Int J Biol Med Res. 2025; 16(3): 8149 -8160

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International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Review article

PHYTOSOME: UNVEILING PREPARATION METHODS, PHARMACOLOGICAL POTENTIAL, AND PHYSICOCHEMICAL PROFILING IN DRUG DELIVERY

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A R T I C L E I N F O

Keywords:
Phytosome technology,
drug delivery,
preparation methods,
pharmacological potential,
physicochemical profiling,
encapsulation efficiency,
bioavailability,
therapeutic application,
plant-derived compounds,
and modern drug delivery systems.

A B S T R A C T

This review article delves into the innovative field of phytosome technology, focusing on its preparation methods, pharmacological potential, and physicochemical profiling within drug delivery systems. The study examines various preparation techniques, including solvent evaporation, coacervation, and supercritical fluid technology, and their impact on encapsulation efficiency and formulation stability. Highlighting the pharmacological benefits, the review underscores the superior bioavailability and therapeutic efficacy of phytosomes in applications such as anti-inflammatory, antioxidant, antimicrobial, and anticancer treatments. The importance of physicochemical profiling, including parameters like particle size, zeta potential, and drug-loading capacity, is emphasized to optimize phytosome formulations. This comprehensive review presents phytosome technology as a promising avenue for enhancing the bioactive potential of plant-derived compounds, positioning it as a significant innovation in modern drug delivery systems. By integrating advanced preparation methods and thorough physicochemical analysis, phytosomes offer a robust platform for improving the delivery and efficacy of bioactive compounds, paving the way for more effective and targeted therapeutic interventions.

Introduction

Phytosomes represent an exciting frontier in plant science and health. Those special molecular complexes,derived from the Greek wordsphyto(plant) and soma(body), encapsulated the essence of the plant and its bioactive compounds, which promotes better absorption and bioavailability in the human body(1,2). This innovative approach to exploiting the therapeutic potential of plants has attracted considerable attention in the fields of medicine,nutraceuticals, and others(1,2).

A phytosome is a complex of phospholipids in its core, which is formed by combining bioactive compounds of plant origin with phospholipids[3]. Phospholipids are essential components of cell membranes and their amphiphilicity allows them to form a lipid bilayer structure(4).This unique property plays a key role in the creation of phytosomes because it enables the encapsulation of hydrophobic plant compounds in the lipophilic environment of phospholipids(5).

The development of phytosomes is based on the challenge of poor bioavailability of certain plant extracts. many bioactive compounds found in plants, such as flavonoids and polyphenols, are poorly soluble in water, which limits their absorption in the gastrointestinal tract.By forming phytosomes, these compounds can be covered with phospholipid layers, creating a structure that improves their solubility and absorption(6).

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The basic structure of phytosome was (depicted in fig1.)(7).

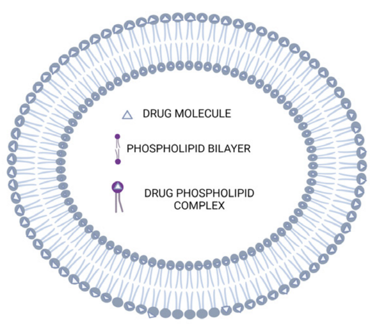


Fig 1: The basic structure of phytosome

Various Techniques Such As Solvent Evaporation And Coacervation Are Used To Ensure The Formation Of Stable And Bioactive Phytosome Complexes.The Resulting Structures Have Better Stability, Solubility, And Absorption Properties Compared to Their Parent Extracts[5]Phytosomes Have Found Application in Various Therapeutic Areas, From Traditional Herbal Medicine To Modern Medicine.In Herbal Medicine,Phytosome Technology Has Been Used to Improve The Bioavailability Of Medicinal Plants With A Rich History Of Traditional Use. In Addition, Pharmaceutical Companies Are Investigating the Potential Of Phytosomes In The Development Of New Drug Delivery Systems, Exploiting The Synergy Between Plant-Derived Compounds And Phospholipids[3] phytosomes are an example of the convergence of botany and health, offering a complex solution to the bioavailability problems of plant-derived bioactive compounds. Their applications include traditional herbal medicines, medicines, and skin care, demonstrating the versatility and potential impact of this innovative technology[5]. As research in this field continues, phytosomes promise to open new dimensions in the therapeutic use of plant compounds that will promote the development of health and well-being (4).

Phytosomes are a fascinating innovation in the realm of herbal medicine and supplementation. These novel compounds have garnered significant attention due to their potential for enhancing the bioavailability and efficacy of various herbal extracts(4).

At their core, phytosomes are specialized complexes formed by combining natural plant extracts with phospholipids, typically phosphatidylcholine. This unique structure allows for a more efficient absorption of the active constituents present in the botanical extracts. The phospholipid "shell" envelops the phytoconstituents, creating a molecular complex that mimics the body's cell membranes, aiding in their absorption(12).

Research has shown promising results across various applications of phytosomes. For instance, in the realm of traditional herbal remedies, phytosome technology has been employed to improve the bioavailability of botanicals like curcumin, green tea extract, ginkgo biloba, milk thistle, and many others(1).Studies indicate that phytosomal formulations of these herbs exhibit increased absorption and improved efficacy compared to standard extracts[1].

