Efficient delivery of phytoconstituents is almost challenging task for scientific community owing to their imbalanced hydrophilicity and lipophilicity considerations. The majority of phytoconstituents is mainly hydrophilic and has large molecular size, resulting in low absorption and bioavailability. Phytosomes and vesicular systems are a unique and revolutionary way of increasing the solubility and bioavailability of phytoconstituents and plant extracts. These are phytosphospholipid complexes or herbosomes, which are complex form of phytoconstituents and phospholipid molecules. In compared to conventional dosage form, phytosphospholipid complex has showed improved pharmacokinetic and pharmacodynamic properties. Solvent evaporation, anti-solvent precipitation, co-solvent lyophilization, and other methods have been used to prepare phytosomes all over the world. The current review focuses on the numerous methods for preparing phytosomes that are routinely used. Significant attributes, characterization methods, role of phospholipids in the preparation of phytosomes, various marketed and patented phytosomal products and recent investigations on phytosomes have also been highlighted.

KEYWORDS: Phyto-phospholipid complex, phytoconstituents, herbosomes, bioavailability, herbal extracts.

INTRODUCTION

The use of various herbal plants as a source of medicine is a prehistoric tradition that continues to be an integral part of India’s healthcare system. Around 20000 medicinal plants have been identified in India, but traditional healers use only 7000-7500 of them to treat various diseases. The popularity of herbal medicines is rapidly increasing as a result of
increased attention provided to it by governmental agencies and various non-governmental organisations comprised the general population and analysts, as the enhanced side effects and adverse drug reactions of current medicines.

However, herbal medicine have a problem with bioavailability,\textsuperscript{[1]} which is due to the fact that mainly all the bioactive constituents of herbal medicines are polar in nature,\textsuperscript{[2]} which prevent them from penetrating GIT trachea’s the outermost cell membrane, and have large multi ring structure which makes passive diffusion impossible (like flavonoids, tannin, glycosidic aglycones, and so on).

To address these issues, the \textit{A Novel Drug Delivery Mechanism for Plant based Medicines is Phytosomes}, has arise,\textsuperscript{[3,4]} The word “Phyto” refers to plant, whereas “some” refers to like cell structure. It is a Vesicular Drug Delivery System (VDDS) in this phytoconstituent of herbal crude extract are bounded through lipid (one molecule of phytoconstituent must be linked at least one phospholipid molecule),\textsuperscript{[5]} that’s why these are also called \textit{phytophospholipid complex}.

Phytosome prevents essential components of herb extract from being damaged by digestive fluids and enteric bacteria, and show enhanced absorption results in increased bioavailability,\textsuperscript{[6,7]} pharmacological and pharmacokinetic parameters when correlate to traditional herb extracts.\textsuperscript{[5,8,9]} The following section illustrates a number of important characteristics of phytophospholipid complex.

\begin{itemize}
  \item Phytosome improves bioavailability by increasing the absorption of hydrophilic phytoconstituents through oral and topical routes.\textsuperscript{[2]}
  \item Enhance the permeation of hydrophilic herbal constituents, allowing for better intestinal absorption.\textsuperscript{[8]}
  \item Increased bioavailability of liver protecting flavonoids and phosphatidylcholine has a synergistic impact on liver safety and hepatoprotective function.\textsuperscript{[9]}
  \item The bonds form among the herbal constituents and phospholipid molecules results in a better stability profile.\textsuperscript{[10]}
  \item Reduce dosage requirements and increased absorption of Phytoactive constituents result in positive outcome.\textsuperscript{[11]}
\end{itemize}
Phytosome Technology and ITS advantages

Indena S.P.A of Italy invented the phytosome technology that significantly improves bioavailability of phytomedicines that are selected via integrating phospholipids into standardised herbal extracts, which enhances absorption and also utilisation. Both water and lipids doesn’t allow polyphenols to soluble in them. The charged phosphate head of phospholipids interacts with polar functionalities of lipophilic guest’s through hydrogen bond and polar interactions forming a specific arrangement that can be observed using spectroscopy.\textsuperscript{[12]} Some advantages of phytosomes are described below:-

- Absorption of fatty insoluble polar plant extract via topical and oral routes is significantly improved, resulting in greater therapeutic efficacy.
- As absorption is increased, thus small dose is required.
- Drug entrapment efficiency is improved via phytosomes.
- PC (phosphatidylcholine) is not just a transporter, besides this, it has liver protective and nutritive properties.
- Greater clinical benefits.
- Chemical bonds are formed in phytosomes therefore they exhibit higher stability profile.
- Phytosomes can easily transfer from a hydrophilic (water loving) part to lipophilic part of enterocyte cell membrane, and then into the cell. Therefore, they are employed for systemic targeting of herbal medication.
- Phytosomes formulation can be used for beautifying products and other dermal uses of plant constituents.

