INTERNATIONAL RESEARCH JOURNAL OF PHARMACY

www.irjponline.com ISSN 2230 – 8407

Review Article

PHYTOSOMES AN EMERGING TECHONOLGY IN PHYTOMEDICINE: A REVIEW

Roy Chowdhury Santanu*, Bhandari Neeraj, Verma Pooja

Department of pharmaceutics Sri Sai College of Pharmacy, Badhani, Pathankot, Punjab, India

Article Received on: 10/08/12 Revised on: 20/09/12 Approved for publication: 07/10/12

*Email: santanu4ualways@yahoo.co.in

ABSTRACT

Phytosomes are little cell like structure. This is advanced forms of herbal formulations which contains the bioactive phytoconsituents of herb extract which surrounds and bound by a lipid. Most of the bioactive constituents of phytomedicines are water-soluble compounds like flavonoids, glycosides, terpenoids. Only, a few natural drugs have been formulated and are available in the market as phytosomes. Phytosomes are recent advanced forms of herbal formulations that have enhanced absorption rate, producing better bioavailability than conventional herbal extracts. Phytosomes are prepared by non conventional method due to their improved pharmacological and pharmacokinetic parameters. Phytosomes absorption in GIT is greater which result in increased plasma level than individual component. They act as a bridge between novel delivery system and conventional delivery system. These drug-phospholipids complex can be formulated in the form of solutions, suspensions, emulsions, syrup, lotion, gel, cream, etc. Thus, this review aims to provide complete information about phytosome.

Keyword: Phytosomes, Herbal extract, Phytoconsituents, Flavonoids, Phospholipds.

INTRODUCTION

During the last century chemical and pharmacological studies have been performed on a lot of plant extracts in order to know their chemical composition and confirm the indications of traditional medicine. Most of the bioactive constituents of herbal drugs are water soluble molecules. However, water soluble phyto constituents like many flavonoids are poorly absorbed[1] either due to their multiple-ring, large size molecules which cannot be absorbed by simple diffusion, or due to their poor miscibility with oils and other lipids, severely limiting their ability to pass across the lipid-rich outer membranes of the enterocytes of the small intestine[1]. Phytomedicines, complex chemical mixtures prepared from plants, have been used in medicine since ancient times and continue to have widespread popular use. Phytosome dietary supplements are the modern culmination of this great tradition. Phytosome is a patent developed by Indena, a leading supplier of nutraceutical ingredients, to incorporate phospholipids into standardized extracts and so vastly improve their absorption and utilization. Over the past century, chemical and pharmacologic science established the compositions, biological activities and health giving benefits of numerous plant extracts. But often when individual components were separated from the whole, there was loss of activity—the natural ingredient synergy became lost. Standardization was developed to solve this problem[2] .The Phytosomes process produces a little cell because of that the valuable components of the herbal extract are protected from destruction by digestive secretions and gut bacteria. Phytosomes are better able to transition from a hydrophilic environment into the lipid-friendly environment of the enterocyte cell membrane and from there into the cell finally reaching the blood [3]. Phytosomes have improved pharmacokinetic and pharmacological parameter. Advanced technology used in the treatment of the acute and chronic liver disease of toxic metabolic or infective origin are of degenerative nature. It can also be used in anti-inflammatory activity as well as in pharmaceutical and cosmetology[4]. The term "phyto" means plant while "some"means cell-like. The use of phytosomes is a new advanced modern dosage formulation technology to deliver herbal products and drugs by improved better absorption and, as a result, produce better results than those obtained by conventional herbal extracts[4] . The phytosome technology developed by Indena meets this challenge by markedly enhancing the bioavailability of selected phytomedicines . As standardized extracts became established, poor bioavailability often limited their clinical utility. Then it was discovered that complexation with certain other clinically useful nutrients substantially improved the bioavailability of such extracts. The nutrients so helpful for enhancing the absorption of other nutrients are the phospholipids. Figure 1

"Phytosome" versus "Liposome''

Liposomes are used primarily in cosmetics to deliver water-soluble substances to the skin. A liposome is formed by mixing a water-soluble substance with phosphatidylcholine. No chemical bond is formed, the phosphatidylcholine molecules collectively surround the water-soluble substance. There may be hundreds or even thousands of phosphatidylcholine molecules surrounding the water-soluble compound. In contrast, Phytosome possesses the phosphatidylcholine and the individual plant components actually from a 1:1 or a 2:1 complex depending on the substance. This difference results in Phytosomes being much better absorbed than liposomes. Phytosomes are also superior to liposomes in skin care[5]. Figure 2

Advantages of Phytosomes

Phytosomes show following advantages:-

- They enhance the absorption of lipid insoluble polar phytoconstituents through oral as well as topical route showing better bioavailability, hence, they have significantly greater therapeutic benefit.
- They improve the absorption of active constituent(s) which further reduce its dose requirement.
- Phosphatidylcholine used in preparation of phytosomes, besides acting as a carrier also acts as a hepatoprotective, hence giving the synergistic effect when hepatoprotective substances are employed.
- Chemical bonds are formed between phosphatidylcholine molecule which added nutritional benefit of Phospholipids.
- They have appreciable drug entrapment.
- Significantly greater clinical benefit.
- Assured delivery to the tissues.

