A REVIEW ON "PHYTOSOMES-NOVEL TREND IN HERBAL DRUG DELVIERY"

LALITHA CHEMBETI*[1],N.HARIKRISHNAN [2]

[1]Research scholor,Dept of pharmaceutical chemistry,Narayana pharmacy college,chintha reddy palem,Nellore-524004,India.

[2] Dept of pharmaceutical analysis ,Faculty of pharmacy, Dr.M.G.R.Educational and research institute ,Deemed to be university,velappanchavadi,Chennai,Tamilnadu-600077,India

Corresponding author

ABSTRACT

Plant-based medications have been used to treat people for millions and billions of years, despite the fact that their therapeutic efficacy has been questioned due to factors such as limited lipid solubility, poor stability, large moiety size, and superfluous metabolism in the gut. Phytosome technology has emerged as a dedicated and promising method to novel medicine delivery that enhances the potency, purity, and targetability of active plant components while preserving or enhancing efficacy. The researchers are confident in their capacity to deliver plant-derived secondary metabolites to their systemic targets using new herbal formulation techniques. This research focuses on the distinct properties of phytophospholipid complexes, as well as their use in the development of novel natural drug delivery systems. This research goes into depth on the various methods utilised in phytosomal synthesis and characterization, as well as the advantages that phytosomal preparations offer over standard herbal extracts. The prospective of the phytosome technique, as a novel medicine regimen, may open up new possibilities and an infinite frontier in terms of study and development.

Keywords: Phytosomes, Herbal, Drug entrapment, Phospholipid

I.INTRODUCTION

The majority of biologically active components in plants are polar or water soluble, however owing to difficulties in absorption, the use of these types of chemicals is restricted, resulting in a reduction in bioavailability. Herbal products must have adequate equilibrium between hydrophilic (for absorption into gastrointestinal tract fluid) and lipophilic (for cross-lipid biomembrane balancing) properties in order to optimise bioavailability. Plant preparations are frequently utilised in both traditional and modern health systems, and they have a long history of success. Various pharmacological investigations have been carried out using several plant extracts and their components during the traditional period in order to determine their medicinal potential [Khanzode et al., 2020]. Significant progress has been achieved in the development of new drug delivery systems (NDDS) for a variety of plant extracts and active components over the course of the last year. The use of novel drug delivery methods, such as targeted drug delivery, which delivers the active ingredient directly to the site of action, and delivery systems that provide targeted and sustained release of the medication,

allowing for greater pharmacological impact at lower doses are being explored. The development of herbal medicine began much earlier in order to heal human ailments with fewer negative effects and has continued to this day. A number of the most important constituents of herbal medicine are easily soluble in water (glycosides and flavonoids); however, the potency of these constituents is limited because they may be partially soluble or hydrophobic in nature, and therefore have less therapeutic efficacy when applied topically [Ghanbarzadeh et al., 2016]. There have been a number of efforts made to improve the bioavailability of such drugs by designing them to target drug delivery systems like as phytosomes and liposomes, which are both excellent choices. It is possible that the application of these approaches throughout the formulation creation process would result in improved bioavailability of herbal medications in comparison to standard herbal extracts.

Phytosomes are herbal drugs that have been packaged into vesicles and are accessible in the Nano form. As a result, the active ingredient of the medication is protected from destruction by digestive secretion and bacteria because the phytosomes serve as an envelope-like covering around the active constituent of the drug [Kalita et al., 2013]. After being absorbed from a water-loving environment, phytosomes can be transported to the cell membrane, where they can then be transported to the blood circulation. The current review emphasizes the future potential and developing technologies in the realm of NDDS for the benefit of herbal and traditional remedies derived from plant sources. The terms "Phyto" and "some" refer to plants and cell-like structures, respectively. Herbosomes are another name for this substance. As a result of this innovative patented process, highly standardised plant extracts or water-soluble phytoconstituents are complexed with phospholipids to form lipid compatible molecular complexes, which significantly improve absorption and bioavailability [Jadhav et al., 2014]. There are several types of phospholipids that can be used, but phosphatidylcholine is the most commonly used because of its certain therapeutic value in the treatment of liver diseases such as alcoholic steatosis, drug-induced liver damage, and hepatitis. Phosphatidylserine, phosphatidylethanolamine, and phosphatidylinositol are also used. Native digestion aids and transporters for both fat-soluble and water-soluble nutrients are also made use of by phospholipids in their natural form. Enterohepatic cell membranes and the stratum corneum layer of the skin are both easily traversed by phytosomes, which have a lipophilic route of their own [Amith Kumar et al., 2016].