Structure of phytosome

In phytosomal structure the active constituents of herb is surrounded by phospholipid (as shown in Fig:-1). Phytophospholipid complex (phytosomes) were formed when interaction between herbal active constituents and phospholipid take place in solvent. In this the phospholipid head group (polar) is anchor but the two long fatty chains don’t participate in complex formation. To make a lipophilic surface, two fatty acids chains can enclose the polar part of phospholipid complex. The presence of phospholipid in the molecule protect the product from water degradation and also leading to enhance adherence to the product, the surface with which it comes into contact, and the interaction of various molecules with the cell structure.
Fig. 1: Structure of phytosome.

Like phosphatidylcholine (PC) is a bifunctional compound in which the hydrophilic choline head bound to herbal active constituents, while the lipophilic phosphatidyl portion (tail and body) envelope the choline bound material and forms a phyto-phospholipid complex.\cite{5,9,13}

Features of phytosomes

Physiochemical properties

- The phytosome/herbosome is made by combining a stoichiometric volume of lecithin with standardised herbal extract as a substrate. The spectroscopic data reveals the formation of H-bond among the substrate’s polar functionalities and polar head (i.e., phosphate & $\text{NH}_4^+$ group).\cite{10}
- Phytosomes range in size from 50 nanometres to a few hundred micrometres.\cite{14}
- Both in free phospholipid and in complex, the signals are unchanged, given by fatty chains, indicating that active principle are wrapped by the aliphatic chains forming a lipophilic covering, according to H1 NMR and C13 NMR results.\cite{15}
- In aprotic solvents, the phytophospholipid complexes are usually freely dissolvable, slightly soluble in fats, doesn’t soluble in water, and comparatively not stable in alcohol. However, when lipophilic phytoconstituents like curcumin are complexed with phospholipids, their phytosomes give an increase in water solubility.\cite{16}
- When mixed with water, phytosome takes on micellar form that resembles a liposome and photon correlation spectroscopy (PCS) shows that liposome structure has been attained by phytosome.\cite{17}
Biological properties

- Herbosomes are novel compounds that are well absorbed and used, resulting in higher bioavailability and better results than herbal plants extracts or non-complex extracts, according to pharmacokinetic and pharmacodynamic studies in laboratory animals and human subjects.\(^{[17]}\)

Table 1: Components involved in the formulation of phytosomes.

<table>
<thead>
<tr>
<th>S. No</th>
<th>Components</th>
<th>Property</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Phospholipid</td>
<td>Used for producing vesicles</td>
<td>Soya-phosphatidylcholine, Egg- phosphatidylcholine, etc</td>
</tr>
<tr>
<td>2</td>
<td>Aprotic solvent</td>
<td>It is used as a solvent in preparation of phytosome</td>
<td>Dioxane, Acetone, Methylene chloride</td>
</tr>
<tr>
<td>3</td>
<td>Non solvent</td>
<td>Precipitating solvent for complexes</td>
<td>n-hexane, Aliphatic hydrocarbon</td>
</tr>
<tr>
<td>4</td>
<td>Buffering agent</td>
<td>Hydrating agent</td>
<td>Ethanol Tris buffer, Saline phosphate buffer</td>
</tr>
<tr>
<td>5</td>
<td>Alcohols</td>
<td>Organic solvent</td>
<td>Ethanol, Methanol</td>
</tr>
</tbody>
</table>

Impact of phospholipid on phytosome preparation

In the composition of cellular and subcellular membranes, phospholipid is a prominent component. They are also necessary component for life’s activities. The human body uses phospholipid as emulsifiers and to improve fat soluble substance portion. In joints, pericardium, pleura, alveoli of lungs and other tissues it acts as a surface active agent.\(^{[19]}\) By using mechanical or chemical processes they can be extracted from soybean and egg yolk by addition of n-hexane. Phosphatidylcholine is made up of two different groups as shown in fig. 2.

