

## **Phytosomes: Preparation, Evaluation and Application**

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### **ABSTRACT**

*The phytosomes are made by two word “phyto” means plant while “some” means cell-like. Phytosomes was prepared by solvent evaporation method. It may be either within the ratio of 1:1 and 1:2. The phytosomes used different type of drug delivery systems such as liposomes, niosomes, transfersomes, ethosomes, phytosomes, colloidosomes etc. The phytosomes are developed in order to carry the drug. Its metabolism and it is also target to the specific site of the body. The chemical based phytosomes like reaction are vesicles of phospholipids bonded with a hydrogen bond to phytochemicals. The main parts of this review in highlights the main therapeutic applications of phytosomes. The review discussed about some latest and novel drug delivery system. Phytosome technology where general force has been provided on the various therapeutic applications of phytosomes and its crucial role in managing the traditional complications that are encountered for the delivery of phytoconstituents. Applications of phytosomes like incremented bioavailability of drugs, anti-cancer and anti-oxidant agent, transdermal drug distribution, increment wound rejuvenating capacity etc.*

**KEYWORDS-** Preparation, Evaluation and Application.

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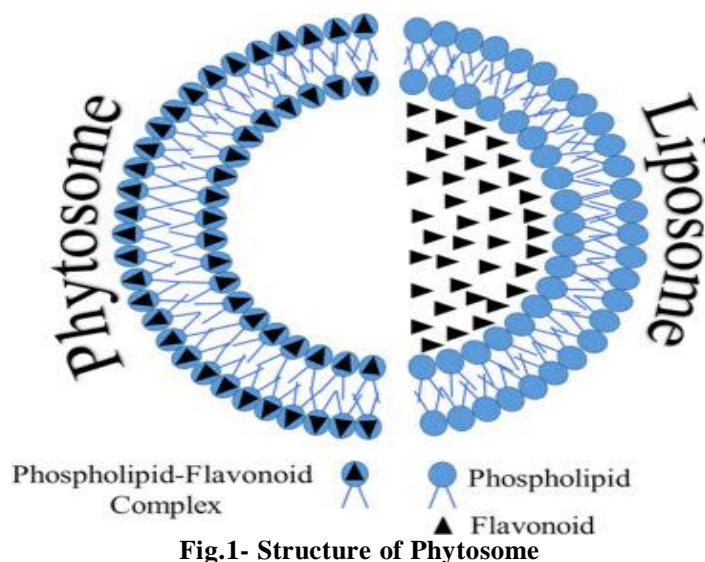
Date of Submission: 06-02-2021

Date of acceptance: 20-02-2021

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### **I. INTRODUCTION**

The Phytosome technology developed by Indena S.P.A. of Italy [1]. Phytosome can be a patented technology including to include standardized plant extracts or dihydrogen monoxide soluble phytoconstituents into phospholipids to supply lipid compatible molecular complexes. The phytosomes process produces a touch cell due to that the precious components of the herbal extract are shielded from destruction by digestive secretions and gut bacteria. Phytosomes have improved pharmacokinetic and pharmacological parameter[2]. More bioavailability of phytosomes as compared to herbal extract due to their increase capacity to cross the lipid rich biomembranes and eventually reaching into the blood [3]. Novel drug delivery system encompasses differing types of pharmaceutical carriers like polymeric micelles, particulate systems, macro- and micro molecules. The vesicular systems are more authoritatively mandated meeting of one or sundry concentric lipid bilayers culminated. When certain amphiphilic building blocks are confronted with dihydrogen monoxide. These systems contribute in prolonging the existence of the drug in circulation reducing toxicity and delaying elimination of rapidly metabolizable drugs [4]. The Italian pharmaceutical and nutraceutical company first time developed the complexation of plant extracts containing water-soluble constituents with phospholipids to enhance their bioavailability. They patente the technology as ‘PHYTOSOME’ [5]. Due to the creation of an H-bond between phospholipids and therefore the phytoconstituents, phytosomes show better physical stability enhancing absorption of hydrophilic polar phytoconstituents leading to enhanced bioavailability and greater therapeutic benefits.



## PREPARATION OF PHYTOSOMES

### Mainly 4 type

#### 1- Solvent evaporation method

The solvent evaporation method involves integration of the phytoconstituents and PC during a flask containing organic solvent. This reaction mixture is kept at an optimum temperature usually 40°C for specific interval of 1 hr to achieve maximum drug entrapment within the phytosomes formed. Thin film phytosomes are separated by 100 mesh sieves and stored in desiccators for overnight [6,7].