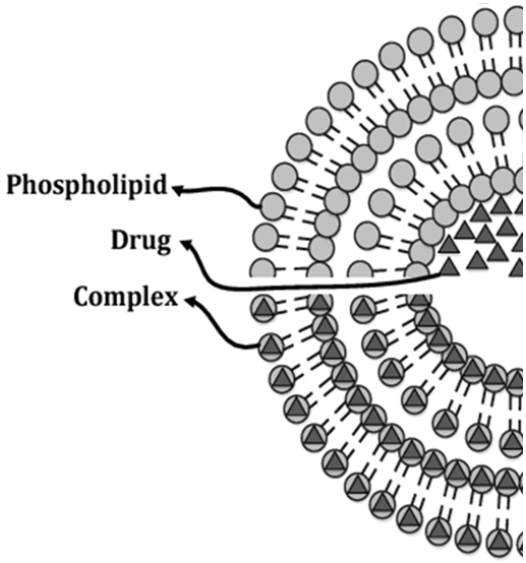

Figure 1: Structure of a phytosome

II.DESIGN AND PREPARATION OF PHYTOSOMES

Phytosome complexes are often produced using unconventional ways. [Karimi et al., 2015] Modernistic herbal complexes are produced by the interaction of an equimolar combination of natural or synthetic phospholipids with active components or herbal extract in aprotic organic solvents. Supercritical fluids, which include the gas solvent technique, the compressed solvent procedure, and the supercritical solvent method, are among the new approaches for phospholipid complexion being explored. The following are examples of different techniques of preparation in a conventional way

2.1 Ether injection

The interaction of lipids dissolved in an organic solvent with herbal extracts in an aqueous phase is the basis for this method. Phospholipids that have been solubilized in diethyl ether are slowly injected drop by drop into an aqueous solution containing the phyto-constituents that will be encapsulated, resulting in a gel-like structure. It leads in the creation of cellular vesicles, which are then removed by solvent removal, resulting in the formation of complexes [Khan et al., 2013]. The structure of phytosomes is dependent on the concentration; when the concentration is low, amphiphiles in mono state are produced; however, when the concentration is high, a variety of structures with different shapes, such as round, cylindrical, disc, and cubic or hexagonal vesicles, can be formed.

2.2 Rotary evaporation

Herbal extract and phospholipids were combined in 30 mL of water miscible organic solvent such as acetone in a round bottom glass container, and the mixture was left to stand for 2 hours at a temperature less than 50°C with stirring in the rotational evaporator. Antisolvents such as n-hexane can be applied to a thin film that has been formed after continuous stirring with a stirrer [Singh et al., 2014] has been produced. The precipitate of phytosomes that has

been produced can be kept in an amber-colored glass container at a regulated temperature and humidity under prescribed conditions.

2.3 Precipitation of Anti-solvent

A particular amount of herbal extract and phospholipids is refluxed with 20 ml of organic solvents such as acetone for 2-3 hours under specific experimental settings below 50°C. Concentration of the reaction mixture is reduced to a minimum volume of up to 10 mL, and then precipitates are formed by adding low-polarity solvents, such as n-hexane, while stirring the reaction mixture. Desiccators are used to hold the filtered precipitates. The dried precipitates are crushed, and the powdered complex is kept at room temperature in a dark amber tinted glass container [Rathore et al., 2015].

III ADVANTAGES OF PHYTOSOMES

3.1 Lack of toxicity and ease of addition

Because phosphotidylcholine, which is utilised in complexation, is a vital component of the cell membrane, the additives used in the phytosome formulation have been authorised, assuring that the idea is safe and secure. Because phosphotidylcholine alone contains hepatoprotective properties, it has been found to have a synergistic impact when complexed with hepatoprotective medications. When it comes to defending the skin against exogenous or endogenous toxins under harsh environmental circumstances, synergistic benefits are readily apparent [Das et al., 2014]. Because of improved absorption of the active component, the Phytosome idea ensures longer duration of action at low doses with a reduced risk profile, compared to other approaches.

3.2 Cost-effectivity

This technique allows for the supply of phytoconstituents at a reasonable cost. The cellular vesicular system is subservient and readily available for future growth at any point in time. It is quite simple to manufacture phytosomes since no difficult technological investment is necessary, and no complex practical speculation is required in the process of manufacturing phytosomes.

