STABILITY STUDIES OF PHYTOSOMES FOR ENHANCING BIOAVAILABILITY

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ABSTRACT

In order to do this, the neutraceutical industry employs a number of tactics when dealing with naturally produced substances that are poorly absorbed. The first one may also correspond to the medicinal chemistry approach: the goal is to generate molecules with better bioavailability through chemical derivatization of the chemical product. Numerous chemical analogues are produced by this advancement and must be properly vetted. Combining the active molecules with other substances as adjuvants to increase the absorption of the active molecules is another tactic that is being investigated. This method entails a thorough formulation study of structures that can stabilize natural chemicals and facilitate intestine absorption. Several innovative delivery systems, such as liposomes, niosomes, and phytosomes, can increase the rate of release and the ability to pass through biomembranes, thereby improving the bioavailability. The phytosome exhibits superior potency and acceptability among the vesicular systems. The creation of liposomes, micelles, nanoparticles, nanoemulsions, microspheres, or other complexes is a component of formulative research. To improve oral bioavailability, a variety of tactics have been developed, including structural modification, trapping with lipophilic carriers such phospholipids, and solubility and bioavailability enhancers. A well-known illustration of the aforementioned strategy is the presence of flavonoids, which have been shown to protect the liver, in the fruit of the milk thistle plant.

KEY WORDS: Phytosomes, Bioavailability, Stability, Neutraceutical Industry.

INTRODUCTION

Modern medicine has made use of phytoconstituents from herbal extracts that were historically employed in home treatments. Some phytoconstituents' lengthy side chains and strong polarity

prevented them from passively diffusing through lipidic membranes. The compositions, medicinal properties, and general health-promoting potential of various plant products have all been validated by phytochemical research. The bioavailability of many herbal medications and phytoconstituents, which are poorly lipid soluble and have low bioavailability, is of major concern.

Despite their extraordinary potential, many herbal extracts have low bioavailability, as evidenced by in vitro and in vivo studies, because of their poor lipid solubility. When taken orally, several hydrophilic herbal extracts may lose their active ingredients in the stomach because of their incorrect molecular size. There have been numerous research conducted to improve the bioavailability of herbal extracts using a variety of techniques, including trapping with lipophilic carriers, structural alteration, and the addition of solubility and bioavailability enhancers. To increase the phytoconstituents' bioavailability, the crude extract's chemical structure seems to be essential.

PHOSPHOLIPIDS

Glycerol is connected to two fatty acids in phospholipids, which are tiny lipid molecules. The third hydroxyl, which is typically one of the two main methylene, has a phosphate group attached to either an amino acid or a biogenic amino. A significant part of every cell membrane is made up of phospholipids, a class of lipids. Phospholipids are also used by humans and other animals as natural digestion aids and as carriers of nutrients that are hydrophilic and lipophilic. They are well absorbed when taken orally and are miscible in lipid and water environments. Phospholipids from soybeans (Glycine max), primarily phosphatidylcholine, are used extensively to create phytosomes because they are lipophilic and easily complex polyphenolics. A key molecular component of cell membranes, phosphatidylcholine is miscible in both water and oil/lipid environments.

Phospholipids are compounds that have hydrophilic head groups joined to alcohol by hydrophobic acyl chains. There are many different types of phospholipids because of the differences in head groups, aliphatic chains, and alcohols. Different kinds of formulations frequently employ different phospholipids, such hydrogenated phosphatidylcholine, soybean phosphatidylcholine, egg phosphatidylcholine, or synthetic phosphatidylcholine. Phospholipids

become interesting since they can provide a number of choices. However, because phospholipids come in a variety of species, choosing the right phospholipid to accomplish a therapeutic goal becomes a critical issue when designing a drug delivery system.

Two fatty acid tails and a phosphate group head make up a phospholipid. Long chains of hydrogen and carbon make up fatty acids, while phosphate groups are made up of four oxygen molecules joined to a phosphorus molecule. Glycerol binds these two phospholipid constituents together.

