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Review Article

PHYTOSOMES AS NOVEL DRUG DELIVERY SYSTEMS FOR PHYTOCONSTITUENTS: A COMPREHENSIVE REVIEW

Modi Prince, Khathuriya Rajesh, Sharma Ranu, Sharma Maya *

Pacific College of Pharmacy, Pacific Academy of Higher Education and Research University, Udaipur Rajasthan, India (313024)

Phytosomes are the novel drug delivery carriers for enhancing the bioavailability and efficacy of the phyto-constituents. These vesicular systems consist of phospholipids and plant based active compounds, forming a complex that improves solubility, stability and absorption. Phytosomes have shown promise in delivering various phytochemicals including flavonoids, polyphenols and terpenoids for therapeutic applications such as antioxidant, anti-inflammatory and anticancer activities. This review highlights the potential of phytosomes in improving phytochemical delivery and their applications in various diseases.

Keywords: phytosomes, phytochemicals, drug delivery systems, bioavailability, phospholipids, vesicular systems, antioxidant, anti-inflammatory and anticancer.

INTRODUCTION

Phytosomes are a lipid-based nanocarrier system that incorporates phospholipids to encapsulate active phytoconstituents. This system augments the bioavailability of poorly soluble compounds by creating a vesicle structure capable of interacting with both polar and nonpolar compounds [1]. The efficient delivery of phytosomes across biological membranes makes them suitable for various administration routes, including oral, topical, and parenteral applications. Compared to conventional systems, phytosomes offer several advantages, including enhanced stability, reduced toxicity, attenuated variability in absorption, improved skin penetration, and controlled drug release. Phospholipid structures in phytosomes also protect bioactive components from degradation by digestive enzymes and gut bacteria, ensuring better therapeutic outcomes. These advantages make phytosomes promising candidates for a wide range of therapeutic applications [1, 2].

Phytosomes are lipid-based nanocarriers that incorporate phospholipids to encapsulate plant-based nutraceuticals and medications. Also referred to as phyto-phospholipid complexes (Figure 1), phytosomes effectively address

challenges related to the solubility and bioavailability of these compounds [3].

The term "Phyto" means plant and "some" means cell like. It is also mentioned as herbosomes. This is a new 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 [4]. Phosphatidylcholine, phosphatidylserine, phosphatidylethanolamine, phosphatidylinositol are the phospholipids used, but phosphatidylcholine are widely used because of their certain therapeutic value in case of liver diseases, alcoholic steatosis, drug induced liver damage and hepatitis. Phospholipids are also employed as natural digestive aids and as carriers for both fat miscible and water miscible nutrients [5]. Phytosomes can easily traverse the lipophilic path of the enterohepatic cell membranes and also stratum corneum layer of the skin [6].

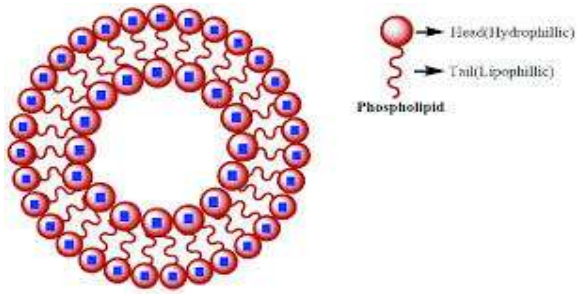

Figure 1: A typical phytosome

Standardized plant extracts mainly flavonoids are derived as phytosomes. Selection of flavonoids are done from the groups consisting of quercetin, kaemferol, quercretin-3, rhamnoglucoside, quercetin-3-rhamnoside, hyperoxide, vitexin, diosmine, 3-rhamnoside, (+) catechin, (-) epicatechin, apigenin-7-glucoside, luteolin, luteolin glucoside, ginkgonetine, isoginkgonetine and bilobetine etc [7,8].