3.3 Biodegradability

Due to the fact that phosphatidylcholine is used in phytosome formulation as a carrier transporter and is an integral component of the cell membrane, there is no difficulty in assembling the drug frame during formulation manufacture [Salazar et al., 2014].

3.4 Bioavailability

Improved absorption of hydrophilic herbal extracts from the intestinal lumen is made possible by the presence of a phytophospholipid complex. When secondary metabolites are complexed with the lipophilic head of phospholipids, there is a significant increase in the bioavailability of these compounds [Agarwal et al., 2014].

3.5 Entrapment efficiency

The efficiency of drug entrapment is extremely high, and no hazardous metabolites are generated as a result. On top of that, when the biomarker bonds with soybean lipids, it creates nanocellular vesicles, from which medication release may be predicted in advance [Agarwal et al., 2014].

IV EVALUATION OF PHYTOSOMES

The prepared phytosomes are evaluated using various techniques [Rosa direto et al., 2019] as mentioned below

4.1 Fourier transform infrared spectroscopy (FTIR)

The FTIR analysis was performed in order to determine the structure and chemical stability of the medication, phospholipid. To obtain pellets at 600 kg/cm2 pressure, the phytosomal medicine will be crushed with potassium bromide to obtain a powder. Approximately 4000-400 cm-1 of space will be scanned during the scan.

4.2 Differential Scanning Calorimetry (DSC)

An aluminium cell containing a physical mixture of drug extract and Phosphatidyl choline, as well as a drug phospholipid complex, was placed in the nitrogen environment and heated at a rate of 50-250 Celsius per minute from 0 to 400 Celsius to estimate the thermal degradation of the drug due to interaction with the phospholipids.

4.3 Scanning electron microscopy (SEM)

The particle's size and appearance were determined using a scanning electron microscope (SEM). In an ion sputter, a dry sample was placed on an electron microscope brass stub that had been coated with gold. At 100, a random scan of the complex is performed.

4.4 Transition electron microscopy (TEM)

When magnified to 1000 times, the size of phytosomal vesicles was determined using transmission electron microscopy (TEM).

4.5 Size analysis and zeta potential

To determine the particle size and zeta size of phytosomal complexes, the Malvern Zetasizer is employed. This particle size and zeta sizer characterization is carried out using an Argon laser.

4.6 Drug entrapment efficiency

In order to separate the phytosome from the untrapped drug, the complex of drug phytosomes was centrifuged at 10000 rpm for 90 minutes at 4°C. A technique known as UV spectroscopy can be used to determine the concentration of free drug in a sample.

V DESIGN ASPECTS OF PHYTOSOMES

The design of phytosomal formulations is influenced by the mode of administration of the substance, which can be either topical or oral. Because of advancements in pharmaceutical sciences, phytosomes are finding use in the formulation of different dosage forms, including medicines, nutraceuticals, and cosmeceuticals, among other things. Indena, Thorne research, Jamieson natural resources, Natural factors, and Nature herb are only a few of the pharmaceutical firms that are involved in the manufacturing of phytosome products.

5.1 Suitability of Dosage form

Phytosome complexes can be formed into oral and topical dose forms; however, the most appropriate dosage form for drug release can be determined by evaluating the efficacy and efficiency of biomarker chemicals in each formulation. It is crucial to consider the solubility of a complex when determining the stability of a complex and the choice of solvent may be made based on the phytoconstituents, which can be either hydrophilic or lipophilic. Suspension produced by distributing phytosomes in biocompatible edible or semi-synthetic oily carriers has been shown to be effective. The formulation of a phytosomal capsule containing herbal extract and a lipid complex can be done manually or by using an automatic filling process that does not compress the complex. The phytosome complex can be chemically integrated into an emulsion or ointment base that has been produced. After optimising the solubility of the components and other pharmacokinetic characteristics, different topical phytosomal formulations such as solution, emulsion, and lotion are recommended for use on the skin.

5.2 Suitability of herbal extract

Because phytosomes are formed by chemical contact between hydrophilic herbals and lipophillic phospholipid moieties, aqueous extraction can be used to provide the best bonding possible between the two groups of molecules. Because terpenoids, tannins, and flavonoids form the strongest possible interaction with phospholipids, herbal extracts may be phytochemically tested for these compounds. Furthermore, by maximising the intrinsic characteristics of phytoconstituents, it is possible to specify the drug release from a phytosomal complex in greater detail. If you are picking phytoconstituents, it is important to examine their fundamental intrinsic features such as hydrophilicity, lipophillicity, cell permeability, biodegradability and release characteristics, as well as the size of the phytosomal complex.