- No compromise of nutrient safety.

Properties of Phytosomes

Chemical properties

Phytosomes is a complex between a natural product and natural phospholipids, like soy phospholipids. Such a complex is obtained by reaction of stoichiometric amounts of phospholipid and the substrate in an appropriate solvent. On the basis of spectroscopic data, it has been shown that the main phospholipid-substrate interaction is due to the formation of hydrogen bonds between the polar head of phospholipids (i.e. phosphate and ammonium groups) and the polar functionalities of the substrate[5]. while in phytosomes the active principle is anchored to the polar head of phospholipids, becoming an integral part of the membrane for formation of H-bonds between the phenolic hydroxyls of the flavone moiety and the phosphate ion on the phosphatidylcholine side[6]. Molecules are anchored through chemical bonds to the polar head of the phospholipids, as can be demonstrated by specific spectroscopic techniques[4]

Phosphatidylcholine

This can be deduced from the comparison of the NMR of the complex with those of the pure precursors. The signals of the fatty chain are almost unchanged. Such evidences inferred that the two long aliphatic chains are wrapped around the active principle, producing a lipophilic envelope, which shields the polar head of the phospholipid and the catechin.

Biological Properties

Phytosome are advanced forms of herbal products that are better absorbed, utilized and as a result produce better results than conventional herbal extracts the increased bioavailability of the phytosome over the non complexed botanical derivatives has been demonstrated by pharmacokinetics studies or by pharmacodynamic tests in experimental animals and in human subjects

Preparation of Phytosome

Phytosomes are novel complexes which are prepared by reacting from 3-2 moles but preferably with one mole of a natural or synthetic phospholipid, such as phosphatidylcholine, phosphatidylethanolamine or phosphatidylserine with one mole of component for example flavoliganans, either alone or in the natural mixture inaprotic solvent such as- dioxane or acetone from which complex can be isolated by precipitation with non solvent such as aliphatic hydrocarbons or lyophilization or by spary drying. In the complex formation of phytosomes the ratio between these two moieties is in the range from 0.5-2.0 moles. The most preferable ratio of phospholipid to flavonoids is 1:1[3]. In the phytosome preparations, phospholipids are selected from the group consisting of soy lecithin, from bovine or swine brain or dermis, phosphatidylcholine, phosphatidylethanolamine, phosphatidylserine in which acyl group may be same or different and mostly derived from palmitic, stearic, oleic and linoleic acid. Selection of flavonoids are done from the group consisting of quercetin, kaempferol, quercretin-3, rhamnoglucoside, quercetin-3-rhamnoside**,** hyperoside, vitexine, diosmine, 3- rhamnoside, (+) catechin, (-) epicatechin, apigenin-7-glucoside, luteolin, luteolinglucoside, ginkgonetine, isoginkgonetine and bilobetine[7] either alone or in the natural mixture in aprotic solvent such as dioxane or acetone from which complex can be isolated by precipitation with non solvent such as aliphatic hydrocarbons or lyophilization or by spray drying. In the complex formation of phytosomes, the ratio between these demonstrated by pharmacokinetic studies or by pharmacodynamic tests in experimental animals and in human subjects[5]. Phytosomes are formulated by patented processes in which the standardized extract (having a standardized content of active principles) and/or active ingredients of herbs (like flavoliganans and terpenoids) are bound to the phospholipids like phosphatidylcholine (PC) through a polar end. The phytosome process produces small cells which protect the valuable components of the herbal extract from destruction by digestive secretions and gut bacteria [5]. They improve transition of constituents from the water phase to the enterocytes of the gut wall and ultimately they reach the circulation. The phytoactive components of these herbal extracts are well suited to direct binding to phosphatidylcholine from soy. PC is also the principle molecular building block of cell membranes and is miscible with both water and oil/lipid mixtures, and is well absorbed orally. Phospholipids are small lipid molecules in which the glycerol is bound to only two fatty acids, instead of three as in triglycerides, with the remaining site is occupied by a phosphate group. Specifically, the choline head of the phosphatidylcholine molecule binds to phytoconstituents while the fat-soluble phosphatidyl portion, comprising the body and tail, then ratios of EFP-PVP precipitates by means of dissolution release. Silybin and phospholipids were resolved into the medium, after the organic solvent was removed under vacuum condition, and a silybin-phospholipid complex was formed [4].