1) Lipophilic phosphatidyl group
2) Hydrophilic choline group

![Fig. 2: Phosphatidylcholine.](image)
The choline moiety enhances muscle control and memory. The hydrophilic part binds to the plant extract, whereas the phosphatidyl group act as a shell covering the phytoconstituents, further protecting the active constituents from digestion. The bioavailability of the active ingredient is raised, and duration of action is also prolonged, due to the formation of drug-phospholipid complexes.\[19\]

**Preparation techniques of phytosomes**

Herbal extract and lipids combine to form phytosomes/herbosomes which are novel complexes. Phytosomes are formed by binding the standardised extract of herb’s active ingredient to a phospholipid such as phosphatidylcholine (PC), phosphatidylethanolamine and phosphatidylycerine via polar end.\[20\]

Herbosomes produced by mixing two three units of phospholipid (natural or synthetic) with one unit of plant extracts. The process take place in an aprotic solvent like acetone or dioxane, and phytophospholipid complex were removed via precipitation by addition of non-solvent like aliphatic hydrocarbons and with lyophilization, or by spray drying. The proportion of two parts in complex formation ranges from 0.5-2 moles. The most ideal phospholipid to flavonoid ratio is 1:1. The preparation of phytosomes is illustrated in a step-by-step manner in diagram below (fig. 3).

![Diagram](image-url)

**Fig. 3:** General steps for phytosomes preparation.
Solvent evaporation, co-solvent lyophilization and anti-solvent precipitation are three commonly used techniques for the preparation of phytosomes, as shown in the diagram (Fig. 4).

1) **Solvent evaporation method**

This technique has been used to create phytosomal vesicles. A 250ml round bottom flask is use to combine the anhydrous ethanol with phytosomal complex. A rotator evaporator is connected to the flask. At 60°C solvent will start evaporating and a thin layer film will formed around the flask. The lipid layer peels off in the phosphate buffer (pH 7.4), also hydrates the film, generating vesicles suspension. Probe sonication with 60 percent amplitude is used on the phytosomal suspension. Until characterization, the phytosomal suspension then kept in the refrigerator for one day.\(^\text{[21]}\)

2) **Co-solvent lyophilisation**

Separate solvents are used to dissolve the phytoconstituents and phospholipid. Both solutions were mixed together using continous stirring or slow agitation until a clear mixture was formed. Complexes are obtained and deposit after co-solvent lyophilization of a clear mixture under vacumm under few hours.\(^\text{[16,22,23]}\)
3) **Anti-solvent precipitation technique**

Weigh the polyphenolic extract and phospholipid accurately. Kept it in a round bottom flask of 100ml and heat for 3 hours at 60°C with 30ml DCM, then reduce it to 5-10ml and then add 30ml n-hexane with constant agitating to obtain the precipitates. After this collect the precipitates and store them overnight in vacuum desiccator. The desiccated precipitates are then passed from #100 mesh & place into a tightly sealed container.[24]