#### 2- Mechanical Dispersion method

In the experiments, the lipids dissolved in organic solvent are brought in contact with aqueous phase containing the drug (Sikarwar MS et al., 2008). The next removal of the organic solvent under reduced pressure results in the formation of phyto-phospholipid complex. Recently methods for the phospholipid involute preparation include super critical fluids (SCF), which include gas anti-solvent technique (GAS) compressed anti solvent process (PCA), supercritical anti solvent method (SAS) (Li Y et al., 2008).

#### 3-Salting out technique

An important method of phytosome preparation that done by dissolving both PC and therefore the plant extract during a suitable organic solvent then n-hexane was added until the extract-PC complex precipitation occurs [9].

#### 4- Lyophilization methods

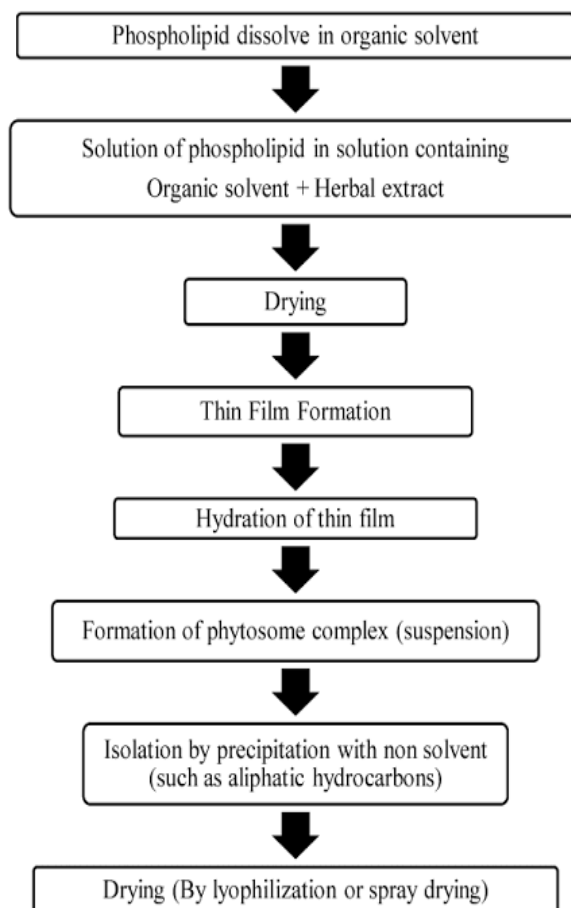
The lyophilization technique DSN was plenary dissolved in DMSO. The resulting DSN solution (2.5% weight/volume) was added to the answer of SPC dissolved in t-butylalcohol (1.5% weight/volume) followed by stirring for 3 hours on a magnetic stirrer until complex formation. The complex was then isolated by lyophilization. After abstracting the samples from the freeze drier, the resultant DSN:SPC involute (yield 90.4%, weight/weight) was placed during a desiccator over P2O5 at 4°C until testing. For the culled developing technique the influence of variable formulation factors was assessed including SPC type (Lipoid® S100, Lipoid® S75 and Lipoid® S PC-3), drug phospholipid ratio (1:1, 1:2, and 1:4) and co-solvent type of chemical (methanol, ethanol, chloroform, acetone, and TBA). Non-conventional methods are customarily employed in construction of phytosome complexes. Modernistic herbal complexes are composed by reaction between equilar amalgamation of natural or synthetic phospholipid and active constituents or herbal extract in acrostic organic solvents [10,11].

Common stages in formulation of phytosomes Various methods of preparation are as follows:

**Anti-solvent precipitation process:** Certain amount of herbal extract and phospholipids is refluxed with 20 ml of organic solvents like acetone at specific experimental conditions below 50°C for 2-3 hr. The reaction mixture is concentrated to minimum volume up to 10 ml then on addition of solvent with low polarity like n-hexane with stirring precipitates are obtained. Filtered precipitates are stored in desiccators. The dried precipitates are pulverized and powdered involute are stored in dark amber colored glass bottle at temperature [12].

**Rotary evaporation process:** Specific weight of herbal extract and phospholipids were mixed in 30 ml water miscible organic solvent like acetone in round bottom glass container followed by stirring for two hours at a temperature but 50°C in rota evaporator. Antisolvent like n-hexane are often added to thin film which is obtained after uninterrupted stirring employing a stirrer [13]. Precipitate of phytosomes obtained are often stored in amber colored glass container at controlled temperature under specified humidity.

Phospholipids solubilized in ether are slowly injected drop wise in an solution of the phytoconstituents which is to be encapsulated. It leads to the formation of cellular vesicles on subsequent solvent abstraction, resulting in involute formation [14]. Structure of phytosomes depends upon concentration amphiphiles in mono state are produced when the concentration is a smaller amount, but sort of structures with different shapes viz. round, cylindrical, disc and cubic or hexagonal vesicles could also be formed on increasing the concentration [15].



