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A REVIEW: PHYTOSOMES – NOVEL DRUG DELIVERY SYSTEM

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Abstract: The term Phyto signifies plant and some implies cell. It is additionally referenced as ribosomes this is the new licensed innovation, where normalized plant concentrates or water solvent phytoconstituents are complexed with phospholipids to deliver lipid viable atomic complexes, there by incredibly expanding ingestion and bioavailability. The new turn of events and led works of different specialists have been concentrated completely to lay out the transdermal repetition as a likely method for conveying phytoconstituents. The effective use of phytosomes for beauty care products reason has proactively been demonstrated. This survey likewise contains a relative record of liposomes and phytosomes alongside late headways in the field of phytosomes innovation with an extraordinary worry to transdermal medication conveyance. The unfortunate oral bioavailability of polyphenol compound can be upgraded through the fuse of them into phospholipids based self-collected conveyance system, i.e. prevalently known as phytosome. There are number of items accessible in the market that contain phytosome drug conveyance framework, for example, Ginkgo biloba, Silybum marianum, and Camellia sinesis.

KEYWORDS: - **:** Novel Drug Delivery System, Phytosomes, Phytophospholipds, liposomes, Phosphatidylcholine

INTRODUCTION

The majority of plant elements that are physiologically active are polar or water soluble; nevertheless, limited absorption limits the use of these chemicals, hence lowering their bioavailability. For development of bioavailability, natural items should have legitimate homeostasis among hydrophilic and plant arrangements are generally utilized in customary as well as present day medication framework.[1] During the conventional times, different pharmacological investigations have been done with many plants extricates and their constituents to really look at their restorative application. Throughout the last year, extraordinary progression has been made for advancement of novel drug delivery system (NDDS) for different plant separates and their dynamic constituents. Novel medication conveyance, for example, designated drug conveyance which straightforwardly channels the dynamic element on the site of activity and such conveyance framework could offer designated and supported arrivals of medication so pharmacological impact could be accomplished at lower portion. The improvement in the space of home grown medication began before to fix human sicknesses with lesser secondary effects. [2] Various boss constituents of home grown medication are effectively solvent in water (glycosides, flavonoid) in any case, these constituents are limited in their power since they might to be some extent dissolvable or hydrophobic in nature, so when applied topically shows less helpful viability. [3]

THE PHYTOSOMES TECHNOLOGY

The flavonoids and torpedoed constituents of plant extracts loan themselves very well for the immediate restricting to phosphatidylcholine. Phytosomes are framed by the response of a stoichiometric measure of phospholipid (phosphatidylcholine) with the normalized extract or polyphenol constituents (like straightforward flavonoids) in a non-polar dissolvable. [4] Phosphatidyl moiety is hydrophilic in nature. Explicitly the choline top of the phosphatidylcholine atom ties to polar mixtures while the lipid dissolvable phosphatidyl part involving the body and tail envelopes the choline bound material. In these manner the phytoconstituents structures a lipid viable sub-atomic complex with phospholipids complex. Particle are bounce through substance securities to the polar choline top of the phospholipids, as can be shown by unambiguous spectroscopic procedures. [5, 6] Exact compound investigation shows the unit phytosomes is generally a flavonoid particle connected with something like one phosphatidylcholine atom. The outcome in the development of a miniature cell. The phytosomes innovation creates a little cell by which the plant extracts or its dynamic constituents is safeguard from obliteration by gastric discharges and stomach microorganism due to the gastro protective property of phosphatidylcholine. [7]

ADVANDATGE OF PHYTOSOMES

1) Small dose is required, as absorption is expanded manifolds.
2) Phytosomes posses better drug entrapment efficiency.
3) Phosphatidylcholine is a not simply a transporter; it is likewise having hepatoprotective action and healthy benefit.
4) Cosmetic and other topical use of phytoconstituents should be possible by phytosomes formulation.
5) Because of arrangements of compound bonds, phytosomes shows better stability profile.[8]
6) Time period of action is increased. [9]
7) Phytosomes have fundamentally more prominent clinical advantage.
8) Phytosomes increases the solubility of bile to herbal constituents. [10]

