

Available online on 15.10.2024 at <http://ajprd.com>

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research

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Review Article

Pharmacosomes: In Targeted Drug Delivery System

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ABSTRACT

Pharmacosomes are a cutting-edge method of medication delivery based on a lipid transport system. A novel approach to drug delivery called "drug targeting" seeks to deliver the medication to the intended site of action or absorption while preventing any other non-target site from being exposed to it. Drug targeting is a practical delivery method that allows medicinal agents to be delivered to a particular location without endangering other organs. Pharmacosomes are colloidal drug dispersions that are hexagonally assembled into micelles, vesicles, or nanometric- size micelles that are covalently attached to the phospholipid. They function pretty accurately as appropriate carriers for drug administration because of their unique characteristics, which include small size, amphiphilicity, active drug loading, high entrapment efficiency, and stability.

This paper focus on about the Pharmacosomes, there advantages, disadvantages, and matters that are needed for the formulation, and there characterization and also application.

Key Words: Drug delivery system, Pharmacosomes, Characterization of Pharmacosomes.

ARTICLE INFO: Received 10 April 2024; Review Complete 28 June 2024; Accepted 15 Sept 2024. ; Available online 15 Oct. 2024



Cite this article as:

Abhishek Yadav, Mohd Amaan, Adarsh Dubey, Dheeraj Kushwaha, Pharmacosomes: In Targeted Drug Delivery System, Asian Journal of Pharmaceutical Research and Development. 2024; 12(5):41-45, DOI: <http://dx.doi.org/10.22270/ajprd.v12i5.1476>

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INTRODUCTION:

During the course of treatment, the novel targeted drug delivery system seeks to administer the medication at a rate determined by the body's requirements [1]. One novel form of medication delivery technique is pharmacosomes. In 1968, Vaizoglu and Speriser introduced them for the first time [2]. A special kind of vesicular medication delivery is pharmacosomes. Concentric lipid bilayer assemblies generated by specific amphiphilic structural elements make up vesicular systems. Components come into contact with water. Drugs covalently bound to lipids form colloidal dispersions known as pharmacosomes [3]. It is a type of medication delivery technology based on vesicles. By directing the medication to the exact location, the vesicle-based drug delivery method lowers toxicity and increases the medicine's bioavailability [4].

Targeted medication delivery aims to improve therapeutic efficacy and minimize side effects by delivering the therapeutic agent to the targeted tissues while lowering the therapeutic agent's relative concentration in the other tissues. The delivery of medications to receptors, organs, or any other particular area of the body to which the entire medication is intended is known as drug targeting. Paul Ehrlich created the targeted drug delivery system in 1909, demonstrating the therapeutic agent's direct delivery to damaged cells [1].

VESICULAR DRUG DELIVERY SYSTEM:

These days, one of the most cutting-edge, innovative medication delivery methods is vesicular drug delivery. The phrase "Bingham bodies" refers to the vesicles' biological origins, which were initially documented by Bingham in 1965 [5]. For many years, vesicular systems have been used as drug delivery vehicles. They were used to accomplish a number of

goals, including as extending and regulating drug release, improving drug transport across diverse biological membranes, and delivering drugs with specificity [9]. During the course of treatment, novel vesicular drug delivery carriers aim to route the active moiety to the target site of action while delivering the drug at a rate determined by the body's needs [9].

Advantage of vesicular drug delivery system: [1, 7, 6, 8]

- Enhanced bioavailability.
- Medicines that are lipophilic and hydrophilic may be combined.
- They are biocompatible and biodegradable.
- Delays the removal of medications with a fast metabolism.
- Prolonging the duration of drug exposure in the blood.

Table 1: Type of vesicular drug delivery system [1].

