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International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

REVIEW ARTICLE ON PHYTOSOME

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ABSTRACT :

Phytosomes, a phospholipid-based self-assemble delivery system, are a popular way to improve the poor oral bioavailability of polyphenolic compounds. "Some"symbolizes a covering for a structure, while "phyto" refers to plants. In most cases, one or two moles of phospholipid andpolyphenolicphytoconstituents react to form a phytosome. The ratios of 1:1 and 1:2 are both possible. Aside from protecting acid-labile herbal medications in the gastrointestinal tract, phytosomes can also be used to increase the rate and extent of lipophilic herbal ingredients' transit across lipid membranes, which explains their role as carriers. Products like Ginkgo biloba and Silybum that incorporate phytosomal drug delivery systems are readily available in the market.

KEY WORDS :

- Phospholipid
- Phytosome
- Lipid bilayer
- Hydrophilic tail
- Phytoconstituent

INTRODUCTION TO PHYTOSOMES[1]

A novel drug delivery is a new approach that utilizes new technologies, innovative ideas, and methodologies to deliver the active molecules in safe yet effective concentration to produce desired pharmacological action. Phytosomes are one of the novel drug delivery system containing hydrophilic bioactive phyto-constituents of herbs surrounded and bounded by phospholipids.

By forming these complex structures, phytosomes enhance the solubility and stability of the plant extracts, leading to improved absorption and bioavailability when consumed orally or applied topically. This makes them a popular choice in the formulation of herbal supplements and topical products.

The term “phyto” means plant while “some” means cell like.They are little cell like structure in which the herbal drug is loaded in vesicles, which is available in nano form. They provide an envelope, like coating around the active constituent of drug and due to this the chief constituent of herbal extract remains safe from degradation by digestive secretion and bacteria.

Phytosome is effectively able to absorb from a water loving environment into lipid loving environment of the cell membrane and finally reaching to blood circulation . It can be used in the treatment of various fatal diseases without denaturing the active phyto-compounds and enhanced bioavailability.

The first phytosomes were developed by Indena company (Milan, Italy) in the late 1980

STRUCTURE OF PHYTOSOMES[2]

The strucural comoponents are:

A.*Plant Extracts*: These are the active ingredients derived from plants. They can be botanical extracts, herbal extracts, or other natural substances known for their medicinal properties.

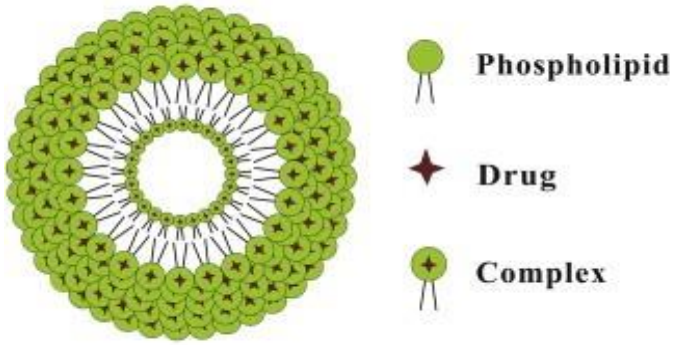
B.Phospholipids: Phospholipids are a class of lipids that are essential components of cell membranes. In phytosomes, phospholipids such as phosphatidylcholine are used to encapsulate the plant extracts. These phospholipids have a hydrophilic (water-attracting) head and a hydrophobic (water-repelling) tail, allowing them to form a protective layer around the plant extract.

Hydrophilic head: This part of the phospholipid molecule is attracted to water molecules, making it water-soluble.

Hydrophobic tail: This part of the phospholipid molecule repels water and is attracted to fat molecules, making it lipid-soluble.

Binding: The hydrophilic heads of the phospholipids bind to the hydrophilic compounds of the plant extract, while the hydrophobic tails surround the lipophilic (fat-soluble) components of the extract.

Microstructure: The resulting microstructure of a phytosome is a complex, spherical structure where the plant extract is enclosed within a phospholipid bilayer.



