Review article:

An Overview of Phytosome Novel Drug Delivery System

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ABSTRACT:

In recent days, most common diseases and nutritional disorders have been treated with natural remedies. Despite excellent in vitro bioactivity, many plant extracts and phytoconstituents have less or no activity in vivo due to poor lipid solubility or incorrect molecular size or both, resulting in poor absorption and bioavailability. Thus, much work is directed towards the development of a new concept of herbal delivery system, namely phytosomes, which are better absorbed, utilized and thus provide better results than traditional plant extracts. Phytosomes are often called herbosomes. The term "phyto" means a plant, while "some" means a cell. Phytosomes are small cellular structures. The phytosome consists of phospholipids, mainly phosphatidylcholine, which form a lipid-compatible molecular complex with other components. Phytosomes are better than liposomes due to 2:1 and 1:1 complex ratio of components and phospholipids, much better absorption and stability profile. Phytosome is anti-inflammatory and antioxidant. In animal studies, it improved resistance to atherosclerotic lesions, strengthened the protective prostaglandin and protected the ventricular myocardium against damage caused by lack of blood flow.

Keywords: Phytosomes, medicine, Drug Development, Phospholipid

INTRODUCTION:

The word "phyto" means plant, while others mean cellular. “Phyto”means a plant. Phytosomes have been used for vesicular delivery of phytoelectric constituents and lipid-bound (a single molecular phytocomponent, at least molecularly bound to a phospholipid) herbal extract. absorption pharmacological and pharmacokinetic biological and better availability. Phytosomes are an innovative lipid-based delivery system with a liposome-related structure that can be used to capture different types of polyphenol-based phytoconstituents to improve their absorption upon administration.

The first phytosomes were developed by the company Indena (Milan, Italy) in the late 1980s with the aim of increasing the bioavailability of medicines by converting them into phospholipids. The structure of phytosomes consists of a standardized polyphenolic plant extract incorporated into phospholipids, mainly phosphatidylcholine (PC)[1-2].

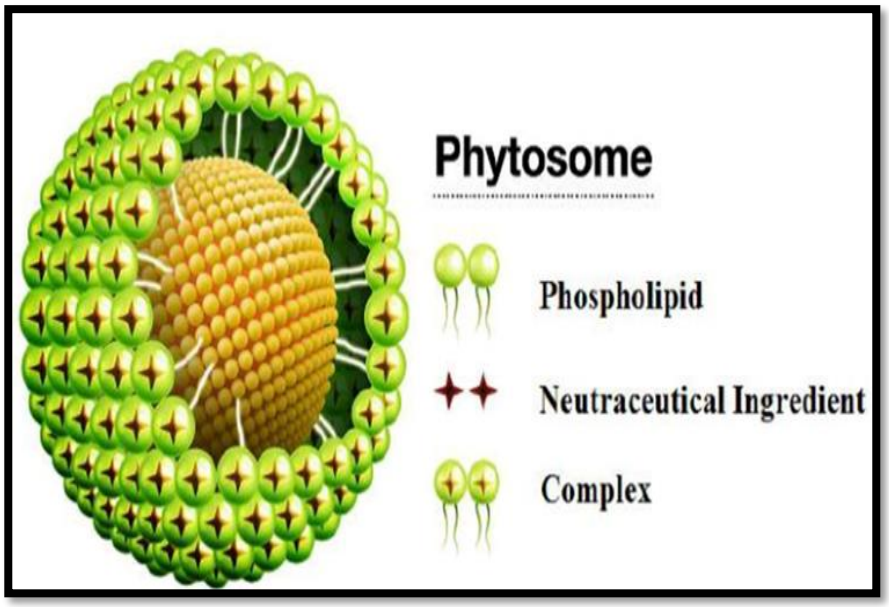


Figure1:Structure of phytosomes

ADVANTAGES:

1) Phytosomes produce a small cell in which the valuable components of plant extracts are protected against digestive secretions and destruction by intestinal bacteria
2) It ensures proper delivery of the drug to the appropriate tissues.
3) There is no need to jeopardize the nutritional safety of plant extracts by delivering herbal drugs as a phytosomal medium.
4) Due to the maximum absorption of the main ingredients, the dosage requirement has been reduced

5) Encapsulation efficiency is high and more predetermined because the drug itself is conjugated with lipids to form vesicles.
6) When preparing phytosomes, there is no problem of drug retention.
7) Phytosomes have a better stability profile due to chemical bonds between phosphatidylcholine molecules and phytocomponents
8) The phosphatidylcholine used in the composition of the phytosomal process not only nourishes the wearer but also the skin, because it is an integral part of the cell membrane.
9) Phytosomes are also better than liposomes in skin care products.
10) The phosphatidylcholine used in the production of phytosomes, in addition to the carrier, also acts as a hepatoprotective substance, as a result of which it gives a synergistic effect when using substances that protect the liver [3, 4,5].