Characterization of Phytosomes

The behavior of phytosomes in both physical and biological system is governed by the factors such as physical size, membrane permeability, percent entrapped solutes, chemical composition as well as the quantity and purity of the starting materials. Therefore, the phytosomes are characterized for physical attributes i.e. shape, size, percentage drug capture, its distribution, entrapped volume, percentage drug released and chemical composition [3] as well as the quantity and purity of the starting materials[1]. The phytosome is a unit of few molecules, this makes difference, so the phytosomes being much better absorbed than liposomes. Not surprisingly, Phytosomes are also superior to liposomes in skin care products while the liposome is an aggregate of many phospholipid molecules that can enclose other phytoactive molecules but without specifically bonding to them. Liposomes are touted drug delivery vehicles, but for dietary supplements their promise has not been fulfilled. But for phytosome products numerous studies prove that they are markedly model for better absorption and have substantially greater clinical efficacy. Companies have successfully applied this technology to a number of standardized flavonoid preparations.

- Different spectroscopic and in-vitro and in-vivo evaluations are applied on phytosomes. These complexes can be characterized by Transmission Electron Microscopy (TEM), 1HNMR, 13C-NMR, 31P-NMR and FT-IR. Models of in-vitro and in-vivo evaluations are selected on the basis of expected therapeutic activity of biologically active phytoconstituents present in phytosomes. Complexation increases the activity of the active ingrdients. A chemical spectral characteristic is determined in phospholipids complexes using IR and UV spectroscopic study. Liquid chromatography/atmospheric pressure, chemical ionization and mass spectrometry (LC/APCI-ITMS) proved to be a very powerful tool for pharmacokinetic studies of phytochemicals.
- This technique is applied to evaluate the levels of ginkgolides A and B and bilobalide in plasma of

volunteers after administration of Ginkgo biloba extracts in free (Ginkgoselect) or phospholipid complex (Ginkgoselect Phytosome) forms. The effects of Ginkgo biloba dimeric flavonoids in Phytosome form on the vasomotor activity and skin microcirculation of the cheeks, hands, limbs and female breast are studied in human subjects by Infrared-Photo- Pulse-Plethysmography, Laser Doppler Flowmetry, High Performance Contact.

- Thermography, Computerized Videothermography, and Optic Probe Videocapillaroscopy. In-vivo studies are performed on Beagle dogs, rodents, wistar rats to compare pharmacokinetics parameters between pure extracts and its phospholipid complex[6].

Therapeutic Applications of Phytosomes

To examine the various advantages of phytosomes, especially their ability to enhance the bioavailability of polar phytoconstituents, various therapeutic applications of phytosomes have been explored. Phytosome by complexing hesperetin with hydrogenated phosphatidylcholine. This complex was then evaluated for antioxidant activity in CCl4 intoxicated rats along with pharmacokinetic studies. It was found that the phytosome had asustained release property for over 24 h and enhanced antioxidant activity. Pharmacokinetic study revealed that the phytosome had higher relative bioavailability than that of parent molecule at the same dose level. In the study of bioavailability of silybin in rats was increased remarkably after oral administration of prepared silybinphospholipid complex due to an impressive improvement of the lipophilic property of silybin-phospholipid complex and improvement of the biological effect of silybin. Ravarotto et al., reported silymarin phytosome show better antihepatotoxic activity than silymarin alone and can provide protection against the toxic effects of aflatoxin B1 on performance of broiler chicks[3]. Phytosomes are advanced form of herbal extract that are better absorbed which results better than conventional herbal extract. Phytosomes have improved pharmacokinetic and pharmacological parameter, which in result can can advantageously be used in treatment of acute liver diseases, either metabolic or infective origin. Absorption of phytosome in gastro-intestinal tract is appreciably greater resulting in increased plasma level than the individual component. This means more amount of active constituent becomes present at the site of action (liver, brain, heart, kidney etc) at similar or less dose as compared to the conventional plant extract[3]. advantageously be used in treatment of acute liver diseases, either metabolic or infective origin[5].

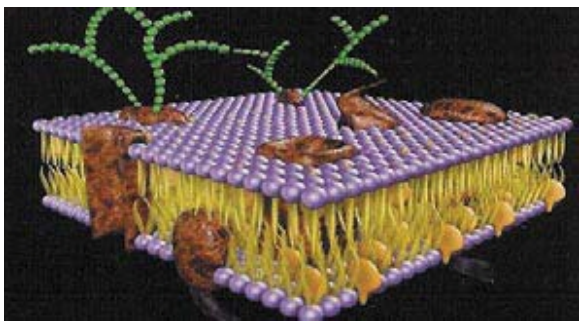

Figure 1: Cell membranes are largely lipid phase. A double molecular layer consisting of PC and other phospholipids provides a continuous matrix into which the proteins inserted.

