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REVIEW ON PHARMACOSOMES

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ABSTRACT

Pharmacosomes are a new type of drug delivery system in vesicle form. They aim to solve problems with older vesicular carriers like liposomes, niosomes, and transferosomes. These systems bond drugs to lipids, which makes them more stable. This also helps to trap more of the drug and stop it from leaking out. Pharmacosomes have both water-loving and fat-loving parts. This dual nature helps drugs dissolve better, reach the body more, and go to specific targets. Scientists can make pharmacosomes in different ways. They can shake them by hand, remove solvents, or inject ether. These methods allow pharmacosomes to be used for many types of medicine. This paper looks at how pharmacosomes are built, what makes them special, and how we can study them. It also talks about how doctors might use them and how they could change the way we give drugs to patients.

KEYWORDS: Pharmacosomes, vesicular drug delivery, amphiphilic compounds, lipid-drug conjugates, bioavailability, controlled release, nanocarriers, stability, therapeutic applications, targeted delivery.

INTRODUCTION

Drug distribution using vesicular systems has been practiced for many years. They were used to accomplish a variety of goals, including as improving drug transport across different biological membranes, extending and regulating drug release, and targeted drug delivery.[1]

When specific amphiphilic building blocks come into contact with water, they form vesicular systems, which are highly ordered assemblies of one or more concentric lipid bi layers. When specific building blocks that are amphiphilic are exposed to water. Numerous different amphiphilic building blocks can be combined to make vesicles.[2]

Novel vesicular system such as including pharmacosomes, liposomes, transferosomes, niosomes, polymeric nanoparticles.[3] However another nanocarrier **Pharmacosomes** are used as an alternative to traditional vesicles and have special advantages over other vesicles, such as liposomes and transferosomes.

Additional benefits include stability, high entrapment efficiency, no medication leakage or loss, and others. Pharmacosomes are also known as colloidal dispersions of medications covalently bonded to lipids, can be ultrafine vesicular, micellar, or hexagonal in shape Depending on the chemical composition of aggregates the lipid-drug complex.[4] Because a medicine (pharmakon) is linked to a carrier (soma), they are appropriately called "pharmacosomes."[5]

Pharmacosomes can also be thought of as a neutral molecule with positive and negative charges. Both hydrophilic and hydrophobic qualities, as well as a suitable ratio of polyphenol to phospholipids in the complex form.[6]

The zwitterionic, amphiphilic, stoichiometric compounds of pharmaceuticals are known as pharmacosomes these are specifically used in phospholipids, polyphenolic compounds. Surface and bulk interactions of lipids with the drug are necessary for the creation of vesicular pharmacosomes. Any medication that has an active hydrogen atom (-COOH, -OH, -NH2, etc.) may be esterified to a lipid, with or without the presence of a spacer chain that strongly produces an amphiphilic molecule.[3]

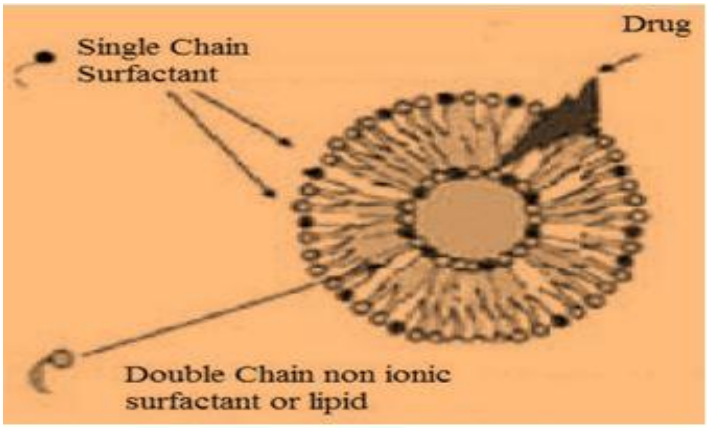


Figure No. 1: Schematic illustration of pharmacosomal system.

