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Review Article

A REVIEW ON PHYTOSOMES, IMPORTANCE AND ITS APPLICATIONS

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ABSTRACT

Phytosomes are said to be natural extracts contains plant constituents which are bound in phospholipids mainly phosphotidylcholine by producing a lipid stable molecular complexes. This will become better formulation with high grade of stability to attain peak pharmacokinetic and pharmacodynamic profiles. Such degree of freedom will pave to chart out many therapeutic interventions towards the treatment of most of diseases. Hence, The authors has taken a lead to emphasize the importance of phytosomes, its preparations and characterization and also current scenario towards phytosomal technology in detailed way.

Key words: Nanotechnology; Plant products; Nanophytosomes.

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INTRODUCTION

Phytosomes are said to be containing natural herbal formulations. Most of the Plants are having medicinal properties due to the presence of many active constituents which are mainly the secondary metabolites like flavonoids, terpinoids, tannins, glycosides, alkaloids etc. The active constituents present in the plants are mostly hydrophilic in nature. The therapeutic efficacy of

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herbal extracts are quickly destroyed by the enzymes present in the intestinal gut. Hence, advanced researches are done for the specific site delivery of these plants derived products (Middleton and Kandaswami, 1994). The term "phyto" means plant and "some" means cell like (Mukherjee and Wahile,2006). It is also called as herbosomes. This is an advanced methodology, where extract of the plant or the hydrophilic phytoconstituents are mixed with phospholipids to produce more lipid stable molecular complexes, thereby it enhances the absorption and bioavailability of phytoconstituents (Manach et al., 2004; Mascarell, 1993). Phospholipids are naturally used as an aid for digestion and act as carriers for both fat soluble and water soluble nutrients (Shivan and Kinjal, 2010). Phytosomes can easily cross the cell membranes and also stratum corneum layer of the skin (Bombardelli et al., 1989; Bombardelli, 1991; Bombardelli and Spelta, 1991; Loggia *et al.*, 1996; Forster *et al.*, 2009; Chanchal and Swarnlata, 2008). In the last century numerous research have been performed on a lot of plant extracts to know their biological importance and their use in medicinal field (Middleton and Kandaswami,1994). Phytosomes have better ability to penetrate into the membrane of the cell and from there it enter into the cell and finally reaching the systemic circulation (Bombardelli *et al.*,1989).

Phytosome Technology and Its Advantages

Hydrophilic phytoconstituents has the ability to bind with phospholipids. A specified amount of phospholipid (phosphatidylcholine) react with the herbal extract in a non-polar solvent. The phospholipid (phosphatidylcholine) used in this formulation was obtained from soybean with both lipophilic (phosphovidyl part) and hydroplilic (choline) portions. The body portion has choline group which is hydrophilic and the tail portion has phosphotidyl group which is lipophilic in nature, thereby the hydrophilic group is encoded within the lipophilic group to form a stable complex, phytosomes are formed (Goyal et al., 2011; Keerthi et al., 2014). The bonds formed are chemical in nature, which in additional provides better stability for the drug molecule in complex with wide range of advantages (Table 1). Phosphatidylcholine used in this formulation has dual function, it act as a carrier for drug moiety with nutritional value (Amin and Bhat, 2012; Singh et al., 2013).

Preparation of Phytosomes

Though there was not enough data available throughout the phytosome research, authors tried maximum to provide all inputs for the preparation of phytosomes. The method for the preparation of phytosomes are as follows: In the first step, phospholipids are obtained from either natural or synthetic sources are to be dissolved in a organic solvent such as acetone or dioxane. To the solution of phospholipids, herbal extract is added with constant stirring. Then the solution is allowed to evaporate on a spray dryer. The ratio between the portions in the range of 0.5 to 2.0 moles but the most preferable ratio is1:1(Karimi et al., 2015; Rani et al., 2007). Thin flim is formed after evaporation of the solvent. Futher hydration of the flim leads to formation of phytosomal suspension. The formed phytosomes will be collected by precipitation technique. The collected phytosomes are futher subjected to drying by lyophilisation method (Pandey and Patel, 2010; Saha et al., 2013). The entire preparations are illustrated in schematic way for better understanding to the users (Fig 2).