The enhanced bioavailability of phytosomes has implications beyond traditional herbal medicine. They have found utility in cosmetic and pharmaceutical formulations, where improved absorption of active herbal ingredients can lead to more potent skincare products or enhanced drug delivery systems(8).

4. HISTORICAL DEVELOPMENT OF PHYTOSOME

The concept of Phytosomes emerged in the late 20th century as a breakthrough strategy aimed at bolstering the bioavailability of phytoconstituents sourced from botanical extracts. Dr. Gianni Belcaro, an Italian researcher, was instrumental in pioneering this approach in the 1980s. Dr. Belcaro, along with his research team, sought innovative methods to overcome the inherent limitations of conventional herbal extracts in effectively delivering therapeutic compounds within the body(14,15).

The historical genesis of Phytosomes primarily revolves around leveraging phospholipids to create complexes with phytoconstituents. This strategic approach stemmed from the understanding that phospholipids, crucial structural elements of cell membranes, possessed the potential to significantly augment the absorption and bioavailability of bioactive compounds sourced from plants(16).

Initially, research efforts were centered on the synthesis of these complexes through the conjugation of phospholipids, particularly phosphatidylcholine, with botanical extracts. This fusion process facilitated the formation of Phytosomes, encapsulating or binding the phytoconstituents within the phospholipid structure(6).

The innovation driving Phytosomes was spurred by the imperative need to surmount challenges associated with the limited solubility and absorption rates of specific herbal compounds. By orchestrating these complexes, researchers aimed to revolutionize the delivery of active constituents, thereby amplifying their therapeutic efficacy within targeted tissues(17).

Since its inception, Phytosome technology has undergone remarkable advancements. Research endeavors undertaken by both scientific scholars and pharmaceutical entities have extensively investigated diverse combinations, manufacturing methodologies, and applications of Phytosomes across nutraceuticals, pharmaceuticals, and cosmetics. This ongoing evolution in the field continues to refine and broaden the spectrum of potential applications for Phytosomes in the domain of natural product-based therapist[14].

Phytosomal formulation(19)

Components and structures (20)

Phytosomes are primarily composed of two key elements (21)

1. Phospholipids: These vital constituents are fundamental building blocks present in cell membranes. Varieties like phosphatidylcholine or phosphatidylserine serve as pivotal components within Phytosomes. They play a crucial role in constituting the outer layer, crafting a lipid bilayer structure akin to natural cell membranes(22).

2. Phytoconstituents: These active compounds stem from botanical extracts and encompass diverse bioactive molecules such as flavonoids, polyphenols, or other therapeutic plant-derived substances (23).

The structural framework of Phytosomes involves the entwining or encasement of phytoconstituents within the lipid layer shaped by phospholipids. This interaction fosters a complex structure where the hydrophilic heads of the phospholipids face outward while the hydrophobic tails orient inward, enveloping the phytoconstituents securely within(15).

This structural arrangement is strategically devised to heighten the solubility of phytoconstituents, catering to both water-based and lipid-based environments. It's theorized that the formation of this intricate complex bolsters the stability, absorption, and bioavailability of phytoconstituents, thereby enhancing their therapeutic effectiveness upon ingestion or application(14).

5.MANUFACTURING PROCESSES OF PHYTOSOME

5.1Preparation of phytosomes:

Phytosomes are advanced forms of herbal formulations where the active constituents of botanical extracts are combined with phospholipids to enhance their absorption and bioavailability. Here's a detailed method of preparing phytosomes(24).

5.2Materials Needed:

1. Botanical Extract: Choose the herb or plant extract you want to formulate into phytosomes[10]

2. Phospholipids: Typically, phosphatidylcholine or lecithin are used. These can be sourced from soybeans, sunflowers, or other plant-based sources (16).

3. Solvents: Ethanol or methanol for extracting the active constituents from the botanical extract [21]

4. Equipment: Glassware, beakers, heating mantle/stirrer, rotary evaporator, centrifuge, and a lyophilizer (optional but recommended for drying)(26).

5.3Method:

5.3.1.Extraction Of Active Constituents:[20]

Measure the desired quantity of the botanical extract.Use a suitable solvent (ethanol or methanol) to extract the active constituents from the botanical material. This can be done through maceration, percolation, or other extraction methods.Evaporate the solvent under reduced pressure using a rotary evaporator to obtain the concentrated extract[20].

5.3.2.Preparation of Phospholipid Solution:

Dissolve the phospholipids (phosphatidylcholine or lecithin) in a suitable solvent (usually alcohol) to form a clear solution. Ensure proper dissolution by stirring and heating gently if needed.[20]

5.3.3. Formation Of Phytosomes:

1.Mix the concentrated botanical extract obtained from step 1 with the phospholipid solution prepared in step

2. Stir the mixture thoroughly to allow the constituents to form phytosomes. The combination of phospholipids and botanical extract should lead to the formation of complexes[20].

5.3.4. Removal Of Solvent:

Remove the solvent from the mixture using a rotary evaporator under reduced pressure. This step is crucial to obtain a concentrated phytosome complex.

Optionally, further remove any remaining traces of solvent by subjecting the mixture to a lyophilizer (freeze-drying)[20]

5.3.5. Characterization And Storage:

Characterize the obtained phytosome complex for its particle size, shape, and encapsulation efficiency using appropriate analytical techniques like dynamic light scattering (DLS) or electron microscopy.