IMPORTANCE OF PHARMACOSOME

- Pharmacosomes can be used to incorporate both lipophillic and hydrophilic medications.
- The efficiency of entrapment is not only great but predetermined, as the medication is conjugated produces vesicals with lipids.
- There is no loss from drug leakage because the drug is covalently bound.
- The entrapment efficiency of pharmacosomes is not affected by captured volume or interactions between the drug and the bilayer.
- The physicochemical characteristics of the drug-lipid complex influences the physicochemical stability of the pharmacosome.[8]

ADVANTAGES

- Efficient means of accomplishing targeted treatment objectives, such as medication targeting and controlled release
- High and preset entrapment efficiency
- Effective instrument for achieving targeted drug delivery and controlled release
- Volume of inclusion has no effect on entrapment efficiency

- There's no need to take out the loose, untrapped medication.
- Enhances the bioavailability of medications that are poorly soluble.

DISADVANTAGES

- Covalent bond required to protect leakage of drugs
- Amphiphillic nature is important for synthesis of compounds
- On storage undergoes fusion, aggregations & chemical hydrolysis[8]

Table No 1: Pharmacosomes differs from Liposome, Niosome and Transferosome.[9]

Vesicular System	Issues Encountered	Advantage of Pharmacosome
Liposome	1. Expensive 2. Degradation by oxidation 3. Lack of purity of natural phospholipids 4. Chances of leaching of drug	1. Cheaper 2. Oxidation resistant 3. Pure natural phospholipid not needed 4. Covalent linkage prevents drug leakage.
Niosome	1. Time consuming prepn 2. Comparatively less efficient 3. Instability	1. Less time consuming preparation 2. More efficient 3. More stable
Transferosome	1. Expensive 2. Chemical instability	1. Cheap 2. Chemically stable

MATERIALS

Drug

When drugs with active hydrogen atoms (-COOH, OH, or NH2) are esterified to lipids, they can form amphiphilic complexes with or without spacer chains, which help organisms move their membranes, tissues, and cell walls.[10]

Solvent

The solvents used in the pharmacosome manufacturing process need to be volatile and of a high purity. For the manufacture of pharmacosomes, an intermediately polar solvent is chosen.

Lipids

Two major forms of phospholipids, phosphoglycerides and spingolipids, are used as the structural component of biological membranes. Protidylcholine is the most prevalent kind of phospholipid. Using a hydrophilic phosphocholine polar head group, phosphotidyl choline is an amphiphilic molecule that is formed when a glycerol bridge connects two hydrophobic acyl hydrocarbon chains.[10,11]

Table No.2: Composition of Pharmacosomes.

Component	Requirement
Drugs	Functional hydrogen atom from amino, carboxyl, or hydroxyl group that can be esterified
Solvents	High purity, volatile, and intermediate polarity
Lipid	Phospholipids-phosphoglyceride or sphingolipids

Assemblies and pharmaceutical components of pharmacosome[12]

