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A Comprehensive Review on Pharmacosomes – Emerging Amphiphilic Vesicular Drug Carrier

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ABSTRACT
Pharmacosomes are lipid based amphiphilic vesicular carrier drug delivery system, which holds the potential to improve the solubility and bioavailability of selected drug. Due to its amphiphilic nature, it has a capability of encapsulating both poorly soluble hydrophilic as well as lipophilic drugs, and also alters the drug release rate for the enhancement of drug absorption across the biological barriers. Pharmacosomes possess some exceptional advantages like efficient delivery of drug directly to the site of infection, leading to reduction of drug toxicity with minimal adverse effects, also reduce the cost of therapy by enhanced bioavailability of medication especially in case of drugs which are poorly soluble. The amphiphilic nature of Pharmacosomes helps to reduce interfacial tension, decreases in the interfacial tension consecutively leads to an increase in the contact surface area thereby increasing bioavailability of drugs. Pharmacosomes are emerging as one of the novel potential vesicular carrier because of their better stability in comparison with other vesicular carrier systems liposomes, niosomes, transferosomes. Pharmacosmes often considered to be better tool to attain desired therapeutic effects in case of targeted and control release formulation. This article reviews the potential prospective of Pharmacosomes as a carrier mediated drug delivery system which is useful in the treatment of various diseases and describes the methods of preparation,characterization and applications.
Keywords: *Pharmacosomes, amphiphilic, bioavailability, vesicular system.*

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INTRODUCTION

Vesicular drug delivery plays a crucial role in modelling biological membrane as well as in the targeting and release of the active constituents. Carriers are the substance used in the process of drug delivery, and they help to improve the drug efficiency, selectivity, and safety in the administration of a drug. Delivering and release of the drug through drug carriers in systemic circulation involves a controlled manner (1). This can be attained either by slow release of the drug over an extended period or by actuated release at the drug target by use of few stimulants such as changes in pH, application of heat. Particularly, in the case of drugs with poor water solubility and/or membrane permeability, drug carriers are used to get better pharmacokinetic and thus improving their bioavailability (2). In recent time's vesicular drug delivery gaining more attention and vesicles has become the vehicle of choice in most of the delivery systems. Vesicular drug delivery has more benefits over conventional therapies due to its limited permeation into membranes. Vesicular drug delivery system is considered to one of the systems that can improve the bioavailability of medication especially in case of poorly soluble drugs and helps to reduce the toxicity effects by the targeting drug to the specific site (3). The benefits of encapsulating drugs in vesicular structures are to get better solubility of poorly water-soluble drugs and prolong the existence of the drug in bloodstream and reduce toxicity. Recent advances in the area of vesicular drug delivery system, leading to the development of systems that helpful in drug targeting, sustained, controlled, and transdermal drug delivery (4). Lipid-based vesicular systems were set to be of greater value in areas like immunology, membrane biology, and diagnostic techniques and most recently in genetic engineering. As an outcome, many vesicular carriers like liposomes, niosomes, transfersomes, ethosomes, Pharmacosomes came into the existence (5). Pharmaceutical carriers are classified into different types like particulate type, macromolecular, polymeric, and cellular carriers. Particulate type of carriers are known to be colloidal carriers which includes lipid particles of both low and high-density lipoproteins (6). A wide variety of drug carriers are being studied and each of them has unique advantages and ailing effects. Major types of drug

carriers include liposomes, niosomes, polymeric micelles, microspheres, ethosomes, transferosomes, and nanoparticles. Differentiation of these carriers is based on their composition, adsorption, encapsulation, type of bonding, or conjugation between drug and carrier. Different types of drug carriers utilize different kinds of attachment methods (7).

