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PHYTOSOMES AS A DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

The term “Phyto” means plant and “some” means cell. Additionally, it is referred to as herbosomes, a novel, patented method in which phospholipids and standardized plant extracts or water-soluble phytoconstituents combine to form lipid-compatible molecular complexes that significantly improve absorption and bioavailability. Phytosomes, a type of self-assembled delivery system based on phospholipids, are a popular way to improve the poor oral bioavailability of polyphenolic compounds. The review analyzes "Phytosome technology," a cutting-edge and innovative drug delivery method. A focus on the various therapeutic uses of phytosomes and their critical role in addressing the common issues that arise during the delivery of phytoconstituents is placed heavily. Phytosomes have been discussed for their potential uses in wound healing, transdermal administration, bioavailability, and anti-cancer. The comparative analysis of the medicinal properties of the medication in its free form and its phytosomes reveals that the complex offers several benefits over standard therapies.

KEYWORDS: Phytoconstituents, Phytosome, Bioavailability, Cancer, Transdermal delivery, Wound healing.

INTRODUCTION

The majority of plant elements that are physiologically active are polar or water soluble; nevertheless, limited absorption leads to restricted usage of these chemicals, ultimately lowering their bioavailability. Herbal products need to have the right balance between hydrophilic (for absorption into gastrointestinal tract fluid) and lipophilic (to pass lipid biomembrane balance) in order to increase bioavailability.[1]

In both conventional and modern medicine, plant remedies are commonly employed. Many plant extracts and their constituents have been the subject of numerous pharmacological investigations throughout history to determine their potential medicinal uses. The development of innovative drug delivery systems (NDDS) for different plant extracts and their active ingredients has advanced significantly in the last 12 months. A novel approach to drug administration is targeted drug delivery, which delivers the active ingredient directly to the site of action. This type of delivery system allows for both focused and prolonged drug release, resulting in a pharmacological impact at a lower dosage. Herbal therapy has advanced earlier in order to treat illnesses in people with less adverse consequences.[2] Many of the main ingredients in herbal medicine, such as glycosides and flavonoids, are readily soluble in water. Nevertheless, the effectiveness of these ingredients is limited since they may be hydrophobic or only partially soluble, which results in reduced therapeutic benefit when administered topically. Many attempts have been made to increase the medicine's bioavailability by forming it into a specific drug delivery system; liposomes and phytosomes are two viable choices. When compared to traditional herbal extracts, the formulation development process using these methodologies may result in better bioavailability of herbal medications.[3] Phytosomes are herbal medications contained in vesicles that are sold in nanoscale form. Because the phytosomes surround the drug's active ingredient with an envelope-like covering, the principal ingredient in the herbal extract is shielded from bacterial and digestive secretion destruction. A phytosome can efficiently absorb from an environment that loves water to one that loves lipids in the cell membrane before entering the bloodstream. For the benefit of traditional and herbal medicines made from plant sources, the current study emphasizes the potential applications and cutting-edge technology in the field of NDDS.[4] The words "some" and "phyto" refer to plants and cells, respectively. It is referred to as herbosomes as well. This is a novel, patented process that produces lipid-compatible molecular complexes by complexing phospholipids with standardized plant extracts or water-soluble phytoconstituents. This dramatically increases absorption and

bioavailability. Among the phospholipids used are phosphatidylcholine, phosphatidylserine, phosphatidylethanol amine, and phosphatidylinositol; however, phosphatidylcholine is most frequently utilized due to its potential therapeutic benefit in cases of hepatitis, drug-induced liver damage, alcoholic steatosis, and liver disorders. Additionally, phospholipids are used as natural digestion aids and as carriers of nutrients that are both water and fat miscible. Phytosomes are able to pass through the stratum corneum layer of epidermis and the lipophilic route of enterohepatic cell membranes with ease.[5] Standardized plant extracts are obtained as phytosomes, primarily from flavonoids. Flavonoids are selected from groups that include luteolin, luteolin glucoside, apigenin-7-glucoside, kaemferol, quercetin, quercretin-3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoxide, vitexin, diosmine, 3-rhamnoside, (+) catechin, (-) epicatechin, and ginkgonetine, isoginkgonetine, and bilobetine, among others.

STRUCTURE OF PHYTOSOMES

PC, or phosphatidylcholine, is a chemical with two functions. In particular, the hydrophilic choline head attaches itself to these substances, and the lipophilic phosphatidyl portion—which consists of the body and tail—envelops the choline-bound material to form a phyto-phospholipid complex.