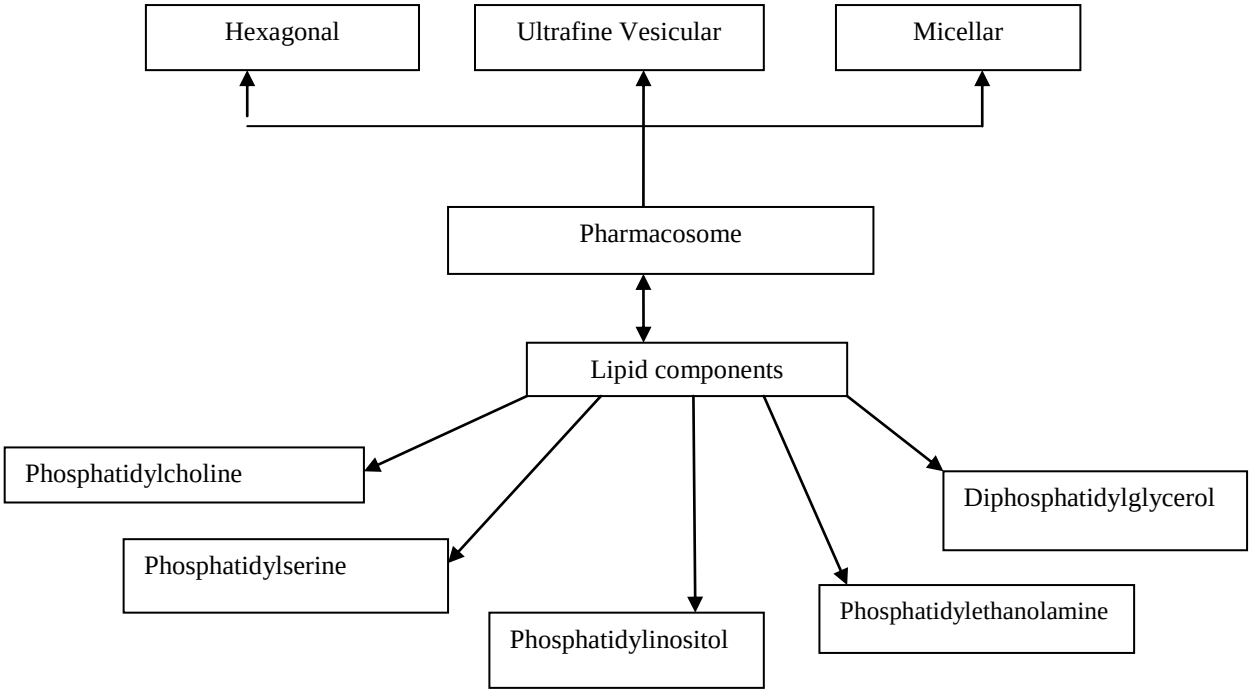


Figure No. 2: Assemblies and pharmaceutical components of pharmacosomes.

Mechanism of drug entrapment in the pharmacosomes

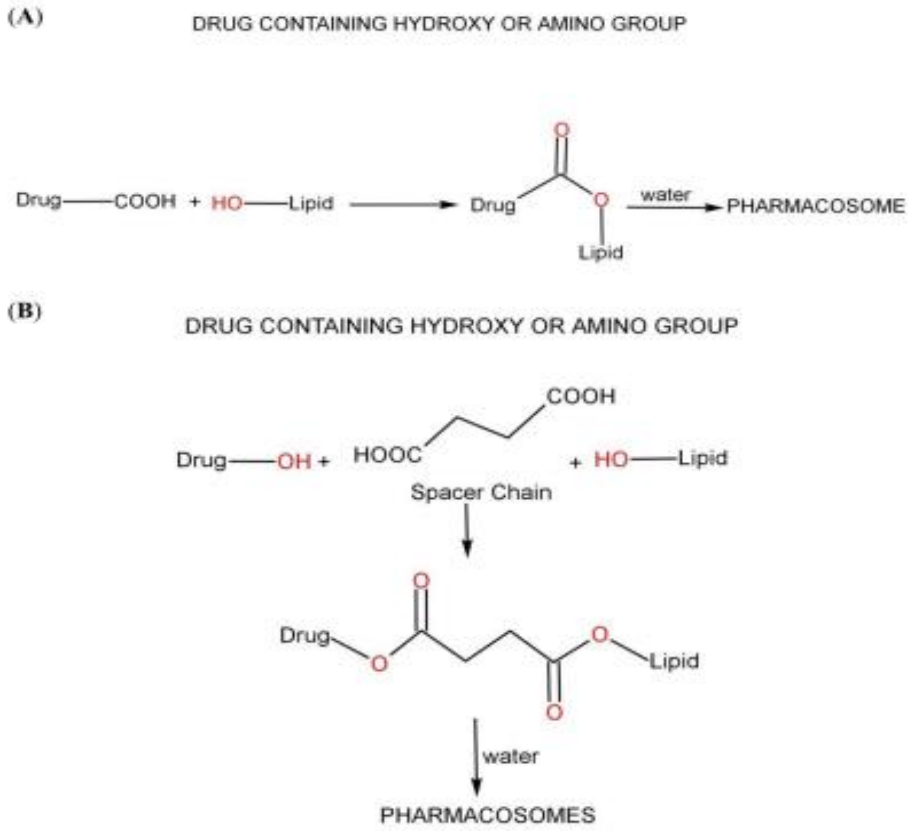


Figure No. 3: Mechanism of drug entrapment in the pharmacosome.