PHARMACOSOMES

Pharmacosomes are part of a novel drug delivery system and emerging as one of the potential vesicular carrier because of their better stability aspects, increased entrapment efficiency, no drug leakage due to drug - lipid conjugation. (8, 9). Pharmacosomes are defined as amphiphilic lipid-based vesicular systems posses' drug-Phospholipid complex that is helpful to improve the bioavailability of drugs. Pharmacosomes imparts better biopharmaceutical properties to the drug, resulting in enhanced bioavailability. Drugs bearing an active hydrogen atom from (-COOH,-OH,-NH_2) can esterified to the lipid with or without spacer chain leads to the formation of the amphiphilic compound which enhances the permeation towards the target site. Based on their chemical structure Pharmacosomes, can exist as ultrafine, micellar or hexagonal aggregates (10). Pharmacosomes indicate **Pharmakon** means a "drug" and **soma** means "carrier". The formulation of Pharmacosomes is dependent on surface and bulk interactions of lipids with drugs. When compared with other vesicular carriers pharmacosomes are one of emerging lipid-based vesicular amphiphilic carrier that has a capability of encapsulating both poorly soluble hydrophilic and lipophilic drugs, due to its amphiphilic nature it helps to reduce interfacial tension, thereby increasing the contact surface area and bioavailability of drugs and has a ability to efficiently pass through the bio membranes and thereby improve the pharmacokinetic and pharmacodynamic properties of various types of drugs. So far pharmacosomes act as good carrier for encapsulating various classes of drugs like non-steroidal anti-inflammatory drugs, cardiovascular, anti-neoplastic drugs and for proteins (11). Formulated drug based Pharmacosmes can be administrated in different routes like oral, topical extra or intra vascular (12). In comparison with other categories of lipidbased delivery systems, Pharmacosomes exhibit improved results in numerous ways. The drug-lipid complex depends upon the phase transition temperature but it does not depend on the rate of release as it is covalently bounded to the lipid. Pharmacosomes aid in drug targeting and controlled release of drug to get desired dose.

Advantages: (13, 14)

1. They serve as effective tools for attaining desired therapeutic goals such as drug targeting and controlled release.
2. Predetermined entrapment efficiency as drug and carrier conjugation.
3. Besides the above, as drug and carrier conjugation, predetermined entrapment efficiency is also available, which may be expressed as entrapment efficiency (Banduda et al.,)
4. In the case of liposomes, there is no need to remove the free, unentrapped drug from the formulation.
5. It helps to improve bioavailability especially in the case of poorly soluble drugs.
6.Many problems that are associated with Drug carriers such as liposomes, nanoparticles, micro-emulsions which have lead to low drug-loading efficiency, physical stability such as fusion, aggregation, sedimentation and drug leakage during preparation, preservation etc is absent in case of pharmacosomes.
7. It shows less toxicity and adverse effects.
8. Drug can be directly delivered to specific site.

Disadvantages: (15)

1. Some water insoluble drugs are encapsulated relatively in a less hydrophobic region within membrane bilayer rather than relatively bulk surface area.
2. pharmacosome storage undergoes fusion and aggregation problem as well as chemical hydrolysis [14].

Limitations of Pharmacosomes :(16)

1. Synthesis of a compound in Pharmacosomes mainly depends upon its amphiphilic nature.
2. The second limitation involved required surface and bulk interactions from the leakages of drugs.
3. It requires covalent bonding to protect from leakage of drugs by selecting structure with functional groups (COOH, -NH2, OH).

COMPONENTS OF PHARMACOSOMES: (17-19)

The three main components required for the preparation of pharmacosomes is based on selection of drugs, solvent and lipid.

1. **Drug:** Drugs which are having an active hydrogen atom (-COOH, - OH,-NH2 etc) can be esterified to the lipid, after esterification conjugate of drug with carrier produces a compound, which is amphiphilic in nature. These amphiphilic complexes which are synthesized, facilitates easy membrane, tissue, or cell wall transfer, in the organism.

2. **Lipids:** A class of Phospholipids consider as molecular building blocks of biological membranes. Generally, two types of phospholipids used are phosphoglycerides and spingolipids. The most common lipid is phosphotidyl choline.