Store the prepared phytosomes in airtight containers protected from light and moisture to maintain stability and efficacy.

Dosage Form: Phytosomes can be incorporated into various dosage forms like capsules, tablets, creams, or solutions based on the intended use.

Quality Control: Regular quality checks should be performed to ensure consistency and potency of the phytosome formulation.

Consultation: It's advisable to consult with a qualified herbalist, pharmacist, or scientist experienced in phytosome preparation for precise formulations and dosages[20]

6.SELECTIONOF PHYTOCONSTITUENTS FOR PHYTOSOMES

The selection of phytoconstituents for Phytosome preparation is a critical process that involves considering various key factors:

1. Bioactivity and Therapeutic Potential: Phytoconstituents chosen for Phytosome formulation should demonstrate well-documented bioactivity and therapeutic potential. Examples include flavonoids, polyphenols, alkaloids, or other known bioactive compounds with medicinal properties[23]

2. Solubility and Stability: Optimal phytoconstituents for Phytosomes often exhibit poor solubility in water or limited bioavailability due to their hydrophobic nature. Phytosome technology aims to enhance the solubility and stability of these compounds, thereby improving their absorption and efficacy [16]

3. Clinical Relevance: Preference is given to phytoconstituents with established clinical relevance and proven health benefits for Phytosome formulation. These are compounds that have shown efficacy in treating specific health conditions or ailments [24]

4. Compatibility with Phospholipids: The interaction between chosen phytoconstituents and the phospholipids used in Phytosome formulation is pivotal. Certain compounds may exhibit better interactions or form stronger complexes with specific phospholipids, influencing the overall effectiveness of the Phytosome [25]

5. Safety Profile: The safety profile of selected phytoconstituents at intended dosage levels is crucial. Compounds chosen for Phytosome preparation should have well-documented safety profiles, ensuring minimal adverse effects[26]

6. Research and Development Support: The availability of research backing the efficacy and enhanced bioavailability of specific phytoconstituents through Phytosome technology is a guiding factor in their selection[27]

7. Market Demand and Application Potential: Consideration of the market demand for certain phytoconstituents and their potential applications in nutraceuticals, pharmaceuticals, or cosmeceuticals may influence their selection for Phytosome preparation[28]

7.METHOD FOR PREPARATIONS OF PHYTOSOMES

7.1.Solvent evaporation method

The solvent evaporation method involves integration of the phytoconstituents and PC during a flask containing an organic solvent. This reaction mixture is kept at an optimum temperature usually 40°C for specific interval of 1 hr to achieve maximum drug entrapment within the phytosomes formed. Thin film phytosomes are separated by 100 mesh sieves and stored in desiccators for overnight[29][20]

7.2 Mechanical Dispersion method

In the experiments, the lipids dissolved in organic solvent are brought be in contact with aqueous phase containing the drug (Sikarwar MS et al., 2008). the next removal of the organic solvent under reduced pressure results in the formation of phyto-phospholipid complex. Recently methods for the phospholipid involute preparation includes super critical fluids (SCF), which include gas antisolvent technique (GAS) compressed anti solvent process (PCA), supercritical anti solvent method (SAS)[30] (Li Y et al., 2008).

7.3 Salting out technique

An important method of phytosome preparation that done by dissolving both PC and therefore the plant extract during a suitable organic solvent then nhexane was added until the extractPC complex precipitation occurs[31,32]

7.4 lyophilization methods

The lyophilization technique DSN was plenarily dissolved in DMSO. The resulting DSN solution (2.5% weight/volume) was added to the answer of SPC dissolved in tbutylalcohal (1.5% weight/volume) followed by stirring for 3 hours on a magnetic stirrer until complex formation. The complex was then isolated by lyophilization. After abstracting the samples from the freeze drier, the resultant DSN:SPC involute (yield 90.4%, weight/weight) was placed during a desiccator over P2O5 at 4°C until testing.

For the culled developing technique, the influence of variable formulation factors was assessed including SPC type (Lipoid® S100, Lipoid® S75 and Lipoid® S PC3), drug phospholipid ratio (1:1, 1:2, and 1:4) and cosolvent type of chemical (methanol, ethanol, chloroform, acetone, and TBA). Nonconventional methods are customarily employed in construction of phytosome complexes. Modernistic herbal complexes are composed by reaction between Equilar amalgamation of natural or synthetic phospholipid and active constituents or herbal extract in acrostic organic solvents[20]

Common stages in formulation of phytosomes Various methods of preparation are as follows:[32–34]

7.5 Antisolvent precipitation process:

A certain amount of herbal extract and phospholipids is refluxed with 20 ml of organic solvents like acetone at specific experimental conditions below 50°C for 23 hr. The reaction mixture is concentrated to minimum volume up to 10 ml then on addition of solvent with low polarity like nhexane with stirring precipitates are obtained. Filtered precipitates are stored in desiccators. The dried precipitates are pulverized and powdered involute are stored in dark amber colored glass bottle at temperature[20].

