Review Article

Int J. Pharm. Drug. Anal, Vol: 13, Issue: 2, 2025; 26-34

International Journal of Pharmaceutics and Drug Analysis

Content Available at www.ijpda.org ISSN: 2348:8948

NATURE MEETS NANOTECHNOLOGY: EVOLUTION OF PHYTOSOMES

Kondumahanti V.N Lakshmi [1], Nallamilli Satya Jaya Krishna Reddy [2], Devanaboyina. Narendra [3]

[1]Assistant Professor, Department of Pharmacology, VJ's College of Pharmacy, Diwancheruvu, Rajahmundry - 533296, Andhra Pradesh, India.

[2]III/IV, Bachelor of Pharmacy, VJ's College of Pharmacy, Diwancheruvu, Rajahmundry-533296, Andhra Pradesh, India.

[3]Professor and Principal, Department of Pharmacognosy, VJ's College of Pharmacy, Diwancheruvu, Rajahmundry-533296, Andhra Pradesh, India.

Received: 14 Apr 2025 Revised: 27 Apr 2025 Accepted: 09 June 2025

Abstract

Since ancient times, herbal plants have served as traditional medicines for the treatment of various diseases. These herbal plants contain phyto constituents that have excellent pharmacological activity and bioactivity and help in the management of diseases like cancer, liver damage, inflammation, and heart disease. The supply of these phytomedicinals, which have some physicochemical limitations such as poor absorbability and bioavailability due to their multiple ring structures and poor solubility. Phytosome technology was introduced to overcome the physicochemical limitations of herbal medicines. "Phyto" means plant, and some meanings relate to cell-like structures. Phytosomes are the complex structures produced by the envelopment of phyto constituents like flavonoids, terpenoids, tannins, and xanthones into phospholipids like phosphatidylcholine. The formed phytosomal complex exhibits enhanced solubility, absorbability, and bioavailability compared to crude drug forms. A number of phytosomal products are available in the market, such as CURCUMIN, SILYMARIN, GREEN TEA, RUTIN, CATECHIN, and GINSENG. This article contains a comparative study of phytosomes along with recent advancements, including their preparation methods, properties, formulations, characterization, and applications. Particle size, zeta potential, morphology, and entrapment efficacy help determine their stability in the formulation. TEM and SEM are used to characterize the phytosomal complex. Phytosomes represent a potential drug delivery system with enhanced bioavailability and therapeutic efficacy compared to normal phyto constituents. Further research on this phytosomal technology brings the medicinal field into a new era.

Keywords: Phytosome, herbal extract, phosphotidylcholine, SEM, TEM.

***Corresponding Author**

Kondumahanti V N Lakshmi

DOI: https://doi.org/10.47957/ijpda.v13i2.628

Produced and Published by

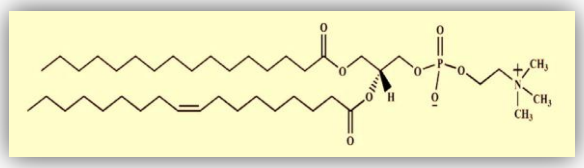
South Asian Academic Publications

Introduction

Phyto medicines (or) herbal medicines are having its origin from plants and botanicals to improve health and help to treat various diseases [1]. Phytoconstiuents are present in all parts of these herbal plants that are leaves, flowers, fruits, stems and roots [2]. Examples of such medicinal plants include TERMINALIA CHEBULA RETZ, SCUTELLARIA BAICALENSIS [3] CURCUMIN [4], PIPER LONGUM [5], GINKGO BILOBA, which are helps in treatment of various diseases. Most of the herbal plants contain polyphenol as a secondary metabolite which is a water soluble and have molecular weight about 500 to 4000 daltons [6], However the presence of these polyphenolic rings in their structure leads to poor absorption and decreased bioavailability of phytomedicinals in the body.It is primarily due to two reasons, Firstly, these polyphenols have multiple ring in their structure that is Impediment passage through cell membrane through passive via diffusion process and secondly solubility of this herbal constituents is low in lipid membrane that makes them poor permeable through gastrointestinal membrane and leads to poor bioavailability [7]. For enhancing their absorption and bioavailability a perspective had that is envelopment of phytoconstituents within the lipophilic carrier like phytosomes [8], Niosomes [9], Nanoparticles [10], ethosomes, transferosomes, nanocapsules [11]. Among that above all phytosomes enhances the absorption and

bioavailability of herbal medicines which are poor lipid solubility and does not penetrate easily through Cell membrane. Most of them shows invitro potent pharmacological action, but they often to failed to show effectiveness in in-vivo studies [12]. INDENA S.P.A of Italy was first to develop phytosome technology to enhances the bioavailability of phytoconstituents in blood which is achieved by envelopment of phospholipid into herbal extract for improved utilization [13].This technology is enhances the absorption of many plant extracts like CURCUMIN, SILYMARIN, GREENTEA, RUTIN, CATECHIN AND GINSENG [14].

Fig 01: Structure of Phosphotidyl Choline [55].



