Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Spl Issue [1] January 2023: 58-65

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Phytosomes: The future of Herbal Drug Delivery

Poonam Karekar[a]*, Dr. Suresh Killedar[b], Dr. Amir Shaikh[c], Manali More[d], Sneha Joshi[e], Rahul Buchade[f], Yash Dongre[g], Harinath More[h], Pradnya Zambare[i]
: a,h- Bharati Vidyapeeth College of Pharmacy, Kolhapur, Near Chitranagri, Kolhapur-416013, Maharashtra, India
b -Sant Gajanan Maharaj College of Pharmacy, Mahagaon, Chinchewadi, Mahagaon Gadhinglaj-416503, Kolhapur, Maharashtra, India
c,d,e,f,g- Indira College of Pharmacy, Pune, Niramay, New, Old Mumbai Rd, Tathawade, Pune-411033, Maharashtra, India
i-Rayat Institute of research and Development, Satara, Maharashtra, INDIA
Corresponding author: Poonam S. Karekar
Email Id: poonamkarekar16@rediffmail.com

ABSTRACT
Phyto-constituents of herbal origin are gaining importance in day today life due to their nutritional and medicinal properties. They have the potential to treat severe ailments, but they remain unexplored for ages due to poor bioavailability. Thus, various methods have been explored in recent years to enhance their bioavailability. Phytosome drug delivery is one of the methods developed in recent years and it uses the polymer to increase bioavailability and is compatible in-vivo. The methods used in the preparation of phytosomes are also easy and be done at the laboratory level. Further, they can be characterized by techniques like FTIR, PXRD, DSC, SEM, TEM, and HNMR. Thus, such novel drug delivery can be exploited to augment the bioavailability of otherwise poorly absorbable constituents of plants and utilized in incurable disease treatment with lesser side effects.
Keywords: *Phytosomes; bioavailability; drug delivery*

Received 22.10.2022 Revised 23.11.2022 Accepted 24.12.2022

INTRODUCTION

Medicinal plants are abundant bio-source of drugs, neutraceuticals, food supplements intermediate chemical systems for synthetic drugs [1]. 'Phyto-constituents' can be simply called 'Plant-chemicals'. Phyto-constituents can have medicinal as well as nutritive value, occur naturally in plants, and are observed to be beneficial for human health [2]. The key role played by Phyto-constituents is the protection of plants from damage and disease and imparting colour, flavour, and aroma to different plant parts. It has been observed that phyto-constituents can curb the impact of hazards like stress, pollution, UV exposure, drought, and pathogenic attack on plants, recently a lot of research is going on to prove the implications in the betterment of human health [1]. A variety of vegetables, fruits, beans, whole grains, nuts, and seeds consists of diversities of active constituents and most of these are found concentrated in plant parts like roots, stems, flowers, fruit, seed and leaf [1].
Phyto-constituents can be classified as Primary and secondary metabolites.
1. Primary metabolites consists of amino acids, sugars, proteins, and nucleic acids.
2. Secondary metabolites consist of flavonoids, terpenes, glycosides, alkaloids, plant steroids, glycosides and saponins.
Pharmacological properties like antioxidant, antimicrobial, anti-inflammatory, modulation of hormones, hepato-protective, anti-depressant, a decrease of platelet aggregation, cardio-protective and anti-cancer are depicted by various phyto-constituents present in different parts of plants [1].

- How do Phyto-constituents help in preventing diseases?
  1. They activate an immune response against pathogenic bacteria, micro-organisms, and viruses in the body

2. They prohibit the formation of carcinogens in the body from eatables, drinkables and other substances from surroundings.
3. Prevent the cell damage that might occur due to some free radicals and exposure to pollution by reducing oxidation.
4. They may deduct the growth rate of cancerous cells, and may contribute to the regulation of hormones
5. They might help in DNA repair mechanisms

Types of phyto-constituents:

1. Phenolics:

It occurs widely in different varieties of plants, and gained importance since ancient times, for its role as a safeguard against damage due to oxidative stress. They are classified as secondary metabolites and found to be present as hydroxybenzoates and hydroxycinnamic acid. Some of the phenolic compounds in plants are polymerized to form larger molecules like proanthocynadines and lignins[1, 2].

