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Areview on phytosomes

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ABSTRACT
Nowadays, medicinal herbs and the phytochemicals in them have emerged as effective treatments for a variety of conditions.However, their clinical application may be limited by their limited bioavailability and selectivity.As a result, improving bio-efficacy in transporting dietary phytochemicals poses a significant challenge in terms of bioavailability.To increase phytochemicals' bioavailability, a variety of approaches have been proposed for the development of efficient carrier systems.Nano-vesicles have been introduced as potential delivery vehicles for insoluble phytochemicals.The bilayer vesicles have been widely used and praised in the scientific literature for their adaptability and ease of preparation.The introduction of phytosome technology and its applications, with an emphasis on formulation and characterization principles, make up the first section of the review.A comprehensive overview of the biological activities of commercial and non-commercial phytosomes is provided in the second section, which is broken down into systems and related pathologies.Curcumin and silymarin are the most commonly formulated compounds, highlighting phytosomes' superior efficacy in terms of biological activity and dosage reduction. These findings confirm phytosomes' superior efficacy.The promising clinical and experimental results regarding the applications of phytosomes are then discussed.The study's conclusion inspires the researchers to bring their expertise from the lab to the market to further develop these products.

Keywords: phytochemical, nanomedicine, phytosome, delivery, vesicle, disease

INTRODUCTION

A phospholipid, mostly lecithin, and a natural active ingredient make up the Phytosome complex.Several well-known herbal extracts and active molecules, such as Ginkgo biloba extract[1], bilobalide from Ginkgo biloba[2], silybin from milk thistle (Silybum marianum),[3] curcumin from turmeric,[4] and green tea extract (Camellia sinensis),[5] have been subjected to complexation with phospholipids. An attempt to trademark the term in the United States was unsuccessful on appeal.Applicant's fatal error, according to the Board, was in using the term as the sole designation for its new product[6]. Some refer to cell-like, while "Phyto" refers to the plant. [7] The vesicular drug delivery system known as phytosomesalso known as herbosomes—improves the bioavailability and absorption of low-soluble drugs.[8] The reaction between phosphatidylcholine (or any hydrophilic polar head groups) and plant extracts in an aprotic solvent produces phytosomes, which are a complex of phospholipids and natural active phytochemicals bound in their structures. [9] These details display worked pharmacological and pharmacokinetic properties when contrasted with pervasive arrangements.The hydrophilic phytoconstituent-choline complexes are completely covered by the lipid-soluble phosphatidyl portion.The remarkable advantages of phytosomes include high drug encapsulation, improved stability (chemical bonds are formed between the polar head of the amphiphile molecule and the phytoconstituent),[10] and improved bioavailability[11] Additionally, polar phytoconstituents, as well as active constituents with a higher absorption rate, require a lower dosage to have a biological effect.

ADVANTAGES

1. Enhance the bioavailability

Multiple studies have revealed that Phyto-phospholipid complexes can boost the absorption of oral topical routes, hence they can increase the bioavailability and reduce the required dose for therapeutic benefit.

2. Enhance percutaneous absorption

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Phyto-phospholipid complexes can easily transition from a hydrophilic environment into the lipophilic environment of the cell membrane and then enter the cell [12]. Therefore, a large number of studies have displayed that the percutaneous absorption of phytoconstituents is improved because of the application of phytoconstituents in form of phytosome [13], [14].

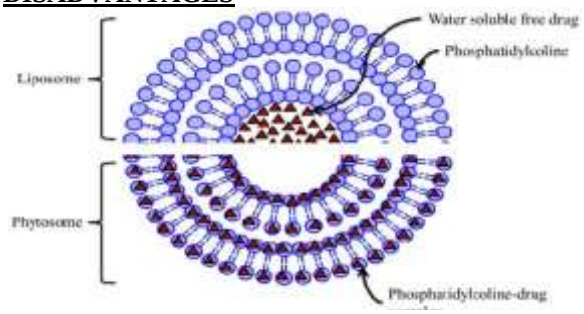
3. Hepatoprotective effect

Compare with carriers employed in other drug delivery systems, phosphatidylcholine isa crude ingredient that also revealsgreat therapeutic benefits [15]. Phosphatidylcholine acts as a hepatoprotective with nutrient value. So, when phosphatidylcholine is taken by the patient, it will show the synergistic effect to protect the liver

4. another advantage

Phyto-phospholipid complexes possess a better drug complexation rate and the preparation of Phyto-phospholipid complexes is not complicated [16].