Characterization and Evaluation of Phytosomes

The characterization techniques for the evaluation of phytosomes are as follows (Patel *et al.*, 2013)

Characterization techniques:

Vesicle size and Zeta potential: The particle size and zeta potential can be determined by DLS using a computerized inspection system (Patel *et al.*, 2004).

Surface morphology analysis: By using scanning electron microscopy (SEM) the surface morphology analysis of phytosomes can be determined (Tripathy *et al.*, 2013).

Transition temperature: By using differential scanning calorimetry the transition temperature of the vesicular lipid system can be determined.

Surface tension measurement: Du novy ring densitometer is used to find out the surface tension activity of a drug dissolved in aqueous solution (Pawar and Bhangale, 2015).

Entrapment efficiency: By using ultracentrifugation technique the drug entrapment ability of phytosomes can be measured (Patel *et al.*, 2004).

Drug content: Drug content present in the phytosomes can be determined by High performance liquid chromatographic method or any other spectroscopic methods (Bhattacharya, 2009).

Stability studies: Stability studies were carried out for two months on the optimized formulation of phytosomes. For stability study the optimized formulation were placed in humidity chamber (sonar) at 75%RH,45^oc. After two months, the formulation was evaluated for weight variation, hardness, friability, disintegration and percentage drug content (Kumari *et al.*, 2011).

SPECTROSCOPIC EVALUATIONS

The spectroscopic evaluation provides more information about phytosomes. They are as follows:

FT-IR:The FT-IR spectra data will be taken to determine the structure and chemical shift of the extract, phosphotidylcholine and phytosomes (Pawar and Bhangale, 2015).

¹H-NMR: The ¹H-NMRspectra is used to determine the development of complex formed between active phytoconstituents and phosphotidylcholine molecules. In non polar solvents, there will be an evident change in ¹H-NMR signal commencing from atoms included in the complex formation. The signals from protons are broadened. In phospholipids there is broadening of signals whereas the singlet correlative to the Ntrimethyl portion of choline yields an upfield shift (Tripathy et al., 2013).

¹³C-NMR: The ¹³C-NMR of phytosomes, when recorded at room temperature all the carbons in phytoconstituents are unobservable. The signals equivalent to the choline and glycerol portion was broadened, whereas some are shifted and most of the resonance of the fatty acids chains maintains their initial sharp lines (Gupta and Dixit, 2011).

Current Research Towards Nanophytosomes

Since the phytosomes are novel in upcoming era, few extensive studies are done on silymarin, grape seed extract, quercetin, curcumin etc (Wellington and Jarvis, 2001; Hikino et al, 1984). Some are enlisted have for the reading: In Schandalik et al., 1992, 1994, has used human volunteer patients and tested the nine hepatoprotective activity of silymarin and reported that phytosomal form of silvbin possess four times greater passage through the liver (Schandalik and Perucca, 1994; Schandalik et al., 1992). In 1993, Mascarella et al, conducted similar work by using 232 patients with chronic hepatitis and reported the better bioavailability of silymarin phytosome[La Grange et al., 1999]. Grape seed phytosome is composed of oligomericpolyphenols, proanthocyanidins or procyanidins (Vitisvinifera) of varying molecular size, complexed with phospholipids. The main properties of procyanidin flavonoids are with increased antioxidant capacity and stimulation of physiological antioxidant defenses of plasma, protection against ischemia/reperfusion induced damages in the heart, protective effects against atherosclerosis thereby offering marked protection for the cardiovascular system and other organs through a network of mechanisms that extend beyond their great antioxidant potency. In the year of 2001. Jhiang prepared herb epimedii flavanoidphytosome (EPF). The precipitate was investigated and the study showed that the dissolution of the precipitate was significantly higher than that of its physical mixture and Herba epimedii extract tablets (Jiang et al., 2001). In 2005Bombardelliet al, reported that the silvmarin phytosomes showed much site specific activity