3. **Solvents:** Intermediate and high polarity organic solvents of analytical grade is used in development of pharmacosomes. It should be of high purity and volatile in nature. Then selected phospholipids and the drug must be dissolved in the selected high polarity solvent. Based on the polarity of the drug and the lipid the solvent is selected.

PREPARATION METHODS OF PHARMACOSOMES (20-22)

Pharmacosomes are prepared by various methods;

Hand shaking method

In this method, the first step is mixing of drug and lipid with an organic solvent. The solvent is then evaporated by subjecting the solution under vaccum. Solvent evaporation leads to the formation of thin film on the inner surface of round bottom flask. By hydrating the thin film with addition of aqueous medium (buffer), vesicular suspensions of pharmacosomes are readily obtained. The equipment rotary evaporator is mostly used for the formation of thin film.

Solvent evaporation method

In this method drug is first acidified so that the active hydrogen might be available for complexation. The drug acid is then extracted into suitable selected solvents like chloroform and subsequently recrystallized. The complex of drug-Phosphatidylcholine (PC) is prepared by associating drug acid with PC in various molar ratios. The accurately weighed PC and drug acid are placed in a 100 ml round bottom flask and dissolved in sufficient amount of high polarity solvent like dichloromethane. The mixture is refluxed for one hour. The dried residues are then collected and kept in vacuum dessicator for complete drying.

Ether injection method

In this method, firstly drug lipid complex was dissolves in organic solution then injected slowly into the aqueous medium. Here the drug lipid complex is mixed with ether which acts as a solvent and then it is injected slowly into the aqueous medium leads to spontaneous formation of vesicles.

Anhydrous co-solvent lyophilisation method

In this method, drug powder and phospholipids are co-dissolved in solution of dimethyl sulfoxide (DMSO) containing 5% glacial acetic acid upon gentle agitation a clear mixture obtained, this mixture subjected to freeze dried process at a condenser temperature overnight, and then formed complex is flushed with nitrogen and stored at 4^0C.

Supercritical fluid process method

Complex formation of drug-lipid are dissolved in a supercritical fluid of Co_2, then mix-up into nozzle mixing chamber. Generally, gas anti-solvent and solvent enhanced dispersions like SEDDS techniques are used in this process.

CHARACTERISATION OF PHARMACOSOMES :(23,24)

Pharmacosomes are characterised for different parameters like:

Surface morphology, Drug-lipid compatibility (FT-IR and DSC), crystalline state measurement, in-vitro drug release studies

Solubility studies:

Solubility of the drug, phospholipids and their physical mixture composition of prepared Pharmacosomes can be determined by using shake flask method. In these method equal volumes of buffer solutions with different pH varies from 2 to 7.4 and 1-Octanol containing phospholipids complex are mixed properly in the screw capped bottles and equilibrated under constant stirring or shaking at 37^0 C for 24hrs.After separating the aqueous phase is determined by selected methods or procedures of HPLC or UV spectrophotometry.

Surface morphology:

Scanning electron microscopy (SEM) and transmission electron microscopy (TEM) useful to detect the surface morphology i.e., shape and size of the Pharmacosomes, which depends on the purity and nature of phospholipids used, method of preparation, structural changes, etc. Pharmacosomes which prepared from low purity phospholipids tend to be greasy and form sticky aggregates. On other hand, Pharmacosomes which are prepared from very high purity grades (>90%) phospholipids may undergo oxidative degradation and hence form poorly stable complexes. Thus, phospholipids having around 80% purity should be selected.

Complex determination:

The formation of the complex can be determined by IR spectroscopy comparing the spectrum of the complex or conjugate of drug with the spectrum of each individual component and their physical mixture.

Stability of Pharmacosomes can be characterized by comparing the spectrum of its micro dispersion in water after the lyophilisation at different time intervals.