Phytoso
ME- A New Revolution

Phytosomes symbolize a rapid growth in herbal drug delivery system. Phytosomes, are composed of phytochemical, the word PHYTO means plant; SOME means cell like structure[15].These are produced by phospholipids like phosphatidylcholine reacts with plant extracts or polyphenolic compounds in the presence of non polar solvents [16]. Some phyto constituents like flavonoid and terpenoid extracts easily bind to the phosphatidylcholine. Among all phytochemicals polyphenols whose having by hydrogen atom (-OH,-NH2, COOH etc.), easily included into phytosome structure. In the phytosomes hydrogen bonds were directly formed between Hydrophilic parts (choline) with herbal extract [17]. This results in incorporation of phytochemicals into phytosomal structure. These phytosomes are consisting of phosphatidylcholine and herbal extract in a specific ratio typically 1:1 or 1:2 molar ratios [18].

Difference between Phytosome and Liposome

By observing the High permeability and bioavailability studies, some of the differences observed were given in below table.

Table 01:

CHARACTERISTICS	PHYTOSOME	LIPOSOME
SIZE	Smaller in size	Larger in size [19].
BIOACTIVE COMPOUND	Chemically bonded to polar heads to PC	No bonds invovles and entrapment by membrane [19].
DRUGPHOSPHOLIPID RATIO	1:2 or 2:1 molecular complex	Thousands of phospholipid. Molecules around the drug [20].

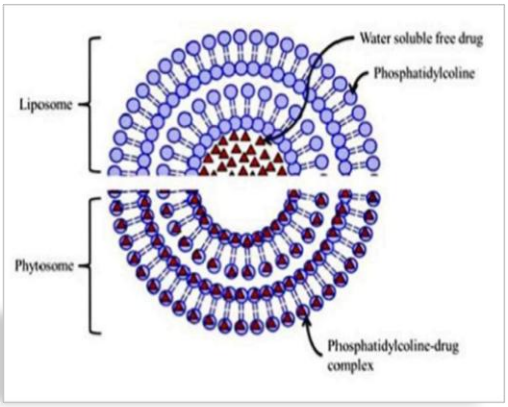


Fig 02: Drug Complex with Liposome and Phytosome [21].

Properties of Phytosomes

Physico-Chemical Properties: As above discussed that reaction between substrate and phospholipid gives phytosomes. Mostlyphytosomes have a size range from 50 nanometres to 100 micrometers. When phytosome mixed with water it resembles liposome such as micellar shape and Photon correlation spectroscopy [PCS] reveals that phytosomes Attains overall structural characteristics of liposomes [22]. The central Part of liposomes consist of active moiety therefore, there is no direct contact occurs between the extracted material and lipid. But in phytosomes there is a direct contact between the extract and the polar head of phospholipid (specifically phosphate and -NH3 group) and this creates an extensive arrangement that improves bioavailability [23].

Biological Properties

Phytosomes are the advanced technology, so they have improved absorbability and Bio -availability compared to natural herbal extracts or other Novel drug deliverysystem [24]. Pharmacokinetic and pharmacodynamic studies have shown that there is an enhanced bioavailability of phytosomal complex than non complexed herbal phytoconstiuents [25].

Types of Expients Used to Formulate Phytosomes [26]

Phospholipids:

1. Distearoylphosphatidyl Choline
2. Soy Phosphatidyl Choline
3. Egg Phosphatidylcholine.

Aprotic Solvent:

1. Dioxane
2. Methylene Chloride
3. Acetone [27].

Alcohol:

1. Ethanol
2. methanol.

Non-Solvent

1. N-Hexane
2. Methanol
3. Ethanol
4. Aliphatic Hydro Carbon
5. Ethyl Acetate

Equipments Required Preparing Phytosomes [26, 28]

- Digital ph meter
- melting point apparatus
- Single pan electronic balance
- different scanning calorimeter
- scanning electron microscopy(SEM)
- transmission electron microscopy(TEM)
- Chromatographic instrument
- UV visible spectrophotometer
- IR-spectrometer

Preperation Methods for Phytosomes

Method-A

With the help of a thin layer rotatory evaporator, vacuum method, The phytosomal vesicles are maded, then an anhydrous ethanol is placed in 250ML round bottom flask that containing phytosome complex. Then attachment of this flask to the rotatory evaporator is doned. A thin layer is formed to the flask by evaporating the solvent at above temperature 60° Celsius. the hydration of film occurs with the help of phosphate buffer with a pH 7.4, and A vesicle suspension is formed by peeling off the lipid layer Into phosphate buffer sonication is done with 60% amplitude to the phytosomal suspension then stored in a refrigerator about 24 hours, before characterization [29], soy phytosomes and bitter melon phytosomes [30] are prepared by using this method [31].

Method-B

Until the evaporation process, the polyphenolic extract is reacted with soya lecithin in the equal amount, in presence of 5ML of dichloromethane with continuous stirring process. Then evaporated dichloromethane is obtained, to that thin film add 5ml of n-hexane with continuous stirring and remove solvent by placing on a fume hood that for certain time. Then, n-hexane is completely removed and to obtain the phytosomal complex film is hydrated and sonicated [32].