ADVANTAGES[3]

Phospholipid, i.e., phosphatidylcholine one of the valuable components of phytosome has a bifunctional activity by acting as a vehicle as well as health benefit such as hepatoprotective activity.
The absorption of hydrophilic active constituents is increased which also increase the efficacy.As the efficacy increases the dosage requirement is also reduced.
Have better stability.
Have the ability to permeate through skin due to its lipid layer around the phytoconstituent and thus enhance the effectiveness.
By increasing the solubility of bile to herbal origin phytoconstituents, phytosomes enhance the liver targeting
They increase the solubility of bile to herbal constituents
Time period of action is increased

DISADVANTAGES

- when administered orally or topically,they limit their bioavailability
- phytoconstituents is quickly eliminated from phytosomes
- stability problem

PROPERTIES OF PHYTOSOMES[4]

PHYSIOCHEMICAL PROPERTIES

- Phytosomes are the complex between phytoconstituents and natural phospholipid, and the complex is obtained by reacting an appropriate amount of phospholipid and chief constituents in particular solvent.
- The interaction between phospholipid and substrate is due to the development of hydrogen bonds between the polar head of phospholipid and the polar functionalities of the chief constituents.
- On treatment with hydrophilic environment phytosome shows a cell like structure like liposomes, but in a liposome, the chief constituent interacts within the internal pocket while in phytosome the chief active constituents are enveloped the polar head of phospholipid and becoming an integral part of the membrane.

BIOLOGICAL PROPERTIES

- Phytosome increases the active absorption of active ingredients
- Increase the systemically bioavailability when administered orally.
- Having better efficacy as per compare to conventional herbal extract.
- Better pharmacokinetic as compare to simple herbal drugs

PREFORMULATION STUDIES[5]

Preformulation studies of phytosomes involve a systematic examination of the physical,chemical,and mechanical properties of phytosomal formulation before their development and manufacturing. Phytosomes are little cell like structure in which the herbal drug is loaded in vesicles, which is available in nano form. They provide an envelope, like coating around the active constituent of drug .Preformulation studies are critical for understanding and optimizing these formulations.

Preformulation studies are typically conducted in the early stages of product development to guide formulation optimization, identifying potential issues, and enhance the safety, efficacy,and quality of phytosomal formulation. These studies are important for a wide range of applications, including pharmaceutical, cosmetics,and even food products, where controlled release and stability are essential factors

Objectives of preformulation studies

- To generate useful data needed in developing stable and safe dosage forms that can be manufactured on a commercial scale
- To provide in-depth knowledge and understanding of the physical characteristics of a candidate drug molecule prior to dosage form development

Goals of preformulation studies

- To determination of all the properties of drug and the best suitable dosage form for the drug molecule
- To formulate new dosage form of already existing drug
- To formulate an elegant,safe,efficacious dosage form with good bioavailability.

CHARACTERIZATION AND EVALUATION OF PHYTOSOMES[6]

The behavior of phytosomes in both physical and biological systems is governed by factors such as the physical size, membrane permeability, percentage of entrapped solutes, and chemical composition as well as the quantity and purity of the starting materials. Therefore, phytosomes can be characterized in terms of their physical attributes i.e. shape, size, distribution, percentage drug captured, entrapped volume, percentage of drug released and chemical composition.

Different characterization techniques used in phytosomes are:

visualization

Visualization of phytosomes can be achieved using transmission electron microscopy (TEM) and by scanning electron microscopy (SEM)

Vesicle size and Zeta potential

The particle size and zeta potential can be determined by dynamic light scattering (DLS) using a computerized inspection system and photon correlation spectroscopy

Entrapment efficiency

The entrapment efficiency of a drug by phytosomes can be measured by the ultracentrifugation technique.

Transition temperature

The transition temperature of the vesicular lipid systems can be determined by differential scanning calorimetry.

Surface tension activity measurement

The surface tension activity of the drug in aqueous solution can be measured by the ring method in a Du Nouy ring tensiometer.

Vesicle stability

The stability of vesicles can be determined by assessing the size and structure of the vesicles overtime. The mean size is measured by DLS and structural changes are monitored by TEM

Drug content

The amount of drug can be quantified by a modified high performance liquid chromatographic method or by a suitable spectroscopic method.

Spectroscopic evaluations

To confirm the formation of a complex or to study the reciprocal interaction between the phytoconstituent and the phospholipids, spectroscopic methods are used .

Fourier tranform infrared spectroscopy analysis

The formation of the complex can be also be confirmed by IR spectroscopy by comparing the spectrum of the complex with the spectrum of the individual components and their mechanical mixtures. FTIR spectroscopy is also a useful tool for the control of the stability of phytosomes when micro-dispersed in water or when incorporated in very simple cosmetic gels. From a practical point of view, the stability can be confirmed by comparing the spectrum of the complex in solid form (phytosomes) with the spectrum of its micro-dispersion in water after lyophilization, at different times. In the case of simple formulations, it is necessary to subtract the spectrum of the excipients (blank) from the spectrum of the cosmetic form at different times, comparing the remaining spectrum of the complex itself.