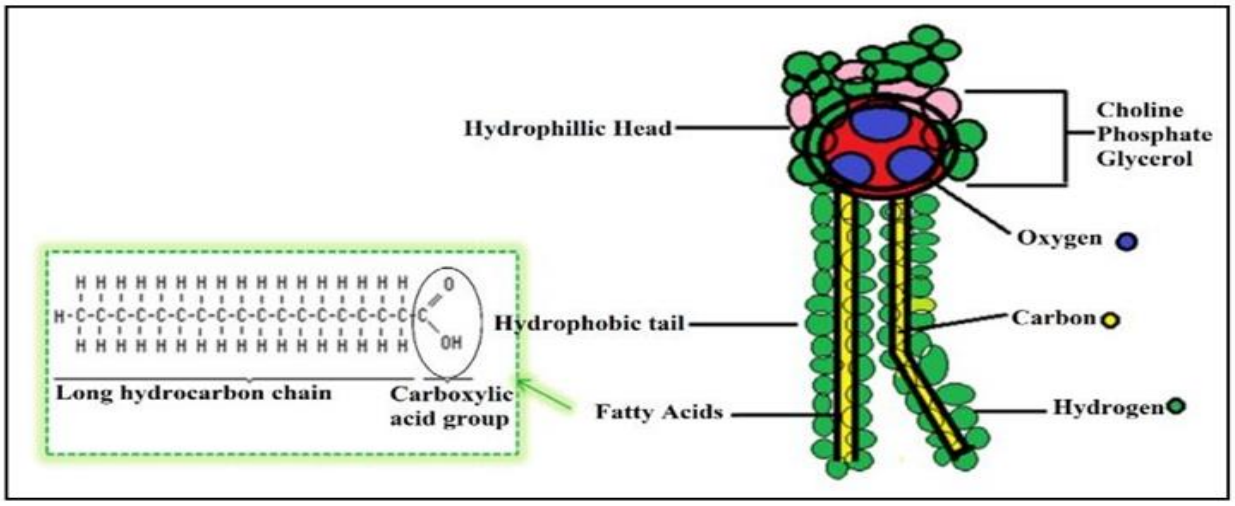

Fig. 1: General structure and constituents of phospholipids (phosphatidyl choline) Structure of Phospholipids

In their structures, phospholipids contain phosphorus, a polar potion, and a non-polar potion. Glycerophospholipids and sphingolipids are two categories of phospholipids based on the alcohols they contain.

GLYCEROPHOSPHOLIPIDS

Glycerol is the backbone of phospholipids known as glycerophospholipids, which are the predominant phospholipids found in eukaryotic cells. The head group, the length and saturation of hydrophobic side chains, the type of bonding between the aliphatic moieties and the glycerol backbone, and the number of aliphatic chains determine the chemical structures and

classification of glycerophospholipids, all of which exhibit the L-configuration. Glycerophospholipids, including phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidic acid (PA), phosphatidylinositol (PI), phosphatidylglycerol (PG), and cardiolipin (CL), differ depending on the head group.

SPHINGOLIPIDS

The phospholipids known as sphingolipids are made up of two nonpolar tails and a polar head group. Sphingosine is the primary component of sphingolipids. Sphingomyelins and glycosphingolipids (cerebrosides, sulfatides, globosides, and angliosides) are examples of sphingolipids. Although they are found in membranes, sphingolipids are particularly prevalent in the myelin sheath. Essential structural lipid elements of nerve cell membranes are sphingomyelins. Ceramide units with phosphorylcholine moiety connected to position 1 of the sphingoid base component make up sphingomyelin, also known as ceramide 1-phosphocholine. As a result, it is the sphingolipid analogue of phosphatidylcholine and shares its zwitterionic properties.