Method-C

The DSN was entirely dispersed using the dispersant DMSO through the lyophilisation technique. A complex is formed by stirring SPC, dissolved in t-butyl alcohol (1.5percent weight/volume) with the DSN solution for 3 hours using a magnetic stirrer. Then, with the help of lyophilisation method the complex was segregated. until the testing process the resultant DSN:SPC involutes(90.4% weight/weight) sample, Which is taken from freeze dryer was stored in a desiccators overP205 at 4°c.The impact of various formulation Factors including drug phospholipids ratio(1:1,1:2,and1:4),SPC type(®SPC-3) and co-solvents Like methanol, ethanol, acetone , carbon tetra chloride ,and TBA were evaluated. For the developed technique phytosome complexes are formed by involving non conventional methods also including amalgamation of natural or synthetic phospholipid and active phyto constituents. It gives Modern herbal complex with influence of aerosticorganic solvent [33].

Method-D

Take 200 ml round bottom flask And place extract and soy by addition of lecithin and keeping the temperature not exceeding 60°C for 2 hours To get a solid, and add 20 ML of hexane and the precipitate is collected by filtration process place a overnight in vacuum sealed containers for drying. With the help of a mortar and pestle, crush the dry precipitate, and then pass it through 100 mesh sieve. The very fine phytosomes complex is obtained.after completion of the process.thenstore it in an amberedcoloured bottle and maintains the temperature [34]. For example MORINGA phytosomes are prepared by this anti solvent method [35].

General Method

Phospholipids are dispersed in a drug-containing organic solvent.

↓

It forms a thin film.

↓

Then hydration occurs.

↓

Formation of phytosome suspension occurs.

↓

Phytosomes are finally formed after several steps [36].

Table 02: Various Herbals and Herbal Compounds as Phytosomes

HERBAL PLANT	TYPE OF PHYTOSOME	METHOD OF PREPERATION	PHARMACEUTICAL APPLICATION
CARVACROL	PHOSPHOLIPON	Thin film hydration method	Anti-microbial, anti-oxidant, anti-inflammatory , anti-septic, and anti-cancer propertie [37]
DIOSPYROS KAKI L.	PHOSPHOTIDYL CHOLINE	-----	Infectious diseases, gastrointestinal problems, skin conditions and insomnia [38].
SPIRULANA PLATENSIS	SOY LECITHIN	Solvent evaporation	High blood pressure, diabetes, Anemia and allergy [39].
L-CARNISONE	LIPOID S 75	Solvent evaporation	Protection against aging, oxidative stress, inflammation, autism and glycation [40].
QUERCETIN	PHOSPHOTIDYL CHOLINE	Thin layer hydration method	Anti oxidant, anti inflammatory, anticancer and heart problems [41].
SOYBEAN	PHOSPHOTIDYL CHOLINE	Solvent evaporation	Cardiovascular disease, stroke, coronary heart disease (CHD) and improving bone health [42].
TETRA HYDRO CURCUMIN	SOY-PHOSPHOTIDYL CHOLINE	THIN FILM HYDRATION METHOD	Anti cancer, antioxidant, anti inflammatory and neurological disorder [43].
GINKGO BILOBA	SOY PHOSPHOLIPID	---------	To traet dementia, eye problem, memory loss [44].
DIOSMIN	PHOSPHOTIDYL CHOLINE	Solvent evaporation	To treat hemorrhoids and bleeding eyes [45].
PIPER LONGUM	SOY PHOSPHOTIDYL CHOLINE	Thin layer method	General tonic, digestive issues respiratory tract infection [46].
SILYMARIN	SPC(LECITHIN P3644)	----------	To treat chronic Liver disease, liver cirrhosis, and alcoholic fatty liver [46].
ADIANTUM CAPILLUS VENERIS	PHOSPHOTIDYL CHOLINE	Anti solvent method	To treat bronchitis, cough diabetes and hair loss [47].
UMBILLIFERONE	PHOSPHOLIPON 90-H	----------	Anti inflammatory, anti hyperglycemic agent and anti tumor agent [49].
MORINGA	PHOSPHOLIPID	Anti solvent method	Anti oxidant, digestive issues and to promote skin health [49].
GINGER-RHIZOME	PHOSPHOTIDYL CHOLINE	Thin layer hydration method	Chemotherapy treatment, pain relief, Anti inflammatory and to treat cardio vascular diseases [50].
BITTER MELON (MOMORDICA CHARANTIA)	PHOSPHOTIDYL CHOLINE	Thin layer method	To improve bone health, boosting immunity and wound healing [51].
AMALTAS(CASSIA FISTULA)	SOY LECITHIN	Anti solvent method	Anti pyretic, carminative, antioxidant, anti inflammatory and laxative [52].
COCAO POD HUSK CONTAING CHROMOSOMES	PHOSPHOTIDYL CHOLINE	Thin layer method	It shows anti oxidant and tyrosinase inhibitor effects [53].
OCIMUM BASILIUM	PHOSPHOTIDYL CHOLINE	----------	Used as anti oxidant, anticonvulant, anti microbial and anti hyper lipidemic agent [54].

