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Review Article

Phytosomes: A Newer Approach towards Drug Delivery System

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ABSTRACT

The objective of this review is to focus on the application of herbosome technology along with its preparation, various properties, and characterization. The term "Herbo" means plant while "some" indicates cell-like. It is also known as phytosome. It is a novel technique in herbal drug technology that removes the limitations of traditional drug delivery systems and enhances the bioavailability of herbal extracts. They are produced by a process whereby the standardized plant extract or its constituents are bound to phospholipids, mainly phosphatidylcholine producing a lipid compatible molecular complex. The product and extract which are obtained from plant source are increasingly receiving attention as dietary supplements for the homeostatic management, toxicities, cancers, weight loss, and other chronic or acute degenerative disorders. After isolation of plant products, they prone to instability and are potentially incapable to cross the biomembrane as such. Hydrophobic nature is shown by some plant product and their delivery to the systemic circulation is a quite difficult task. The ribosome technique reduces these tasks to reasonable extents.

Keywords: Herbosome, phospholipids, phytoconstituents, bioavailability

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INTRODUCTION

The term Herbosome Consists of two words 'Herbo' means plant and 'Some' means cell like. It is also mentioned as 'Phytosome'. This is the modern patented technology, where standardized plant extracts or water soluble phytoconstituents are complexed with phospholipids to produce lipid compatible molecular complexes, there by greatly increasing absorption and bioavailability. The some phospholipids (Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine, phosphatidylinositol) are used, but phosphatidylcholine are mostly and widely used because of their certain therapeutic value in case of liver diseases, alcoholic steatosis, drug induced liver damage and hepatitis. Phospholipids are depeuted as natural digestive aids and as carriers for both fat miscible and water miscible nutrients. Herbosomes can easily travels the lipophilic path of the enterohepatic cell membranes and also stratum corneum layer of the skin.[1] Mainly standardized plant extracts of flavonoids are derived as Herbosomes. The various flavonides are selected from the groups consisting of quercetin, campherol, quercretin-3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoside, vitexine, diosmine, 3-rhamnoside etc.

Plants are prosperous with health promoting substances which are mainly the secondary metabolites like flavonoids. Mostly the biologically active component of plants is polar or water soluble molecules. These toxicity and absorption issue limit the use of this component. Apart from that the herbal extracts are destroyed by the digestive secretions and gut bacteria. Vast researches have been done for successful delivery of these plant derived products since the last century.[2]

Mostly the biologically active components of plants are polar or water soluble molecules. Water soluble phytoconstituents are meanly absorbed due to their large molecular size or due to their poor lipid solubility, therefore reduced their ability to across the lipid rich biological membrane, resulting poor bioavailability when administered orally or applied topically. Also isolation and purification of individual components from whole herbal extract lead to partial or total loss of therapeutic activity, the natural synergy become lost which is due to chemically related constituents in herbal extract. The active components of the herbal product (or medicament) are responsible for the effectiveness.[3] To counter these problems pharmaceutical research has been geared towards the development of novel lipid-based drug delivery systems to improve the bioavailability of drugs while maintaining the therapeutic activity of the drug. One delivery system designed to improve the in vivo solubility and hence bioavailability of poorly soluble herbal drugs involves the incorporation of standardized herbal extracts into phospholipids to form a ―lipid- friendly complex known as herbosome. In case of their ampiphilic properties, herbosomes are more bioavailable (as demonstrated by pharmacokinetics and activity studies in animals), when applied topically or orally, as compared with simple herbal extracts owing to their enhanced capacity to cross into the blood through the lipid-rich biomembranes. It is confirm by various research the active components of herbal formulation are also well protected from destruction by the gastric environment. Lipid drug delivery systems have more beneficial over polymer based systems. The advantages include: heightened drug absorption, reduced side effects, controlled drug release and site specific targeting. Also, most lipid formulations have been higher stability and higher carrier capacity [4].