5.3 Suitability of additives

The additives used in phytosomal formulations can be chosen based on the dosage form and the mechanism of drug administration that will be employed. In the preparation of phytosomes suitable phospholipids, solvents, dyes, and buffering agents are employed.

VI PHYTOSOMES IN MARKET

Numerous plant products have had their compositions, biological activities, and health-promoting properties determined during the past century by the fields of phytochemical and phytopharmacological science and research. Polar or water soluble molecules make up the majority of the physiologically active components of plants. However, water-soluble phytoconstituents (such as flavonoids, tannins, terpenoids, and so on) are poorly absorbed, either because of their large molecular size, which prevents passive diffusion from taking place, or because of their poor lipid solubility, which severely limits their ability to pass across lipid-rich biological membranes, resulting in poor bioavailability. Various herbal extracts used in phytosomes as listed below.

Table 1: Currently marketed phytosomes

Plant name	Commercial formulation	Phytodrug	Indication
Aesculus hippocastanum	Phytosome	Saponins	Vasoactive
Ammi visnaga	Visnadex	Visnadine	Improving microcirculation
Camellia sinensis	Epigallocatechin	Green tea	Antioxidant
Centella asiatica	Centella	Asiatic acid	Skin disorders, Hair fall prevention
Citrus aurantium	Naringenin	Naringenin	Antioxidant
Crataegus Mexicana	Vitexin-2'-O-rhamonoside	Crataegus	Antioxidant
Crategus oxyacanthoides	Hyperin	Hawthron	Cardioprotective
Cucurbita pepo	Tocopherols, Carotenoids	Cucurbita	Anti-inflammatory, BPH
Curcuma longa	Curcumin	Curcuvet®	Anti-inflammatory, Osteoarthritis
Echniacea angustifolia	Echinacosides	Echniacea	Immunomodulatory
Fraxinus ornus	Esculoside	Esculoside	Vasoactive
Gingko biloba	Ginkgolides	Gingkoselect	Cognition enhancer
Glycine max	Genistein	Soyselect	Antiangiogenic
Glycyrrhiza glabra	Glycyrrhetinic acid	Glycyrrhetinic acid	Anti-inflammatory
Melilotus officinalis	Melilotoside	Lymphaselect	Anti-inflammatory
Olea europaea	Verbascoside	Oleaselect	Antioxidant

Panax ginseng	Ginsenosides	Ginseng	Immunomodulatory
Pinus maritime	Procyanidins	Pycnogenol	Antiwrinkle
Polygonum cuspidatum	Resveratrol	Rexatrol	Antioxidant
Radix puerariae	Puerarin	Puerarin	Cardiovascular
Santalum album	Ximenynic acid	Ximilene	Improving microcirculation
Serenoa repens	Fatty acid	Sabalselect	Beningn prostate hyperplasia
Silybium maranium	Silybin	Siliphos	Hepatoprotective
Syzygium cumini	Tannins	Madeglucyl	Antihyperglycemic
Terminalia sericea	Sericosides	Sericoside	Skin improvement
Vaccinium angustifolium	Anthocyanoside	VitaBlue	Antioxidant
Vaccinum myrtillus	Anthocyanosides	Mirtoselect	Antioxidant
Vitis vinifera	Resveratrol	Biovin	Cardioprotective
Zanthoxylum bungeanum	Hydroxy-a-sanshool	Zanthalene	Anti-reddening

VII CONCLUSION

A new approach for determining systemic absorption of herbal extracts, the phytophospholipid complex technique, has emerged as a cutting-edge frontier in the field. This method has proven to be successful in resolving unreasonable questions about plant-based medicines. Aiming for specified lipid penetration at a higher concentration with prolonged and stable therapeutic levels in plasma, enables for a greater number of active biomarkers to reach the intended site of action, therefore increasing their effectiveness. The importance of comprehensive characterisation with optimization, quantitative and qualitative study of the lipid-based system, and its influence in different disease states, must be emphasised further. These new complexes, on the other hand, have the potential to be trustworthy candidates for enhanced medication dose treatment. Phytosomes has demonstrated the importance of herbals in current medication targeting techniques once again through the use of this new formulation technology.

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