Characterization of Phytosomes

Particle Size and Zeta Potential

To study the stability and reproducibility of complexes, particle size and zeta potential are major aspects.

Generally, 50 nm to 100 nm is the particle size for phyto-phospholipid complexes. mazumder prepared a phytosomal complex called singrin phytosome which has an average particle size and zeta potential around were153 ± 39 and 10.09±0.98 appropriately [55].

Entrapment Efficacy [56]

Entrapment of chemical constituents within the phospholipid is an important aspect. It was determined with the help of UV-visible spectroscopy (uv1601, shimadzu). Prachi pudapurkar measured the entrapment efficacy of the diosmin. The following formula was used to measure the Entrapment efficacy (%):

EE(%)=T-S/T×100

Where:

T = Total amount of Diosmin

S = Diosmin in filtrate

Drug Content [57]

To determine drug content, take 10 mL of sample and a 100milligrams of solvent of phyto-phospholipid complex and mix both to dissolve. After dissolution, the UV spectrophotometer was used to measure the absorbance.

The formula below was used to determine drug content (%):

% drug content=Total amount of drug-Amount of free Drug/total amount of drug×100

Crystallinity

By losing crystallinity, the phytosomal complex shows results in occlusion or enhanced solubility/hydrophilicity of poorly water-soluble phytoconstituents. The DSC & XRD analysis helps to provide crystallinity of the phytosomal complex. An uncomplexed (or) unformulated drug shows a sharp peak at a high melting point on the DSC thermogram, but phytosomes show broad peaks and less melting point and intensity than the pure form of the drug. So, phytosomes show more solubility [58].

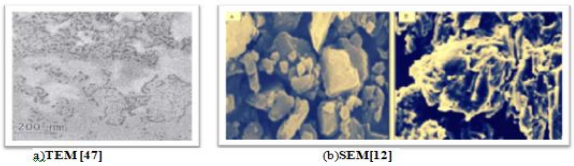


FIGURE 3: SEM AND TEM OF PHYTOSOMAL COMPLEX

Fig 03:

Visualization

- With the help of atomic force microscopy (AFM), SEM & TEM are used to determine the morphology of phytosomes. The surface characteristics, presence or absence of impurities on surface, texture, and smoothness of the surface are determined with the help of surface morphology.
- The entrapment of the drug within the phospholipid is studied by TEM.

Vesiclestability [59]

- Zeta potential measures size and polarity. Polydispersity Index (PDI) describes vesicle stability when the PDI value is lower than 0.5. It determines that the formed phytosomal complex is stable.

Spectroscopy [60]

To observe complex formation between two herbal extracts and phospholipid, the spectroscopic methods used are:

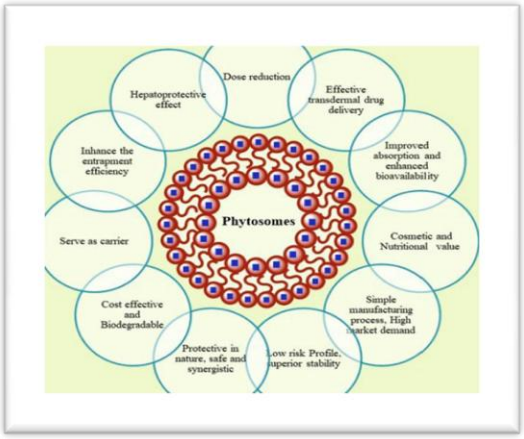
1H-NMR, 13C-NMR, FTIR, UV

Applications of Phytosomes [46-54]

Phytosome-As Hepato Protective Agent

sonam Sharma developed phytosomes of Abutilon indicum and PIPER LONGUM. He studied (using) the solution in adult Charles Foster albino rats. CCl_4 (carbon tetrachloride) administration results in toxicity to liver enzymes like alkaline phosphatase (ALP), total bilirubin (TB), etc. This oxidative stress with CCl_4 results in the formation of free radicals in the liver,by interfere with CYP450,which causes damage to liver cells.When they administered the phytosomal solution, it exhibited defence against carbon tetrachloride-induced hepatotoxicity. When compared to crude drugs, the lipid solubility and hepatoprotective action of the phytosomal complex was significantly higher. Another example, Gohari Mahmoud Abad introduced Silymarin phytosomes. When they administered alcohol to mice (as a model), it resulted in oxidative stress, water retention, and inflammation of liver cells and enzymes. When silymarin phytosome is introduced into the rats, it results in blockage of inflammatory cell penetration. This study shows that the silymarin phytosomal complex is more effective than silymarin alone in the treatment of alcoholic liver disease.

Fig 04: Various Benefits of Phytosomes [57].



Phytosome-As an Anti Microbial Agent

Ganesh Jagtap formulated phytosomes of Adiantum capillus-veneris (ACV). These phytosomes were examined against Gram-negative (Escherichia coli) and Gram-positive (Staphylococcus aureus) bacteria to test their antimicrobial activity. The phytosomal complex showed higher antimicrobial effects than crude ACV.