Phosphatidylcholine and Herbal extract:

Phospholipids are complex molecules which are used in all known life forms to make cell membranes. Which are cell membrane building blocks, form the matrix into which fit a large variety of proteins that are enzymes, transport proteins, receptors, and other biological energy converters. The phospholipids are also employed as natural digestive aids and as carriers for both fat-miscible and water miscible nutrients in humans and other higher animals. Phospholipids are a major component of biological membrane and can be isolated from either egg yolk or soy beans from which they are mechanically extracted or chemically extracted using hexane.

Phosphatidylcholine is a bifunctional compound, the choline moiety being hydrophilic and phosphatidyl being lipophilic in nature. The choline head of the phosphatidylcholine molecule Specifically binds to the components of herbal extract while the lipid soluble phosphatidyl portion then envelopes the choline bound material that results in a formation of little micro sphere or cell. The Herbosome process produces is a microsphere cell that protects valuable components of the herbal extract from destruction by digestive secretions and gut bacteria.[5]

Properties and Morphology of Herbosome:

Physico-chemical Properties:

- Herbosomes are lipid compatible molecular complexes. Which are lipophilic substances with a clear melting point.
- They are freely soluble in nonpolar solvents (in which the hydrophilic drug moiety are not), and moderately soluble in fats.

- Herbosomes assume a micellar shape when treated with water.
- The size customarily varies from 50 nm to about 500 μm of the phyto- phospholipid complex molecules.
- In herbosomes, phytomolecules are anchored through chemical bonds to the polar head of the phospholipids.
- From the 1HNMR and 13CNMR data, it can be deduced that the fatty chain gives unchanged signals both in free phospholipid and in the complex, which indicates that the active principle wrapped by long aliphatic chains, producing lipophilic envelope.

Biological Properties:

- They shows better absorption and utilization, therefore they shows more bioavailability and better result than the conventional herbal extract or non-complexed extracts, which has been proven by pharmacokinetic studies and pharmacodynamic tests in experimental animals and in human subjects.[6]

- Herbosomes express their behaviour in physical or biological system because of their physical size, membrane permeability, percentage entrapment, chemical composition, quantity and purity of the materials used. The Herbosomes should not be confused with liposomes where hydrophilic drug molecules are entrapped within a cavity or spaces between the membranes. The liposomes may involve several hundred phospholipid molecules for this entrapment and are usually now being used for cosmetic purposes. Instead, the Herbosomes involves interaction of 1- 4 phospholipid molecules with the phytoconstituents which are chemically anchored to each other. Several researches have shown the Herbosomes to be a better alternative for liposomes in terms of membrane permeability and stability.

METHODS OF PREPARATION :

1. The preparation of novel complex (HERBOSOME) are done by reacting from 3-2 moles but preferably with one mole of a natural or synthetic phospholipid, (like, phosphatidylcholine, phosphatidylethanolamine or phosphatidyiserine) with one mole of component (for example- flavolignanans), either with or without in the natural mixture in aprotic solvent (such as dioxane or acetone) from which complex can be isolated by different technique like, precipitation with non solvent (such as aliphatic hydrocarbons) or lyophilization or by spray drying. The ratio between these two moieties is in the range from 0.5- 2.0 moles in the complex formation of Herbosome. The most preferable ratio of phospholipid to flavonoids is 1:1.[7]

2. Taking naringenin with an equimolar concentration of phosphatidylcholine (PC) to formed Naringenin–PC complex. Taking a 100 mL round bottom flask and the equimolar concentration of phosphatidylcholine and naringenin were placed. Then refluxed in dichloromethane for 3 h. When the concentration of the solution reached to 5–10 mL, 30 mL of n-hexane was added to get the complex as a precipitate followed by filtration. The precipitate was collected and placed in vacuum desiccators.