2. Alkaloids:

Alkaloids are basic in nature made up of amino acids and have heterocyclic nitrogen in structure, categorized as a heterogeneous class of secondary metabolites. The name 'alkaloid' is acquired from its alkaline nature and is most probably related to a base containing nitrogen [2]. Their main implication is being used as remedies, phychoactive drugs and are bitter in taste [1]. Depending upon the presence of different heterocyclic rings in structure alkaloids are classified as Pyrrolidine alkaloids, Pyridine-piperidine alkaloids and isoquinoline alkaloids. As they are toxic in nature their major function is the protection of plants against micro-organisms, insects and herbivores. In addition to this alkaloid have many pharmacological activities like anti-hypertensive effects, anti-arrhythmic effect, anti-malarial activity, and anti-cancer actions [2].

3. Saponins:

They tend to form stable soaps in aqueous solutions that's why named 'Saponins'. Glycosylated steroids, steroidal alkaloids and triterpenoids make the group of compounds called saponins. Spirostan and furostan derivatives are categorized as two main steroid aglycons [2]. A variety of vegetables, beans and herbs including peas, soya beans and some herbs indicating foaming properties in a name like soapwort, soaproot, soapbark and soapberry are considered as best sources of saponins [1]. Saponins are regarded as good anti-microbial agents.

4. Glycosides:

Glycosides have two parts carbohydrate and non-carbohydrate in the same structure. Out of this, the carbohydrate part is called glycone and the non-carbohydrate part is called aglycone. They are classified into anthraquinone, saponin, Coumarin and furocoumarin, flavonoids, cyanophore, phenol, and aldehyde glycoside [1].

5. Terpenes/Terpenoids:

Turpentine is a volatile oil obtained from a pine tree and thus is named 'Terpene' [1]. Terpenes are multicyclic compounds with basic carbon skeletons having different functional groups. They are divided into hemiterpenoids, monoterpenoids, sesquiterpenes, diterpenes, triterpenes, and tetraterpenoids [2].

6. Tannins:

Tannins have antioxidant activity and act by scavenging free radicals, complex formation with transition metals, inhibiting peroxidase enzyme and preventing lipid peroxidation [3]. They are bitter in taste, polyphenols that precipitate proteins hence called astringents. There are three different types of tannins categorized depending on structural differences. Hydrolysable tannins are formed by phenolic acids. Condensed tannins are composed of carbon-carbon bond polymerization of flavane-3-ol-like catechins or their derivative gallocatechin. Third class is of complex tannins which consist of flavane-3-ol, the unit of condensed tannins, and hydrolyzed tannins, which are partially joined by carbon-carbon bonds [4].

PHYTOSOMES AND THEIR ADVANTAGES:

The term phytosomes word is originated from two words, “phyto" means "plant" and "some". Indena, Italy was the one that developed phytosomal technology. Phytosome drug delivery is one type of vesicular delivery (5). They are fabricated by using standardized extract and phospholipids wherein the interaction between the former and the latter is on a molecular level. There is strong physical interaction between the active ingredient of extract and phospholipids in phytosomes [6]. It consists of micelles formed by conjugation of either herbal extract or aromatic active constituents of herbs like terpenoids, flavonoids,

and tannins which are polar in nature to phospholipid components which are usually carried out in nonpolar solvents [5].

Advantages of phytosomes:

- ✓ Bioavailability of polar phytoconstituents through oral and topical routes is enhanced as phytosomes involve the formation of micelles that are lipid soluble.
- ✓ Phytosome indicates the cell-like structure and thus, would be able to protect herbal extract from destruction by different digestive enzymes and gastric acid.
- ✓ Increased stability of phytosomes is indicative of the formation of stable bonds between phytoconstituents and phospholipids on a molecular level.
- ✓ Due to the lipid solubility of phytosomes they can easily traverse across cell membranes.
- ✓ Phytosomes show sustained release of encapsulated Phyto-constituents.
- ✓ Pharmacological action is not affected
- ✓ Entrapment efficacy is better

PHOSPHOLIPIDS

Structurally phospholipid molecule is made up of a long chain of fatty acids hydrocarbon chain which accounts for its lipophilic character and hydrophilic character is imparted by hydrophilic choline molecule which can attach to polar phytoconstituents, thus known as an amphiphilic molecule. Moreover, it has a negatively charged phosphate group in structure. The binding between phospholipids and phytoconstituents is stronger in nature due to hydrogen bond formation between the phosphate group of the former and the polar functional group of the latter [7, 8].