**Fig. 2 Preparation of Phytosomes**

## **EVALUATION OF PHYTOSOMES**

### **A) Visualisation -**

Morphology of phytosomes was observed by digital microscopy transmission microscope and scanning microscope.

#### **1) Digital microscopy -**

Phytosome formulation shake in water and view under digital microscope at 400X objective lens.

#### **2) TEM analysis -**

The complex was shaken in water and viewed using Transmission Electron Microscope (Hitachi, Japan).

#### **3) SEM analysis -**

Approximately 5  $\mu$ L of the phytosomal suspension was transformed to a canopy slip, which successively was mounted on a specimen tab. The samples were allowed to dry at temperature Then the particle size of the formulation was viewed and photographed using Scanning microscope (Sigma scan, Carl Zeiss scan). The particles coated with platinum by using vacuum pressure and thus, the coated samples were viewed and photographed in JEOL JSM-6701F emission SEM.

### **B) Particle size analysis**

Diameter of particles and polydispersity index was noted down by BECKMAN COULTER, Delsa<sup>TM</sup> Nano. Phytosome formulations were diluted with solvent methanol then evaluated.

### **C) FTIR**

Spectral data were taken to work out the structure and chemical stability of extract, PC and phytosome. Spectral scanning was exhausted the range between 4000 and 5000cm.

#### **D) DSC**

The sample with, phospholipon and phytosome were placed within the aluminum crimp cell and heated at 100C/min from 0 to 4000°C within the atmosphere of nitrogen (TA Instruments, USA, Model DSC Q10 V24.4 Build 116). Peak transit time onset temperatures were recorded by means of an analyzer.

#### **ADVANTAGES OF PHYTOSOMES**

Phytosomes furnishes with the following advantages:[16,17]

- 1) It is assured proper delivery of drug to specific in the respective tissues.
- 2) The nutrient safety of the herbal extracts needn't be compromised by conveying the herbal drug as means of phytosomes.
- 3) Dose requirement has been reduced due to the maximum absorption of minor constituents.
- 4) Marked enhancement in the bioavailability of drug occurs.
- 5) Entrapment capacity is very high and more over predetermined because drug itself is in conjugation with lipids in forming vesicles.
- 6) There is no any problem in drug entrapment while formulating of phytosomes. Phytosomes produce good stability profile due to the formation of new chemical bonds between phosphatidylcholine molecules and the herbal phytoconstituents.
- 7) Phosphatidylcholine used in formulating phytosome process besides as a carrier also known as nourishes of the skin.
- 8) Phytosomes provesto be of significantly greater clinical benefit.

#### **DISADVANTAGE OF PHYTOSOMES**

- 1) Regarding all advantages phytosome may rapidly exclude the phytoconstituent [18].
- 2) phospholipid can encourage proliferation on MCF-7 breast cancer cell line.
- 3) Phytosomes predominant limitation is reported as leaching of the phytoconstituent off the some which reduced the anticipated drug concentration [19].

#### **APPLICATION OF PHYTOSOMES**

- 1) Enhancing Bioavailability
- 2) Delivery of large and diverse drugs, eg. peptides and proteins
- 3) Safe composition
- 4) Hepato-Protective
- 5) Approved for cosmetic and pharmaceutical applications
- 7) Low-risk profile
- 8) Toxicological properties have been well documented
- 9) High market attraction [20].

## **II. CONCLUSION**

Phytosomes or herbosomes are advanced and novel form of botanicals and phyto-constituent that are better absorbed both orally topically and transdermally. Phytosomes improved pharmacological properties and having wide scope in cosmeticology. The methods of preparation of phytosomes are non-conventional, simple and reproducible. Apart from that the phospholipids used have their own beneficial effect to the body. Several areas of phytosomes are to be reported within the future prospect of pharmaceutical application. The phytosome technology forms a link between the traditional delivery system of phytoconstituents and novel drug delivery systems. An attempt was made to explore the continued research with reference to phytosomes and its applications like wound-healing, anti-oxidant, anti-cancer activities, etc. The information gathered herein are going to be useful for the researchers who wish to explore a vesicular drug delivery system which encompasses effective drug on track site without its metabolism. The technology of phytosomes should be discovered for the treatment of other neurodegenerative, cardio-vascular and auto-immune diseases and skin-related disorders. Although, various phytosomes products are available within the market, yet there are many other phytoconstituents which have remarkable ability to treat life threatening diseases, haven't been implemented into phytosome technology. Further research are often done to develop highly target-specific phytosomes

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