Drugs with an active hydrogen atom can be esterified into lipids with or without a spacer chain, which greatly contributes to the production of an amphiphilic molecule that facilitates improved drug penetration into the target location. The prodrug imparts amphiphilic characteristics because it possesses both lipophilic and hydrophilic qualities. Pharmacosomes' amphiphilic nature aids in the reduction of the interfacial property and the production of mesomorphic behavior at greater contraction. Because of this increase in contact area caused by the decrease in interfacial tension, the drug's bioavailability is increased. With their hydrophobic tails arranged against one other and their hydrophilic headgroup facing the water on both sides, the phospholipids form micelles or lipid bilayers when submerged in water. Phospholipids are suited to be employed as excipients for medications that are poorly soluble in water because of these special qualities.

The ways in which pharmacosomes vary from other vesicular systems / How other vesicular systems vary from pharmacosomes

The creation of pharmacosomes was initiated to address issues with alternative vesicular systems and to integrate medications that are not well soluble in water.

Pharmacosomes, which offer distinct advantages over liposome and niosome vesicles, have emerged as a possible substitute for traditional vesicles. The information about the advantages of pharmacosomes and the structure and uses of other vesicular systems demonstrates the structural variations between other vesicles.[13,14]

Preparation of pharmacosomes

1) Hand-shaking method
2) Solvent evaporation method
3) Ether injection method
4) Supercritical Fluid Process
5) Anhydrous co-solvent lyophilization method

1. Hand-shaking method

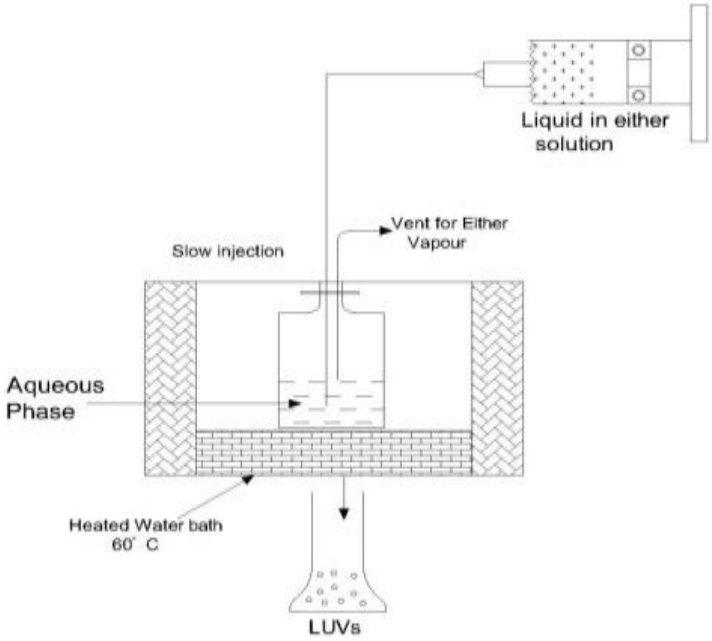
- In the hand-shaking method, both the drug and lipid shell be mixed in the round bottomed flask.
- The organic solvent is evaporated by using rotary vaccum evaporator at room temperature, results in formation of a thin film of deposition on the walls.
- The dried film is then hydrated with buffer and rotated in one direction with hand which results in the formation of vesicular suspension.[14]

2. Solvent evaporation method

The drug is initially acidified in the solvent evaporation process of pharmacosomes preparation in order to potentially release the active hydrogen for complexation.