Phytosome-As Anti-Oxidant Agent

Itadwar conducted experiments on albino rats using umbelliferone phytosomes. He applied both the UMB-

HSPC gel formulation and UMB gel on the skin of rats and observed the permeability of the gel through the skin.
The results showed that the UMB-HSPC gel had higher permeability and more antioxidant activity than the UMB gel. He proved that the UMB-HSPC complex has more stability and photoprotective action than the UMB gel formulation.

Phytosomes-as Cardioprotective Agent

R. Naik conducted experiments on wister albino rats using Ginkgo bilobap hytosomes. Firstly, he introduced ISO (isoproterenol, a catecholamine that induces acute myocardial infarction in humans) into rats, which caused a decreased amount of AST, LDH, and CPK enzymes, and an increased heart rate due to enzyme leakage into the blood. When he introduced Ginkgo biloba phytosomes into the rats, he observed that the phytosomes showed increased enzyme activity in the heart compared to normal crude Ginkgo biloba, resulting in less damage. The phytosomal complex showed higher cardio protective activity than crude Ginkgo biloba.

Phytosome- as Herbal Supplement

Mahdi Jufri prepared Moringaphytosomes. He studied that Moringa leaves contain vitamins, minerals, and proteins, which help treat stunted growth in children. He proved that the phytosomal complex of Moringa extract showed better absorption than crude Moringa plant drugs, resulting in increased therapeutic activity of Moringa.

Phytosome-as an Anti -Inflammatory Agent

Mariana decenee and toma introduced GINGER. RHIZOME phytosomes which are primarily treated with LPS (Lipopolysaccharide–an agent that induces inflammation) in rats. This significantly increases the levels of PON1, SOD, and CAT (antioxidant enzymes), and phytosomes also reduce TNF-α levels in the plasma of rats. These results in the phytosomal complex showing: 36% more anti-inflammatory action and 50% more antioxidant action than crude extracts of ginger based on the extract's bioavailability.

Phytosome- as an Anticancer Agent

Nehal Raouf and Darwish formulated tetra hydrocurcumin (THC) phytosomes. They studied that drug release from the THC-phytosomal complex is 40% higher compared to normal THC in crude form. This THC-phytosome is more capable of inhibiting the proliferation of cancer cells compared to the original drug. They also introduced THC-phytosomes into SCC4 cells, which caused apoptosis (cell death). These THC-phytosomes are easily taken up by cells compared to crude drugs. Overall, the study shows that THC-phytosomes exhibit more anti-cancer activity than the crude form of THC.

Future Perspective of Phytosomes

Phytosomes have emerged as a significant innovation in herbal drug delivery, enhancing the bioavailability and therapeutic efficacy of plant-derived compounds. These complexes, formed by binding phytoconstituents with phospholipids, facilitate better absorption of herbal extracts when administered orally or topically. The efficiency of phytosome formation varies across studies, with reported yields ranging from approximately 25% to over 90% [58]. This variation is influenced by factors such as the molar ratio of active compounds to phospholipids, drug concentration, and reaction temperature during formulation.
Initially explored for cosmetic applications, phytosome technology has been increasingly adopted in the pharmaceutical field over recent years [59]. The integration of nanotechnology into phytosome development holds promise for creating more efficient delivery systems, potentially transforming the treatment landscape for various diseases.
Researchers have highlighted the potential of phytosomes in improving the pharmacokinetic profiles of herbal formulations, suggesting their significant role in future pharmaceutical applications [60]. Innovative approaches in phytosome technology underscore its adaptability and potential in delivering a wide range of phytochemicals. These advancements point towards the expanded use of phytosomes in personalized medicine and targeted therapy [61].

Conclusion

Phytosomal complexes have shown excellent results in enhancing the bioavailability, pharmacological and pharmacokinetic activity of herbal phyto-constituents like flavonoids and terpenoids through gastro intestinal tract and skin. The characterization of phytosomes reveals that the stability and efficacy of phytosomal complex. Due to their entrapment efficacy and biocompatibility, they enhance the therapeutic benefits of herbal products. Phytosomes improves the therapeutic benefits of herbal products by obtaining maximum pharmacological actions. Continue research and innovation into phytosomal complex have demonstrated that potential for the development of novel drug delivery systems with increased therapeutic efficacy, improved clinical utility, and better formulation of hydrophilic plant products.

Acknowledgement

We sincerely acknowledge and extend our gratitude to the management of VJ's College of Pharmacy for their support and resources, which greatly facilitated the completion of this work.

Conflict of Interest

The authors declare no conflicts of interest.

Funding

This work is written with the support from VJ's College of Pharmacy, Diwancheruvu, Rajahmundry - 533296, Andhra Pradesh, India.

Authors Contribution

All authors have read and agreed to the published version of the manuscript.

