



## Formulation and Evaluation of Phytosome, A Novel Biomedicine

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### ABSTRACT

“Phyto” denotes plant and “some” implies something that resembles a cell. Any herbal medication's efficacy depends on the therapeutically active component being delivered at an effective dosage. But when given orally or through topical treatments, their bioavailability is severely constrained. The novel drug delivery systems called phytosomes have superior bioavailability and effects than traditional phyto compounds or botanicals since they are more absorbed. By binding the standardised plant extract or its contents to phospholipids, primarily phosphatidylcholine, a lipid-compatible molecular complex called a phytosome is created. The pharmacokinetic and pharmacodynamic profile of phytosome is superior to those of conventional herbal extracts.

**Keywords:** Phytosome, phospholipid, phytoconstituents, phosphatidylcholine, novel drug delivery system, herbal extract.

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### INTRODUCTION

Novel drug delivery techniques can increase bioavailability.<sup>1</sup>The goal of a novel drug delivery system is to route the active ingredient to the site of action while delivering the medicine at a rate determined by the body's needs during the treatment period. A number of novel vesicular drug delivery systems such as liposomes, niosomes, transferosomes and pharmacosomes have been emerged for controlled and targeted drug delivery. Developments in the field of vesicular drug delivery have allowed for the creation of systems that enable drug targeting and prolonged or regulated release of traditional medications.<sup>2</sup> By binding the plant extract or its contents to phospholipids, phytosome is created.<sup>3</sup>

Traditional medical practises and phytomedicines have been used therapeutically for centuries to maintain health through a variety of techniques. The development of herbal medicine delivery, a modern initiative aims to effectively manage human diseases. Every country is turning to herbal medicines for self-medication as a means of obtaining health care outside the conventional scope of contemporary medicine. The majority of bioactive components of phytomedicine are water-soluble compounds, while the rest are water-insoluble. However, the efficiency of phytoconstituents is constrained because they are not well absorbed when given internally or

topically<sup>4</sup>. Many methods have been discovered to increase the oral bioavailability of drugs, including structural modification, the addition of solubility and bioavailability enhancers.<sup>2</sup>

### Phytosomes

Plants are referred to as “phyto” and cells are referred to as “some”. A phytosome is a vesicular drug delivery mechanism in which lipid surrounds and binds phytoconstituents of herbal extract. When compared to ordinary herbal extract, phytosomes exhibit greater absorption, better bioavailability and improved pharmacological and pharmacokinetic parameters because phospholipid shield vital herbal extract components from being destroyed by digestive secretions and gut bacteria.<sup>2</sup> Physical size, membrane permeability, the amount of solutes that are trapped inside and chemical composition all have an impact on how phytosomes behave in physical and biological system.<sup>3</sup>

### Principle

Standardised extract or polyphenolic component in a non-polar solvent with a stoichiometric amount of the phospholipid produces a phytosome. Flavonoids and terpenoids, which are phytochemical components of the extracts, allow for their direct complexation with phosphatidylcholine. The lipophilic phosphatidyl and hydrophilic choline moiety make up the bifunctional phosphatidylcholine molecule. The phosphatidylcholine molecule's choline head binds to phytoconstituents, while the lipid-soluble phosphatidyl portion's body and tail enclose the choline-bound substance. Because of this, the phytoconstituents form a lipid-compatible molecular complex with phospholipid that is also known as the phyto-phospholipid complex.<sup>2</sup>



There are two basic reasons for the reduced bioavailability and absorption of polyphenolic components. These main components comprise of many ringed molecules and are not too tiny to be absorbed via diffusion process. The second factor is that the main components of polyphenols, flavonoid molecules, are less soluble in lipids. These limitations limit their uptake through cellular membranes.<sup>5</sup>

### Properties of Phytosome

#### 1) Biological properties:<sup>5</sup>

- When taken orally, phytosome improves the overall bioavailability of active substances as well as their active absorption.
- Phytosome has a superior pharmacokinetic profile than conventional herbal medicines.
- These herbal remedies are more innovative than conventional herbal extracts and are more effective.

#### 2) Physicochemical properties:<sup>2</sup>

- A stoichiometric quantity of phospholipid is reacted with standardised plant extracts as the substrate to create phytosomes. The interaction between the phospholipid and substrate is by the formation of hydrogen bond between the polar head of phospholipid and the polar functionalities of the substrate.
- When exposed to water, phytosome adopts a micellar shape resembling a liposome and photon correlation spectroscopy (PCS) demonstrates that phytosome acquired these liposomal structures.
- Phytosomes range in size from 50 nm to a few hundred meters.
- Using data from the H1 NMR and C13 NMR, it was determined that the fatty chain emits the same signals in both free and complex phospholipid. This shows that the active ingredient is encased in lengthy aliphatic chains, creating a lipophilic envelope.

