation of diverse products that optimize formulation manageability and enhance bioavailability [30].

1. Soft Gelatin Capsules

Soft gelatin capsules present an excellent option for formulating Phytosome complexes. These complexes can be suspended in oil-based carriers and subsequently encapsulated in soft gelatin capsules, using either vegetable or semi-synthetic oils. Indena recommends achieving a granulometry of 100 percent for optimal capsule production. Not all Phytosome complexes behave identically when suspended in oily vehicles, so preliminary feasibility tests are necessary to identify the most efficient transporter [30].

2. Hard Gelatin Capsules

Phytosome complexes can also be incorporated into hard gelatin capsules. The naturally low density of these complexes may limit the total powder amount that can be encapsulated; typically, a size 0 capsule can hold no more than 300 mg without pre-compression. A piston tamp filling technique can enhance the powder fill, though this may affect the disintegration time. Throughout the product and process development, Indena recommends closely monitoring relevant parameters. A preliminary dry granulation method is suggested as the most effective manufacturing approach [30].

3. Tablets

Dry granulation is preferred for producing tablets with greater unit doses while ensuring appropriate technical and biopharmaceutical characteristics. The direct compression

technique is advisable only for low unit doses due to the Phytosome intricates restricted flow properties, potential stickiness, and low evident density. If direct compaction is chosen, diluting the Phytosome intricates with 60-70 percent excipients is recommended to enhance its mechanical attributes and achieve tablets with acceptable configuration. Conversely, wet granulation should be prevented because the effects of water and heat (during granulation and drying) can compromise the stability of the phosphatide complex [30].

4. Topical Dosage Forms

Phytosome complexes can also be utilized in topical applications. To penetrate the Phytosome intricate into an emulsion, the phospholipid complex should be dissolved in a small volume of the lipid phase and poured into an already prepared emulsion at low temperatures (below 40°C). Phytosome intricates are soluble in common lipid solvents used in topical formulations. For formulations with low lipid content, the Phytosome complex should be integrated into the aqueous phase and then combined into the final product at a temperature below 40°C [30].

Materials and techniques

- Acetonitrile (MeCN): A solvent used in HPLC for compound elution and separation.
- Acetic acid is frequently utilized in HPLC as a mobile phase addition or modifier.
- Dimethyl sulfoxide (DMSO): This substance can be a solvent for some substances or used to prepare samples.
- Chloroform (CHCl3): Because it can dissolve many organic substances, it is most likely utilized for extraction.
- EtOH (Ethanol): This may be used as a solvent for sample preparation or extraction.
- Diluted samples and mobile phases for analytical techniques require deionized water.
- Lipoid S 40 (PC): This PC source, which is 40% phosphatidylcholine, is made from soybean lecithin. It is frequently utilized in Phytosome preparations to increase the phytoconstituents' solubility and bioavailability [31].

BIOLOGICAL ACTIVITIES*:*

- The rats were maintained in typical laboratory settings with unrestricted access to food and water and were housed in standard metal cages (6 animals per cage). The ambient temperature was kept at 23 ± 2°C, and a 12-hour light/dark cycle was used.

1. Group I (ND + vehicle): Rats in this group were fed a normal diet and treated with a vehicle solution.
2. Group II (HCHF + vehicle): Rats in this group were given a high-carbohydrate, high-fat (HCHF) diet and treated with a vehicle solution.
3. Group III (HCHF diet + vitamin C): Rats in this group received an HCHF diet and were administered vitamin C at a dosage of 250 mg/kg body weight.
4. Group IV (HCHF diet + simvastatin): Rats in this group were fed an HCHF diet and treated with simvastatin at a dose of 1.3 mg/kg body weight.
5. Group V-VII (HCHF diet + PMG) (PMG50, PMG100, and PMG200): Rats in these groups were provided an HCHF diet and treated with varying doses of PMG, including 50 mg/kg, 100 mg/kg, and 200 mg/kg body weight.

- Animals exhibiting a more than 40% change in body weight, fasting plasma glucose levels exceeding 100 mg/dl, systolic blood pressure greater than 130 mmHg or diastolic blood pressure higher than 85 mmHg, and an atherosclerosis index (calculated as total serum cholesterol divided by total serum HDL-C) elevated compared to the control group were selected for further investigation.
- These animals were administered the designated substances orally once daily for 21 days. Daily monitoring of food and water intake and body weight was conducted throughout the study.
- After the study period, parameters such as percentage of body weight gain, cholesterol levels, triglycerides, LDL-C, HDL-C, atherogenic index, plasma glucose, HOMA-IR, and ACE were assessed. Additionally, changes in adipose tissue, including its size, density, weight, and adiposity index, were evaluated, along with oxidative stress status. The expression levels of histone deacetylase 3 (HDAC3), PPAR-γ, and proinflammatory cytokines (TNF-α, IL-6) in adipose tissue were also measured. A schematic representation outlining the experimental protocol is provided [32].