Conventional techniques for preparation of phyto*somes* [9, 10]

Various techniques are employed to prepare phytosomes, which involve the interaction of natural or synthetic phospholipids, primarily phosphatidylcholine, with phytoconstituents. The optimal ratio for forming these complexes typically ranges from 0.5 to 2.0 moles.

The following methods are commonly used to prepare phytosomes:

Solvent evaporation technique

This method involves dissolving a precise stoichiometric ratio of active constituents and phosphatidylcholine in an appropriate solvent. The mixture is then heated at an optimal temperature, typically 40 ◦C for one hour, to achieve maximum drug entrapment in the resulting phytosomes. After heating, the solvent is removed using rotary vacuum evaporation. A variety of solvents can be used, with recent trends favoring protic solvents like ethanol over

traditional aprotic solvents such as chloroform and dichloromethane due to safety concerns [11].

Lyophilization method

In this approach, both phospholipids and phytoconstituents are dissolved in various solvents. The solutions are then combined and agitated using a magnetic stirrer to form the complex, which is subsequently isolated by lyophilization [10, 11].

Salting-out method

This technique involves dissolving a standardized extract or phytoconstituent with phosphatidylcholine in an aprotic solvent such as acetone or dichloromethane. After thoroughly mixing overnight using a magnetic stirrer, a non-solvent-like n-hexane is added to precipitate the complex [2, 12].

Co-solvency method

In this method, phospholipids and dried extracts are dissolved separately in individual flasks containing a solvent such as methanol [11, 13].

PROPERTIES OF PHYTOSOMES [14, 15, 16]

1. Physicochemical properties

a. Phytosome**s** are the complex between phytoconstituents and natural phospholipid, and the complex is obtained by reacting an appropriate amount of phospholipid and chief constituents in particular solvent [14].

b. The interaction between phospholipid and substrate is due to the development of hydrogen bonds between the polar head of phospholipid and the polar functionalities of the chief constituents [15].

c. On treatment with hydrophilic environment phytosome shows a cell-like structure like liposomes, but in a liposome, the chief constituent interacts within the internal pocket while in phytosome the chief active constituents are enveloped the polar head of phospholipid and becoming an integral part of the membrane [16, 17].

d. The phytosome is a combination of few molecular complex which bounded together, while the liposome is a combination of number of phospholipids which react with chief constituent but without complete bonding with them [18].

2. Biological properties [19, 20]

a. Phytosome increases the active absorption of active ingredients and also increase the systemically bioavailability when administered orally.

b. These are the advance form of herbal products and having better efficacy as per compare to conventional herbal extract.

c. Phytosome has better pharmacokinetic as compare to simple herbal drugs [21, 22].

ADVANTAGES OF PHYTOSOMES [23, 24, 25]

a. Phospholipid, i.e., phosphatidylcholine one of the valuable components of phytosome has a

bi-functional activity by acting as a vehicle as well as health benefit such as hepatoprotective activity.

b. The absorption of hydrophilic active constituents is increased which also increase the efficacy.

c. As the efficacy increases the dosage requirement is also reduced.

d. Phytosomes have better stability.

e. Phytsosome has the ability to permeate through skin due to its lipid layer around the phytoconstituent and thus enhance the effectiveness.

f. By increasing the solubility of bile to herbal origin phytoconstituents, phytosomes enhance the liver targeting [26].

g. Phytosome increase the solubility of bile to herbal constituents.

h. Time period of action is increased [27].

Evaluation Techniques of Phytosomes [28, 29]

1. Differential scanning calorimetery

Drug polyphenolic extract, phosphatidylcholine, a physical mixture of drug extract and Phosphatidylcholine, and drug-phospholipid complex were placed in an aluminum cell and heated to a temperature of 50-250°C/minutes from 0 to 400°C in the atmosphere of nitrogen.