PHYTO-PHOSPOLIPID COMPLEX VESICLES: PHYTOSOME

One of the primary strategies for enhancing the bioavailability of phytopharmaceuticals is the novel phyto-phospholipid complexation approach known as "phytosome," which is crucial in boosting absorption and bioavailability. There are certain phytoconstituents that are poorly soluble and do not pass through biological membranes. Despite having strong pharmacological properties in vitro, a number of plant actives have not shown comparable in vivo responses. These plant actives have been made more effective systemically by combining them with dietary phospholipids, such as phosphatidylcholine, which creates new, amphipathic cellular structures. One of the most popular ingredients in neutraceuticals is phytosome, which is used to standardize extracts of phospholipids and enhance their absorption, bioavailability, and usage.

Phytosomes are shaped like cells. "Some" implies cell-like, and "phyto" indicates plant. One innovative method of medication distribution that addresses the shortcomings of traditional methods is the phytosome. The bioactive phytoconstituents of herbal extracts are encased in phospholipids and found in phytosomes. To create lipid-compatible molecular complexes that

enhance absorption and bioavailability, standardized herbal extracts or water-soluble phytoconstituents are combined to create phytosomes. The phytosome process produces cells that are shielded from gut bacteria and digestive secretions and contain a valuable component of herbal extract. Phytosomes are more adept at changing from a hydrophilic environment to the enterocyte cell membrane's lipid-friendly environment before the cell eventually reaches the blood.

Clinically beneficial phospholipids can bind with hydrophilic and lipiphilic phytoconstituents to form lipid-soluble complexes. These complexes can be utilized to create phytosomes, which are vesicles that resemble liposomes. Phosphatidylcholine complexation occurs in phytosomes, and the active plant component forms chemical bonds, making it more stable.

The bioavailability of plant bioactive components is significantly increased by phytosomes. Phospholipids such as soy phospholipids, egg lecithin, phosphotidylcholine, and others have been reported to be used in the production of phytosomes. By enhancing absorption in the gastrointestinal system, phytosomes can penetrate lipid biomembranes and raise the bioavailability of lipid soluble extracts that are poorly absorbed. Extracts of ginkgo biloba, grape seed, hawthorn, milk thistle, green tea, olive oil, ginseng, and other plant components are among those included in phytosomes.

ADVANTAGES OF PHYTOSOME

- Phytosomes readily enter cells by transporting from the cell membrane.
- A discernible improvement in the drug's bioavailability takes place.
- For herbal preparation, phytosomes guarantee a longer duration of action.
- Phytosomes increase the bioavailability and enhance the oral, topical, and other routes of absorption of hydrophilic phytoconstituents.
- Phytosomes form a tiny cell that shields the active ingredients in herbal extracts from being broken down by gut bacteria and digestive secretions.
- Proper medication distribution to the appropriate tissues is induced by phytosomes.
- Using phytosomes to provide herbal medications does not have to compromise their nutritional safety.

- Because of the principal ingredients' maximal absorption, the dose required has been lowered.
- They lower the dose requirement and enhance the absorption of physiologically active constituents.
- Phosphatidylcholine molecules and phytoconstituents form chemical bonds, which demonstrate the phytosomes' strong stability profile.
- Because of their high lipid profile and greater skin penetration, phytosomes are utilized extensively in cosmetics to enhance the transdermal absorption of phytoconstituents.
- The phytoconstituent in phytosomes is more readily absorbed and can pass through intestinal tissue barriers.
- Drug entrapment is not an issue with phytosomes, and the complex is biodegradable.
- Phytosomes are a good choice for a drug delivery system because they improve absorption, increase biological activity, and deliver to the target tissue, all of which magnify the effects of herbal ingredients.
- Because the medication is conjugating with lipids to generate vesicles, the entrapment efficiency is high.
- When creating phytosomes, drug entrapment is not an issue.
- As a crucial component of a cell membrane, phosphatidylcholine, which is employed to formulate phytosomes, not only serves as a carrier but also nourishes the skin.
- In skin care products, phytosomes work better than liposomes.
- The clinical benefits of phytosomes are significantly higher.
- When hepatoprotective compounds are utilized, phosphatidylcholine, which is used to form phytosomes, works as a carrier and a hepatoprotective, resulting in a synergistic effect.
- Because of their limited solubility in aqueous fluids, stable semisolid dosage forms can be formed, and their increased solubility in bile salt makes liver targeting easier.