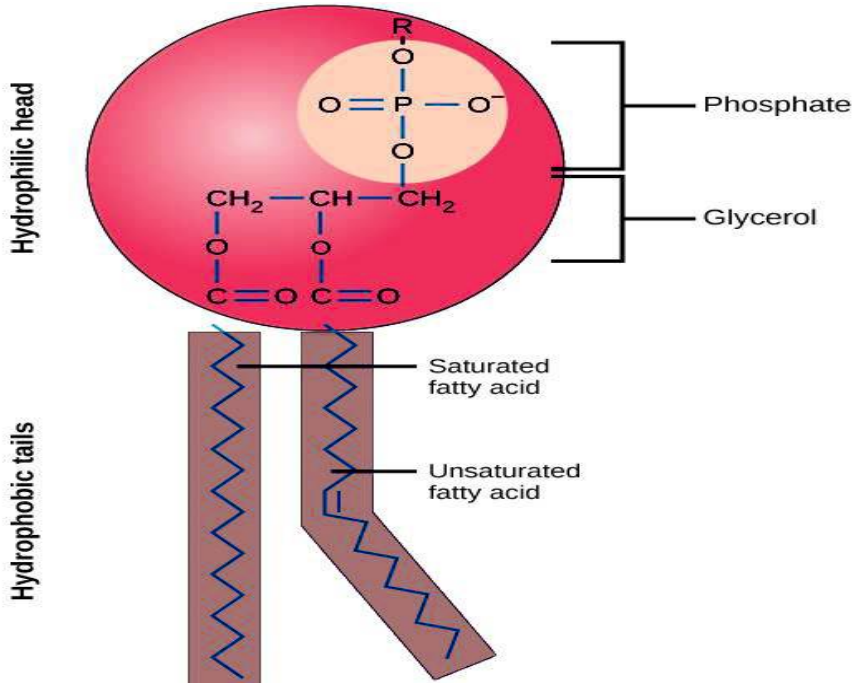

Fig no. 1 Structure of Phospholipid

Advantages of Phospholipids:(8)

1. Enhancement in bioavailability of Phyto-constituents by imparting lipid characteristics to the whole molecule
2. The dose of a drug may be reduced by delivering it through phytosomes
3. Due to the formation of vesicles, there is augmentation of stability as well as entrapment efficacy was also found to be improved
4. With the use of phospholipids patient compliance may be improved as they are having very minimum toxic potential

PREPARATION METHOD OF PHYTOSOMES: [9]

1. Anti-solvent Precipitation method:

Herbal extract and phospholipids are weighed in molar ratio and placed into a round bottom flask. It is then refluxed using organic solvents like dichloromethane or acetone for 2 hours at 60°c. The process is continued until the reaction mixture becomes half of the original volume. Then reaction mixture is

allowed to cool and precipitated by means of adding non-polar solvent such as benzene. The precipitate obtained is filtered and allowed to remove moisture or any remains of solvent by putting it into desiccators. The dried precipitate is subjected to pulverization through screens of suitable size and complex in powder form and is kept in an amber coloured glass bottle at normal temperature.

2. Rotary evaporation method:

Herbal extract and phospholipid were weighed in suitable proportion and dispersed in suitable water miscible organic solvent in round bottom flask. Then it is stirred for 2 hours at 60°c in rotary evaporator. After continuous stirring followed by addition of n-hexane, a thin film is obtained. The precipitate so obtained in the form of thin film and is stored in an amber coloured bottle under specific conditions of temperature and humidity

3. Solvent ether injection method:

In this method advantage is taken of the reaction which occurs between phospholipids dissolved in suitable organic solvent and herbal extract dissolved in aqueous solution. The herbal extract'saqueous solution, to be encapsulated is prepared, into which a solution of phospholipids dissolved in diethyl ether is injected dropwise and slowly. On subsequent removal of solvents, cell-likevesicles are formed, resulting into complex formation. The structure of phytosomes is dependent upon concentration lesser concentration favours formation of monomers while higher concentration favours different shapes of phytosomes like cylindrical, round,disc and cubic or hexagonal.