References

1. Furhad S, Bokhari AA. Herbal Supplements. [Updated 2024 Sep]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2025 Jan–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537255/ PMID: 30725649.
2. Sun W, Shahrajabian MH. Therapeutic Potential of Phenolic Compounds in Medicinal Plants-Natural Health Products for Human Health. Molecules. 2023Feb15;28(4):1845.
3. Ancuceanu R, Anghel AI, Ionescu C, Hovaneț MV,Cojocaru-Toma M, Dinu M. Clinical Trials with Herbal Products for the Prevention of Dental Caries and Their Quality: A Scoping Study. Biomolecules. 2019Dec17;9(12):884.
4. Zhang J, Tang Q, Xu X, Li N. Development and evaluation of a novel phytosome-loaded chitosan microsphere system for curcumin delivery. Int JPharm. 2013 May 1;448(1):168-74.
5. Vijayarani KR, Govindarajulu M et al. Enhanced Bioavailability of Boswellic Acid by Piper longum: A Computational and Pharmacokinetic Study. Front Pharmacol. 2020 Dec 15;11:551911.
6. Bolat E, Sarıtaş S, DumanH,et al.,. Polyphenols: Secondary Metabolites with a Biological Impression. Nutrients. 2024 Aug 3;16(15):2550.
7. Kumar Vishwakarma, Dhaneshwar, etal.' Phytosomes as a Novel Approach to Drug Delivery System'. Pharmaceutical Science, IntechOpen, 21 Aug. 2024.
8. Patel J, Patel R, Khambholja K, Patel N. An overview of phytosomes as an advanced herbal drug delivery system. Asian J Pharm Sci. 2009 Apr;4(6):363-71.
9. Bartelds R, Nematollahi MH, Pols T, Stuart MC, Pardakhty A, Asadikaram G, Poolman B. Niosomes, an alternative for liposomal delivery. PloS one. 2018 Apr 12;13(4):e0194179.
10. Harwansh RK, Deshmukh R, et al.., Recent Advancements in Gallic Acid-Based Drug Delivery: Applications, Clinical Trials, and Future Directions. Pharmaceutics. 2024 Sep 13;16(9):1202.
11. Singh, Hardeep & Sharma, Gauri. (2023). Recent Development of Novel Drug Delivery of Herbal Drugs. RPS Pharmacy and Pharmacology Reports.10.1093/rpsppr/rqad028.
12. Udapurkar, Prachi& Bhusnure, Phyto-phospholipid complex vesicles for phytoconstituents and herbal extracts: A promising drug delivery system. International J. Of herbal medicine. 14. 14-20.
13. Ravindran, Vinod & S, A review on genesis and characterization of phytosomes. International Journal of Pharmaceutical Sciences Review andResearch. 4. 69-75.
14. Demirci M, Caglar MY, Cakir B, Gülseren İ. Encapsulation by nanoliposomes. Nano encapsulation technologies for the food and nutraceutical industries. 2017 Jan 1:74-113.
15. Pandey R, Bhairam M, Shukla SS, Gidwani B. Colloidaland vesicular delivery system for herbal bioactive constituents. Daru. 2021 Dec;29(2):415-438.
16. Jain N, Gupta BP, Thakur N, Jain R, Banweer J, Jain DK, Jain S. Phytosome: a novel drug delivery system for herbal medicine. Int J Pharm Sci Drug Res. 2010 Oct;2(4):224-8.
17. Barani M, Sangiovanni E, Angarano M, Rajizadeh MA, Mehrabani M, Piazza S, Gangadharappa HV, Pardakhty A, Mehrbani M, Dell'Agli M, Nematollahi MH. Phytosomes as innovative delivery systems for phytochemicals: A comprehensive review of literature. International journal of nanomedicine. 2021 Oct 15:6983-7022.
18. Ting, Yuwen& Jiang, Yike& Ho, Chi-Tang & Huang, Qingrong. (2014). Common delivery systems forenhancing in vivo bioavailability and biological efficacy of nutraceuticals. Journal of Functional Foods. 7. 10.1016/j.jff.2013.12.010.
19. Talebi M, Shahbazi K, Dakkali MS, Akbari M, Ghale RA, Hashemi S, Sashourpour M, Mojab F, Aminzadeh S. Phytosomes: A promising nanocarrier system for enhanced bioavailability and therapeutic efficacy of herbal products. Phytomedicine Plus. 2025 Mar 7:100779.
20. Gaikwad SS, Morade YY, Kothule AM, Kshirsagar SJ, Laddha UD, Salunkhe KS. Overview of phytosomes in treating cancer: Advancement, challenges, and future outlook. Heliyon. 2023 Jun 1;9(6).
21. Fathima Shana A.*, Afnan K. V., Afra, Phytosomes As Novel Drug Delivery System, Int. J. of Pharm. Sci.,2024, Vol 2, Issue 8, 2446-2454.
22. Joshi R, Bhardwaj M. Novel Approach on Herbal Drug Delivery System: Phytosome A Brief Overview. Int J Pharm Biol Sci. 2019;9(2):856-62.
23. S.Shabanpour, 'Phytosome: A Novel Drug Delivery Approach in Herbal Medicine', Pharmaceutical Science. IntechOpen, Feb. 06, 2025.
24. Sriya KC, Sai D, Sankar PR. Phytosomes: A novel approach for herbal phytochemicals for enhancing the bioavailability. Int. J. Pharm. Sci. Rev. Res. 2020;6:21-6.
25. Gandhi A, Dutta A, Pal A, Bakshi P. Recent trends of phytosomes for delivering herbal extract with improved bioavailability. J. Pharmacogn. Phytochem. 2012 Nov 1;1(4):6-14.
26. Sharma D, Bhujbale AA. Phytosomes is a novel drug delivery system based herbal formulation: An review. PharmaTutor. 2018 Jun 7;6(3):23-6.
27. Dwivedi J, Sachan P, Wal P, Kosey S, Khan MM. Progressive journey of phytosomes: preparation, characterization, patents, clinical trials & commercial products. J Res Pharm. 2023 Sep 1;27(5):1687-733.