**Table 2: Preparation of phytosomes using various techniques.**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Method Used</th>
<th>Characterization Technique</th>
<th>Inferences</th>
<th>Author(s)</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk thistle phospholipid complex+ Vit C +Vit E</td>
<td>Solvent Evaporation</td>
<td>FTIR, DSC, UV-spectra, In-vitro digestion and absorption assay</td>
<td>Shows better invitro stability as compare to liposomes</td>
<td>Huang et al</td>
<td>[25]</td>
</tr>
<tr>
<td>Triterpene</td>
<td>Solvent Evaporation</td>
<td>SEM, TEM, In-vitro drug release, Ex-vivo permeation, In-vivo pharmacokinetic studies</td>
<td>Improved bioavailability</td>
<td>Freag et al</td>
<td>[17]</td>
</tr>
<tr>
<td>Resveratol</td>
<td>Solvent</td>
<td>SEM, TEM,</td>
<td>Increased</td>
<td>Kalita et al</td>
<td>[17]</td>
</tr>
<tr>
<td>Compound</td>
<td>Method</td>
<td>Studies</td>
<td>Properties</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>-------------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Puerarin</td>
<td>Solvent Evaporation and Freeze Drying Method</td>
<td>SEM, XRPD, DSC, IR, solubility and dissolution studies</td>
<td>Enhanced solubility and In-vitro dissolution rate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Icariin</td>
<td>Antisolvent Precipitation</td>
<td>Vesicle size, TEM, FTIR, In-vitro release, Cytotoxic effect on ovarian cancer cells</td>
<td>Enhanced cytotoxic activity on OVCAR-3 cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lawsone</td>
<td>Antisolvent precipitation</td>
<td>Percentage yield, particle size, entrapment efficiency, drug content and SEM</td>
<td>Better antifungal activity, enhanced permeation rate &amp; anti-inflammatory activity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gingerol</td>
<td>Antisolvent precipitation</td>
<td>Particle size, entrapment efficiency, FTIR, SEM, zeta potential, in-vitro, in-vivo evaluation</td>
<td>Sustained antibacterial, anti-inflammatory action through oral administration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rutin</td>
<td>Co-solvent lyophilization</td>
<td>UV, IR, X-ray diffraction, free radical scavenging activity</td>
<td>Enhanced free radical scavenging activity, improved rutin antioxidant property</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin phospholipid complex</td>
<td>Co-solvent lyophilization</td>
<td>IR, X-ray diffraction, in-vitro release studies, hypoglycaemic effect and relative bioavailability studies</td>
<td>Enhanced solubility and intestinal absorption of insulin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Woodfordia fruticosa</td>
<td>Ethanol reflux method</td>
<td>Percentage yield, entrapment efficiency, FTIR,</td>
<td>Improved solubility &amp; increased</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Spectroscopic analysis and characterization

Physical characteristics of phytosomes are shape, size, distribution, percentage drug capture, entrapped volume, percentage of drug release, and chemical compositions etc. As a result particle size, proportion entrapment of drug, chemical compositions, purity and quantity of raw material all influences the phytosome behaviour in both physical and biological systems.

Table 3: Some characterization Methods and Techniques.

<table>
<thead>
<tr>
<th>Characterization techniques</th>
<th>Characterization methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visualization</td>
<td>Transmission Electron Microscopy (TEM)</td>
</tr>
<tr>
<td>Entrapment Efficiency</td>
<td>Ultracentrifugation</td>
</tr>
<tr>
<td>Transition Temperature</td>
<td>DSC</td>
</tr>
<tr>
<td>Surface Tension Activity</td>
<td>Ring method in a Du Nouy ring transiometer (in aqueous solution)</td>
</tr>
<tr>
<td>Vesicle stability</td>
<td>Mean size by DLS (Dynamic Light Scattering), Structural changes (TEM)</td>
</tr>
<tr>
<td>Drug Content</td>
<td>Modified HPLC</td>
</tr>
<tr>
<td>Vesicle size and Zeta potential</td>
<td>DLC &amp; PSC</td>
</tr>
<tr>
<td>In-vitro drug release</td>
<td>Franz Diffusion Cell (Phytosomal Suspension)</td>
</tr>
<tr>
<td>Drug Content</td>
<td>UV-Spectrophotometer at 269nm</td>
</tr>
</tbody>
</table>

Recent investigations on phytosomes
There are various research articles on phytosomes which shows the benefits of Phytosomal Drug Delivery System over conventional drug delivery systems. Few researches are given below:-

i) In a study, the metabolic parameters, nervousness like behaviour, and inflammatory factors in rats that had been bared to stress and given a curcumin nano-phytosome. Four groups (n=20), are made with eighty female rats.
With A & B group (negative control) being non-stressed rats treated with 0.9% Nacl and nano-phytosome. C and D groups (positive control) being stressed rats were treated with 0.9% Nacl and nano-phytosome.

The stressed rats were given a 13-days stress phase before being given a 21 day treatment.