3. The 100 ml round-bottom flask were taken and placed required amounts of drug and phospholipids and dissolved in anhydrous ethanol. After ethanol was evaporated off under vacuum at 40 ◦C, the dried residues were gathered and placed in desiccators overnight, then crushed in the mortar and sieved with a 100 mesh. Silybin–phospholipid complex(the resultant) was transferred into a glass bottle, flushed with nitrogen and stored in the room temperature .[8]

PHARMACEUTICAL SCOPE OF PHYTOSOMES:

1. They show better bioavailability by enhancing the absorption of lipid insoluble polar phytoconstituents through oral as well as topical route, hence significantly greater therapeutic benefit.
2. Appreciable drug entrapment
3. Its dose requirement is also reduced, as the absorption of active constituent(s) is improved,.
4. The Phosphatidylcholine(PC) besides acting as a carrier also acts as a hepatoprotective, therefore they providing synergistic effect when hepatoprotective substances are employed.
5. The chemical bonds are formed between phosphatidylcholine molecule and phytoconstituent so phytosomes show better stability profile.
6. The percutaneous absorption are improved byapplication of phytoconstituents in form of phytosome and act as functional cosmetics.
7. Added nutritional benefit of phospholipids.[9]

Limitations of herbosome:

Herbosomes, despite of having numerous advantages as drug delivery system, are not prevalent in the market. Yamila B. Gándola et al. 2014, mentioned that phospholipids (lecithin) can induce proliferation on MCF-7 breast cancer cell line.30 A major drawback of Herbosome could be

leaching of the phytoconstituents off the 'some' which reduces the desired drug concentration indicating their unstable nature.

CONCLUSION

Recent research shows improved absorption and bioavailability with Herbosomes as compared to then conventional means. The most of the phytosomal studies are focused to Silybum marianum (milk thistle) which contains premier liver-protectant flavonoids. Hepatoprotective effects are show by the fruit of the milk thistle plant contains flavonoids.[10] Yanyu et al. prepared the silymarin Herbosome and studied its pharmacokinetics in rats. In the study after oral administration of prepared silybin-phospholipid complex the bioavailability of silybin in rats was increased remarkably due to an impressive improvement of the lipophilic property of silybin-phospholipid complex.[8] They shows better absorption and utilization, therefore they shows more bioavailability and better result than the conventional herbal extract or non-complexed extracts, which has been proven by pharmacokinetic studies and pharmacodynamic tests in experimental animals and in human subjects.[6] They are produced by a process whereby the standardized plant extract or its constituents are bound to phospholipids, mainly phosphatidylcholine producing a lipid compatible molecular complex. Phytosomes have been therapeutically used for hepatoprotective and liver diseases as mentioned in the literature. After screening and selection for phytoconstituents for therapeutics use, herbosomal technique of drug delivery can be developed for various categories like anticancer, cardiovascular and anti-inflammatory activities.

Table.1 – Commercial product available[11, 12, 13]

Trade name	Phytochemical	Indication
18ß-glycyrrhetinic acid Herbosome	18ß-glycyrrhetinic acid from licorice rhizome	Soothing
Centella Herbosome	Triterpenes from Centella asiatica leaf	Cicatrizing, trophodermic
Crataegus Herbosome	Vitexin-2″-O-rhamnoside from Hawthorn flower	Antioxidant
Escin ß-sitosterol Herbosome	Escin ß-sitosterol from horse chestnut fruit	Anti-oedema
Ginkgoselect® Herbosome	Ginkgoflavonglucosides, ginkgolides, bilobalide from Ginkgo biloba leaf	Vasokinetic
Ginselect® Herbosome	Ginsenosides from Panax ginseng rhizome	Skin elasticity improver, adaptogenic
Ginkgo biloba Terpenes Herbosome	Ginkgolides and bilobalide from Ginkgo biloba leaf	Soothing
Ginkgo biloba Dimeric Flavonoids Herbosome	Dimeric flavonoids from Ginkgo biloba leaf	Lipolytic, vasokinetic
Greenselect Herbosome	Polyphenols from green tea leaf	Prevention of free radicalmediated tissue damages and weight management
Leucoselect Herbosome	Polyphenols from grape seed	Antioxidant, capillarotropic

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