Drug-lipid compatibility:

Differential scanning calorimetry (DSC) is a thermo analytical technique utilised to determine drug–lipid compatibility and their interactions.The thermal response is studied using separate samples and heated them in a sample pan which is closed. The nitrogen gas is purged, and the temperature is maintained in a definite range with a specific heating rate.

Crystalline state measurement:

The crystalline nature of pure drug can be determined by using X-ray diffraction technique. The tube voltages and tube current can be regulated in the X-ray generator. For the source of radiation copper lines are used. The overall intensity of all reflection peaks from the spectrum projected by area under curve of X-ray powder diffraction pattern that specifies the sample attributes.

***In-vitro* Drug Release studies:**

Based upon the resultant therapeutic activity of biological active components, models of invivo and invitro evaluation have been carried out. Invitro dissolution studies of drug-Phosphatidylcholine complex as well as pure drug with media of different pH in standard dissolution apparatus used to determine the pH dependent dissolution profile.

Applications of Pharmacosomes:(25)

1. Shelf stability of Pharmacosomes is greater.
2. Pharmacosomes can improve the permeation rate by improving the membrane fluidity by using suitable permeation solvents.
3. Amphiphilic prodrug forms pharmacosomes, when diluted can modify corneal drug transport and release profile.
4. Vesicular carrier -Pharmacosomes interact with biomembranes enabling a better transfer of active ingredients.
5. Pharmacosome prepared for various drugs which are poorly soluble like Diclofenac, Aspirin, Fenoprofen and studies shows that pharmacosomes has ability to enhance the dissolution rate and also transdermal permeation.
6. Pharmacosomes as building particles capable of transporting biologically active substances which includes composition of proteins and nucleic acids.
7. Prepared geniposide pharmacosomes was characterized and found that they can improve absorption and permeation of biologically active constituents.

Table 1: Effect of drug after incorporation into a carrier (Pharmacosomes) (26-28)

Drugs	Effect of drug after incorporation in Pharmacosomes
Amoxicillin (antibiotic)	Helpful in treatment of H.pylori infections in male rats and increased cytoprotection
Dermatan sulphate (mucopolysaccaride)	Improved and increased biological activity
Taxol (anti-neoplastic drug)	Improved and increased biological activity
Cytarbin (anti-cancer drug)	Improved biological activity
Bupranolol hydrochloride (Beta blocking agents)	Enhanced effect on intraocular pressure and lymph transport.
Pindolol diglyceride (beta blocker used in treatment of angina pectoris and Hypertension)	Increase in plasma concentration three to five folds.
Isoniazid (used in tuberculosis)	Improved permeability and macrophage targeting

CONCLUSION

Over the years, vesicular systems have been investigated as a major drug delivery due to its flexibility for varied desirable purposes and it has been realized as extensively useful carrier systems in various scientific domains. Pharmacosomes has more advantages over other novel delivery system because of its high entrapment efficiency as it forms drug-lipid conjugate and prevents leakage of drug. Despite the certain drawbacks, such as (fusion, aggregation), Pharmacosomes still play a significant role in the selective targeting, and the controlled delivery of various drugs. Pharmacosomes have immense potential, to improve the drug delivery for both synthetic and natural active ingredients and further advantages of the

vesicular system can be exploited by expanding this approach to additional drugs. Researchers around the world continue to set in their efforts to improve the vesicular system by making them steady in nature in order to prevent leaching of contents, oxidation, and their uptake by natural defence mechanisms.