PROPERTIES OF PHYTOSOMES

Physiochemical Properties:

1) Phytosome are ready by response of stoichiometric amount with the standardized plant extract as substrate. The spectroscopic data reveals that phospholipids-substrate interaction is due to the formation of hydrogen bond between polar head (i.e. phosphate and ammonium group) and the polar functionalities of the substrate. [11]
2) The size of phytosome changes from 50nm to few 100
3) Phytosomes when treated with water, they except a micelle shape looking like liposomes and photon connection spectroscopy (PCS) uncovers these liposomal structures gained by phytosomes.
4) From the 1HNMR and 13CNMR data, it can be concluded that the fatty chain gives unaltered signals both in free phospholipids and in the complex, which demonstrates that long aliphatic chains are folded around the active principal, producing lipophilic envelop.
5) Regarding the solubility of phytosomes, the complexes are often freely soluble in aprotic solvents, moderately soluble in fats, insoluble in water and relatively unstable in alcohol.

Biological properties:

1) Exploration on pharmacokinetics and pharmacodynamics properties in animal research and healthy human workers have shown that the phytosomes has a higher bioavailability than the complexed natural subsidiaries.
2) Phytosomes are herbal preparation that are easily utilized, absorbed and thus greater outcomes than traditional herbal extracts.
3) Freely soluble in non- polar and aprotic solvent; solvents in which hydrophilic moiety is not present.
4) Insoluble in water.
5) Moderately soluble in fats.[12]

COMPARISON BETWEEN LIPOSOMES AND PHYTOSOMES.

In like manner phytosomes, a liposomes is formed by blending water dissolvable substance in with phosphatidylcholine in clear proportion under specific conditions. Here no synthetic bond is formed; the phosphatidylcholine atoms encompass the water solvent substance. There might be hundreds or even a large number of phosphatidylcholine particles encompassing the water-soluble compound. Conversely, with the phytosome process the phosphatidylcholine and the plant parts really structure a 1:1 or a 2:1 sub-atomic complexes relying upon the substance buildings, including synthetic bonds. This distinction results in phytosomes being vastly improved retained than liposomes showing better bioavailability. Phytosomes have likewise been tracked down better than liposomes in effective and healthy skin items. [13]

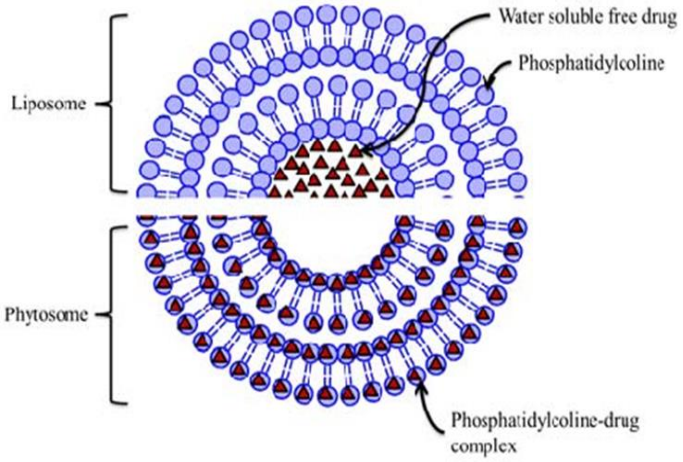

Fig 1; Shows difference between Liposomes and Phytosomes
The molecular organization of the Liposomes (upper segment)
The molecular organization of the Phytosomes (lower segment)

METHOD PREPARATION OF PHYTOSOMES

- **ANTI-SOLVENT PRECIPITATION TECHNIQUE**
  A 100 ml round-bottom flask containing the prescribed dosage of medication and soy lecithin was refluxed for two hours at a temperature higher than 60°C using 20 ml of dichloromethane. 5–10 millilitres of the mixture are concentrated. The precipitate was obtained by carefully adding 20 millilitres of hexane while stirring continuously. The precipitate was then collected, filtered, and kept in vacuum desiccators for the night. A mortar is used to smash the dry precipitate, which is then sieved through #100 meshes. The powdered complex was kept at room temperature in a glass container with an ambered colored. [14]