28. Dhase AS, Saboo SS. Preparation and evaluation of phytosomes containing methanolic extract of leaves of Aegle marmelos (bael).
29. Maryana W, Rachmawati H, Mudhakir D. Formation of phytosome containing silymarin using thin layer-hydration technique aimed for oral delivery. Materials today: proceedings. 2016 Jan 1;3(3):855-66.
30. Sasongko RE, Surini S, Saputri FC. Formulation and characterization of bitter melon extract (momordica charantia) loaded phytosomes. Pharmacognosy Journal. 2019;11(6).
31. El-Menshawe SF, Ali AA, Rabeh MA, Khalil NM. Nanosized soy phytosome-based thermogel as topical anti-obesity formulation: an approach for acceptable level of evidence of an effective novel herbal weight loss product. International journal of nanomedicine. 2018 Jan 9:307-18.
32. Kumar A, Kumar B, Singh SK, Kaur B, Singh S. A review on phytosomes: Novel approach for herbal phytochemicals. Asian J Pharm Clin Res. 2017 Oct 1;10(10):41-7.
33. Gaurav V, Paliwal S, Singh A, Pandey S, Siddhiqui M. Phytosomes: Preparation, evaluation and application. Int J Res Eng Sci. 2021;9(2):35-9.
34. 31. S Raja Sekhara Reddy and Dr. Anuj Kumar Sharma, Characterization, properties and formulation of Phytosomes IJMT 2022; 4(2): 229-234
35. Wardana MS, Jufri M, Mun'im A. Physicochemical properties and nutrition of moringa oleifera lam. leaf extract: a preliminary study on preparation phytosomes as herbal supplement for children. International Journal of Applied Pharmaceutics. 2022 Jan 1;14(1):281-7.
36. Vighne RC, Deore SL, Baviskar BA. A Comparative Investigation on the Phytosomes of Diverse Bioactive Nootropic Medicinal Herbs. Pharmacognosy Reviews. 2024 Jul;18(36):117-26.
37. Tafish AM, El-Sherbiny M, Al-Karmalawy AA, Soliman OA, Saleh NM. Carvacrol-loaded phytosomes for enhanced wound healing: molecular docking, formulation, DoE-aided optimization, and in vitro/in vivo evaluation. International Journal of Nanomedicine. 2023 Dec 31:5749-80.
38. Direito R, Reis C, Roque L, Gonçalves M, Sanches-Silva A, Gaspar MM, Pinto R, Rocha J, Sepodes B, Rosário Bronze M, Eduardo Figueira M. Phytosomes with persimmon (diospyros kaki l.) extract: Preparation and preliminary demonstration of in vivo tolerability. Pharmaceutics. 2019 Jun 22;11(6):296.
39. Adela N, Sari UK, Karim DD, Ratnasari D. Formulation and Antioxidant Activity Test of Phycocyanin Phytosomal Gel from Green Algae Extract (Spirulina platensis). Jurnal Aisyah: Jurnal Ilmu Kesehatan. 2024 Mar 20;9(1).
40. Abdelkader H, Longman MR, Alany RG, Pierscionek B. Phytosome-hyaluronic acid systems for ocular delivery of L-carnosine. International journal of nanomedicine. 2016 Jun 14:2815-27.
41. Rasaee S, Ghanbarzadeh S, Mohammadi M, Hamishehkar H. Nano phytosomes of quercetin: A promising formulation for fortification of food products with antioxidants. Pharmaceutical sciences. 2014 Sep 16;20(3):96-101.
42. El-Menshawe SF, Ali AA, Rabeh MA, Khalil NM. Nanosized soy phytosome-based thermogel as topical anti-obesity formulation: an approach for acceptable level of evidence of an effective novel herbal weight loss product. International journal of nanomedicine. 2018 Jan 9:307-18.
43. Raouf N, Darwish ZE, Ramadan O, Barakat HS, Elbanna SA, Essawy MM. The anticancer potential of tetrahydrocurcumin-phytosomes against oral carcinoma progression. BMC Oral Health. 2024 Sep 26;24(1):1126.
44. Panda VS, Naik SR. Cardioprotective activity of Ginkgo biloba phytosomes in isoproterenol-induced myocardial necrosis in rats: a biochemical and histoarchitectural evaluation. Experimental and toxicologic pathology. 2008 Aug 5;60(4-5):397-404.
45. Udapurkar PP, Bhusnure OG, Kamble SR. Diosmin phytosomes: development, optimization and physicochemical characterization. Indian J Pharm Educ Res. 2018 Oct 1;52(4):S29-36.
46. Mahmoudabad AG, Gheybi F, Mehrabi M, Masoudi A, Mobasher Z, Vahedi H, Gharravi AM, Bitaraf FS, Sorkhabadi SM. Synthesis, characterization and hepatoprotective effect of silymarin phytosome nanoparticles on ethanol-induced hepatotoxicity in rats. BioImpacts: BI. 2023 May 30;13(4):301.
47. Jagtap SG, Kajale VV, Abhyankar MM, Kulkarni AS, Ghante MR. Formulation and evaluation of phytosomes of hydroalcoholic extract of Adiantum capillus-veneris for antimicrobial activity. Pharmacognosy Research. 2023;15(3).
48. Ittadwar PA, Puranik PK. Novel umbelliferone phytosomes: development and optimization using experimental design approach and evaluation of photo-protective and antioxidant activity. Int J Pharm Pharm Sci. 2017;9(1):218.
49. Wardana MS, Jufri M, Mun'im A. Physicochemical properties and nutrition of moringa oleifera lam. leaf extract: a preliminary study on preparation phytosomes as herbal supplement for children. International Journal of Applied Pharmaceutics. 2022 Jan 1;14(1):281-7.
50. Deleanu M, Toma L, Sanda GM, Barbălată T, Niculescu LȘ, Sima AV, Deleanu C, Săcărescu L, Suciu A, Alexandru G, Crișan I. Formulation of phytosomes with extracts of ginger rhizomes and rosehips with improved bioavailability, antioxidant and anti-inflammatory effects in vivo. Pharmaceutics. 2023 Mar 25;15(4):1066.
51. Sasongko RE, Surini S, Saputri FC. Formulation and characterization of bitter melon extract (momordica