REFERENCES

1. Dawoud, M., Zaafan, M., Saleh, S., Mannaa, I., & Sweed, N. (2023). Response surface optimization of a cardioprotective compound through pharmacosomal drug delivery system: in vivo bioavailability and cardioprotective activity potential. Drug Delivery and Translational Research, 13(9), 2315-2339. https://doi.org/10.1007/s13346-023-01315-w
2. Supraja, B. and Mulangi, S. (2019). An updated review on pharmacosomes, a vesicular drug delivery system. Journal of drug delivery and Therapeutics, 9(1-s), 393-402. https://doi.org/10.22270/jddt.v9i1-s.2234
3. Agrawal, U., Gupta, M., & Vyas, S. (2016). vesicular carriers for transcutaneous immunization., 319-335. https://doi.org/10.1007/978-3-662-47862-2_21
4. Pandita, A., & Sharma, P. (2013). Pharmacosomes: an emerging novel vesicular drug delivery system for poorly soluble synthetic and herbal drugs. *ISRN pharmaceutics*, *2013*, 348186. https://doi.org/10.1155/2013/348186.
5. Singh, D., Pradhan, M., Nag, M., & Singh, M. R. (2015). Vesicular system: Versatile carrier for transdermal delivery of bioactives. *Artificial cells, nanomedicine, and biotechnology*, *43*(4), 282–290. https://doi.org/10.3109/21691401.2014.883401.
6. Semalty, A., Semalty, M., Rawat, B. S., Singh, D., & Rawat, M. S. (2009). Pharmacosomes: the lipid-based new drug delivery system. *Expert opinion on drug delivery*, *6*(6), 599-612. https://doi.org/10.1517/17425240902967607.
7. Limongi, T., Susa, F., Marini, M., Allione, M., Torre, B., Pisano, R., & di Fabrizio, E. (2021). Lipid-Based Nanovesicular Drug Delivery Systems. *Nanomaterials (Basel, Switzerland)*, *11*(12), 3391. https://doi.org/10.3390/nano11123391.
8. Pandita, A. and Sharma, P. (2013). pharmacosomes: an emerging novel vesicular drug delivery system for poorly soluble synthetic and herbal drugs. isrn pharmaceutics, 2013, 1-10. https://doi.org/10.1155/2013/348186.
9. Azeem, A., Anwer, M., & Talegaonkar, S. (2009). niosomes in sustained and targeted drug delivery: some recent advances. Journal of drug Targeting, 17(9), 671-689. https://doi.org/10.3109/10611860903079454
10. Pathak, K., Keshri, L., & Shah, M. (2011). Lipid nanocarriers: influence of lipids on product development and pharmacokinetics. *Critical reviews in therapeutic drug carrier systems*, *28*(4), 357–393. https://doi.org/10.1615/critrevtherdrugcarriersyst.v28.i4.20.
11. Fang, C., Al-Suwayeh, S., & Fang, J. (2013). Nanostructured lipid carriers (nlcs) for drug delivery and targeting. Recent Patents on Nanotechnology, 7(1), 41-55. https://doi.org/10.2174/187221013804484827.
12. Semalty, A., Semalty, M., Singh, D., & Rawat, M. S. (2009). Development and physicochemical evaluation of pharmacosomes of diclofenac. *Acta pharmaceutica (Zagreb, Croatia)*, *59*(3), 335–344. https://doi.org/10.2478/v10007-009-0023-x
13. De, P., Saha, M., Das, D., & Maji, H. (2020). Formulation and characterization of atorvastatin pharmacosomes as an alternative approach to conventional vesicular system. international research journal of pharmacy, 11(3), 45-49. https://doi.org/10.7897/2230-8407.110329
14. Dawoud, M. H. S., Zaafan, M. A., Saleh, S. S., Mannaa, I. M., & Sweed, N. M. (2023). Response surface optimization of a cardioprotective compound through pharmacosomal drug delivery system: in vivo bioavailability and cardioprotective activity potential. *Drug delivery and translational research*, *13*(9), 2315–2339. https://doi.org/10.1007/s13346-023-01315-w.
15. Hardwick, J., Taylor, J., Mehta, M., Satija, S., Paudel, K. R., Hansbro, P. M., Chellappan, D. K., Bebawy, M., & Dua, K. (2021). Targeting Cancer using Curcumin Encapsulated Vesicular Drug Delivery Systems. *Current pharmaceutical design*, *27*(1), 2–14. https://doi.org/10.2174/1381612826666200728151610.
16. Alenzi, A. M., Albalawi, S. A., Alghamdi, S. G., Albalawi, R. F., Albalawi, H. S., & Qushawy, M. (2023). Review on Different Vesicular Drug Delivery Systems (VDDSs) and Their Applications. *Recent patents on nanotechnology*, *17*(1), 18–32. https://doi.org/10.2174/1872210516666220228150624.
17. Breitsamer, M., & Winter, G. (2019). Vesicular phospholipid gels as drug delivery systems for small molecular weight drugs, peptides and proteins: State of the art review. *International journal of pharmaceutics*, *557*, 1–8. https://doi.org/10.1016/j.ijpharm.2018.12.030.
18. Kumar P B, Debnath S, Babu N M. Pharmacosomes as a novel vesicular drug delivery system. *Int J Novel Trends Pharm Sci.* 2013; 3(3): 46-52.
19. Chatap, V., Patil, P., & Patil, S. (2014). In-vitro, ex-vivo characterization of furosemide bounded pharmacosomes for improvement of solubility and permeability. Advances in Pharmacology and Pharmacy, 2(5), 67-76. https://doi.org/10.13189/app.2014.020501
20. Suksaeree, J., Charoenchai, L., Monton, C., Chusut, T., Sakunpak, A., Pichayakorn, W., … & Boonme, P. (2013). Preparation of a pseudolatex-membrane for ketoprofen transdermal drug delivery systems. Industrial & Engineering Chemistry Research, 52(45), 15847-15854. https://doi.org/10.1021/ie402345a.
21. Binh, N., Xuan, H., & Yen, N. (2020). Preparation and characterization of flurbiprofen/β-cyclodextrin inclusion complex. Vnu Journal of Science Medical and Pharmaceutical Sciences, 36(3). https://doi.org/10.25073/2588-1132/vnumps.4259.