Following treatment with nano-phytosome, anxiety-like behaviour, inflammatory markers IL-6, IL-1, TNF, and COX-2, as well as glucose and triglyceride concentrations, were measured. The result revealed that stress induction raised anxiety symptoms (P0<05), inflammation (P0<05), and blood parameters but curcumin nano-phytosome treatment reduced anxiety symptoms (P0<05), inflammation (P0<05), and blood parameters (P0<05).[46]

ii) In another study, the purpose of this study was to design and analyse a phosphatidylcholinated phytosome system base on the TFTA (Triterpenoid Fraction of Terminalia Arjuna) for safe & proficient triterpenoid administration with increased absorption and as a result increased bioavailability. By using thin layer film hydration method herbosomes, a novel transporter for drug delivery of TFTA, were successfully prepared using a ratio of 3:7 of PC-TFTA complex and cholesterol in chloroform: methanol (3:1) and then evaluated for various spectroscopic techniques like SEM, DSC, FTIR, and physical evaluation etc. The average diameter of Plantersome was 381.2 ± 1.82 nm. TFTA had an entrapped efficiency of 87.94 ± 0.41%. [47]

iii) Icariin (ICA) is a flavonol glycoside with pharmacological properties that are pleiotropic. It is cytotoxic to cancer cells of ovary and improves their chemosesitivity to chemotherapeutic drugs. In a study, ICA’s cytotoxic activities in OVCAR-3 ovarian cancer cells might be improved by putting it in phytosomes. A box-Behnken design was used to optimise the ICA phytosomal formulation. The optimized formula was characterized by particle size, shape, and in-vitro drug release. ICA in phytosomes may improve its cytotoxicity action in OVCAR-3 ovarian cancer cells. A box-Behnken model was used to optimise the ICA-phytosomal formulation. The cytotoxicity of ICA-phytosomes against ovarian cancer cells was increased. [48]

iv) For the treatment of hepatocellular carcinoma (HCC), the most effective isoflavone is Genistein (Gen).The primary impediments to low gen oral bioavailability are low water solubility and first pass metabolism. Another study was done to shield the gen from its
metabolism and increase the bioavailability through the complex forming between gen and phospholipid and assimilate Gen lymphatic delivery to PL. For this, in the synthesis of GP, GPM, and GPL phytosomes, many types of PL were employed including Lipiod® S100, Phosal® 53 MCT, and Phosal® 75 SA. Following oral administration to rats, the influence of formulated components was assessed. [48]

v) Grape seed extract (GSE) is high in phenolic compounds, which have strong antioxidant properties. Because of its hydrophilicity, phenolic chemicals in GSE have poor penetration. A research was done to develop a GSE phytosome serum that would solve the problem of penetration. In this study thin layer hydration method was used for preparing phytosomes. Prepared plantersomes was also characterized for their physical and chemical properties. A gel based serum was created using specified phytosome. The serum was then subjected to physiochemical tests (colour, odour and syneresis), homogeneity, and pH, viscosity, and rheology properties. On phytosome and non-phytosome serum, an in-vitro penetration study was done using Franz diffusion cells. Thus study concluded that plantersomes enhance the diffusion of the drug in serum dosage form. [49]

vi) Illnesses caused by oxidative stress have been treated with Bergamot since ancient times. The goal of this study was to analyze if bergamot phytosomes might improve the plasma lipid profile and reduce visceral fat in obese class 1 patients with mild hyperlipidemic. Sixty-four individuals were arbitrarily assigned to one of two groups. After just 30 days of supplementation, this study found that bergamot phytosomes have positive benefits such as decreased VAT and regulation of metabolic changes. [50]

vii) Coenzyme Q10 (CoQ10) is a lipid-soluble substance that acts as an antioxidant and transfer electrons in the mitochondrial transport chain by boosting the transmembrane, which may be used by the ATPase to generate ATP. However, CoQ10 is hydrophobic in nature, which limits its absorption. This study looked at the cellular and mitochondrial content of CoQ10, as well as its redox state after being incubated with UBQ (UBIQSOME®). The results of this study show that UBQ formulation improves cellular bioenergetics parameters in in-vitro models. [52]