- Phosphatidyl-choline - phospholipid
- Phosphatidyl moiety - lipophilic
- Choline moiety – Hydrophilic

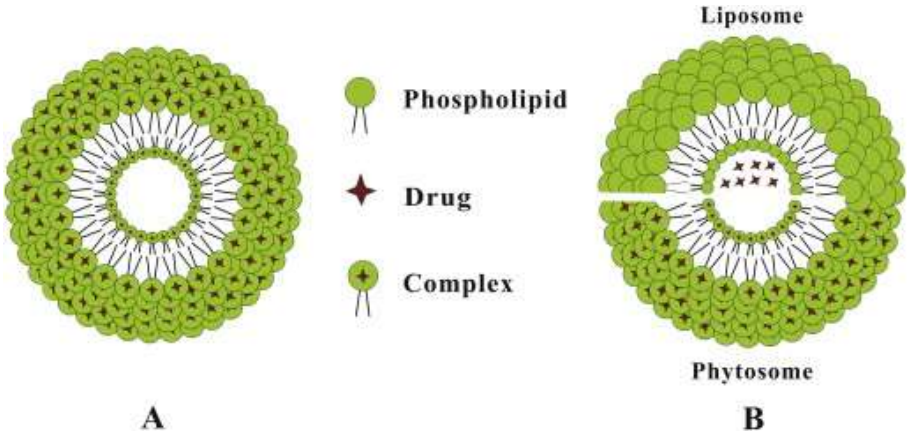

Fig.1- Structure of Phytosomes.

PROPERTIES OF PHYTOSOMES

Chemical properties

A compound of natural products and natural phospholipids, such as soy phospholipids, is called a phytosome. This kind of complex is produced when a chosen polyphenol (such as

simple flavonoids) reacts in a nonpolar solvent with stoichiometric levels of phospholipid.[6] Based on their spectroscopic and physicochemical data, it has been demonstrated that the primary phospholipid-substrate interaction results from the hydrogen bonding of the polar functional groups of the substrate with the phospholipids' polar head (phosphate and ammonium groups). They are hydrophilic compounds that are lipophilic and have a transparent melting point. They are also easily soluble in nonpolar solvents (but not in lipids), and they are moderately soluble in fats. Phytosomes take on a micellar shape and form structures like liposomes when they come into contact with water. Whereas the active principle of phytosomes is attached to the polar head of phospholipids and becomes a permanent component of the membrane, the active principle of liposomes is dissolved in an internal pocket or floats in the layer membrane.[7,8,9] Certain spectroscopic methods can show that molecules are chemically bonded to the polar head of the phospholipids.[10,11]

Biological properties

In order to show the biological activity of phytosomes, pharmacokinetic and pharmacodynamic studies have been conducted on humans and experimental animals.[12] Based on these investigations, the phytosomes' superior bioavailability over non-complexed botanical derivatives has been assessed.[7]

PREPARATION TECHNIQUES FOR PHYTOSOMES

a. The process of thin layer rotary evaporator vacuum was used to create phytosome vesicles. The 250 ml round bottom flask containing the phytosomal complex was filled with anhydrous ethanol. On top of a rotating evaporator, the flask was fixed. Around 60°C will cause the solvent to evaporate, encircling the flask in a thin circle. Phosphate buffer (7.4) is used to hydrate the film. The lipid layer separates and forms a suspension of vesicles in the phosphate buffer. We used 60% amplitude probe sonication on the phytosomal solution. Before characterizing the phytosomal suspension, it will be refrigerated for a full day.[13]

b. Phospholipid, or soy lecithin, was reacted in an equal proportion with polyphenolic extract in 5 milliliters of dichloromethane (DCM), stirring until the mixture evaporated. Following the evaporation of the DCM, 5 mL of n-hexane was added to the thin film while stirring, and it was then placed in a fume hood to ensure all of the solvent was gone. Following the whole n-hexane removal, the thin film was sonicated and hydrated to produce the required phytosomal complex.[14]

c. Weigh the polyphenolic extract and phospholipid precisely. It should be placed in a 100 ml round-bottom flask and refluxed with 30 mL of DCM at 60°C for three hours. It should then be decreased to 5–10 mL and stirred continuously to produce precipitate. Gather the precipitate and leave it overnight in a vacuum desiccator. After being dried, the precipitate is filtered through #100 mesh and placed in a container with a closed amber color.[15]

d. The reflux approach is one way to prepare phytosomes. A 100 mL round-bottom flask containing phospholipid and polyphenolic extract was refluxed in DCM for one hour at a temperature not to exceed 40°C. After evaporating the clear solution, 15 mL of n-hexane was added until a precipitate formed. After being extracted, the precipitate was put in a desiccator.[16]

e. Phospholipid and cholesterol should be precisely weighed into a round-bottom flask, dissolved in 10 mL of chloroform, and then sonicated for 10 minutes using a bath sonicator. It is possible to remove organic solvent by exposing it to a rotating evaporator at 40°C with reduced pressure. In a rotary evaporator, a thin layer that has been completely solvent-freed is hydrated with the drug's polyphenolic extract. To dissipate heat, the phospholipid mixture was sonicated in an ice bath. The prepared phytosomes were kept in a bottle with an amber hue.[17]