2. Scanning electron microscopy (SEM)

SEM was used to determine the size of the particle and its appearance. Dry sample was placed on electron microscope brass stub coated with gold in an ion sputter. Random scanning of the complex at 100 [30].

3. Transition electron microscopy (TEM)

TEM was used to characterize the size of phytosomal vesicles with 1000 magnification.

4. Fourier transform infrared spectroscopy (FTIR) analysis

FTIR analysis will be done for checking the structure as well as chemical stability of drug, phospholipid. The phytosomal drug will be crushed with potassium bromide to obtain pellets at 600 kg/cm2 pressure. Scanning will be done between the ranges of 4000-400 cm−1.

5. Drug entrapment and loading capacity

Drug phytosomal complex was centrifuged at 10000 rpm for 90 minutes at 4°C to separate phytosome from the untrapped drug [31]. The concentration of free drug can be measured by doing ultraviolet spectroscopy. The percentage drug entrapment can be calculated as given formula:

$$\%\boldsymbol{Entrapment\ Efficiency} = \frac{\boldsymbol{Weight\ of\ total\ drug - Weight\ of\ free\ drug}}{\boldsymbol{Weight\ of\ total\ drug}}\ \boldsymbol{x\ 100}$$

6. Size analysis and zeta potential

Malvern Zetasizer is used to check the particle size and zeta size of phytosomal complex. Argon laser is used for this particle size and zeta sizer characterization.

***7. In vitro* and *in vivo* evaluations**

In vitro and *in vivo* evaluation will depend on the properties of the drug, their chief phytoconstituents bounded by phospholipid layer and on the bases of that particular animal model is selected for its evaluation [32, 33].

Recent Advances in Phytosome Technology

A number of research articles have revealed the importance of phytosomal delivery system over conventional herbal extract. Advances in phytosomal delivery system are as follows:

a. **Bacopaside** well-known chief constituents present in *Bacopa monnieri* plant having antiamnesic activity. This study is an attempt to prepare phytosome from bacopaside and its *in vivo* evaluation on rodents. There is remarkably great change in the therapeutic efficacy of the compound prepared by phospholipid as compare to simple *B. monnnieri* extract [34].

b. Another study also reveals that there is the preparation of **berberine** phospholipid complex solid dispersion, which not only increase the solubility of the compound but also increase its flow ability and dissolution rate for industrial production [35].

c. Another research state that there is the preparation of **sinigrin** phytosome. The study was carried out for *in vitro* wound healing capacity and the result is also appreciable as compare to sinigrin alone [34, 35].

d. One research reported **silymarin** phytosomes with better antihepatotoxic activity as compare to silymarin alone and also having great role for the protection against B1 aflatoxin on broiler chicks [36].

e. The phytosomes from standardized extract of seeds of *S. marianum* have administered orally which is having great effect on foetus from maternally ingested alcohol.

f. One clinical research reveals that the study of 232 patient with chronic hepatitis when treated with **silybin** phytosome at a dose of 120 mg twice or thrice a day up to 120 days having great role for recovery of liver function [37].

g. **Grape seed** phytosome also having great role in ischemia induced damage in the heart, also having protective against atherosclerosis. The main chief constituents responsible for this is proanthocyanidins/procyanidins [38].

h. *Camellia sinensis* or the extract of **green tea** when incorporated in phytosomes having improved oral bioavaiability as compared to uncomplexed green tea extract.

Epigallocatechin 3-o-gallate is the main active constituents present in green tea.

i. Further clinical trial suggested that phytosomes of green tea free from caffeine also having a significant effect on anti obesity and antioxidant activity. Its also having effect on low-density lipoprotein.

j. **Quercitin** phytosomal complex reveals the better therapeutic property in rat liver injury induced by carbon tetra chloride.