7.6 Rotary evaporation process:

Specific weight of herbal extract and phospholipids were mixed in 30 ml water miscible organic solvent like acetone in round bottom glass container followed by stirring for two hours at a temperature but 50°C in Rota evaporator. Antisolvent like nhexane are often added to thin film which is obtained after uninterrupted stirring employing a stirrer Precipitate of phytosomes obtained are often stored in amber colored glass container at controlled temperature under specifiedhumidity[32][20,34]

7.7 Thin Flim hydration technique:

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 32 moles of an herbal extract are combined to form a phytosome.

The reaction takes place using an aprotic solvent like the complex is derived from dioxane or acetone may be separated by precipitation combined with nonsolvent 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. (Figure 2&3) illustrates the step-by-step method of phytosome preparation. The steps below make up the general technique of making phytosomes[34][35]

Phospholipid dissolved in organic solvent containing drug/ extract (1:1).

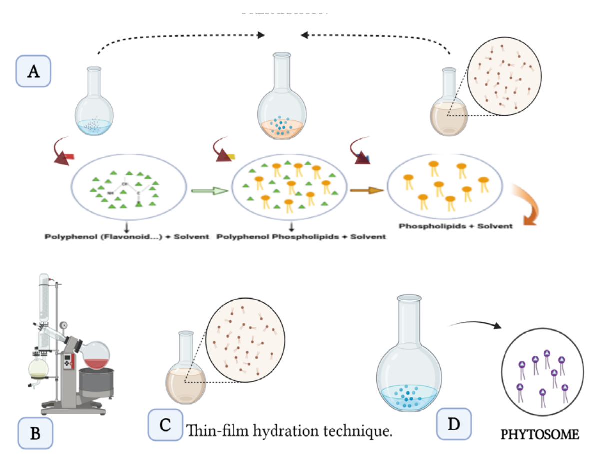
Solution of phospholipid in organic solvent with drug/extract

Drying

Formulation of thin film

Formulation of phytosomal complex

Isolation by precipitation (Lyophilization spray drying)



A:Preparation B :Refluxing and concentration under reduced pressureC :drying and thin layer formation D: Hydration and size reduction.

Thin hydration technique (depicted in Figure 2.)

8.MECHANISM OF PHYTOPHOSPHOLIPID COMPLEX FORMATION

The poor absorption of flavonoid nutrients is likely due to two main factors. First, these are multiple ring molecules not quite small enough to be absorbed from the intestine into the blood by simple diffusion, nor does the intestinal lining actively absorb them, as occurs with some vitamins and minerals. Second, flavonoid molecules typically have poor miscibility with oils and other lipids. This severely limits their ability to pass across the lipid rich outer membranes of the enterocytes, the cells that line the small intestine.

The phytosome technology meets this challenge. Phytosomes results from the reaction of a stoichiometric amount of the phospholipid (phosphatidylcholine) with the standardized extract or polyphenolic constituents (like simple flavonoids) in a nonpolar solvent. Phosphatidylcholine is a bifunctional compound, the phosphatidyl moiety being lipophilic and the choline moiety being hydrophilic in nature. Specifically, the choline head of the phosphatidylcholine molecule binds to these compounds while the lipid soluble phosphatidyl portion comprising the body and tail which then envelopes the choline bound material.

Hence, the phytoconstituents produce a lipid compatible molecular complex with phospholipids, also called as phyto-phospholipid complex. Molecules are anchored through chemical bonds to the polar choline head of the phospholipids, as can be demonstrated by specific spectroscopic techniques. Precise chemical analysis indicates the unit phytosome is usually a flavonoid molecule linked with at least one phosphatidylcholine molecule. The result is a little microsphere or cell is produced[6]

9. LIST OF RECENT PHYTOSOMAL PREPARATIONS

Table1. summarizes the List of recent research on phytosomes, along with their methodology and solvents.

Different phospholipid complexes	Technique for preparation	Solvents	Ref.
Complex of luteolin and phospholipid	The use of Quality by Design for solvent evaporation	Ethanol	(35)
Nanophytosomes that contain rutin	Thin layer hydration method Solvent evaporation method	A mixture of methanol and hloroform(1:4).	(36)
Terminalia Arjuna phytosome combination of methanolic extract (TBE) Complex of rosmarinicacid (RA) and phospholipids	Solvent evaporation method Salting out	Methylene chloride and methanol (6:1) hexane Anhydrous ethanol	(37)
Complex of Standardized Centella Extract on Phospholipids	Solvent evaporation method	Ethanol, n-hexane	(38)
Extract from Phyllanthusemblica phospho lipid complex	Solvent evaporation method	Dichloromethane or methanol as solvent	(39)
Complex of oleanolic acid with phospholipid	Solvent evaporation method	Anhydrous ethanol	(40)
Complex of echinacoside phospholipids	Solvent evaporation method	Tetrahydrofuran	(41)
Complexes of silymarin with phospholipid	Solvent evaporation method	Ethanol	(42)