DISADVANTAGES



PROPERTIES OF PHYTOSOME

- **Chemical properties**

A combination of a natural product and natural phospholipids, like soy phospholipids, is known as a phytosome.The reaction of stoichiometric amounts of phospholipid and the substrate in a suitable solvent yields this kind of complex.According to spectroscopic data, hydrogen bonds between the polar head of phospholipids (phosphate and ammonium groups) and the polar functionalities of the substrate are the primary mechanism by which phospholipids and substrate interact.The phytosomes take on a micellar shape when exposed to water, resulting in structures that resemble liposomes.The active principle in phytosomes is anchored to the polar head of phospholipids. For instance, in the case of the catechindistearoylphosphatidylcholine complex, there is the formation of H-bonds between the phenolic hydroxyls of the flavone moiety and the phosphate ion on the phosphatidylcholine side. In liposomes, the active principle is dissolved internally by comparing the nuclear magnetic resonance (NMR) values of the complex and the pure precursors, this can be inferred.The fatty chain's signals are virtually unchanged.As a result of this evidence, it was deduced that the polar head of the phospholipid and the catechin are protected by a lipophilic envelope created by the two long aliphatic chains surrounding the active principle.

- **Biological properties**

Pharmacokinetics studies or pharmacodynamic tests in experimental animals and human subjects have demonstrated the increased bioavailability of phytosomes over non-complexed botanical derivatives produces better herbal products similar to the extracts.

CLASSIFICATION

1.THE LIPOSOME

The Greek words "Lipos" and "Soma," which mean "body," gave rise to the liposome.[17] The spherical, 0.05–5.0 micrometer-diameter vesicles that makeup liposomes are cholesterol and phospholipids.Due to their hydrophobic and lipophilic properties, they represent an extremely promising carrier for drug delivery in a variety of architectures.[18–20] The goal of this drug delivery system is to direct the drug to the intended action site.[21] Liposomes are biocompatible, stable, and biodegradable. They also have a unique property that allows them to control the release of hydrophilic and lipophilic substances inside their compartments.[22] Various pathological conditions, including cancer, inflammation, eye and skin disease, malaria, and osteosarcoma, are treated with liposomes.[23–28] A variety of methods can be used to design liposomes.

The solvation of the lipids in an organic solvent, in general, is the foundation of the majority of liposome preparatory methods.(2) obtaining a thin film of lipids through evaporation(3) a hydrophilic solvent hydrating the lipid layer; (4) Liposome purification (5) and defining the final liposome's properties.Additionally, the loaded drug's encapsulation may be enhanced by other synthesis techniques. [29]

2. THE NIOSOME

Niosomes are nanometric lamellar vesicles generated by mixing a nonionic surfactant with a li pid like cholesterol helper.[30] The non-ionic

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surfactants create a stable bilayer vesicle in hydrophilic systems by using energy (physical agitation and heating). [31] Hydrophobic parts in the bilayer structure are guided aside from the aqueous phase, while the hydrophilic heads stay in contact with the aqueous side. The surfactants used in the preparation of niosomes should be biocompatible, biodegradable, and not immunogenic. [32] Niosomes act like liposomes in vivo and in vitro, extending the circulation of the encapsulated phytochemical, adjusting its organ distribution, and improving bioavailability.

Niosomal compositions with the same cho lesterol value are leakier than liposomes. [33] Previous research has shown that cholesterol concentration is an important influence factor on vesicle leakage. [34] As a result, the efficiency of liposomal drug trapping becomes lower than niosomes. [35]

3. THE TRANSFERSOME

The first deformable or elastic nanocarrier, transfersomes, appeared in the early 1990s.[36] The customary liposomes don't penetrate the layers of the skin and stay bound to the external layer corneum layer. [37] As a result, improved liposomes have been developed into new types of lipid vesicles like transfersomes.The membranes of a transfersome, a lipid carrier that is highly deformable and elastic, facilitate the transfer of compounds to deeper skin tissues. [38] The transfersome consists of a bilayer softening agent for vesicle flexibility (usually a surfactant) and at least one amphipathic molecule (soy phosphatidylcholine).When transfersome components are added to aqueous systems, they self-assemble into a lipid bilayer that eventually forms a lipid vesicle.Transfersomes have been shown to penetrate the skin further in studies of deformability and penetration.Peptides, small molecules, proteins, and especially herbal components can be carried by transfersomes in medications.[39]

4. THE ETHOSOME

Ethosomes are carriers that don't hurt and let medicines get into the deep layers of the skin and circulate throughout the body.[40] Ethosomes are soft vesicles that have been designed to enhance the delivery of active agents, such as pharmaceuticals and natural products.Deionized water, high concentrations of ethanol, and phospholipids (phosphatidylserine, phosphatidylcholine, and phosphatidic acid) make up the majority of them.[41] Because of the impairment of the skin lipid bilayer caused by the high concentration of ethanol, ethosomes are the best option for the skin.As a result, when ethanol is incorporated into the membrane of the vesicle, it makes it possible for the vesicles to reach the stratum corneum.Because of the presence of ethanol, the ethosomes' lipid membrane is also packaged less tightly than that of other vesicles, which improves the stratum corneum lipids' capacity for drug trafficking.[42] The ethosomes were found to be useful for a variety of applications in the biotechnology, pharmaceutical, cosmetic, veterinary, and nutraceutical industries.As a result, these new vesicular carriers for improved skin delivery are these soft vesicles.[43]

CHARACTERISATION OF PHYTOSOMES

1.AVERAGE SIZE AND SHAPE

A crucial phytosome analysis that provides valuable insight into the quality and various forms of a sample is the evaluation of size and morphology.Microscopical observation4 (TEM, SEM, optical, atomic force, fluorescence, etc.), diverse techniques like DLS[44]what's more, and stream and size-avoidance chromatography[45] can be utilized for phytosome size portrayal.The most common types of electron microscopy for phytosome visualization are cryo-TEM and freeze-fracture-TEM. [46] To avoid phytosomal disruption, cryo-TEM could directly demonstrate phytosomes in the frozen state.[47] Liposomal morphology and size can be precisely observed using freeze-fracture TEM without causing any structural distortion.