- **ROTARY EVAPORATION TECHNIQUE**
  In a rotating round-bottom flask, the prescribed dosage of medication and soy lecithin were dissolved in 30 millilitres of tetrahydrofuran, and the mixture was stirred for three hours at a temperature higher than 40° c. After the sample was thinned out, n-hexane was added, and a magnetic stirrer was used to continually agitate the mixture. The resulting precipitate was collected, put in an amber-colored container, and kept in room temperature storage. [15]

- **SOLVENT EVAPORATION TECHNIQUE**
  A 100 ml round-bottom flask containing the prescribed dosage of medication and soy lecithin was filled, and for two hours, it was refluxed with 20 ml of acetone at 50–60°C room temperature. In order to acquire the precipitate, which was filtered and collected, the mixture is concentrated to 5–10 ml. The amber-colored glass bottle containing the dried precipitate phytosome complexes was kept at room temperature. [16]

Different Additives Used In the Formulations of Phytosomes: [17]

1) Phospholipids: Soya phosphatide choline, Egg phosphatidylcholine, Dipalmityl phosphatidyl choline, Distearyl phosphatide choline.
2) Aprotic solvent: Dioxane, acetone, methylene chloride.
3) Non solvent: n-hexane and non-solvent i.e. aliphatic hydrocarbon.
4) Alcohol: Ethanol, Methanol

List of Equipment Used In Preparation of Phytosomes

1) UV – Visible 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 electronic microscopy (SEM)
9) Transmission electron microscopy (TEM)

General Method for Preparation of Phytosomes:

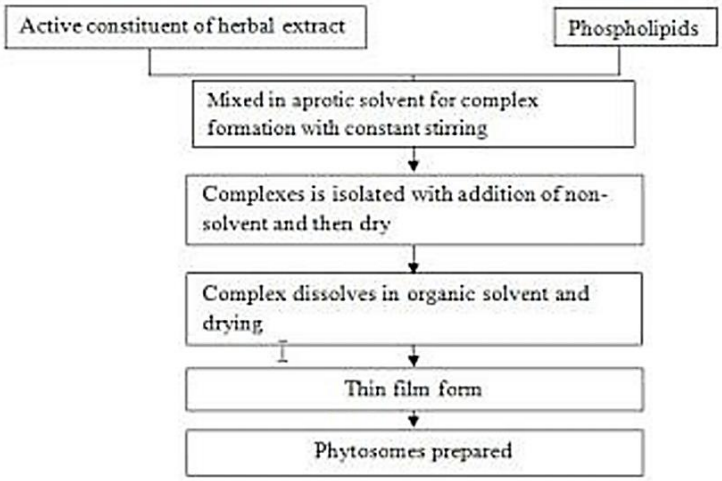

Fig 2: General method for Preparation of Phytosomes

CHARACTERIZATION OF PHYTOSOMES

- **Solubility and Partition Coefficient**:
  To describe the primary components, active ingredients, phyto-phospholipid complexes, and physical mixture (P), it is very required to analyse the solubilisation in organic and inorganic solvents as well as the n-octanol and water partition coefficient. Generally speaking, hydrophlicity and lipophilicity are processed at higher levels by phytosomes than by active components. [18]

- **Particle Size and Zeta Potential:**
  Two important characteristics that are related to their stability and repeatability are particle size and zeta potential. Phospholipid complexes typically have particle sizes between 50 and 100 m. The complexes average zeta potential and particle size were determined to be 10.09 ± 0.98 mV and 153 ± 39 nm, respectively. [19]

- **Scanning electron microscopy (SEM) and transmission electron microscopy (TEM):**
  SEM gave important details regarding the surface morphology and solid-state properties of complexes. The transmission electron microscope (TEM) is widely employed to investigate the crystallization and dispersion of nanoparticles, in addition to ascertaining the size of individual particles. Using SEM, active compounds may be observed in highly crystalline settings; however, complexation causes the structural crystals to disappear. TEM showed that when phyto-phospholipid complexes are diluted in distilled water and gently agitated, they take on the shape of vesicles. [19]

STRUCTURAL VERIFICATION OF PHYTO PHOSPOLIPID COMPLEXES

- **Ultra Violet Spectra (UV Spectra):**
  Samples with varying UV absorbance can be utilised to determine their own structural qualities.The properties of components UV absorbance including during and after complexation have not been shown to alter in most experiments When chemicals are mixed with phospholipids , their chromophore are unaffected.