Complex of epigallocatechin gallate and phospholipid	Solvent evaporation method	Ethanol	(43)
Extractphospholipid of pomegranates	Spray drying	Equal volumes of dioxane and methanol	(44)
Complexation of phospholipids in (W. somnifera) NMITLI118RT	Solvent evaporation method	Ethanol	(45)
Phytosomes Containing NaringeninLoaded DipalmitoylPC	Solvent evaporation technique	Methanol, ethanol, and ethyl acetate	(42)
Phytosome-loaded complex of gingerol Soya Lecithin	Antisolvent precipitation technique	Methanol	(46)
Phytosome Made of Polyphenols from Moringa Oleifera Leaf Tofu PC	Thin layer hydration technique	Dichloromethane, ethanol	(47)
Phytosome with apigenin and phospholipid the Phospholipon® 90H complex	Solvent evaporation technique	1, 4–dioxane, methanol	(48)
Combination of phospholipid and curcumin	Solvent evaporation technique	Dichloromethane	(49)
Complex of soybean PC and mitomycin C	Solvent evaporation technique	Dichloromethane	(50)
Phytosomes of Piper longum	Solvent evaporation technique	Distilled water	(51)
Phytosomes based on berberinephospho lipid complex	Solvent evaporation technique	Aprotic solvent	(52)
Aloe vera extract phytosomal gel	Thin-layer hydration method	Chloroform	(45)
Extract of Euphorbia neriifolia Linn. Phospholipids Complex	evaporation method	Dichloromethane	(53)

10.PHYTOSOMES ADVANTAGES:

1. Enhanced Bioavailability: Phytosomes significantly improve the absorption of plant extracts with low solubility, making them more accessible to the body [19].

2. Improved Solubility: They boost the solubility of compounds that repel water, enabling better dispersion within the body for enhanced absorption [36].

3. Increased Stability: Phytosomes often maintain better stability than traditional herbal extracts, preserving their effectiveness over time[37]

4. Targeted Delivery: They facilitate precise delivery to specific cells or tissues, optimizing the impact of the herbal extracts [38]

5. Enhanced Cellular Penetration: Phytosomes penetrate cell membranes more effectively due to their structure, fostering improved cellular level absorption [17]

6. Reduced Dosage Requirement: Increased bioavailability allows for lower doses while maintaining the same therapeutic effects, reducing potential side effects [39,40]

7. Faster Onset of Action: Improved absorption leads to a quicker onset of action, delivering faster relief or benefits [40]

8. Synergistic Effects: Phytosomes enhance the combined benefits of herbal extracts and phospholipids, amplifying their synergistic effects [37]

9. Improved Efficacy: They heighten the efficacy of herbal extracts, ensuring a higher concentration of active compounds reaches the targeted tissues[41]

10. Minimized Gastric Irritation: Phytosomes potentially reduce gastric irritation linked to certain herbal extracts by facilitating better absorption and distribution [42]

11. Compatibility with Various Compounds: Phytosomes can be combined with diverse herbal extracts, broadening their applications across different plant compounds [17]

12. Clinically Supported: Numerous phytosome formulations have undergone clinical trials, verifying their efficacy and safety [17]

13. Versatile Applications: They are adaptable for use in different forms such as capsules, tablets, or topical creams, offering versatile applications [43]

14. Extended Duration of Action: Enhanced absorption often prolongs the duration of action, extending the benefits of the herbal extracts [19]

15. Potential for Innovative Formulations: Ongoing research explores new phytosome formulations, expanding the range of herbal extracts benefiting from this technology [44]

Phytosomes exhibit promising advantages in optimizing the therapeutic potential of herbal extracts, contributing significantly to the advancement of natural medicine and supplementation.

11.PHYTOSOMES DISADVANTAGES

1. Limited Long-Term Studies: Since the widespread use of phytosomes is relatively recent, comprehensive, long-term research into their effects and safety might still be developing [45]

2. Higher Production Costs: Creating phytosomes involves a process that can be more expensive than traditional extraction methods, which might translate to higher prices for consumers [36,46]

3. Quality Variability: The effectiveness of phytosomes can differ based on the quality and purity of the ingredients used, potentially leading to variations between products [36]

4. Possible Allergic Reactions: Some individuals might have allergic reactions to specific components used in phytosome formulations, which could result in adverse effects [47]

5. Complex Formulation Challenges: Achieving the right balance between plant extracts and phospholipids for effective phytosomes can be intricate, affecting the consistency and efficacy of the final product [17]

6. Medication Interactions: Phytosomes, like many supplements, might interact with certain medications, affecting their effectiveness or causing adverse reactions in some cases [48]

7. Varied Effectiveness: While phytosomes can enhance the absorption of some herbal compounds, their impact on all plant extracts or compounds may not be universally significant [17]

8. Potential Digestive Discomfort: For some individuals, the addition of phospholipids in phytosomes might lead to digestive discomfort or gastrointestinal issues [20]

9. Reliance on Manufacturer Standards: The reliability and effectiveness of phytosome-based products heavily rely on the quality control and manufacturing standards of the producing company [44]

10. Limited Product Range: Compared to traditional herbal extracts, phytosome-based supplements might have a more restricted range of available options, potentially limiting choices for consumers [49]

12.VARIOUS PROPERTIES OF PHYTOSOMES

12.1 Physiological

Phytosomes are a fascinating innovation in the realm of herbal medicine and supplementation. These novel compounds have garnered significant attention due to their potential for enhancing the bioavailability and efficacy of various herbal extracts[20]

At their core, phytosomes are specialized complexes formed by combining natural plant extracts with phospholipids, typically phosphatidylcholine. This unique structure allows for a more efficient absorption of the active constituents present in the botanical extracts. The phospholipid "shell" envelops the phytoconstituents, creating a molecular complex that mimics the body's cell membranes, aiding in their absorption[9]