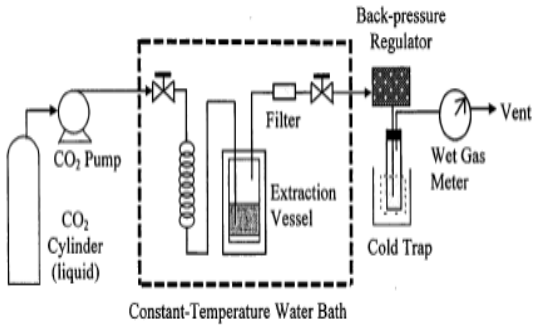
A 100 ml round-bottom flask is filled with precisely weighed PC and drug acid, which are then sufficiently dissolved in dichloromethane. Refluxing the mixture for an hour is done. Next, in a rotating vacuum evaporator, the solvent is removed under vacuum at 40 °C. After drying completely, the leftovers are gathered and put in a vacuum desiccator.[15]

3. Ether injection method



Using the ether injection approach, the drug-lipid complex organic solution was gradually injected into the aqueous medium, causing the vesicles to form easily. Here, the drug-lipid combination is combined with ether, a solvent, and injected gradually into the aqueous media, thereafter vesicles form on their own.[16]

4. Supercritical Fluid Process



Drug + Lipid Complex

↓

Dissolved in supercritical fluid of CO2 and mixed in nozzle mixing chamber

↓

Pharmacosomes are obtained

This method is also known as complicated supercritical fluid enhanced dispersion by solution.

Firstly, the drug and lipid complex mixture is combined with carbon dioxide supercritical fluid. A high super saturation is then achieved by passing the mixture through a nozzle.

Currently, the turbulent flow of carbon dioxide and solvent causes a quick mixing of dispersion, leading to the creation of a pharmacosome.[17]

5. Anhydrous co-solvent lyophilization method

Drug powder and phospholipids broke down in 1 ml of Dimethyl sulfoxide (DMSO)

↓

containing 5% glacial acetic acid,

↓

after that shakes the blend to get a reasonable fluid

↓

Freeze-dried for the time being at condenser temperature.

↓

At that point, resultant complex flushed with nitrogen and put away at 4o C.[18]

6. Recent approaches

- A biodegradable micelle forming drug conjugate was synthesized from the polymer consisting of polyxyethylene glycol and polyaspartic acid with a Adriamycin which is hydrophobic in nature.
- Diluting the micelle without the active constituent getting precipitated in the monomeric drug conjugate.
- Diluting lyotropic liquid crystals of amphiphilic drug by Muller-Goymann and Hamann.
- Phosphotidylethanolamine with various molar ratios of Phosphotidylecholine and cholesterol which significantly enhanced cytoprotection by encapsulating amoxicilin Singh et al. formulated “vesicular constructs”using aqueous domain.[19]

Chracterization of Pharmacosomes

1. Complex Determination

Using Fourier transform infrared spectroscopy, one can see the correlation between the complex sample's correlating spectra and that of its discrete elements, as well as their combination, to indicate the development of the complex or conjugate.[20]

2. Surface Morphology

Using transmission electron microscopy (TEM) or scanning electron microscopy (SEM), the surface morphology of pharmacosomes can be studied. In addition to the lipid purity grade being used in this technique, a few operational factors are also monitored.[20]

3. Drug-liquid compatibility

One thermo analytical method for figuring out drug-lipid compatibility and potential interactions between the two is differential scanning calorimetry. By heating the individual samples in a closed sample pan, the thermal response is investigated. With a particular heating rate and a defined temperature range, the nitrogen gas is evacuated.[21]

4. Solubility

The shake-flask technique can be used to assess the change in solubility brought on by complexation. This method involves mixing an aqueous phase (buffer solution with the drug-phospholipid conjugate at the proper pH) and an organic phase (1-octanol). Constant shaking is then used to maintain equilibrium at 37°C for a day. Following the separation of the aqueous phase, the concentration is ascertained by means of UV or HPLC techniques.[22]

5. *In-vitro* drug release

To assess the *In vitro* drug release rate, utilize the reverse dialysis bag approach. Using this method, the receiver phase is placed outside the dialysis bag and pharmacosomes are placed inside. Every dialysis bag is taken out and its contents checked for medication leakage. The donor phase is contained in a vessel with dialysis bag holding the continuous phase, which are periodically agitated. This approach has the advantage of increasing the membrane surface area that is available for transfer from the donor to receptor compartment. Another advantage of this approach is the increased staffing efficiency it offers due to the reduced number of processes.[23]