Table 1: Marketed formulations of phytosomes[39]

S. NO.	NAME OF THE PRODUCT	ACTIVE CONSTITUENT	BIOLOGICAL SOURCE	USES
1	Centella phytosomes	Triterpine	*Centella asiatica*	Cicatrizing, trophodermic
2	Ginselect phytosomes	Ginsenosides	*Gingko biloba*	Adaptogenic
3	Greenselect phytosomes	Polyphenols	*Camellia sinensis*	Free radical scavenging activity
4	Leucoselect	Polyphenols	*Vitis vinifera*	Antioxidant
5	Meriva	Curcuminoids	*Curcuma longa*	Anti-inflammatory
6	Silymarin	Silymarin	*Silybum marianum*	Antihepatotoxic
7	Oleaselect TM phytosome	Polyphenols	*Olea europaea*	Anti-inflammatory, antioxidant
8	Crataegus phytosomes	Vitexin-2'-O-rhamonoside	*Crataegus Mexicana*	Antioxidant
9	Visnadine	Visnadine	*Ammi visnaga*	Circulation improver
10	Bilberry	Triterpine	*Vaccinium myritillus*	Potent antioxidant
11	Ruscogenin phytosomes	Steroid saponin	*Ruscus aculeatus*	Anti-inflammatory
12	PA2 phytosomes	Proanthocynidin	*Horse chestnut bark*	Antiwrinkles, UV protectant

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13	Zanthalene phytosomes	Zanthalene	*Zanthoxylum bungeanum*	Soothing, anti-itching
14	Lymphaselect phytosomes	Triterpenes	*Melilotus officinalis*	Indicated in insomnia
15	Sabalselect phytosome	Fatty acid, sterols	*Serenoa repens*	Beningn prostate hyperplasia
16	Sericoside phytosome	Sericosides	*Terminalia sericea*	Skin improver
17	Echinacea phytosome	Echinacosides	*Echinacea angustifolia*	Immunomodulators, nutraceuticals
18	Rexatrol	Resveratrol	*Polygonum cuspidatum*	Antioxidant, antiaging

SUMMARY AND CONCLUSION

Herbal products always have great concern of denaturation and bioavailability. There is so many novel approaches are available in the form NDDS. Despite these approaches liposomes and phytosomes are most suitable novel approaches for herbal drugs to overcome this kind of problems. These delivery systems have improved the pharmacotherapeutics and pharmacokinetics of herbal drugs. This kind of delivery systems is also utilized in the field of nutraceuticals and cosmoceuticals for improving therapeutic effect and permeability in the skin. The formation of phytosomes are simple and reproducible a part of that phospholipids used in the preparation of phytosomes have their own beneficial effects in the body.

In summary, phytosomes represent a novel approach to enhancing the delivery and efficacy of herbal medicines. Their capacity to improve solubility and bioavailability while protecting active ingredients from degradation may lead to broader indications in both pharmaceutical and nutraceutical domains. This review provides an overview of biological activities of phytosomes both for commercial and non-commercial products. The set of collected studies shows a general advantage in the use of these formulations to improve the bioavailability of bioactive phytochemicals, allowing a reduction in

dosage, compared to non-formulated compound, or greater biological activity.

REFERENCES

1.Lu M, Qiu Q, Luo X, et al. Phyto-phospholipid complexes (phytosomes): a novel strategy to improve the bioavailability of active constituents. Asian J Pharm Sci. 2019;14(3):265–274. doi:10.1016/j.ajps.2018.05.011

2. Raeiszadeh M, Esmaeili-Tarzi M, Bahrampour-Juybari K, et al. Evaluation the effect of Myrtus communis L. extract on several underlying mechanisms involved in wound healing: an in vitro study. S Afr j Bot. 2018;118:144–150. doi:10.1016/j. sajb.2018.07.006

3. Poursalehi HR, Fekri MS, Far FS, et al. Early and late preventive effect of Nigella sativa on the bleomycin-induced pulmonary fibrosis in rats: an experimental study. Avicenna J Phytomed. 2018;8(3):263.