### Advantages

- Phytosomes have better stability due to strong chemical bonding with lipid.<sup>5</sup>
- Phytosomes increases cutaneous absorption due to lipid coating.<sup>5</sup>
- Platform for the delivery of large and diverse group of drugs (peptides, protein molecules).<sup>2</sup>
- The vesicular system is passive and non-invasive.<sup>2</sup>
- Phosphatidylcholine, an essential part of the cell membrane used in phytosome technology, acts as a carrier and increases the absorption of active constituents there by reduces the dose.<sup>2,5</sup>

### Preparation

- In solvent evaporation technique weight the phospholipid and cholesterol accurately, dissolve it in

10 mL of chloroform and then sonicate the mixture using a bath sonicator for 10 minutes. By submitting it to lower pressure in a rotary evaporator (40°C), solvent removal can be accomplished. In a rotary evaporator, a thin layer is created after the solvent has been completely removed and is hydrated with the drug's polyphenolic extract. For heat dissipation the phospholipids mixture was sonicated in an ice bath. The prepared phytosome was kept in a bottle with an amber hue.<sup>5</sup>

- The thin layer rotary evaporator vacuum approach was used to create phytosome vesicles. Anhydrous ethanol was combined with the herbal extract and phospholipid in a 250 ml round bottom flask which was connected to rotatory evaporator. Around the flask, a thin layer of will form when the solvent evaporates at a temperature of roughly 60°C. The lipid layer will peel off in the phosphate buffer, creating vesicle suspension. Probe sonication with 60% amplitude was applied to the phytosomal suspension. Before being characterised, phytosomal suspension will be kept for 24 hours in the refrigerator.<sup>5</sup>
- Reflux technique can be used to create phytosomes. In a 100 mL round bottom flask with a maximum internal temperature limit of 40°C, phospholipid and polyphenolic extract were added and refluxed with dichloromethane (DCM) for 1 hour. The solution was evaporated and 15 mL of n-hexane was added until precipitation was formed. In a desiccator, the precipitate was transferred.<sup>5</sup>
- Weigh the polyphenolic extract and phospholipid accurately. Place it in a 100 ml round bottom flask, reflux with 30 mL of dichloromethane (DCM) for 3 hours at 60 °C, then reduce the volume to 5-10 mL and add 30 mL of n-hexane with constant stirring in order to obtain precipitate. Gather the precipitate and keep it overnight in a vacuum desiccator. The precipitate is then stored in a tightly closed, amber coloured container.<sup>5</sup>
- Phospholipid or soy lecithin was combined in an equal amount with polyphenolic extract and added 5 mL of dichloromethane (DCM). The mixture was stirred until the DCM evaporated. 5 mL of n-hexane was added to the thin film while still being stirred and the n-hexane was then completely removed inside of a fume hood. The thin film was hydrated and sonicated for the appropriate phytosomal complex.<sup>5</sup>

### Dosage Form

Based on its ability to increase the effectiveness and efficiency of the bioactive component, a suitable formulation or dosage form for the distribution of phytosomes can be chosen. The final formulation must take into account the inherent characteristics of herbal drugs such as hydrophilic or hydrophobicity; surface properties of systems such as permeability and charges; degree of biodegradability and tonicity, as well as the



release profile and size of the product required. Both oral and topical formulations of phytosome are available. Here are some examples for therapeutic dose formulations for delivering phytosomes.<sup>2</sup>

#### a) Tablet:

A direct compression procedure can only be used for lower unitary doses because the phytosome complex have restricted ability to flow, sticky in nature and possess low apparent density. The complex of phytosomes should be diluted with 60–70% excipients to produce tablets with the desired qualities. Due to the harmful effects of heat and water on the stability of the phyto-phospholipid complex, wet granulation should be avoided.<sup>2</sup>

#### b) Capsule:

To create soft gelatin capsules, the phytosome can be dissolved in oily media (vegetable or semi-synthetic oil) forming suspension which is filled into the shell.<sup>2</sup>

Phytosomes can be filled in to hard gelatin capsules. Precompression is not necessary because it can alter the disintegration time during a straight volumetric filling operation. Due to low density of phytosome the maximum quantity of powder that may be put into a capsule (often no more than 300 mg each size capsule) appears to be constrained. We can increase the amount of powder that is loaded into capsules by using a piston pump during the capsule filling process.<sup>2</sup>