6. Differential scanning calorimetry

The drug-excipient compatibility and potential interactions were demonstrated using this thermo analytical approach.[24] A 2910 Modulated Differential Scanning Calorimeter V4.4E was utilized to record the drug-excipient compatibility interactions utilizing this thermodynamic technique. Each individual sample was heated to 2.0 + 0.2 mg in a covered sample pan with nitrogen gas flow to examine the thermal behavior. The experiments were conducted at a heating rate of 10°C per minute, throughout a temperature range of 25 to 250 °C. The disappearance of endothermic peaks, the emergence of peaks, changes in peak shape and onset, peak temperature/melting point, and relative peak area/enthalpy can all be used to determine the conclusion of the interaction.[25]

7. X-ray powder diffraction

Relative integrated intensity of reflection peaks has been used to calculate the degree of crystallinity. The area under the curves of the XRPD patterns yields the integrated intensity, which is a representation of the specimen's properties.[24]

8. Dissolution Study

In a USP (8) six station dissolution test apparatus, type II (Veego Model No.6 DR, India), *In vitro* dissolution investigations of drug PC complexes as well as plain diclofenac acid were carried out in triplicate at 100 rpm and 37°C. A precisely weighed volume of the complex was added to 900 milliliters of pH 6.8 phosphate buffer, which is equal to 100 mg of drug acid. To keep the sink conditions constant, samples (3 mL each) of the dissolving fluid were taken out at various intervals and replaced with an equivalent volume of fresh medium. The samples that were removed were filtered (using a 0.45-mm membrane filter), appropriately diluted, and then spectrophotometrically measured at 276 nm.[25]

9. Stability of Pharmacosomes: Assessing the stability of the system after the product has been lyophilized is made easier by this correlation between the spectrum in the solid state and the spectrum of dispersion in water, which shows a range of points in time and comprises small particles.[26]

Table No. 3: Therapeutic Application of Drugs after incorporation with Pharmacosomes.[27]

Drugs	Applications
Naproxen	Solubility was improved, and drug release was regulated.
Aceclofenac	Enhanced bioavailability and improved solubility and dissolution profile.
Ketoprofen	Solubility and dissolution profile have been improved.
Etodolac	Solubility, entrapment efficiency, and long-term stability.
Rosuvastatin	Improved bioavailability and sustained medication release
Losartan	Solubility, dissolving profile, and bioavailability have all improved
Pindolol	Bioavailability has improved
Acyclovir	Solubility is increased, as is the hemolytic reaction.

Table No. 4: Comparison between Liposomes and Pharmacosomes.[28,29]

Liposomes		Pharmacosomes
Principle	Incorporation of drug in the aqueous or lipid phase of a mixture of lipid where the physicochemical properties of the carrier and release of drug will be functions of different lipids used	Covalent binding of a drug to a lipid where the resulting compound is the carrier and the active compound at the same time. The physicochemical properties depend on drug as well as the lipid
Loss of drug	Through leakage	No leakage, since drug is covalently bound but loss of drug by hydrolysis is possible.
Manufacturing Cast fill method	Extrusion/sonication Injectable method Reverse phase evaporation etc.	Self dispersion through moderate mixing and sonication
Separation of free drug	By gel filtration, dialysis, ultrafilteration, ultracentrifugation	Not necessary since the drug covalently linked
Volume of inclusion	Decisive in incorporation of drug molecules.	Irrelevant, since the drug is covalently bound
Surface charge	Achieved through lipid combination.	Depends on the physicochemical structure of the drug lipid complex.
Membrane fluidity	Depends on lipid combination and presence of cholesterol fluidity influences the rate of drug release and physical stability of system.	Depends on phase transition temperature of drug lipid complex. No effect on release rate since the drug is covalently bound
Release of drug	Diffusion through the bilayer, desorption from the surface or release through degradation of liposomes	Hydrolysis (including enzymatic).
Physical stability	Relatively good Aggregation through double valenced cation.	Depends on physicochemical properties of the drug-lipid complex

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