4. Oloumi MM, Vosough D, Derakhshanfar A, et al. The healing potential of Plantago lanceolata ointment on collagenase-induced tendinitis in burros (Equus asinus). J Equine Vet Sci. 2011;31 (8):470–474. doi:10.1016/j.jevs.2011.03.014

5. Samareh-Fekri M, Poursalehi HR, Mandegary A, et al. The effect of methanol extract of fennel on bleomycin-induced pulmonary fibrosis in rats. J Kerman Univ Medical Sci. 2015;22(5):470-83.

6. Bhise JJ, Bhusnure OG, Jagtap SR, Gholve SB, Wale RR. Phytosomes: a novel drug delivery for herbal extracts. J Drug Deliv Ther. 2019;9(3–s):924–930.

7. Teng Z, Yuan C, Zhang F, et al. Intestinal absorption and first- pass metabolism of polyphenol compounds in rat and their transport dynamics in Caco-2 cells. PLoS One. 2012;7(1):e29647. doi:10.1371/journal.pone.0029647

8. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. Am J Clin Nutr. 2004;79(5):727–747.

9.Bhattacharya S. Phytosomes: the new technology for enhancement of bioavailability of botanicals and nutraceuticals. Int J Health Res. 2009;2(3):225–232. doi:10.4314/ijhr.v2i3.47905

10. Kidd P, Head K. A review of the bioavailability and clinical efficacy of milk thistle phytosome: a silybin-phosphatidylcholine complex (Siliphos). Altern Med Rev. 2005;10(3):193–203.

11. Ting Y, Jiang Y, Ho C-T, et al. Common delivery systems for enhancing in vivo bioavailability and biological efficacy of nutraceuticals. J Funct Foods. 2014;7:112–128. doi:10.1016/j. jff.2013.12.010

12. Lu W, Kelly AL, Miao S. Emulsion-based encapsulation and delivery systems for

polyphenols. *Trends Food Sci Technol*. 2016;47:1–9. doi:10.1016/j.tifs.2015.10.015

13. Munin A, Edwards-Lévy F. Encapsulation of natural polyphenolic compounds; a review. Pharmaceutics. 2011; 3(4):793–829.

14. He J, Luo L, Zeng L. Recent advances in research on preparation technologies and applications of tea polyphenol nanoparticles. Food Sci. 2011;32:317–322.

15. Das, M.K., Kalita, B., 2014. Design and evaluation of phyto-phospholipid complexes (Phytosomes) of rutin for transdermal application. J. Appl. Pharm. Sci. 4, 51–57.

16. Ameri, A., Khazaeli, P., Behnam, B., Mehrabani, M., Forootanfar, H., 2024. Formulation and optimization of phytosomes of ethanolic extract of Viola tricolor flowers using design of experiment (DOE) to evaluate in vitro photoprotective potential as sunscreen cream. Ind. Crops. Prod. 209, 118057.

17. Di Pierro, F., Settembre, R., 2013. Safety and efficacy of an add-on therapy with curcumin phytosome and piperine and/or lipoic acid in subjects with a diagnosis of peripheral neuropathy treated with dexibuprofen. J. Pain. Res. 6, 497.

18. Ezike, T.C., Okpala, U.S., Onoja, U.L., Nwike, C.P., Ezeako, E.C., Okpara, O.J., Okoroafor, C.C., Eze, S.C., Kalu, O.L., Odoh, E.C., Nwadike, U.G., Ogbodo, J.O., Umeh, B.U., Ossai, E.C., Nwanguma, B.C., 2023. Advances in drug delivery systems, challenges and future directions. Heliyon. 9, e17488.

19. Alqaaf, M., Nasution, A.K., Karim, M.B., Rumman, M.I., Sedayu, M.H., Supriyanti, R., Ono, N., Altaf-Ul-Amin, Md., Kanaya, S., 2025. Discovering natural products as potential inhibitors of SARS-CoV-2 spike proteins. Sci. Rep. 15, 200.