PHYTOSOME SIGNIFICANCE

Many technological and scientific investigations have demonstrated the importance of phytosomes, a significant development in delivering phytochemicals. Here is a summary of their significance and citations to essential literature works.

1. Pharmacological Advantages

Research has shown that phytosomes have higher pharmacological activity than free phytochemicals. This entails fewer adverse effects and improved therapeutic efficacy. For example, quercetin encapsulated in phytosomes has demonstrated enhanced antioxidant and anti-inflammatory properties [33].

2. Technological Developments in Pharmaceuticals

Phytosome formulation, characterization, and optimization are all subjects of research. The method offers a way to enhance the delivery of herbal and plant-based medicines, a breakthrough in pharmaceutical formulations [34].

3. Clinical Implications

Research has demonstrated that the use of Phytosome formulations can both lower the necessary dosage and increase the efficacy of medicinal medicines, which may minimize the likelihood of side effects [34].

Limitations of Phytoconstituents

- According to existing literature, the regular intake of dietary phytoconstituents (PCs) offers a range of health benefits, including potential cancer management.
- The clinical use of PCs as effective chemotherapy agents faces several challenges. One major limitation is their low oral bioavailability, with compounds like curcumin (0.47%), berberine (0.68%), celastrol (3.14%), and resveratrol (<1%) showing poor absorption and limited permeability.
- In addition, variations in dosing, high first-pass metabolism, large volumes of distribution, suboptimal therapeutic efficiency, and poor stability further hinder their therapeutic potential.
- The extraction and isolation processes of PCs can also compromise their therapeutic efficacy.
- Furthermore, targeted delivery remains a significant challenge due to these compounds' low lipophilicity, high molecular weight, and inability to cross biological membranes, which results in poor absorption easily.
- Moreover, the clinical application of PCs in cancer treatment is still limited by the lack of conclusive evidence showing that their consumption can entirely prevent cancer in humans.
- Despite the intake of PCs, cancer cases continue to be reported. Additionally, while in vitro studies on the anticancer potential of PCs have been promising, similar results have not been observed in vivo, especially in complex animal models. This discrepancy creates a gap between preclinical findings and clinical outcomes [35].

DISCUSSION

Enhancing the bioavailability and therapeutic efficiency of bioactive chemicals from medicinal plants has been demonstrated to be a promising application of Phytosome technology. Traditional herbal medicines are hampered by low solubility and absorption; phytosomes efficiently overcome these issues by encasing active components in phospholipid complexes. Optimizing these formulations requires careful consideration of important variables such as phospholipid types, plant extract selection, and stoichiometric ratios. Technological developments in Phytosome synthesis and reliable structural verification techniques like NMR and UV spectroscopy validate the phytosomes' efficacy and stability. Moreover, the focus on sustainability in phytosome production corresponds with consumers' increasing need for ecologically conscious health goods.

CONCLUSION

Phytosome technology presents a groundbreaking approach to overcoming the limitations of conventional drug delivery, especially in enhancing the bioavailability and efficacy of plant-derived compounds. Through advanced formulations that maximize solubility, stability, and cellular absorption, phytosomes pave the way for a new era in therapeutic innovation, offering safer, more effective treatments for chronic diseases such as cancer, rheumatism, and respiratory conditions. By relating traditional herbal knowledge with modern nanotechnology, phytosomes advance pharmaceutical science and reinforce natural medicine's relevance in addressing complex health challenges. This convergence of technology and nature promises significant progress in personalized medicine, enabling a future where patients benefit from targeted, sustainable, and holistic therapeutic solutions. The potential of phytosomes in the pharmaceutical landscape is vast, marking a decisive step toward more integrated, high-performance treatment strategies.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Surendra Kumar M. and Astalakshmi N. conceptualized the idea and conducted the literature survey. Dhivya K. and Sarathi M. drafted the manuscript and further revised it. Lokesh D., Nivethitha S., and Praveen Kumar M. contributed to conducting the literature survey and making the corrections. All the authors contributed to the correction of the manuscript and the final proofreading of the manuscript.

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