PHYTOSOMES'PROPERTIES: [10]

Physicochemical properties:

a) The phytosomes are complexes formed of phospholids and extract and is product of reaction between chief constituent of extract and phospholipid in particular solvent.

b) There is formation of hydrogen bonds between polar functional groups on chief constituent and polar heads of phospholipids.

c) Phytosomes display a cell-like structure similar to liposomes, after interaction between hydrophilic counterparts of extract and phospholipid. However, in phospholipids chief constituents of extract become integral part of membrane as they are enveloped in polar heads.

Biological properties:

a) Phytosomeleads to increase in bioavailability when administered orally by active absorption of active constituents.

b) As compared to herbal extracts phytosomes have better efficacy and are known as advanced form of herbal products.

c) They have better pharmacokinetic profile when compared with simple herbal extract.

DIFFERENCE BETWEEN PHYTOSOMES AND LIPOSOMES: [11, 12]

In phytosomal formulation, there is conjugation between the hydrophilic choline head and the phytoconstituents while in liposomes phytoconstituents or active constituents are dissolved in either lipid bilayer membrane or aqueous internal core.

Phytosomes involve complex formation between choline molecules and phytoconstituents, which are held together by chemical bonds. On the other hand, liposomes merely have the confinement of hydrophilic moieties in numerous phospholipid molecules. Thus, liposomal formulation involves an absence of chemical binding between active constituents andphospholipids.

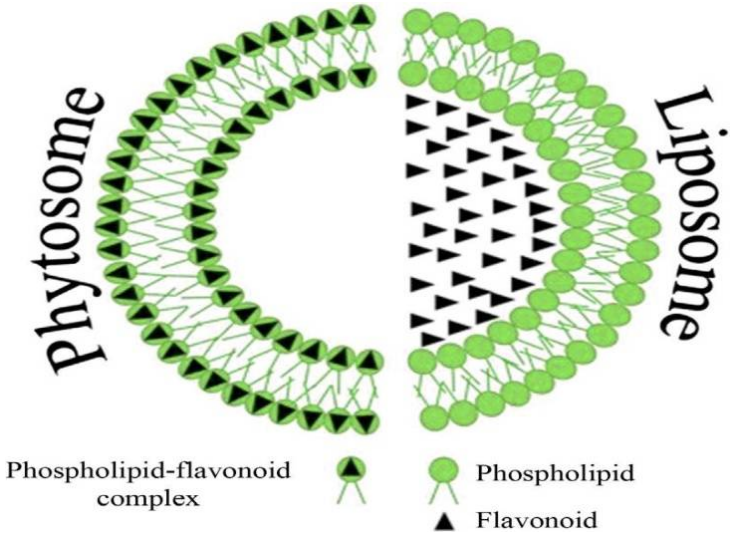

Fig.no.2: Structural difference of Phytosome and Liposome

Thus, as complex is formed between phytoconstituent and phospholipid stability of phytosomal formulation is better than liposomes.
As there is conjugation encapsulation efficiency of active constituents is always better in phytosomes in comparison to liposomes.
The concentration of phospholipids employed in preparation of liposomes is almost five times higher which is used for phytosomal formulation.
It is observed that phytosomes are absorbed to good extent as compared to liposomes.

CHARACTERIZATION OF PHYTOSOMES:

The physical properties of phytosomal formulation were evaluated by means like particle size, particle shape, particle size distribution, release of active constituent from formulation, entrapment efficacy, crystalline and amorphous nature and melting range.Moreover,chemical characteristics of phytosomes are identified with the help of several techniques like Nuclear Magnetic Resonance (NMR), High-Performance Liquid Chromatography (HPLC), Fourier Transform Infra-red Spectroscopy (FTIR), Differential Scanning calorimetry (DSC). The sample must be in dried form for characterization by above techniques [10, 11].

1.Differential scanning calorimeter:

Drug or extract, phospholipid, physical mixture, and phospholipid and extract- phospholipidstoichometric complex was put in aluminium pan and temperature was allowed to increase from 50-250°c / minute from 0 to 400°c in nitrogen atmosphere.

2.Scanning electron microscopy (SEM):

Scanning electron microscopy is used to determine the morphology and particle size of formulation. The dry sample is scanned by putting it on brass stub coated with gold in an ion sputter electron microscope.