22. Alenzi, A. M., Albalawi, S. A., Alghamdi, S. G., Albalawi, R. F., Albalawi, H. S., & Qushawy, M. (2023). Review on Different Vesicular Drug Delivery Systems (VDDSs) and Their Applications. *Recent patents on nanotechnology*, *17*(1), 18–32. https://doi.org/10.2174/1872210516666220228150624.
23. Singh V K, Patel A, Chandra D, Yadav K (2014). Pharmacosomes: A novel carrier for targeted and controlled vesicular drug delivery system. *World J pharm Sci.* 3(5): 1221-1238.
24. Binh, N., Xuan, H., & Yen, N. (2020). Preparation and characterization of flurbiprofen/β-cyclodextrin inclusion complex. Vnu Journal of Science Medical and Pharmaceutical Sciences, 36(3). https://doi.org/10.25073/2588-1132/vnumps.4259.
25. Pandita, A., & Sharma, P. (2013). Pharmacosomes: an emerging novel vesicular drug delivery system for poorly soluble synthetic and herbal drugs. *ISRN pharmaceutics*, *2013*, 348186. https://doi.org/10.1155/2013/348186.
26. Singh, D., Pradhan, M., Nag, M., & Singh, M. R. (2015). Vesicular system: Versatile carrier for transdermal delivery of bioactive. *Artificial cells, nanomedicine, and biotechnology*, *43*(4), 282–290. https:// doi.org/ 10.3109/21691401.2014.883401.
27. Vyas, S., Jaitely, V., & Kanaujia, P. (1999). synthesis and characterisation of palymitoyl propanolol hydrochloride auto-lymphotrophs for oral administration. international journal of pharmaceutics, 186(2), 177-189. https://doi.org/10.1016/s0378-5173(99)00166-0.
28. Kaur, G., Negi, K., Kumar, K., & Teotia, D. (2021). Development and evaluation of pharmacosome formulations of mefenamic acid. GSC Biological and Pharmaceutical Sciences, 16(3), 229-234. https://doi.org/ 10.30574/gscbps.2021.16.3.0286.

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