2.SURFACE CHARGE

The charge of phytosomes in emulsions is defined by the zeta potential (full charge created by medium). Zeta potential may be negative, positive, or neutral depending on the composition of the phytosome. [48] Zeta potential could reflect the stability of phytosomes in a medium; in fact, charged particles repel each other enough to maintain stability. Phytosome emulsion with a zeta potential greater than or less than 30 mV is known to be stable.[49]

3.CHEMICAL COMPOSITION

NMR, [50]FTIR, and mass spectrometry are typically used to assess the chemical composition and interaction between vesicle components and phytochemicals.[51] Additionally, phytosome phospholipid quantification can be accomplished by reaction with a suitable reagent, followed by spectrophotometric quantification.[52] Mass spectrometry is one of the most reliable methods

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for determining the phytochemical composition of plant extracts and phospholipids because of its high sensitivity, selectivity, and signal-to-noise ratio.[53] FTIR techniques have also been used by a lot of authors to figure out how phytochemicals and vesicle components interact with one another.For instance, de Azambuja Borges et al. used HATR-FTIR, high-field 31P NMR, and low-field 1H NMR to investigate how asolectin-loaded liposomes and soy isoflavone genistein interact with one another.The results demonstrated that isoflavone reduces the degree of hydration and mobility of the phosphate group.[54]

4.ENCAPSULATION EFFICIENCY AND RELEASE BEHAVIOUR

Encapsulation efficiency (EE percent) describes the amount of phytochemical that is embedded in the phytosome.

$$EE\% = \frac{IP - EP}{IP} \times 100$$

where EE% is the efficiency of encapsulation, EP is encapsulated phytochemical and IP is the initial content of phytochemicals.The process of encapsulation efficiency determination begins with the removal of free unencapsulated phytochemicals from the phytosome emulsion by the Sephadex gel column, ultracentrifugation, or dialysis method (defined cut-off) for several hours against buffer solution. Step 2 in EE estimation is the ruination of the phytosome bilayer (with Triton X-100, acetonitrile, methanol, and ethanol) and the quantification of the released active agent by different methods, such as enzymatic assays, gel electrophoreses, fluorescence spectroscopy, and field flow fractionation chromatographic methods, such as HPLC, UPLC, or LC-MS.Drug release behavior of vesicle carriers has been the subject of extensive research over the past few years, since the release profile obtained in vitro may provide an indicator of the efficiency of the carrier in vivo.[55]

METHOD OF PREPARATION OF PHYTOSOMES

The rotary evaporator method, anti-solvent precipitation, freeze-drying co-solvency, and salting-out techniques are just a few of the proposed methods for making phytosome.The most common methods for making the phytosome.The evaporator approach and solvent evaporation are popular and frequently utilized methods for producing phospholipid complexes.Liu et al. stated that the solvent evaporation method for preparing the evodiamine phospholipids complex [56] Berberine-loaded phytosomes was made in another study by Yu et al. using a self-assembly method and solvent evaporation.[57] Lipid materials were dissolved in an organic solvent during solvent evaporation, which was followed by vacuum rotary evaporation.Lawsone-loaded phytosomes were made using the anti-solvent precipitation method, as reported by Singh et al.[58] In this method, dichloromethane was refluxed along with lawsone and soy lecithin at a temperature of 60 °C or less.N-hexane was then added to store the precipitate overnight in vacuum desiccators.Anti-solvent precipitation was used by Karole et al. to create phytosomes containing Bombax ceiba extract. [59] El-Menshawe et al. talked about a phytosome-based soy thermogel made with three different ways to prepare it: salting out, co-solvency, and solvent evaporation.[60] The co-solvency method produced the ideal phytosome formulation, which had an ideal entrapment efficiency (EE) of 99.89%, a size of 64.44 nm, and a release rate of up to 93% after two hours.In an innovative study, Demir et al. encapsulated both the extract of Calendula officinalis and AuNPs to create a novel liposomal formulation. [61] The conventional method of thin-film hydration within the extrusion was used to prepare the vesicles.The results demonstrated that this approach enhanced AuNP and calendula extract's biological activity.The lyophilization or anhydrous co-solvent lyophilization of phytosome complexes are two examples of other documented approaches for their preparation.[62]

APPLICATIONS OF PHYTOSOMES[63].

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

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