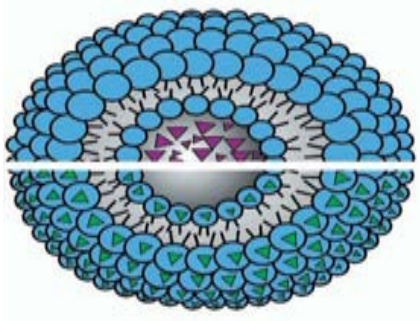

Figure 2: Presenting difference between liposomes and Phytosomes

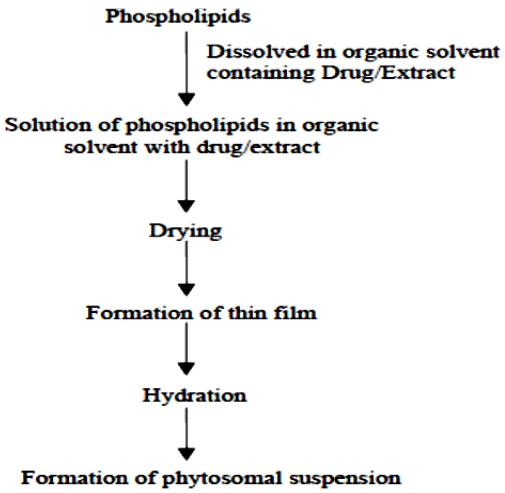

Figure 3: Common stages for prepration of pytosomes[4]

CONCLUSION

Phytosomes results from the reaction of a stoichiometric amount of the phospholipid (phosphatidylcholine) with the standardized extract or polyphenolic constituents (like flavonoids, terpenoids, tannins, xanthones) in a non-polar solvent. They have many distinctive advantages over other conventional formulations. As far as the potential of phytosome technology is concerned, it has a great future for use in formulation technology and applications of hydrophilic plant compounds. Phytosomes have improved pharmacokinetic and pharmacological parameter so they can advantageously be used in treatment of acute liver diseases, either metabolic or infective origin. Absorption of phytosome in gastro-intestinal tract is appreciably greater resulting in increased plasma level than the individual component. After screening and selection for phytoconstituents for therapeutics use, phytosomal drug delivery can be developed for various categories like anticancer, cardiovascular and anti-inflammatory activities etc. It has a great future for use in formulation technology and applications of hydrophilic plant compounds.

REFERENCES

1. Nitesh S Chauhan, et al, Phytosomes: A Potential Phyto-phospholipid Carriers for Herbal Drug Delivery,JPR, 2009,vol 2(7),1267-1270.
2. Anupama Singh,Vikas Anand Sahuran, Manjeet Singh, Phytosome: Drug Delivery System For Polyphenolic Phytoconstituents, Iranian Journal of Pharmaceutical Sciences, 2011,7,(4),209-219.
3. Nilesh Jain, Brahama p Gupta,et al ,Phytosomes: A Novel Drug Delivery System For Herbal Medicine, International Journal Of Pharmaceutical Sciences And Research, 2010,Vol 2(4),224-228.
4. Jagruti Patel, Rakesh Patel, Nirav Patel ,An Overview Of Phytosomes On An Advanced Herbal Drug Delivery System ,Asian Journal Of Pharmaceutics ,2009,4(6), 363-371.
5. Srikanth Vangapelli,Laxmaiah,Ch,Gopi Shankar, Shivraj Gouda et al,Phytosome: A Novel Delivery System For Improving Bioavailability Of Herbal Medicine,IJPRD,2011, Vol 3(6), 175-184.

6. Shalini Sharma, Ram Kumar Roy, Phytosomes :An Emerging Tecnology,IJPRD ,Vol 2,2010,1-7.
7. Pandey shivanand, Patel Kinjal,Phytosomes:Tecnical Revolution in Phytomedicine IJPTR Vol 2, Jan-March2010,627-631.
8. Sanjib Bhattacharya Pytosomes: Emerging Strategy in Delivery Of Herbal Drug and Nutraceuticals, Pharma Times, Vol 41, No.3-March 2009, 9-12.
9. Priyanka Rathore and Gourav Swami,Phytosomes: A Potential Phytophospholipid Carriers for the Bioavalabilabilety Enhancement of Herbal Extracts, IJPSR,2012,Vol 3(3),737-755.
10. Schandalik,Gatti G,Phytosome Herbal Support: Increase The Absoption Of Herbal Extracts ,Arzneim Forsch 1992 , 42 (7), January 20,2011,964-968.

Source of support: Nil, Conflict of interest: None Declared