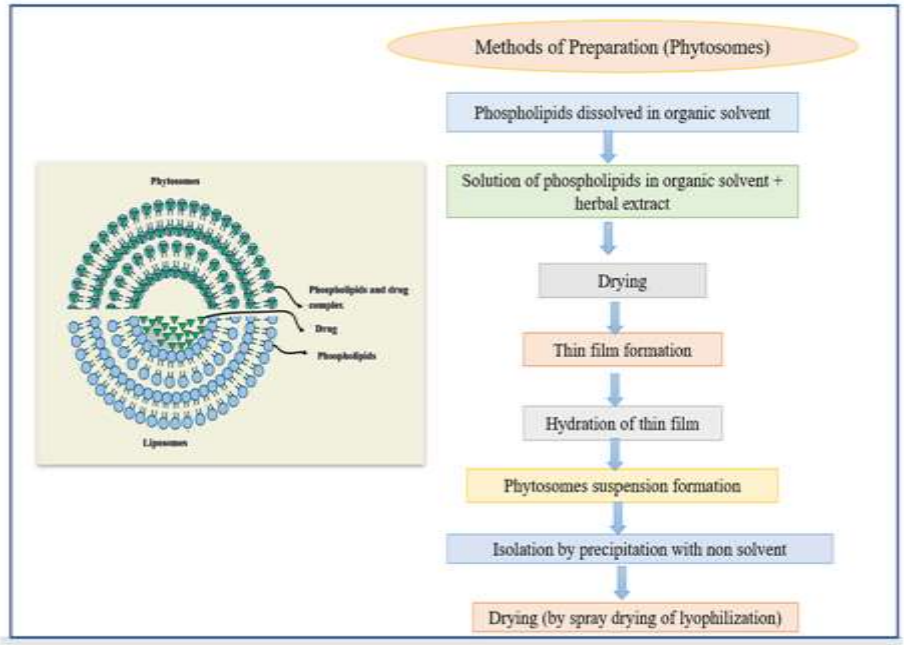

Fig.2: Preparation of Phytosome.

Merits of phytosomes over conventional dosage forms

- Plant extracts exhibit a significant increase in bioavailability as a result of their complexation with phospholipids and enhanced intestinal absorption.[18]
- They penetrate the botanical extract that isn't lipophillic, making it feasible for improved absorption from the intestinal lumen, which would not be achievable otherwise.[19] The components of phytosomes have all been approved for use in cosmetic and medicinal applications, and the formulation is safe.[20, 21]
- Because of their easy bioavailability through phytosomal enzymatic conversion, they have been utilized to provide flavonoids that protect the liver.[22] Plus, phosphatidylcholine has a synergistic effect on liver protection because it is also a hepatoprotective.
- In both normal and stressed environmental settings, this method provides cost-effective delivery of phytoconstituents and synergistic effects when used as functional cosmetics to protect the skin against exogenous or endogenous risks.[21]
- They can also be used to improve drug penetration through the skin for dermal and transdermal administration.[11]
- Because of their rich lipid profile and enhanced skin penetration, they can be widely utilized in cosmetics. Functional cosmetics can be made with phytosomal compositions.[21]
- As a transporter of skin nourishment, phosphatidylcholine is a crucial component of the cell membrane utilized in phytosome technology.
- Throughout the formulation preparation process, there is no issue with drug entrapment. Additionally, due to the drug's formation of vesicles upon conjugation with lipid, the entrapment efficiency is high and more overspecified.
- Because phytoconstituents and phosphatidylcholine molecules create chemical bonds, they provide a superior stability profile.
- The phytosomal system can be immediately commercialized because it is non-invasive, passive, and appropriate.
- The primary constituent's enhanced absorption results in a lower dose required. To obtain the intended effects, they can also be administered in lesser doses.

Demerits of Phytosomes

- When administered orally or topically they limit their bioavailability.
- Phytoconstituents is quickly eliminated from phytosome.

- Stability problem

MECHANISM OF PHYTOSOME TECHNOLOGY[23]

There are two basic reasons for the reduced absorption and bioavailability of polyphenolic components. These main ingredients consist of several ringed molecules that aren't too little to be absorbed through diffusion. The second factor is the low solubility of flavonoid molecules, or the main components of polyphenols, with lipids. These are the restrictions preventing them from being absorbed through biological membranes. The primary outcome of phytosome technology is the complexation of polyphenols with phospholipid in a 1:1 or 1:2 ratio, which forms a phytosomal complex with a lipid layer around the contents.

CHARACTERIZATION TECHNIQUES OF PHYTOSOME[24-26]

Differential scanning calorimetery

Within an aluminum cell, drug polyphenolic extract, phosphatidylcholine, a physical mixing of drug extract and phosphatidylcholine, and drug-phospholipid complex were heated to a temperature of 50–250°C/minutes between 0 and 400°C in a nitrogen atmosphere.