and a longer duration of action than the single constituent, with respect to percent reduction of edema, inhibition of myeloperoxidase activity, antioxidant and free radical scavenging activity (Bombardelli et al., 1991). In 2005*Maitiet al* produced a guercetin phytosome by a simple and reproducible method and reported that the phytosomal complex shows better therapeutic effect than the uncomplexed molecule in rat liver injury induced by carbon tetrachloride (Jiang et al., 2001; Maiti et al., 2005). Maiti et al, 2006, 2007, also developed naringenin and curcumin phytosomes in two different studies and reported that antioxidant activity of the phytosomal complex has better therapeutic efficacy than that of normal one (Maiti et al., 2010). In xiao et al., 2006, prepared silymarin phytosomes and studied its pharmacokinetics in rats and reported that the bioavailability of silvbin has increased markedly with phytosomal formulations. Hepatoprotective activity of silymarin phytosomes was found to be more than silymarin alone against aflatoxin B1, as reported by Tedescoet al, 2008, after performing the experiment on broiler chicks (Tedesco et al., 2004). Hence, In recent years much works are going to focus on standardized herbal extracts to formulate into more bioavailable phytosomes. Extract of Serenoa repens(CO2 extract) extract of Vaccinium myrtillus (Fruit extract), extract of Coleus forskohlii, Ximenoil and Ximenynic acid extracted from Santalum album, Esculoside, glycosylated coumarin obtained from Aesculus hippocastanum, Ruscogenins, group of saponins extracted from Ruscus aculeatus are highly worked upon for better bioavailability through the formation of phytosomes by patented process (Acharya et al., 2011).

Commercial Products in Market

To date, very few products has come in to market and said to be commercially available. The list of available (Table 2) components is enlisted here for readers.

SNO	Advantages of Phytosomes (Kidd and Head, 2005; Semalty et al., 2007; Naik and Panda, 2008;		
SNU	Bhattacharya,2009).		
1.	Hydrophilic herbal extracts absorption is enhanced and has a better therapeutic effect.		
2.	Phytosomes deliver the drug at specific site, so low dose is required to produce therapeutic effect.		
3.	Phytosomes are easy to develop and has more stability than any other herbal formulations.		
4.	The carrier used in this formulation (phosphotidylcholine)has an advantage that it is eco-friendly		
	with nutritional value.		
5.	Drug entrapment capacity of phytosomes is high than compared to any other herbal formulations.		
6	No complex techniques are not required in the production of phytosomes and hence low cost is		
0.	required for its production.		
7	Phytosomal formulations are easily penetrate through the layer of the skin. Hence it can use for		
/.	transdermal delivery.		

 Table 1. Advantages of Phytosomes

S.No	Phytosomes	Phytoconstituents	Therapeutic Applications
1.	Silybin Phytosome	Silybin from Silybummarianum	Hepatoprotective, antioxidant for liver and skin
2.	Ginkgo Phytosome	24% ginkgo flavonoids	Protects brain and vascular linings, anti-skin Ageing
3.	Ginseng Phytosome	37.5% ginsenosides	Nutraceuticals, immunomodulator
4.	Green Tea Phytosome	Epigallocatechin	Nutraceutical, systemic antioxidant, anticancer
5.	Grape Seed Phytosome	Procyanidins	Nutraceutical, systemic antioxidant, cardioprotective
6.	Hawthorn Phytosome	Flavonoids	Nutraceutical, cardio-protective and antihypertensive.
7.	Olive oil Phytosome	Polyphenols	Antioxidant, anti-inflammatory, antihyperlipidemic
8.	Echinacea Phytosome	Echinacosides	Nutraceutical, immunomodulator
9.	Centella Phytosome	Terpenes	Vein and Skin disorders
10.	Palmetto berries Phytosomes	Fatty acids, alcohols and sterols	Non-cancerous prostate enlargement

 Table 2. Commercial products of phytosomes





CONCLUSION

Phytosomes or herbosomes are said to be advances in herbal formulations. Such phytosomal technology forms a strong link among conventional and novel drug delivery systems. Apart, phytosomes will have better pharmacokinetic and pharmacological efficacy. It also has better therapeutic effect at low dose to produce desired pharmacological effect. Phytosomes have wide scope in nutraceuticals and cosmetology. Hence in future, nanophytosomes will play an important role in the field of drug delivery with high peak values at affordable cost to treat many chronic and acute diseases. **CONFLICTS OF INTEREST**

Authors declare no conflicts.

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