- **Differential Scanning Calorimetry (DSC):**
  Interactions can be determined by analysing the DSC's transition temperature, melting points, emergence of new peaks, removal of old peaks, and changes in the relative peaks area. In many cases, the characteristic peaks of phyto-phospholipid complexes differ significantly from those of a physical combination. Strong interactions are thought to provide the active ingredient and prevent the two phospholipid fatty chains from rotating freely. This is accomplished by the polar part of phospholipids. The DSC thermo gram, which shows two unique peaks that are lower than those of the physical combination, lost the rutin and PC peaks. [20]

- **Fourier Transform Infrared Spectroscopy (FTIR)**

  A popular structural analysis method that yields a variety of functional groups with unique band numbers is FTIR. Shape, location, and attributes of intensity. The creation of phyto-phospholipid complexes can be verified by comparing the phospholipid complex spectra to those of physical mixes. Numerous investigations could yield a variety of results. The rutin and phyto-phospholipid complexes' FTIR spectra matched those of pure rutin exactly. [20]

- **X – Ray Diffraction:**
  These days, X-ray diffraction is a great way to find out the morphology of both amorphous and crystal components. It is frequently employed in the investigation of phytophospholipid complexes, or active substances. PCs and the physical configurations of them. Dense crystalline peaks are visible in the X-ray diffraction pattern of a physical mixture containing an active substance, which suggests a high crystal form. Conversely, the absence of a crystalline peak in active element phyto-phospholipid complexes suggests that the components interacting with phospholipids are either amorphous or molecular. The hydrophilicity and lipophilicity of active components were lower than those of phospholipid complexes.[18]

- **Nuclear Magnetic Resonance:**
  In order to determine the complexes' structural characteristics. Methods such as 13C NMR and 1H NMR are employed. The link between phospholipids and polyphenols is established by hydrogen bonds, not chemical ones. The core choline-bioactive part of these complexes can have its membrane contained by the hydrophobic side of lipids. Based on different phyto-phospholipid complexes' spectra.

Mechanism of Phytosome Technology

The primary method of creating phytosomal complexes with lipid coverings around the contents is the complexation of polyphenols with phospholipids at a ratio of 1:1 or 1:2. [21] Chemical bonds hold molecules to the polar choline head of phospholipids. According to precise chemical analysis, a flavonoid or polyphenol molecule connected to at least one phosphatidylcholine molecule often makes up the unit phytosome. A tiny microsphere or cell is created as a result. [22] Phospholipid complexes can be taken up from the GIT by enterocyte-based transport, and drugs can be transported from the intestinal lymphatic system, which is widely distributed throughout the body, to the systemic circulation. The ability to avoid first-pass metabolism and use lymphatic transport for tailored medication administration is its main benefit. [23]

APPLICATION

1) The nutrients so helpful for enhancing the absorption are the phospholipids.
2) Phospholipids are complex molecules that are used in all known life forms to make cell membranes.
3) It is use in cancer treatment.
4) It is used as wound healing.

Limitation of Phytosome:

Phytosomes, despite of having numerous advantages as drug delivery system, are not prevalent in the market. A major drawback of phytosome could be leaching of phytoconstituent off the ‘some’ which reduces the desired drug concentration indicating their unstable nature. [24]

CONCLUSION

Herbal products always have great concern of denaturation and bioavailability. There is so many novel approaches are available in NDDS. Despite these approaches liposomes and phytosomes are most suitable novel approaches for herbal drugs to overcome this kind of problems. These delivery systems have improved the pharmacotherapeutics and pharmacokinetics of herbal drugs. This kind of delivery systems is also utilized in the field of nutraceuticals and cosmeceuticals for improving therapeutic effect and permeability in the skin. The formation of phytosomes are simple and reproducible a part of that phospholipids used in the preparation of phytosomes have their own beneficial effects in the body.

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