3. Transition electron microscopy (TEM):

TEM is undertaken to specify the size of phytosomes as the structure is magnified under it.

4. Drug entrapment and loading capacity:

To separate the untrapped extract or drug from phytsomes, the drug:phytosome complex is centrifuged at 10000 rpm for 90 minutes. A suitable spectrophotometric method like UV-visible spectrophotometer or HPLC is used to estimate the concentration of free drug. Following formula is used for calculation of entrapment efficiency:

$$\frac{(\text{Total amount of drug}) - (\text{amount of free drug})}{(\text{Total amount of drug})} \times 100$$

5.Fourier transform infrared spectroscopy (FTIR) analysis:

FTIR is utilized to confirm physical as well as chemical interaction between drug or extract and phospholipid. For this purpose, extract phospholipid and drug and phospholipid complex are triturated with potassium bromide and converted into pellet. It is then scanned in the range of 4000-400cm^{-1}.

6. Size analysis and zeta potential:

Zeta potential and particle size of extract and drug phytosomal complex is determined using Malvern Zetasizer.

7. H1 NMR:

H1 NMR is undertaken to know either the hydrophilic or lipophilic part of the phospholipid is responsible for interacting with drug or extract to form the complex.
In vitro and *in vivo* evaluations:
The pharmacological property of different constituents present in phytosomes will decide *in-vitro* and *in-vivo* evaluation parameters and upon that suitable animal model is selected.

PHYSIBILITY OF PHYTOSOMES:
In the study, both phytosomes and liposomes were fabricated by combining milk products with phospholipid. Better encapsulation efficiency is observed with phytosomes as compared to liposomes. In-vitro digestibility and bioavailability were studied. The ascorbic acid's cellular uptake was better for phytosomes as compared to liposomes. From the point of view of stability,phytosomes were superior to liposomes and thus could be good option as nutrient food for infants[13].
The study involved the complexation of chitosan with phospholipids for the delivery of gingerol in the treatment of respiratory infection. Gingerol, an antibacterial drug, has issues like less aqueous solubility, and low bioavailability and it is rapidly eliminated from the body. Thus, the anti-solvent precipitation method is used to form phospholipids of gingerol along with chitosan to overcome the above-mentioned problems. GLPC was observed to have superior bioavailability and correlated hematological against the incubated micro-organisms in rabbit blood. Thus, the combined effect of chitosan and phytosomes produced a sustained release profile in the nanoparticle-based formulation. It also improved the oral rate of absorption with the optimum antibacterial activity for the treatment of respiratory infections [14].
This study involved comparison of cytotoxic effectsand wound healing of sinigrin and sinigrin-phytosome complex. The in-vitro wound healingeffect of sinigrin and phytosomeswas observed on HaCaT cells. FTIR and DSC evaluation confirmed the genesis of sinigrin -phytosome complex. The phytosomal complex displayed better wound healing activity as compared to sinigrin alone as former completely healed wound in 42 hours while later displayed only 71% closure ofwound. The phytosomes also shown less toxicity with regards toHaCaT cells and at higher concentration, it displayed potent activity with regards to A-375.Thus,phytosomal complex of sinigrin significantly improved wound healing potential [15].
This study involved apigenin-phospholipid (APLC) formulation and its characterization and study of its enhanced solubility profile, in vivo bioavailability, and antioxidant activity. Full factorial design was employed for formulation of APLC, and method used was solvent evaporation. Theformation of APLC was assisted by FTIR, DSC,1H NMR, and PXRD analysis.There was about 36 folds increase in solubility in optimised formulation in comparison to apigenin. The pharmacological evaluation was carried using suitable rat model by studying its effects on carbon-tetrachloride induced increase inmarker enzymes of liver function.Moreover, rate and extent of drug release were also observed to be enhanced as well as liver function tests also revealed restoration of liver function marker enzyme.Thus, overall study dictated relevance of phytosomes for effective delivery of drugs like apigenin and such substances with low aqueous solubility [16].
The study involved formation of silymarinphytosomes. Silymarin is flavonoid isolated from *Silybum marianum* is an efficient hepatoprotective agent. However, when administered orally it is absorbed to an extent of only 20-50%, thus having poor bioavailability. Thus, study was undertaken to improve bioavailability with sufficient stability. Solvent evaporation method was utilized to prepare phytosomes complex in different ratios.The DSC and FTIR results depicted physical interaction between silymarin, and phospholipids and optimized formulation displayed good stability after freeze thaw stability testing.Thus, overall stability was found to be improved by forming phytosomal complex of silymarin [17].