In vitro and in vivo evaluations

In vitro evaluation of phytosomes involves experiments conducted outside a living organism, typically in a laboratory setting. Here are some key aspects of in vitro evaluation for phytosomes:
Solubility Studies: Determining the solubility of the active compounds in the phytosome formulation can indicate how well they might dissolve in the digestive system and potentially be absorbed.
Permeability Studies: Assessing the ability of the phytosomes to cross biological membranes (like intestinal cells) can predict their absorption potential.
Stability Studies: Examining how stable the phytosomes are under various conditions (pH, temperature, etc.) helps understand their shelf life and effectiveness over time.
Cell Culture Models: Using cell cultures (such as Caco-2 cells, which mimic intestinal epithelial cells) to study absorption and metabolic interactions can provide insights into how phytosomes interact with the body at a cellular level.
In vivo evaluation, on the other hand, involves studies conducted within living organisms to observe real physiological effects. Key aspects of in vivo evaluation for phytosomes include:
Bioavailability Studies: Measuring the concentration of active compounds in blood plasma or tissues after ingestion can determine how much of the phytosome formulation actually reaches systemic circulation.
Pharmacokinetic Studies: Tracking the absorption, distribution, metabolism, and excretion (ADME) of phytosomes provides insights into their behavior in the body.

Efficacy Studies: Assessing the biological effects of phytosomes in animal models or humans to determine if they achieve the desired therapeutic outcomes.
Safety and Toxicity Studies: Evaluating any adverse effects or toxicity associated with phytosome administration is crucial for ensuring their safety for human use.

In summary, combining both in vitro and in vivo evaluations provides a comprehensive understanding of phytosomes, including their absorption mechanisms, biological effects, and safety profile. These evaluations are essential for optimizing phytosome formulations and establishing their efficacy for therapeutic use.

PREPARATION OF PHYTOSOMES[7]

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 standardised extract of the herb's active components to phospholipids like Phosphatidyl choline either phosphatidyl ethanolamine or phosphatidyl serine via a polar end. A phospholipid that is either natural or synthetic and 3-2 moles of an herbal extract are combined to form a 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 non-solvents like Lithium-based hydrocarbons, lyophilization, or by spraying. These two moieties are arranged in a ratio between 0.5 and 2.0 moles during the complicated development of phytosomes. Phospholipids and flavonoids should be used in a 1:1 ratio.

Solvent evaporation technique

Particular quantity of drug polymer and phospolipid (drug and soya lecithin) can be taken into spherical bottom flask and reflux with specific solvent at a temperature 50-60 °C. for 2 hrs.The mixture may be concentrated to 5-10ml to get the precipitate which can be filtered and collected.The dried precipitate phytosome loaded can placed in amber coloured glass bottle and stored in room temperature.

Super-critical fluids being used (SCF)

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

Lyophilization process

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

Gas anti-solvent method

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

Enhancing dispersion using supercritical fluids

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

Anti-solvent precipitation technique

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

Rotary evaporation technique

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

Ether-injection technique

In this procedure, an organic solvent is used to dissolve the drug's lipid complex. The development of vesicles is then triggered by the mixture being gently infused into an aqueous agent that has been heated. Focus determines the condition of amphiphiles. At low concentrations, amphiphiles work as monomers, but as the concentration goes up, different structures can form, such as spherical, cylinder, disc, cubic, and hexagonal structures.

Cosolvent

An organic solvent, such as methanol, is used to dissolve the extract and PC. An hour of swirling with a magnetic stirrer was used to complete the mixing.

Salting out

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

Thin layer hydration

Cholesterol was dissolved in dichloromethane, whereas fraction, PC, and were all dissolved in methanol. Once the solvent has entirely vaporised, with a thin dry layer has developed on the bottom of the container, the mixture is gently evaporated at 45°C using a rotary evaporator. The resulting thin film of lipid is then pumped combined with nitrogen gas kept prior to by one night at room temperature receiving hydration treatment. On a rotary

evaporator set at 45°C, aquabidest was used to hydrate the film layer. Using sonification and a homogenizer, the technique to calculate particle size was also optimised.

APPLICATIONS[8] :

1. **Silymarin phytosome:**

- Most of the phytosomes are focused to silybum marianbum which contains liver protective flavonoids.
- The fruit of milk thistle plant (s.marianum,family steraceae) contain flavonoids known for hepato protective effect
- Silymarin has been showqn to have positive effect in treating liver diseases of various kinds, including hepatitis cirrhosis, fatty infiltation of the liver and inflammation of the bile duct.