Lipoidal Biocarriers	Non-lipoidal Biocarriers
A. Pharmacosomes	A. Niosomes
B. Liposomes	B. Bilosomes
C. Emulosomes	C. Aquasomes
D. Enzymosomes	
E. Sphingosomes	
F. Ethosomes	

PHARMACOSOMES:

A special kind of vesicular medication delivery is pharmacosomes. Concentric lipid bilayer assemblies generated by specific amphiphilic structural elements make up vesicular systems. Components come into contact with water. Drugs covalently bound to lipids form colloidal dispersions known as pharmacosomes [1]. The drugs may be designed as phospholipid complexes (pharmacosomes) to improve permeability and solubility while reducing GI toxicity [8]. The structural components of pharmacosomes provide them both lipophilic and hydrophilic properties [8]. One way to change a medication's initial biodistribution is using pharmacosomes [15].

The system consists of attaching a medication (pharmakon) to a carrier (soma), which is why they call them "pharmacosomes" [6]. Lipid vesicles have been discovered to have applications in immunology, membrane biology, diagnostic methods, and most recently, genetic engineering. Vesicular structures are one type of system that decreases toxicity by selectively absorbing the medication and extending its half-life in systemic circulation. These vesicles, dubbed "Bingham bodies" when Bingham originally described them in 1965, are crucial for transporting and directing active chemicals as well as simulating biological membranes. These can be described as ultrafine vesicular, micellar, or hexagonal aggregates, depending on the chemical nature of the drug-lipid combination. They are colloidal dispersions of medicines covalently bonded to lipids [16].

Vesicles are colloidal particles with a bilayer arrangement of lipids and surfactants (amphiphiles) enclosing a water-filled core. These amphiphiles can create one or more concentric bilayers if the water content is raised. While lipophilic medications become stuck in the bilayered wall by hydrophobic and/or electrostatic forces, hydrophilic pharmaceuticals find a home in the interior aqueous environment [17]. When prodrugs, or pharmacosomes, come into contact with water, they create pharmacosomes and come together to form multilayers. In order to design this approach, the bulk properties of the drug-lipid combination are taken into account while maintaining the surface qualities [4].

Such a chemical's synthesis may be controlled to produce a highly amphiphilic compound, which will aid in the organism's ability to transfer membranes, tissues, or cell walls [12].

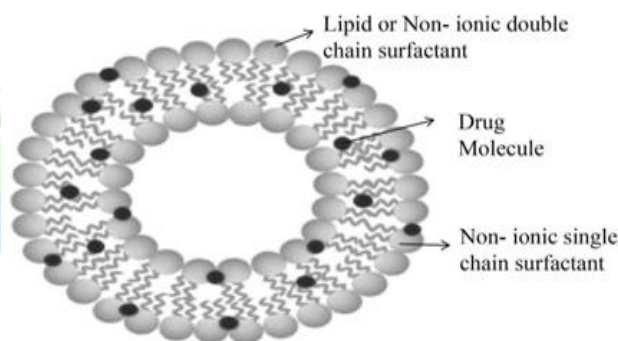


Figure 1: Structure of Pharmacosomes

ADVANTAGES OF PHARMACOSOMES:

- The drug administration procedure gets easier to follow [1].
- Directly administer the medication to the infected site [3].
- delays the removal of medications with a fast metabolism [1].
- When the medication is administered to the intended site, its toxicity is reduced [5].
- The sustained-release mechanism's functioning [9].
- there is a high and specified entrapment efficiency Because the drug and carrier are covalently bonded [11].
- The physicochemical characteristics of the drug-lipid combination determine the physicochemical stability of the pharmacosomes [9].
- It works well with both lipophilic and hydrophilic medications [16].
- Pharmacosomes' phase transition temperature significantly affects how they interact with micellar and vesicular state members [15].

DISADVANTAGES OF PHARMACOSOMES:

- Drug deposition at the target site has the potential to increase toxicity [1].
- High levels of competence in this discipline are needed for the targeted drug delivery systems development, storage, and administration [1].
- Pharmacosomes maintain emulsion, aggregation, and chemical hydrolysis while being stored [3].
- Formulation requires extremely sophisticated technologies [6].
- A compound's ability to synthesise depends on how amphiphilic it is [9].
- Drugs that are insoluble in water are encased in membrane bilayers, with the hydrophobic section being forced against their relatively large surface area [16].
- In order to stop pharmaceutical leaks, covalent bonding is required [15].