The primary advantage of phytosomes lies in their ability to overcome the inherent limitations of poor solubility and low absorption rates associated with certain herbal compounds. By forming these complexes, phytosomes enhance the transport of active compounds across biological membranes, facilitating improved uptake by the body. This, in turn, enhances the therapeutic effects of herbal extracts[50]

Research has shown promising results across various applications of phytosomes. For instance, in the realm of traditional herbal remedies, phytosome technology has been employed to improve the bioavailability of botanicals like curcumin, green tea extract, ginkgo biloba, milk thistle, and many others. Studies indicate that phytosomal formulations of these herbs exhibit increased absorption and improved efficacy compared to standard extracts[6,51]

Moreover, the enhanced bioavailability of phytosomes has implications beyond traditional herbal medicine. They have found utility in cosmetic and pharmaceutical formulations, where improved absorption of active herbal ingredients can lead to more potent skincare products or enhanced drug delivery systems[52]

Phytosomes offer considerable potential, it's important to note that not all herbal extracts can be effectively formulated into phytosomal complexes. The creation of these complexes requires a precise understanding of the molecular structure and properties of both the herbal compound and the phospholipid used in the process[53]

Phytosomes represent an innovative approach to improving the bioavailability and efficacy of herbal extracts. Their ability to enhance the absorption of active constituents has promising implications for traditional herbal medicine, pharmaceuticals, and cosmetic formulations. Continued research and development in this field hold the potential to unlock even more applications and benefits for phytosome technology in the future[54]

12.2 Chemical

Phytosomes, as specialized complexes formed by combining herbal extracts with phospholipids, exhibit distinct chemical properties that contribute to their unique characteristics and efficacy:

1. Phospholipid Composition: Phytosomes predominantly consist of phospholipids, particularly phosphatidylcholine, which forms the major component of the phospholipid bilayer. This composition provides the structural basis for encapsulating and carrying the phytoconstituents[19]

2. Amphipathic Nature: Phospholipids possess both hydrophilic (water-attracting) and hydrophobic (water-repelling) regions within their structure. This amphipathic nature allows them to interact with both water and lipid-based substances, facilitating the encapsulation of hydrophobic herbal compounds [44]

3. Encapsulation Mechanism: The chemical properties of phospholipids allow them to form bilayer structures, creating a protective shell around the hydrophobic phytoconstituents. This encapsulation protects the herbal compounds from degradation and aids in their transportation and absorption [2]

4. Liposomal Characteristics: Phytosomes, owing to their phospholipid composition, exhibit some similarities to liposomes, which are spherical vesicles with a lipid bilayer. However, phytosomes differ in their structure, primarily in the ratio of phospholipids to the encapsulated compounds [20]

5. Intermolecular Interactions: Phytosomes form through intermolecular interactions between the hydrophilic and hydrophobic regions of phospholipids and the herbal constituents. These interactions enable the formation of stable complexes with the encapsulated phytoconstituents [19].

6. Enhanced Solubility: Phytosomes improve the solubility of hydrophobic herbal compounds in both water and lipid-based environments. This increased solubility aids in their absorption and utilization within the body [44]

7. Biocompatibility: Phospholipids used in phytosome formulations are generally biocompatible and well tolerated by the body, reducing the risk of adverse reactions [55]

8. Stability and Shelf-life: Phytosomes possess good stability, preserving the integrity and bioactivity of the encapsulated herbal extracts. This stability contributes to an extended shelf-life of phytosome-containing products [55]

These chemical properties are crucial for formulating phytosomal complexes effectively. The interplay between phospholipids and the phytoconstituents determines the stability, bioavailability, and efficacy of the resulting phytosome formulation[19]

12.3 Biological

Phytosomes are advanced forms of herbal products that are better absorbed and utilized to produce better results than conventional herbal extracts. The increased bioavailability of the phytosomes over the noncomplexed botanical derivatives has been demonstrated by pharmacokinetics studies or by pharmacodynamic tests in experimental animals and human subjects[44,48]

The biological properties of phytosomes, arising from their unique structure and interactions within the body, contribute significantly to their efficacy and therapeutic effects.

1. Enhanced Bioavailability: Phytosomes exhibit increased bioavailability compared to standard herbal extracts. Their structure facilitates improved absorption and transportation of the encapsulated herbal compounds across biological membranes, leading to higher concentrations of active ingredients in the systemic circulation [48,49]

2. Improved Absorption Mechanism: Phytosomes, with their phospholipid bilayer structure, interact effectively with cell membranes. This interaction facilitates the absorption of the complexed phytoconstituents into cells, optimizing their uptake and utilization by various tissues [48]

3. Cellular Uptake and Distribution: Phytosomes can facilitate the cellular uptake and distribution of herbal compounds to target tissues or organs. This property allows for a more targeted delivery of active ingredients, potentially enhancing their therapeutic effects while reducing systemic side effects [48,55]

4. Stability and Protection: Phytosomes protect encapsulated herbal extracts from degradation by enzymes and harsh conditions within the gastrointestinal tract. This protection preserves the integrity and potency of the phytoconstituents until they reach their intended sites of action [56]