viii) Silybin, a natural chemical used to treat liver illness, has been found to have a variety of biological activities including anticancer, antioxidant, and hepatoprotective properties.
However, due to its poor water dissolving power and restricted GIT absorption, developing silybin products remains difficult. To enhance silybin's poor bioavailability, SPCs-NPs, a new formulation of phytosome-nanosuspensions for silybin shielding, has been created for liver protection effectiveness. In the in vivo pharmacokinetic research, they discovered that the SPCs-NPs formulation not only had a faster \textit{in-vitro} dissolution rate, but also had a high plasma concentration. Furthermore, SPCs-NPs showed more powerful hepatoprotective effects in pharmacodynamics studies. Overall, the study intriguing findings showed that SPCs-NPs may be used as a viable formulation for increased drug bioavailability and improve liver protection effectiveness.\cite{52}

ix) Another study focused on the development of a new diosgenin derivative and its phytosome against lung cancer cells, which demonstrated strong cytotoxic action. In preclinical investigations, diosgenin (Di), a sapogenin produced from plants, shown antitumor action. They developed several Di derivatives and tested against FZU-0021-194-P2 (P2), which shown more strong cytotoxic action against human non-small-cell lung cancer A549 and PC9 cells. P2 phytosome (P2Ps), a phytosome derivative, with higher water solubility than P2. The findings suggested that P2Ps might be used to promote anticancer formulations for non-small cell lung cancer.\cite{53}

x) Another study reveals the preparation of berberine phospholipid complex solid dispersion, which not only increases the compound's solubility but also its flow ability and dissolving rate for industrial production.\cite{24}

Table 4: List of marketed phytosomal product.

<table>
<thead>
<tr>
<th>Phytosomes</th>
<th>Phytoconstituents complexed</th>
<th>Dose</th>
<th>Application</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silybin phytosome\textsuperscript{tm}</td>
<td>Silybin from \textit{silybin marianum}</td>
<td>120mg</td>
<td>Hepatoprotective, antioxidant for liver and skin</td>
</tr>
<tr>
<td>Ginselect\textsuperscript{®} phytosome\textsuperscript{®}</td>
<td>37.5% ginsenosides from \textit{panax ginseng}</td>
<td>150mg</td>
<td>Adaptogen, tonic, skin tightener, nutraceuticals</td>
</tr>
<tr>
<td>Greenselect\textsuperscript{®} phytosome\textsuperscript{®}</td>
<td>Epigallocatechin from \textit{camellia sinensis}</td>
<td>50-100mg</td>
<td>Nutraceuticals, systematic antioxidant, anticancer</td>
</tr>
<tr>
<td>Grape seed phytosome\textsuperscript{tm}</td>
<td>Procyanidins from \textit{vitis vinifera}</td>
<td>50-100mg</td>
<td>Nutraceuticals, systemic antioxidant, cardio-protective</td>
</tr>
<tr>
<td>Ginkgo phytosome\textsuperscript{tm}</td>
<td>ginkgo biloba l.</td>
<td>120mg</td>
<td>Cognition, vasokinetic</td>
</tr>
<tr>
<td>Olive oil phytosomes</td>
<td>Polyphenols from \textit{olea europaea} oil</td>
<td>-</td>
<td>Anti-inflammatory and antioxidant</td>
</tr>
<tr>
<td>Super milk thistle</td>
<td>Silybin from</td>
<td>150mg</td>
<td>Antioxidant for liver and skin</td>
</tr>
<tr>
<td>Patent title</td>
<td>Innovation</td>
<td>Inventors Name</td>
<td>Patent No</td>
</tr>
<tr>
<td>------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td><strong>extract</strong>™ silymarin food product</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hawthorn phytosome™</td>
<td>Flavonoids from <em>crataegus sp.</em></td>
<td>100mg</td>
<td>Nutraceuticals, best choice in heart disease and high blood pressure</td>
</tr>
<tr>
<td>Leucoselect®</td>
<td>Procynidine</td>
<td>300mg</td>
<td>Reduce oxidative stress and improves plasma antioxidant defences</td>
</tr>
<tr>
<td>Visnadine phytosome®</td>
<td>Visnadine from <em>ammi visnaga</em></td>
<td>-</td>
<td>Circulation improver</td>
</tr>
</tbody>
</table>