DISADVANTAGES:

1) When administered orally or topically, they limit their bioavailability.
2) Plant ingredients are quickly removed from the phytosome and stable problem

PROPERTIES OF PHYTOSOMES:

Chemical Properties : Phytosomes are a complex between a natural product and natural phospholipids such as soy phospholipids. Such a complex is formed by the reaction of stoichiometric amounts of phospholipids with a selected polyphenol (for example, simple flavonoids) in a non-polar solvent. Based on these physicochemical and spectroscopic data, it is shown that the main phospholipid-substrate interaction is due to the formation of hydrogen bonds between the polar end of the phospholipids (ie phosphate and ammonium groups) and the polar functional groups of the substrate. . They are lipophilic substances with a clear melting point, which dissolve well in non-polar solvents (in which no hydrophilic part was present) and are moderately soluble in fats. When phytosomes are treated with water, they form in the form of micelles, forming liposomal structures. In liposomes, the active ingredient dissolves in an internal pocket or floats in a bilayer membrane, while in phytosomes, the active ingredient is anchored to the polar end of phospholipids, making it an integral part of the membrane [6,7, 8].

Biological properties: phytosomes are advanced forms of plant products that are better absorbed, used and thus provide better results than traditional plant extracts. Increased bioavailability of phytosome compared to complex botanical derivatives has been demonstrated by pharmacokinetic studies or pharmacodynamic tests [9].

Mechanism of phytosomes technology:

The lower absorption and bioavailability of polyphenolic constituents mainly due to two factors. These chief constituents are number of ringed molecule and are not too much small that it will absorbed by diffusion process. Second factor is that flavonoid molecule or chief constituents of polyphenols have poor solubility with lipids. These are the limitations that their absorption through biological membrane .phytosome technology is mainly result with complexation of polyphenols with phospholipid in 1:1 ratio or 1:2 results in the formation of phytosome complex with lipid covering around the constituents [10].

DIFFERENCE BETWEEN PHYTOSOMES AND LIPOSOMES:

Phytosome	liposomes
Here, the active chemical constituent molecule is anchored by chemical bonds to the polar end of the phospholipid.	Here, the active ingredient dissolves in the hollow medium or membrane layer
Chemical bonds are formed	No chemical bonds are formed
In phytosomes, phosphatidylcholine and the plant compound form a 1:1 to 2:1 complex, depending on the substance.	Here, the water-soluble molecule is surrounded by a hundred or a thousand phosphatidylcholine molecules
Phytosomes are better absorbed than liposomes showing better bioavailability.	Bioavailability of liposomes is less than phytosomes
Content of phospholipids is less higher	Content of phospholipid is much higher

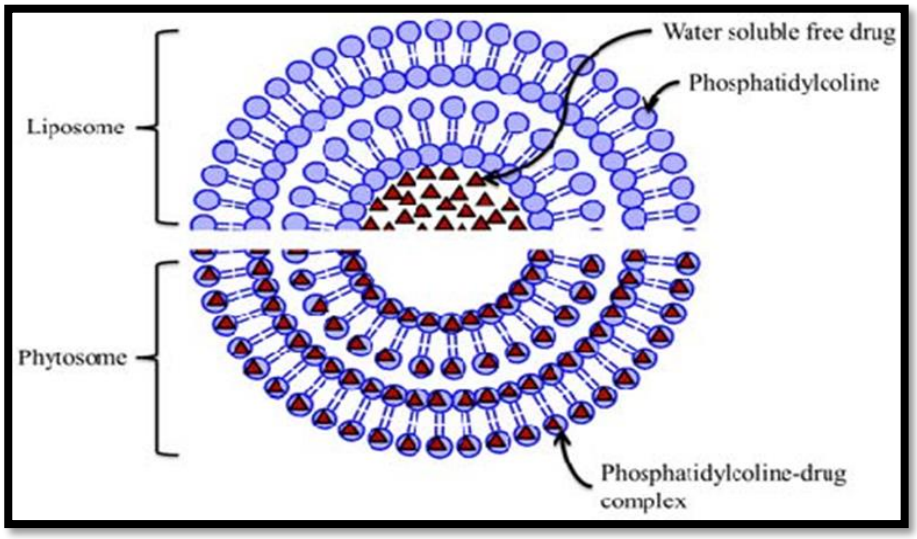


Fig. 1: Difference between liposomes and phytosome

APPLICATION:

1) Silymarin phytosole:

Most phytosomes are concentrated in silybum marianum, which contains flavonoids that protect the liver. The fruits of the milk thistle plant (S. marianum family-steraceae) contain flavonoids to protect the liver. Silymarin has been shown to have a positive effect in the treatment of liver diseases. Various, including hepatitis, cirrhosis, fatty infiltration etc.

2) Phytosomes of grape seed:

The grape seed phytosome consists of oligomeric polyphenols of different molecular sizes complexed with phospholipids. The main properties of grape seed procyanidine flavonoids are to increase the antioxidant capacity and stimulate the physiological defense of plasma.

3) Phytosome of green tea:

Green tea leaves are characterized by the polyphenol compound epigallocatechin-3-0-gallate as a key component. They are powerful modulators of several biochemical processes involved in the breakdown of homeostasis in serious chronic degenerative diseases such as cancer and atherosclerosis. It also has advantages. Functions as antioxidants, anticancer [11, 12].

METHOD OF PREPARATION PHYTOSOME:

1. Antisolvent precipitation technique:

A certain amount of the drug and soy lecithin was placed in a 100 ml round bottom flask and refluxed with 20 ml of dichloromethane at a temperature not exceeding 60 oC for 2 hours. The mixture is concentrated to 5-10 ml. Hexane (20 mL) was carefully added with constant stirring to give a

precipitate, which was filtered and collected and kept in a vacuum incubator overnight. The dried precipitate is crushed in a mortar and sieved through 100 meshe. The powder complex was placed in an amber glass bottle and kept at room temperature.

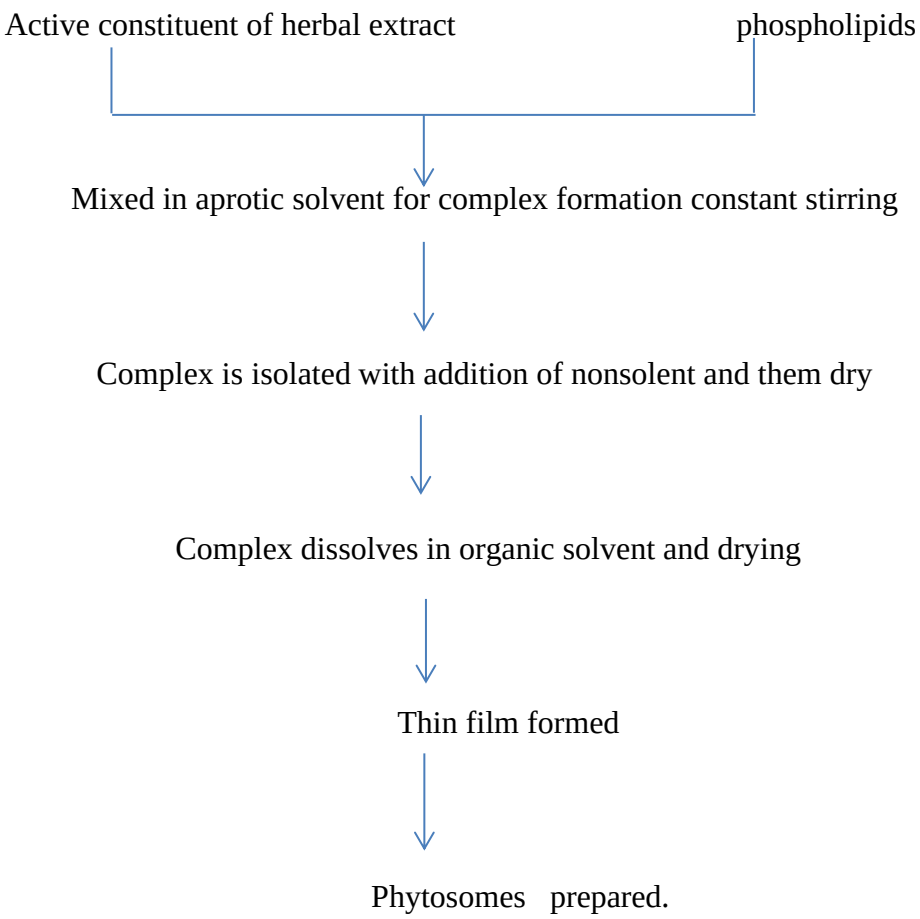
2. Rotary evaporation technique :