RESEARCH METHODOLOGY

FTIR spectra were obtained using an FTIR spectrophotometer in order to characterize SCE, SPE, and SBE.102 Using a differential scanning calorimeter, the drug's thermal behavior was assessed, and the range of its melting and enthalpy points was ascertained.

INFRARED SPECTROSCOPY

The sample was prepared using the potassium bromide disk method. Potassium bromide dispersion was used to measure the drug's infrared spectrum in its solid state. The bands have been given (cm-1).

DIFFERENTIAL SCANNING CALORIMETRY STUDY

Using a differential scanning calorimeter, the extracts' thermal behavior was assessed, and the range of their melting and enthalpies was ascertained. The medication was hermetically sealed in aluminum pans with holes, and it was heated between 50 and 300 degrees Celsius at a steady rate of 10 degrees Celsius per minute.

MELTING POINT

Melting point equipment was used to determine the melting points of SCE, SPE, and SBE.

SOLUBILITY STUDY

To ascertain the extracts' solubility, 10 milliliters of different media were used, and the medication was then added gradually to create a saturated drug solution.

ULTRA VIOLET SPECTROPHOTOMETRY SCAN

SCE, SPE, and SBE were combined in methanol and phosphate buffer (pH 7.4) to create a 10 µg/ml solution. The produced solution was scanned using a twin beam UV-VIS spectrophotometer to check for UV absorption in the 200–400 nm wavelength range. Table No. 6 displayed the maximum absorption of SCE, SPE, and SBE.

STABILITY STUDIES OF PHYTOSOMES

To assess any physical or chemical alterations during storage, stability tests were performed on the optimized phytosomes. The improved phytosomes' storage stability tests were carried out in accordance with ICH regulations. The optimized phytosomes were kept in amber-colored vials that were sealed. To do this, 10 milliliters of phytosome dispersion containing a medication

concentration of 2 milligrams per milliliter was placed in glass vials and kept for three months at two distinct temperatures, 4°C and 25°C.130 It was established how storage affected color and trapping effectiveness. The sampling was carried out once every month.

STATISTICAL ANALYSIS

The mean ± standard deviation is used to display the results. One-way analysis of variance (ANOVA) and the Student's t-test were used for the statistical analysis. Statistical significance was assumed for P values less than 0.05.

RESULTS AND DISCUSSION

STABILITY STUDIES OF CITRUS PHYTOSOME (CP)

Stability experiments were conducted on the improved CP to assess any potential chemical or physical alterations during storage. Table-1 displayed the stability studies of the improved phytosome. Changes in entrapment efficiency were assessed as factors in the storage stability studies of the improved CP under two storage settings. The findings indicated that after three months of storage at 4°C and 25°C, there was a minor shift in entrapment efficiency. The optimized phytosome's EE percentage was 97.18 ±0.17%, and after three months of storage at 4°C and 25°C, it was 90.04 ±0.16% and 88.72 ±0.20%, respectively. The variations in entrapment efficiency as a function of storage time are displayed in Figure 94. Additionally, the percentage of EE dramatically dropped while being stored at 4°C. Consequently, it was discovered that the improved CP remained stable for three months at two distinct storage temperature settings.