5. Modulation of Pharmacokinetics: Phytosomes can modulate the pharmacokinetics of herbal compounds by altering their absorption, distribution, metabolism, and excretion within the body. This modulation leads to optimized and prolonged therapeutic effects [57]

6. Potential Targeting Abilities: Phytosomes may enable the targeted delivery of herbal compounds to specific cells, tissues, or organs. This targeted approach enhances the therapeutic effects of herbal extracts while minimizing adverse effects on nontargeted areas [48]

7. Synergistic Effects Preservation: Phytosomes help maintain the synergistic effects of different phytoconstituents present in herbal extracts by facilitating their efficient absorption and utilization together. This preservation of synergy contributes to enhanced therapeutic outcomes [57]

8. Reduced Dosage Requirement: Due to improved bioavailability, lower doses of herbal compounds encapsulated in phytosomes may achieve comparable therapeutic effects to higher doses of standard extracts. This property potentially reduces the risk of side effects associated with high doses [19]

These biological properties collectively highlight the advantages of phytosomes in enhancing the efficacy, absorption, and targeted delivery of herbal extracts, paving the way for improved utilization of botanical compounds in various therapeutic applications.

12.4 Physical

Phytosomes exhibit several distinct physical properties due to their unique structure and composition, which combine phospholipids and botanical extracts. Here are some key physical properties:

1. Lipid Bilayer Structure:

Phytosomes have a bilayer structure formed by the association of phospholipids with the active constituents of botanical extracts. This structure resembles cell membranes, enhancing their ability to merge with biological membranes for better absorption[55]

2. Particle Size:

Phytosomes typically have a nanosized particle range, often in the nanometer scale (10100 nanometers). Their small particle size contributes to increased surface area, promoting better absorption and bioavailability[2]

3. Enhanced Stability:

Due to their encapsulation within phospholipids, phytosomes tend to have improved stability compared to free botanical extracts. This encapsulation protects the active compounds from degradation due to environmental factors such as light, oxygen, and moisture[20]

4. Solubility and Dispersibility:

Phytosomes demonstrate enhanced solubility in both water and lipid environments. This characteristic improves their dispersibility in various formulations, allowing for easier incorporation into different delivery systems like capsules, tablets, creams, or solutions[57]

5. Improved Bioavailability:

One of the significant advantages of phytosomes is their enhanced bioavailability compared to traditional herbal extracts. The phospholipid complex structure facilitates easier absorption across biological membranes, leading to increased levels of active compounds in the bloodstream[48]

6. Transparent or Translucent Appearance:

Depending on the specific composition and formulation, phytosomes can appear as clear, transparent, or translucent liquids or powders. This physical appearance may vary based on the encapsulated botanical extract and the type of phospholipids used[49]

7. Stability Under Storage:

Properly prepared phytosomes tend to exhibit good stability under appropriate storage conditions. They can maintain their physical properties, including particle size and structure, when stored in suitable environments, away from light and moisture[3]

These physical properties collectively contribute to the efficacy and versatility of phytosomes as advanced delivery systems for herbal extracts, providing improved absorption and therapeutic outcomes.

13. EVALUATION PARAMETERS

Evaluating the effectiveness and quality of phytosomes involves assessing various parameters that encompass their physical, chemical, and biological characteristics. Here are detailed evaluation parameters for phytosomes(76)

13.1 Physical Evaluation :(61)

1. Particle Size and Distribution:

Determined using techniques like dynamic light scattering (DLS) or laser diffraction, assessing the average particle size and uniformity of distribution. Nanoscale particles are desirable for improved bioavailability.

2. Morphology and Shape:

Analyzed through electron microscopy to understand the shape and morphology of phytosomes, which can affect their interactions and absorption.

3. Surface Charge (Zeta Potential):

Zeta potential measurement provides information about the surface charge of phytosomes, impacting their stability and interactions in physiological environments.

4. Physical Stability:

Stability studies assess changes in particle size, aggregation, or sedimentation over time, under different storage conditions (temperature, humidity) to ensure long-term stability.

13.2 Chemical Evaluation :(77)

1. Encapsulation Efficiency:
Quantifies theamount of active constituents encapsulated within the phospholipid bilayer. High encapsulation efficiency indicates better utilization of the active components.

2. Chemical Composition and Purity:
Analyzed through chromatographic techniques (HPLC, GCMS) to verify the presence of specific active compounds and ensure the absence of impurities or contaminants.

3. Drug Release Profile:
In vitro release studies assess the release kinetics of active constituents from phytosomes, determining their sustained or controlled release pattern.

13.3 Biological Evaluation :(66)

1. Bioavailability Studies:
In vivo, studies in animal models or human trials assess the bioavailability of phytosomes compared to conventional herbal extracts. Measurement of blood levels of active compounds helps determine their absorption and distribution.

2. Pharmacokinetic Parameters:

Determine parameters like Cmax (peak plasma concentration), Tmax (time to reach peak concentration), and AUC (area under the curve), providing insights into the absorption and systemic availability of the active compounds.

3. Therapeutic Efficacy:

Assess the efficacy of phytosomes in delivering therapeutic effects. This involves conducting studies on the intended biological activity (e.g., antioxidant, anti-inflammatory, or other specific effects) compared to standard herbal extracts.