8. Physibility of phytosomes on Brain delivery system:
This study was conducted to avoid gastrointestinal degradation of *Annnamuricata*aqueous extract and to enhance its permeability across BBB (blood brain barrier). From the screening study *Annnamuricata* aqueous extract was claimed to havepotent (hMAO-A)monoamine oxidase A inhibitor and strong (H2O2) hydrogen peroxide activity. A peptide ligand was used for promoting passage across the BBB in all phospholipid formulations of liposomes and phytosomes. An *in vitro*transwell model of the BBB, consisted of immortalized human microvascular endothelial cells (hCMEC/D3) were used to carry out cytotoxicity and permeability. Moreover, H2O2 scavenging activities and in vitro hMAO-A inhibition were performed for all samples. Results displayed better performance of phytosomes in terms of scavenging activity,inhibition of enzyme, and binding efficiency as compared to liposomes [18].
Traumatic brain injury (TBI) is considered as a central nervous system condition brought on by head trauma. Because of these situations, re-myelination of nerve is reduced, which contributes to the deterioration of cognitive abilities. Citicoline is reported asa neuroprotective medication which is commonly used in Indonesia to repair and stop future harm to the nerve cells' membranes brought on by trauma. Spade leaf (Centella asiatica) extract phytosome (SEP) is a drug delivery system that is supposed

to improve the therapeutic efficacy of a medicine that is intended to protect the nervous system.To compare and contrast the efficacy of citicolineand SEP as a neuroprotective, which is defined by increasing Krox-20 activation, NRG-1 expression, phospholipid distribution, and improvement in cognitive levels in TBI-induced rats. As compared to spade leaf extract phytosome and citicoline alone, the study found that the combination of the two increased the distribution of phospholipids and sped up performance on cognitive tests.

Spade leaf (CentellaAsiatica) extract phytosome (SEP) production was studied as a model for medication delivery. Traumatic brain injury (TBI), which is brought on by trauma, is regarded as a central nervous system condition. Reduced nerve re-myelination and associated decline in cognitive function are the condition's hallmarks. It was anticipated that the SEP drug delivery system would improve the therapeutic efficacy of neuroprotective medications.Rats with TBI were utilised to compare the efficacy of citicoline and SEP as a neuroprotective, which was accompanied by enhanced Krox-20 activation, NRG-1 expression, phospholipid distribution, and improvement in cognitive function. In contrast to citicoline and phytosome extract alone, the study found thatphytosome of spade leaf extract combined with citicoline demonstrated improved phospholipid distribution and provided the quickest results in cognitive tests [19].

CONCLUSION

Phytosomes which are also known as herbsomes are vesicular drug delivery systems. Thus they can be exploited for phyto-constituients which could be absorbed better both orally, transdermally and topically. Phytosomes are known to have improved pharmacokinetics and pharmacological properties and can serve as targeted drug delivery systems in the coming future. The methods used for the preparation of phytosomes are simple, reproducible, and non-conventional. They also have their own pharmacological activity which is hepatoprotective. In the coming future, phytosomes would be the prime prospectus in pharmaceutical applications. Thus, phytosomal formulation is a connecting link between conventional drug delivery systems of phytoconstituents and advanced drug delivery systems.