20. Kumar A., Kumar B., Singh S.K., Kaur B., Singh S., “A review on phytosomes: Novel approach for herbal phytochemicals” Asian Journal of Pharmaceutical and Clinical Research 2007, 10(10), 42.

21. Semalty A., Semalty M., Rawat M.S., Franceschi F., “Supramolecular phospholipids-polyphenolics interactions, the phytosome strategy to improve the bioavailability of phytochemicals” Fitoterapia 2010, 81(5), 306-14.

22. Gandhi A., Dutta A., Pal A., Bakshi P., “Recent trend of phytosomes for delivering herbal extract with improved bioavailability” J Pharmakon Phytochem 2012, 1(4), 6.

23. Kalita B., Das K.M., Sharma K.A., “Novel phytosome formulation making herbal extract more effective” J Pharm Technol 2013, 6 (11), 1295.

24. Jadhav I.A., Wadhave A.A., Arsul V.A., Sawarkar H.S., “Phytosome a novel approach in herbal drug” Int J Pharm Anal 2014, 2(5), 478.

25. Mukherjee P.K., Wahile A., "Integrated Approaches towards drug development from Ayurveda and other Indian System of Medicine" Journal of Ethnopharmacology, 2006, 103, 25-35.

26. Pandey S., Patel K., "Phytosomes, Technical Revolution in Phytomedicine" International Journal of Pharm Tech Research, 2010, 2 (1), 627-31.

27. Schandalik R.E., "Perucca, Pharmacokinetics of silybin following oral administration of silipide in patients with extrahepatic biliary obstruction" Drugs under Experimental & Clinical Research,1994, 20,37-42.

28. Mascarella S. Therapeutic and antilipoperoxidant effects of silybin-phosphatidylcholine complex in chronic liver disease. Preliminary results, Current Therapeutic Research, 1993, 53 (1), 98-102.

29. Grange L., Wang M., Watkins R., Ortiz D., Sanchez M.E., Konst J., Lee C., Reyes E., "Protective effects of the flavonoids mixture, silymarin, on fetal rat brain and liver" Journal of Ethnopharmacology, 1999, 65, 53-61.

30. Busby A., Grange L., Edwards J., Kings J., "The use of a silymarin/phospholipids compound as a fetoprotectant from ethanol-induced behavioral deficits" Journal of Herbal Pharmacotherapy, 2002, 2 (1), 39-47.

31. Jiang Y.N., Yu Z.P., Yan Z.M., Chen J.M., "Studies on preparation of herbal epimedin flavonoid phytosomes and their pharmaceutics" Zhongguo Zhong Yao Za Zhi, 2001, 26 (2), 105-8. 2007.298.

32. Kleinman H, Goldstein A, Malinda K, Sosne G; Inventors. Treatment of skin, and wound repair, with thymosin beta 4. Google Patents. 2007.

33. Bombardelli E. Oral compositions for the treatment of cellulite. Google Patents. 2010.

34. Bertelli V. Fatty acid monoesters of sorbityl furfural and compositions for cosmetic and dermatological use. EP1690862. 2006.

35. Doering T, Traeger A, Waldmann-Laue M. Cosmetic and dermatological composition for the treatment of aging or photodamaged skin. EP1640041. 2006.

36. Khare AB. Soluble isoflavone compositions. Google Patents. 2005.

37. Merizzi G. Anti-oxidant preparation based on plant extracts for the treatment of circulation and adiposity problems. Google Patents. 2004.

38. Morazzoni P, Bombardelli E. Phospholipid complexes prepared from extracts of Vitis vinifera as anti-atherosclerotic agents. Google Patents. 2001.

39. Bombardelli E, Mustich G. Bilobalide Phospholipide Complexes, Their Applications and Formulations Containing Them. Milano, Italy: Indena Spa; 1991.306