Other Considerations:(22,23)

1. Stability Under Processing and Formulation:

Evaluate the stability of phytosomes during formulation into various dosage forms (capsules, tablets, creams) and processing steps to ensure their integrity is maintained.

2. Toxicity and Safety Studies:

Conduct toxicity assessments to ensure the safety profile of phytosomes, examining acute and chronic toxicity, as well as any potential adverse effects.

Evaluating phytosomes requires a combination of analytical techniques, in vitro experiments, and in vivo studies to comprehensively understand their physical, chemical, and biological properties, ensuring their effectiveness and safety for therapeutic applications.

14.CHARACTERIZATION OF PHYTOSOMES BASED ON VARIOUS ANALYTICAL METHODS

The characterization of phytosomes involves various techniques aimed at understanding their composition, structure, and properties. Here are some common techniques used in the characterization of phytosomes:

1. Morphological Analysis:

Microscopy: Optical microscopy or electron microscopy helps visualize the morphology and size of phytosomes. Electron microscopy, including scanning electron microscopy (SEM) or transmission electron microscopy (TEM), provides high resolution images for detailed structural analysis.

2. Particle Size Analysis:

Dynamic Light Scattering (DLS): DLS measures the particle size distribution of phytosomes in a solution. It provides information about the average particle size and size distribution, which is crucial for understanding their behavior and efficacy.

3. Structural Characterization:

Xray Diffraction (XRD): XRD helps in determining the crystalline structure of phytosomes. It provides information about the arrangement and crystallinity of components within the phytosome formulation.

Fourier Transform Infrared Spectroscopy (FTIR): FTIR identifies chemical bonds and functional groups present in phytosomes. It helps confirm the presence of phospholipids and herbal compounds and assesses any interactions between them.

4. Thermal Analysis:

Differential Scanning Calorimetry (DSC): DSC measures heat flow associated with phase transitions and thermal behavior of phytosomes. It helps in understanding the melting points, transitions, and stability of the formulation components.

5. Encapsulation Efficiency and Drug Release:

High-Performance Liquid Chromatography (HPLC): HPLC is used to determine the encapsulation efficiency of herbal compounds within phytosomes. It also helps in studying drug release kinetics from the phytosomal formulation over time.

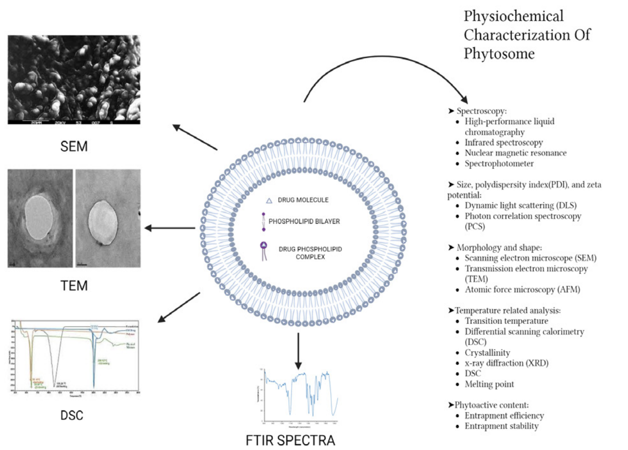
6. Stability Studies:

Accelerated Stability Studies: These studies involve exposing phytosomes to different stress conditions like temperature, humidity, and light to assess their stability over time. Changes in particle size, composition, and efficacy are monitored.

7. Zeta Potential Measurement:

Electrophoretic Light Scattering (ELS): ELS measures the zeta potential of phytosomes, which indicates their surface charge. This information is essential for understanding stability, dispersion, and interaction with biological systems.

These characterization techniques collectively provide comprehensive information about the physical, chemical, and structural properties of phytosomes. They are crucial in optimizing formulation parameters, assessing stability, understanding release kinetics, and ensuring the effectiveness of phytosomal formulations in various applications(34).



Physiochemical characterization of phytosomes is depicted in Fig. 3.

15.CONCLUSION AND FUTURE ASPECTS

Conclusion:

In summary, the review underscores the immense potential of phytosomes in revolutionizing drug delivery. By delving into their preparation methods, pharmacological benefits, and physicochemical properties, it's clear that phytosomes offer a promising solution for enhancing bioavailability, stability, and targeted delivery of phytoconstituents. The wide spectrum of therapeutic effects they demonstrate, ranging from anti-inflammatory to anticancer properties, highlights their versatility and applicability across various medical domains. Furthermore, understanding the structural and functional characteristics through physicochemical profiling provides crucial insights into their efficacy.

Future Directions:

Looking ahead, there is a need for continued refinement and optimization of phytosome preparation techniques to ensure scalability, reproducibility, and cost-effectiveness. Extensive preclinical and clinical studies are essential for validating their efficacy and safety across diverse disease conditions and patient populations. Exploring innovative approaches like combination therapy and targeted delivery systems could unlock novel therapeutic avenues for phytosomes. Additionally, advancements in analytical methods will deepen our understanding of their interactions with biological systems, facilitating the development of tailored formulations. Collaboration among researchers, pharmaceutical firms, and regulatory bodies will be pivotal in translating phytosome research from the lab to clinical settings, ultimately benefiting patients through the development of effective and patient-centric drug delivery systems.

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