**Table 5: Patents of phytosomes.**

<table>
<thead>
<tr>
<th>Patent title</th>
<th>Innovation</th>
<th>Inventors Name</th>
<th>Patent No</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phospholipid complexes of olive fruits or leaves extract having improved bioavailability.</td>
<td>Enhanced bioavailability of olive fruit leaves extract by complexing with phospholipid and composition containing it.</td>
<td>Federico Franceschi, Andrea Giori</td>
<td>WO2007118631A1</td>
<td>[54]</td>
</tr>
<tr>
<td>Treatment of skin and wound repair with thymosin β4</td>
<td>Complex and procedures used for treating dermal related problems with thymosin beta-4.</td>
<td>Hynda kleinman, Allan Goldstein, Katherine malinda, Gabriel sosne</td>
<td>US2007015698</td>
<td>[56]</td>
</tr>
<tr>
<td>Complexes of saponin with phospholipid and pharmaceutical and cosmetics compositions containing them.</td>
<td>Saponin phospholipid complexes with natural or synthesized phospholipids have a high lipophilia and improved lipophilia. They have a high bioavailability and can be used as an active ingredient in pharmaceutical, dermatological and cosmetic formulations.</td>
<td>Ezio Bombardelli, Gian Franco Patri, Roberto Pozzi</td>
<td>EP0283713B1</td>
<td>[57]</td>
</tr>
<tr>
<td>Soluble isoflavone compositions.</td>
<td>Compositions of isoflavones with increased bioavailability.</td>
<td>Anil B. Khare</td>
<td>WO2004045541A2</td>
<td>[58]</td>
</tr>
<tr>
<td>Fatty acids</td>
<td>Having different alkyl</td>
<td>Vittorio</td>
<td>EP1690862</td>
<td>[59]</td>
</tr>
</tbody>
</table>
### CONCLUSION

This review is a cogent attempt to present a concise profile concerning phytosomes benefits, different preparation methods, characterization aspects and salient applications. Phytosomes have elicited improved absorption and enhanced bioavailability as compared to conventional plant extracts. Drug molecules which are incorporated in the structure of phytosomal complex provide more capacity for drug loading, protection against the gastric environment, increased permeation across skin and other biological membranes. Phytosomes also revealed better pharmacokinetic as well as pharmacodynamic properties in comparison to conventional dosage form. Phytosomes can be developed for different purposes like hepatoprotective, anti-inflammatory, immunomodulator, anticancer etc. This advanced frontier technology would surely represent a fruitful avenue for further resolving the queries of various plant based drugs.

### REFERENCES

1. Alexander A, Ajazuddin, Patel R, Saraf S. Recent expansion of pharmaceutical nanotechnologies and targeting strategies in the field of phytopharmaceuticals for the

<table>
<thead>
<tr>
<th>Description</th>
<th>Formulation</th>
<th>Author</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>monoesters of sorbityl furfural and compositions for cosmetic and dermatological use.</td>
<td>Series compounds having side chain straight and branched (C₃-C₁₉) chosen for sorbital furfural fatty acid monoesters.</td>
<td>Bertelli</td>
<td>B1</td>
</tr>
<tr>
<td>Cosmetic and dermatological compositions for the treatment of aging or photo damaged skin.</td>
<td>A chemical that increases collagen formation and a substance that improves the interaction between extracellular matrix and fibroblasts are included in a topical skin therapy composition. For topical treatment, a cosmetic or dermatological component is used.</td>
<td>Anemone TRAGER, Marianne waldmann-Lave, Thomas Doring, Armin waddle</td>
<td>EP1640041 A3</td>
</tr>
<tr>
<td>An antioxidant preparation based on plant extract for the treatment of circulation and adiposity problems.</td>
<td>Formulation based on herbal extracts that have an antioxidant action &amp; especially beneficial in curing circulatory issues like phlebitis, varicose veins, arteriosclerosis and high BP.</td>
<td>Gian Franco merizzi</td>
<td>EP1214084 A2</td>
</tr>
</tbody>
</table>


47. Nabil A. Alhakamy et al Optimized icariin phytosomes exhibit enhanced cytotoxicity and apoptosis-inducing activities in ovarian cancer cells pharmaceutics, 2020; 2-17.


49. Surini, et al.: Cosmetic serum containing grape (Vitis vinifera L) seed extract phytosome, J Young Pharma, 2018; 10(2): s51-s51.52.