2. **Phytosome of grape seed**

- Grapeseed phytosome is composed of oligomeric polyphenols of varying molecular size complexed with phospholipids.
- The main properties of procyanidin flavonoids of grape seed are an in total antioxidant capacity ans stimulation of physiological defenses of plasma

3. **Phytosome of Green tea**

- Green tea leaves is characterized by presence of polyphenolic compound epigallocatechin 3-O-gallate as the key component
- These component are potent modulators of several biochemical process linked to the breakdown of homeostasis in major chronic degenerative disease such as antioxidant , anticarcinogenic, antimutaenic, hypocholesterolemic , cardioprotective effects.

4. **4.Phytosomes of curcumin**

- Maiti et al. developed the phytosomes of curcumin (flavonoid from tudrmeric, Curcuma longa linn) and naringenin (flavonoid from grape, Vitis vinifera).
- Phytosome of naringenin produced better antioxidant activity than the free compound with a prolonged duration of action

COMMERCIALLY AVAILABLE PHYTOSOMAL PRODUCT[9]

SL NO	TRADE NAME	CHIEF CONSTITUENT	SOURCE	DOSE	USE
1	Centella phytosomes	triterpine	Centella asiatica		Cicatrizing,trophodermic
2	Ginselect phytosomes	Ginsenosides	Gingko biloba	120mg	Adaptogenic
3	Greenselect phytosomes	Polyphenols	Camellia sinensis		Free-radicle scavenging activity
4	Leuoselect	Polyphenols	Vitis vinifera	300mg	Antioxidant
5	Silymarin	Silymarin	Silybum marianum		Anti hepatotoxic
6	Oleaselect phytosome	Polyphenols of olive oil	Olea europaea		Anti inflammatory Antioxidant
7	meriva	Curcuminoids	Curcuma longa	200-300mg	Anti-inflammatory
8	visnadine	Visnadine	Ammi visnaga		Circulation improver
9	Bilberry	Triterpene	Vaccinium myritillus		Potent antioxidant

CONCLUSION :

On phytosome, a thorough investigation was done.These are tiny, cell-like structures that hold the herbal medication in vesicles that are sold in nanoscale.In this work, we describe the benefits, drawbacks, and structure of the phytosome. Pre-formulation inquiry was also looked at, covering commercially accessible goods as well as their characterization and evaluation, preparation method, and application. Bioavailability can be significantly improved

With the help of physicians and other researchers, the potential of phytophospholipid complexes has a promising future for therapeutic applications.

REFERENCE :

1. kumar A, kumarB , kumar S S,Barinder kaur ,singh S. A review on phytosomes: Novel approaches for herbal phytochemicalsVol 10(Issue 10); 2017:41

2. 2.Jyotsana dwivedi at.el Progressive Journey of Phytosomes: Preparation, Characterization, Patents, Clinical trials & Commercial products Vol (issue1);2023:1687

3. 3.Vishal Gaurav*, Shivangi Paliwal, Arpita Singh, Swarnima Pandey, Mohd. Aqil Siddhiqui. International Journal of Research in Engineering and Science (IJRES) Phytosomes: Preparation, Evaluation and Application,Vol 9(issue2);2021:35-39

4. kumar A, kumarB , kumar S S,Barinder kaur ,singh S. A review on phytosomes: Novel approaches for herbal phytochemicalsVol 10(Issue 10); 2017:41

5. 5.Jagruti Patela,, Rakesh Patelb , Kapil Khambholjab , Nirav Patel.An overview of phytosomes as an advanced herbal drug delivery system.Asian Journal of Pharmaceutical Sciences Vol 4 (issue6);2009: 363-371

6. 6 Mei LuPhyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents.Asian journal of pharmaceutical science VOL 14(ISSUE 3);2019:265-274

7. 7.Jyotsana dwivedi at.el Progressive Journey of Phytosomes: Preparation, Characterization, Patents, Clinical trials & Commercial products Vol (issue1);2023:1687

8. 8.Jyotsana dwivedi at.el Progressive Journey of Phytosomes: Preparation, Characterization, Patents, Clinical trials & Commercial products Vol (issue1);2023:1687

9. kumar A, kumarB , kumar S S,Barinder kaur ,singh S. A review on phytosomes: Novel approaches for herbal phytochemicalsVol 10(Issue 10); 2017:41