Scanning electron microscopy (SEM)

The particle's appearance and size were assessed using SEM. A dry sample was mounted on an ion sputter-coated brass stub for an electron microscope. scanning the complex at random speed of 100.

Transition electron microscopy (TEM)

Using a 1000 magnification, TEM was utilized to determine the size of phytosomal vesicles.

Drug entrapment and loading capacity

To separate the phytosome from the untrapped drug, the drug phytosomal complex was centrifuged for 90 minutes at 4°C at 10,000 rpm. UV spectroscopy can be used to determine the free drug concentration. You can use the following calculation to determine the percentage of drug entrapment.

$$\text{Entrapment efficiency } (\%) = \frac{\text{Weight of total drug} - \text{weight of free drug}}{\text{Weight of total drug}} \times 100$$

Fourier transform infrared spectroscopy (FTIR) analysis

The FTIR analysis will be performed to verify the phospholipid drug's chemical stability and structure. Using potassium bromide, the phytosomal medication will be crushed to produce pellets under pressure of 600 kg/cm2. The ranges that will be scanned are 4000-400 cm−1.

Size analysis and zeta potential

The Malvern Zetasizer is used to measure the phytosomal complex's particle and zeta sizes. For this particle size and zeta sizer characterization, an argon laser is employed.

In vitro and in vivo evaluations

The drug's qualities, its primary phytoconstituents enclosed by a phospholipid membrane, and the reason that specific animal model was chosen for its assessment will all play a role in both in vitro and in vivo evaluations.

APPLICATIONS[27]

1. Enhancing Bioavailability

The dosage form, low amounts available following chemical degradation, physical inactivation, and excretion through the gut wall and liver may be the causes of the phytoconstituents' limited oral bioavailability. However, improved hydrophilicity, solubility, reduced hepatic metabolism, and improved drug absorption in the systemic circulation all contribute to the phytosomes' greater bioavailability when taken orally.

2. Antioxidant properties

Quercetin was created as a physically stable phytosomal formulation with improved encapsulation efficiency and physical stability to promote intestinal absorption and prevent food from oxidizing.

3. Cancer Treatment

The primary antioxidant qualities of medicinal plants' chemical constituents—flavones, isoflavones, flavonoids, anthocyanins, coumarins, lignins, catechins, and isocatechins—contribute to their potential anticancer effects. Nevertheless, some plant-based substances cause certain negative effects and are hazardous at larger quantities. Numerous adverse effects, including myelosuppression and toxicity to the nervous system, heart, lungs, and kidneys, are associated with the currently accessible and costly traditional cancer therapies, such as radiation and chemotherapy, and they significantly lower quality of life. These

medications made from plants are entrapped with the help of the bipolar moiety, which improves their solubility, dispersibility, and permeability and makes them an effective anticancer agent.

4. Transdermal application

In terms of capillary permeability, vasal protection, and UV radiation protection, the phytosomal complex of saponins and plant extracts (Panax ginseng M.) has been shown to be more effective. Additionally useful for creating pharmaceutical formulations for dermatology and cosmetics, it has a moisturizing effect on the cutis and increases its elasticity by stimulating fibroblasts at the dermal level, which leads to an increase in the synthesis of collagen and proteoglycan. Specific applications for the aforementioned compositions include the treatment of inflammatory conditions, altered capillary fragility and permeability, and general applications in all fields where saponin activity is currently recognized. These applications include oral administration in the form of tablets, capsules, syrups, granules, and solutions (containing 1-500 mg dose of the complex).

5. Wound healing

In 2016, A. Mazumder and colleagues investigated the potential of Sinigrin, a prominent glucosinolate found in Brassicaceae plants, to promote wound healing in both isolated and phytosome-based cultures of HaCaT cells. The phytosome–sinigrin combination exhibits 100% wound healing, but the phytoconstituent alone only demonstrates 71% healing. Furthermore, on A-375 melanoma cells, sinigrin phytosomes exhibit increased anti-cancer activity.

CONCLUSION

A study on phytosomes and their potential uses in wound healing, antioxidant, anti-cancer, and other fields was attempted to be investigated. In comparison to free drugs, phytosome technology is a more significant and effective drug delivery technique. Researchers looking to investigate vesicular drug delivery systems that deliver effective drugs to their target sites without requiring metabolism will find the material gathered here rather helpful. Other neurological, cardiovascular, autoimmune, and skin-related diseases should be investigated for the potential therapeutic uses of phytosome technology. Despite the fact that the market is filled with different phytosome goods, many more phytoconstituents that have the amazing potential to heal serious illnesses have not been included into phytosome technology. More investigation can be conducted to.

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