AQUEOUS ASPECTS OF PHARMACOSOMES:

- It is not difficult to incorporate drugs into lipids; they can be administered directly to the site of infection.
- In most circumstances, including enzymatic, hydrolysis controls drug release from pharmacosomes. The expense of therapy is reduced [2].
- The functional groups and size of the drug, spacer, and length of the lipid chain all have a significant impact on how quickly it breaks down into active drug molecules upon absorption. These can be adjusted rather precisely for better in vivo pharmacokinetics [9].
- They have both hydrophilic and lipophilic characteristics, endocytosis or exocytosis can readily transport them across tissues, cell walls, and membranes [9].
- When paired with lipids, the medication itself forms vesicles, indicating that the entrapment's efficiency is both high and predetermined [10].
- The rate at which the drug molecule breaks down into its active form during delivery is determined by the size, functional group, and length of the fatty acid chain in the lipid [13].
- The physical and chemical bonding characteristics of the complex, which control the overall stability of the formulation [17].

MATTER NEEDED FOR THE FORMULATION:

There are following materials that are use for the formulation of a Pharmacosomes [9, 6].

1. Drugs-

When compounds with an active H₂ atom are esterified to lipids, they can form amphiphilic complexes with or without the inclusion of a spacer chain. An amphiphilic compounds that strongly results from the creation of such

a molecule, which will aid in the organism's transfer of membranes, tissues, or cell walls, may be created.

2. Phospholipid-

Phospholipids are the primary chemicals that build up cell membranes. The two primary phospholipid types used are phosphoglycerides and sphingolipids. Among phospholipids, phosphatidyl choline is the most common kind. In phospholipids, the alcohol is attached to both lipophilic acyl chains and deliquescent head groups. Phospholipids are diverse due to variations in head groups, alcohols, and side chains. Consequently, the changed phospholipid sources lead to the modified phospholipid classes.

3. Solvent-

An analytical-grade, intermediate-polarity organic solvent is used in the production of pharmacosomes. Requirements include high volatility and purity. The drug and the phospholipids need to dissolve in the selected solvent. The choice of solvent is determined by the phospholipid and pharmaceutical polarity.

PREPARATION OF PHARMACOSOMES:

There are various method of preparation of Pharmacosomes that are given below [14, 8, 5]

1. Hand Shaking Method/Solvent Evaporation Method

A volatile organic solvent dissolves the medication and lipid mixture. A small layer of solid mixture is then left on the flask walls after the solvent is removed using a rotatory evaporator in a round-bottom flask. When the dry film is hydrated in an aqueous media, a vesicular suspension is produced quickly.

2. Ether Injection Method-

The medication-lipid combination dissolves in a predetermined amount of ether. The vesicles are then created by gradually injecting the aforementioned combination into a hot buffer solution. The concentration affects the characteristics of the vesicle, particularly its form. Depending on the amphiphilic condition, a range of shapes, including disc, cubic, hexagonal, round, and cylindrical, may occur.

3. Anhydrous Co-Solvent Lyophilization Method-

Initially, the medication and phospholipids are dissolved in a dimethyl sulfoxide solution containing glacial acetic acid. After stirring the mixture to produce a clear liquid, it is freeze-dried for an entire night at condenser temperature. The resulting complex is kept at 4°C after being flushed with nitrogen.

4. Supercritical Fluid Process-

After dissolving the drug and lipid complex in a supercritical CO₂ fluid, the mixture is mixed in a nozzle mixing chamber.

CHARACTERIZATION OF PHARMACOSOMES: [9, 6]

1. Infrared Spectroscopy-

Infrared spectroscopy can also show that the complex was generated by comparing the complex's spectrum to the spectra of its component parts and their mechanical mixing. The compound's infrared spectrum's acute peak for the -OH grp is usually absent from the p'lipid complex, which instead displays a broad peak that indicates interaction within the -OH group. Fourier transform infrared spectroscopy is an additional method for determining the stability of the pharmacosome.