Table 1: Effect of storage condition on % entrapment efficiency of CP

SN	Time (Month)	Temperature Condition	
		25°C	4°C
1	0	97.18 ±0.17	97.18 ±0.17
2	1	94.61±0.24	92.82±0.14
3	2	92.33±0.13	89.15±0.31

4	3	90.04±0.16	86.52 ±0.20
5	6	85.88±0.20	84.12±0.23

a) STABILITY STUDIES OF KUTKI PHYTOSOME (KP)

Changes in entrapment efficiency were assessed as factors in stability experiments of optimized KP under two storage settings. The findings indicated that after three months of storage at 4°C and 25°C, there was a minor shift in entrapment efficiency. The table and figure displayed the impact of storage conditions on the percentage entrapment efficiency of KP. The variations in entrapment efficiency with storage time are displayed in Figure 4.85. Additionally, the percentage of EE dramatically dropped while being stored at 4°C. Consequently, it was discovered that the improved KP remained stable for three months at two distinct storage temperature settings.

Table 2: Effect of storage condition on % entrapment efficiency of KP

SN	Time (Month)	Temperature Condition	
		25°C	4°C
1	0	95.66±0.22	95.65±0.20
2	1	93.01±0.44	90.81±0.14
3	2	92.33±0.13	88.24±0.41
4	3	91.04±0.42	87.25±0.12
5	6	86.88±0.20	85.11±0.23

STABILITY STUDIES OF BOERRHAVIA PHYTOSOME (BP)

Stability studies of optimised BP under two storage conditions were carried out, and the changes in entrapment efficiency were evaluated as parameters. The findings indicated that after three months of storage at 4°C and 25°C, there was a minor shift in entrapment efficiency. Figure 4.86 shows the changes in entrapment efficiency against storage time. Additionally, the percentage of EE dramatically dropped while being stored at 4°C. Consequently, it was discovered that the improved KP remained stable for three months at two distinct storage temperature settings.

Table 3: Effect of storage condition on % entrapment efficiency of BP

SN	Time (Month)	Temperature Condition	
		25°C	4°C
1	0	94.42±0.70	94.42±0.70
2	1	92.30±0.44	92.02±0.14
3	2	91.33±0.13	90.25±0.41
4	3	90.22±0.24	88.26 ±0.10
5	6	87.88±0.20	86.12±0.23

CONCLUSION

Phospholipid (PC) and normalized removes SCE, SPE, and SBE, individually, communicated to effectively get ready phytosomes like CP, KP, and BP. A work was attempted to join SCE, SPE, and SBE with phospholipids to build their dissolvability. Dissolvable vanishing strategies were utilized in the definition of the complex. Reaction surface methodology and focal composite plan were utilized to streamline the definitions. FTIR, DSC, PXRD, and SEM were utilized to describe the streamlined phytosomes. The SEM concentrate on approved the phytosomes' surface morphology, and estimations of molecule size and zeta potential were confirmed. These examinations showed that the vesicular medication phospholipid blend was effectively shaped. The dissolvability and medication arrival of SCE, SPE, and SBE from CP, KP, and BP, separately, were altogether improved, as per the obvious solvency and in vitro disintegration tests.

It has been noticed that the complex really rummaged hydrogen peroxide and DPPH revolutionaries. Phytosomes showed huge cell reinforcement properties. When contrasted with normalized removes, the created phytosomes' cell reinforcement movement was discernibly more grounded, as per the in vitro test. In hepatotoxic models, phytosomes showed predominant hepatoprotection and cell reinforcement movement in contrast with standard concentrates and standard silymarin, further cementing the thought behind this imaginative definition. Histopathology concentrates on in the concentrated on hepatotoxic creatures further affirmed the

detailing's superior in vivo action. Each of the three phytosomes' solidness tests showed that the definition didn't fundamentally adjust over the direction of 90 days.

The phytosomes containing SCE, SPE, and SBE were viewed to have the potential as helpful for expanding its bioavailability. Enormous atoms might have the option to cross the lipophilic organic layer and enter the foundational dissemination on account of this worth added home grown drug transporter innovation. A promising medication conveyance strategy that upgrades the dissolvability and ingestion of plant parts is the phytosome. A promising medication conveyance strategy for working on the quality, targetability, and viability of plant separates is phytosome innovation. The use of phytosomes in plan innovation has a brilliant future. Clinical use of the created phytosomes in a suitable dose structure might show extraordinary commitment.

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