REFERENCES

1. N Varma,Phyto-constituents and Their Mode of Extractions: An Overview, Research Journal of Chemical and Environmental sciences, 4 (2) (2016):08-15.
2. D Koche, M Kawale, R Shirsath,An Overview of Major Classes of Phytochemicals: Their Types and Role in Disease Prevention,HislopiaJournal, 9(1/2) (2016):1-11 .
3. S Njeru, G Kobiad, MMaina, A Review of Some phytochemicals commonly found in Medical Plants, International Journal of Medicinal Plants, Photon 105 (2013):135-140
4. Z Chang, Q Zhang, W Liang, K Zhou, P Jian, G She, L Zhang, A Comprehensive Review of the Structure Elucidation of Tannins from Terminalia Linn. Evidence-Based Complementary and Alternative Medicine, :(2019) https://doi.org/10.1155/2019/8623909
5. A Azeez, S Deepa, V Sivapriya, Phytosomes: emergent promising nano vesicular drug delivery system for targeted tumor therapy Advances in Natural Sciences, Nanoscience and Nanotechnology, 9 (2018):033001
6. A Choudhary, S Verma, A Roy,Phytosomes : A Novel Dosage Form For Herbal Drug Delivery, Journal of Applied Pharmaceutical Research J. App. Pharm. Res., 2 (2) (2014) :44–52
7. S Chandran, S Natarajan, Phospholipid As Versatile Polymer in Drug Delivery Systems, International Journal of Pharmacy and Pharmaceutical Science, Int J Pharm Pharm Sci, 6 (1) (2016):8-11
8. RSingh, Application of Nanometerials Toward Development of Nanobiosensors and their Utility in Agriculture,Springer Nature(2017): 293-303DOI: 10.1007/978-981-10-4573-8_14
9. S Kumar, A Baldi, DK Sharma,Phytosomes: A Modernistic Approach for Novel Herbal Drug Delivery-Enhancing Bioavailability and revealing Endless Frontier of Phytopharmaceuticals, J Develop Drugs, 9, 2 (195) (2020): 1-8.
10. A Kumar, B Kumar, S Kumar,B Kaur,S Singh, A Review OnPhytosomes:Novel Approach For Herbal Phytochemicals, Asian Journal of Pharmaceuical and Clinical Research Asian J Pharm Clin Res, 10(10) (2017): 41-47.
11. B Ghanbarzadeh, A Babazadeh, H Hamishehkar, Nano-phytosomeas a potential food-grade delivery system, Food Bioscience,15 (2016):126-135
12. M Gunay, MKarpuz,A Ozer, Targeted Alpha Therapy and NanocarrierApproach,Cancer Biotherapy and Radiopharmaceuicals, (2020) : https://doi.org/10.1089/cbr.2019.3213
13. Z Huang, CBernnan, H Zhao, J Liu, W Guan, M Mohan, L Stipkovits, H Zheng Fabrication and assessment of milk phospholipid-complexed antioxidant phytosomes with vitamin C and E: A comparison with liposomes, Food Chemistry,324 (2020): 126837
14. R Singh, HGangadharappa , K Mruthunjaya,Phytosomecomplexed with chitosan for gingerol delivery in the treatment of respiratory infection: In vitro and in vivo evaluation European Journal of Pharmaceutical Sciences, 122 (2018):214-229
15. A Mazumder, A Dwivedi, J Preez, J du Plessis,In vitro wound healing and cytotoxic effects of sinigrin–phytosome complex, International Journal of Pharmaceutics, 498(1-2) (2016) : 283-93

16. D Telange, APethe, A Patil, H Fegade, Formulation and Characterization of an apigenin-Phospholipid Phytosome (APLC) for Improved Solubility,in vivo Bioavailability, and Antioxidant Potential,European Journal of Pharmaceutical Sciences, 108 (2016) : 36-49.
17. W Maryanaa, H Rachmawatib, D Mudhakira, Formation of Phytosome Containing Silymarin Using Thin Layer-Hydration Technique Aimed for Oral Delivery , Materials Today: Proceedings3 (3) (2016) : 855-866.
18. S Mancini, L Nardo, M Gregori, I Ribeiro, Functionalized Liposomes and Phytosomes Loading Annonamuricata L. aqueous extract:Potentialnanoshuttles for brain-delivery of phenolic compounds, Phytomedicine.42 (2018) : 233-244
19. A Jazmi, P Alfiantya, S Nurarifah, E Purmitasari, LVitania, W Riawan, Spade Leaf Extract Phytosome Modulates Krox-20, Neuregulin 1 , Phospholipids, and Cognitive Function of Traumatic Brain Injury Model in Rats Indonesian Journal of Cancer Chemoprevention. 6(3) (2015) : 105-110

CITATION OF THIS ARTICLE

P. Karekara, S. Killedarb, A. Shaikhc, M. Mored, S. Joshie, R. Buchadef, Y. Dongreg, H. Moreh and P. Zambarei: Phytosomes: The future of Herbal Drug Delivery. Bull. Env. Pharmacol. Life Sci., Spl Issue [1]: 2023: 58-65.