charantia) loaded phytosomes. Pharmacognosy Journal. 2019;11(6).
52. Yadav H, Singh AP, Vishwakarma D, Mishra J. Formulation and characterization of phytosomal gel by using amaltas for skin problem and as antipyretic. Eur Chem Bull. 2024;13(6). doi:10.53555/ecb.v13i6.17637.
53. Priani SE, Aprilia S, Aryani R, Purwanti L. Antioxidant and tyrosinase inhibitory activity of face serum containing cocoa pod husk phytosome (Theobroma cacao L.). Journal of Applied Pharmaceutical Science. 2019 Oct 5;9(10):110-5.
54. Raj MP, Reichal CR, Manju S, Shobana M, Sangeetha M. Formulation and characterization of phythosomal topical gel of ocimum basilicum. Research Journal of Pharmacy and Technology. 2022;15(10):4649-54.
55. Lu M, Qiu Q, Luo X, Liu X, Sun J, Wang C, Lin X, Deng Y, Song Y. Phyto-phospholipid complexes (phytosomes): A novel strategy to improve the bioavailability of active constituents. Asian journal of pharmaceutical sciences. 2019 May 1;14(3):265-74.
56. Udapurkar PP, Bhusnure OG, Kamble SR. Diosmin phytosomes: development, optimization and physicochemical characterization. Indian J Pharm Educ Res. 2018 Oct 1;52(4):S29-36.
57. SAKURE K, PATEL A, PRADHAN M, Badwaik HR. Recent Trends and Future Prospects of Phytosomes: A Concise Review. Indian journal of pharmaceutical sciences. 2024 May 1;86(3).
58. Joshi G, Tiwari A, Upadhyay P. Development and characterization of herbosomes complex. Journal of Pharmaceutical Research. 2020;10(06).
59. Kattyar SL, Patil PS, Patil SV, Kadam SS. Phytosomes and recent research on phytosomal drugs. Asian Journal of Pharmaceutical Analysis. 2022 Mar 5;12(1):61-9.
60. Joseph AK, Kareparamban PH. Phytosome: a novel revolution in herbal drug. International journal of Research in Pharmacy and Chemistry. 2012;2:2231.
61. Kumar A, Kumar A, Nair R, Bhatt PC, Kumar V, Khan W, et al. Phytosomes: innovative approach to enhance the bioavailability and therapeutic efficacy of herbal extract. World J Pharm Med Res. 2023;9(8):240–52.
62. Singh D, Upadhyay P, Upadhyay S. Phytosomes: an advanced drug delivery system for herbal drug. Sciences. 2018;20:96-101.
63. Poudyal A, Subba B, Bhattarai A, Regmi D, Tiwari B, Pradhan A, Bhutia S. A Comprehensive Review on Phytosomes: A Novel Drug Delivery System of Phytoconstituents.(2022). Int. J. Life Sci. Pharma Res. 2022;12(5):P143-161.
64. Kothamasu S, Sindhuja B, Thangabalan B.Phytosomes as Innovative Delivery Systems for Phytochemicals: A Comprehensive Review. Indo Am J Pharm Sci. 2024;11(12).