The specific amount of drug and soya lecithin were dissolved in 30 ml of tetrahydrofuran in a rotary round bottom flask followed by stirring for 3 hours at a temperature not exceeding 40oC .Thin film of the sample was obtained to which n-hexane was added and continuously stirred using a magnetic stirrer. The precipitate obtained was collected, placed in amber colored glass bottle and stored at room temperature .

3. **Solvent evaporation method :**

A certain amount of the drug and soy lecithin was placed in a 100 ml round flask and boiled with 20 ml of acetone at 50-60 oC for 2 hours. The mixture was concentrated to 5-10 ml to give a precipitate which was filtered and collected.) Phytosome complexes from the dried precipitate were placed in an amber glass vial and stored at room temperature.

GENERAL METHOD FOR PREPARATION OF PHYTOSOMES:



DIFFERENT ADDITIVES USED IN THE FORMULATIONS OF PHYTOSOMES:

- ✓ Phospholipids: Soya phosphatidyl choline, Egg phosphatidyl choline, Dipalmityl phosphatidyl choline, Distearyl phosphatidyl choline.
- ✓ Aprotic solvent: Dioxane, acetone, methylene chloride
- ✓ Non solvent: n-hexane and non-solvent i.e. aliphatic hydrocarbon Alcohol: Ethanol, Methanol

LIST OF EQUIPMENT USED FOR THE PREPARATION OF PHYTOSOMES:

1) UV spectrophotometer
2) FT-IR spectrometer
3) HPLC
4) Different scanning calorimeter
5) Single pan electronic balance
6) Digital pH meter
7) Melting point apparatus
8) Scanning electron microscopy
9) Transmission electron microscopy
10) Different characterization technique used for phytosomes [11,12,13,14,15,16,17,18]

EVALUATION OF PHYTOSOMES:

Differential scanning calorimeter: drug-polyphenol extract, phosphatidylcholine, physical mixture of drug extract and phosphatidylcholine, and drug-phospholipid complex were placed in an aluminum chamber and heated from 50-250°C/min to 0-400°C. Nitrogen to the atmosphere.

Scanning Electron Microscope (SEM): SEM was used to determine particle size and appearance. The dry sample was placed on the gold-plated brass rod of an electron microscope in an ion atomizer. Complex Random Scan 100,

Transmission Electron Microscopy (TEM): TEM was used to characterize the size of phytosomal vesicles at 1000 magnification

Drug entrapment and loading capacity: The drug-phytosome complex was centrifuged at 10,000 rpm for 90 min at 4°C to separate the phytosome from the entrapped drug. The concentration of free drug can be measured by ultraviolet spectroscopy. The percentage of remaining drug can be calculated from the given formula]

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

Fourier Transform Infrared Spectroscopy (FTIR) Analysis: FTIR analysis is performed to check the drug, phospholipid, structure and chemical stability. The phytosome drug is crushed with potassium bromide, resulting in granules under a pressure of 600 kg/cm2. Scanning takes place between 4000 and 400 cm.

Size analysis and zeta potential: The Malvern Zetasizer is used to check the particle size and zeta size of the phytosome complex. An argon laser is used to characterize this particle size and zeta size determinant.

In vitro and in vivo evaluations: In vitro and in vivo evaluations depend on the properties of the drug, their main phytoconstituents limiting the phospholipid layer, and the animal model in question is chosen for its evaluation. Fourier Transform Infrared Spectroscopy (FTIR) Analysis: FTIR analysis is performed to check the drug, phospholipid, structure and chemical stability. The phytosome drug is crushed with potassium bromide, resulting in granules under a pressure of 600 kg/cm2. Scanning takes place between 4000 and 400 cm. Size analysis and zeta potential: The Malvern Zeta sizer is used to check the particle size and zeta size of the phytosome complex. An argon laser is used to characterize this particle size and zeta size determinant. Evaluations in vitro and in vivo: Evaluations in vitro and in vivo depend on the properties of the drug, their main phytocomponents limiting the phospholipid layer, and are chosen based on the animal model considered for its evaluation [19, 20, 21, 22].

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