#### c) Gel:

To the prepared dispersion/emulsion add phytosomal complex.<sup>2,6</sup>

### Evaluation

#### 1. Determination of percentage yield:

Percentage yield of phytosome complex was calculated by the following formula:<sup>6</sup>

$$\text{Percentage Yield} = \frac{(\text{Practical yield})}{(\text{Theoretical yield})} \times 100$$

#### 2. Determination of entrapment efficiency:

Centrifuging the drug phytosomal complex for 90 minutes at 4°C at 10,000 rpm separates the phytosome from the free drug. Utilizing UV spectroscopy, determine the amount of free drug present.<sup>5</sup>

The formula can be applied to determine the percentage of drug entrapment,

Entrapment efficiency (%)

$$= \frac{(\text{Total amount of drug}) - (\text{amount of free drug})}{(\text{Total amount of drug})} \times 100$$

#### 3. Determination of particle size:

Using a Nanophox the average diameter of the phospholipid complex was determined at a specified scattering angle of 90°.<sup>6</sup>

#### 4. Zeta potential:

Malvern Zetasizer is employed to measure the phytosomal complex's zeta sizes.<sup>5</sup>

#### 5. Scanning electron microscopy (SEM):

The size and appearance of the particle were assessed using SEM.

Dry sample was applied to gold-coated brass stub of the electron microscope (JEOL JSM-6360 Scanning microscope). Digital images of phytosome complex were taken by random scanning of the stub at 1000x, 5000x, 10000x and 30000x magnifications.<sup>5</sup>

#### 6. Differential scanning calorimetry (DSC):

Phosphatidylcholine, a physical mixture of drug extract and phosphatidylcholine, drug-phospholipid complex and drug polyphenolic extract were all added to an aluminium cell and heated to a temperature of 400°C at a rate of 50–250°C per minute in the nitrogen atmosphere. Peak transition onset temperatures were recorded by means of an analyzer.<sup>5</sup>

#### 7. Determination of drug content:

By correctly dissolving 100 mg of the phytosome complex in 10 ml of solvent, the drug concentration of the compound was ascertained. Using a UV spectrophotometer, the drug content was calculated from the dilution absorbance.<sup>6</sup>

#### 8. FTIR:

FTIR analysis will be used to examine the drug's phospholipid structure and chemical stability. To create pellets, the phytosomal medication will be crushed with potassium bromide under pressure of 600 kg/cm<sup>2</sup>. 4000-400 cm<sup>-1</sup> will be the range for scanning.<sup>5</sup>

#### 9. Transition electron microscopy (TEM):

The size of phytosomal vesicles was evaluated using TEM at a 1000x magnification.<sup>5</sup>

#### 10. Solubility test:

Take 10ml of solvent in glass containers. On a rotator shaker, the liquid was stirred for 24 hours to get rid of too much extract; it was then centrifuged for 15 minutes. A membrane filter was used to filter the supernatant. Then dilutions were made from 1 ml of filtrate with 9 ml of suitable solvent. Analysed using UV spectrophotometer and calibration curve was used to compute the absorbance of concentration.<sup>7</sup>

#### 11. X-ray:

The microstructure of various amorphous materials as well as crystal materials can currently be examined using X-ray diffraction. X-ray diffraction is typically carried out on phosphatidylcholine, phosphatidylcholine-phytophospholipid complexes. An active component and physical mixture's X-ray diffraction reveals strong crystalline peaks that point to a high crystal form. The absence of a



crystalline peak in active component phyto-phospholipid complexes however shows that the constituents in these complexes have a molecular or amorphous structure.<sup>8</sup>

## 12. Stability studies:

Under three different conditions the physical stability of optimized formulation was checked for six months.<sup>9</sup> At low temperature (4 °C), ambient temperature (28 °C) and high temperature (40 °C), stability tests were conducted.<sup>10</sup>

## CONCLUSION

Phytosomes is a patented technology. Phytosomes are able for transition from hydrophilic surroundings into the lipid friendly surroundings of the enterocyte cell membrane and from there into the cell lastly reaching the blood.<sup>11</sup> Phytoconstituents are sensitivity to degradation and have limited solubility. Vesicular drugs delivery methods contribute to the improvement of these qualities because of their amazing trapping capability, biocompatibility and safety.<sup>12</sup> Vesicles are demonstrated to be very promising cellular delivery platforms for a variety of beneficial phytochemicals. Phytosomes are vesicular drug carriers that promote bioactive molecule absorption and bioavailability as well as overall compound stability by forming a complex between phytochemicals and phospholipids. Since ancient times and till today the use of phyto medicine is prevalent and phytosome is a promising tool to provide anciently using herbal medicines in a more effective contemporary way.

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