2. Surface morphology-

Transmission electron microscopy or scanning electron microscopy can be used to forecast the surface morphology. Pharmacosome size and form can change depending on a number of factors, including the technology employed, the phospholipid purity grade, the speed at which they rotate, and the vacuum applied.

3. Nuclear Magnetic Resonance-

NMR is a crucial technique for confirming conjugate formation since it can analyse the magnetic properties of a wide range of nuclei, including hydrogen, carbon, and phosphorus. The NMR signals of certain nuclei may fluctuate upfield or downfield due to the shielding or deshielding effects of neighbouring nuclei in the phospholipid derivative.

Thirty-one point seven phosphoric acid (ppm) is used to measure the chemical shifts in ³¹P NMR. One example of how this is done is the capacity to discriminate between p'lipids in the hexagonal phase and These assuming a bilayer structure, such as in vesicles.

4. X-ray powder diffraction-

Powder X-ray diffraction is an effective technique for characterisation of materials at the nanoscale. A powder XRD study of a sample can provide crucial information such as crystallite size, phase identification, shape, and sample purity in addition to a number of microscopic and spectroscopic techniques. Because it employs a bulk method, the information it produces can be compared to information from microscopy to determine whether findings on a small sample of particles are representative of the entire sample.

5. Drug lipid compatibility-

Thermoanalytical methods such as differential scanning electron microscopy are used to assess drug-lipid compatibility and interactions. In order to study thermal response, different samples are heated in a closed sample pan. The nitrogen gas is sealed off, and a precise heating rate and temperature range are maintained.

6. Solubility-

To find the solubility of a compound, put a known quantity of the phospholipid complex in a screw-capped penicillin bottle with an aqueous phase buffer solution (pH range of 2- 7.4) and an organic phase (such as 1- Octonol) and shake continuously for 24 hours at 37 degrees Celsius. After separating the two layers, samples were examined with a UV spectrophotometer or an HPLC.

7. In vitro drug release rate-

The reverse dialysis bag technique is used to evaluate the in vitro medication release rate. With this approach, the receiver phase is positioned outside the dialysis bag and pharmacosomes are inserted within. Each dialysis bag containing the continuous phase is taken out and its contents are examined for drug release after being suspended in a vessel holding the donor phase and agitated at prearranged intervals. Increasing the membrane surface area accessible for transport from the donor to receptor compartment is one benefit of this method. Another benefit of this method is that it reduces the amount of stages required, which increases personnel efficiency.

LIMITATION OF PHARMACOSOMES:

- The hydrophilic and lipophilic properties of the medication may have an impact on the creation of this molecule.
- Drug-lipid interactions at the surface as well as systemic levels are required.
- The kind of covalent connection required to stop pharmaceutical leaks.
- Pharmacosomes fuse due to their fragility, and substances kept in containers either aggregate or hydrolyse [17].

APPLICATION OF PHARMACOSOMES:

- Compared to other vesicular drug delivery methods, pharmacosomes are more stable and have a longer shelf life [3].
- The ability of pharmacosomes to transport biological elements such as amino acids and proteins [3].
- Pharmacosomes have the ability to transport drugs to specific sites by modifying the temperature there, particularly when utilising cell-specific drug carriers [9].

- Pharmacosomes can be used to study non-bilayer phases and the mechanisms of action of medications [9].
- The technique has been useful in improving the therapeutic efficacy of many drugs such as in particular, pindolomate, taxol, and acyclovir [16].
- Isoniazid pharmacosome permeability and macrophage targeting were improved [16].
- There has been an increase in the pharmacokinetic and pharmacodynamic effects of phytoconstituents such as xanthenes, glycosides, and flavanoids [17].

ACKNOWLEDGEMENT:

The Authors are especially indebted to Dr. Mukesh Kumar Dubey, Director of Seiko College of Pharmacy, who have been supportive of our career goals and who worked actively to provide us with the protected academic time to pursue These goals.

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