Different lipid based vesicular systems have been developed as controlled and targeted drug delivery systems. Pharmacosomes are novel vesicular drug delivery systems. They are potential alternative to conventional vesicles. Pharmacosomes are the amphiphilic phospholipid complexes of drugs bearing active hydrogen that bind to phospholipids. Similar to other vesicular systems pharmacosomes provide an efficient method for delivery of drug directly to the site of infection, leading to reduction of drug toxicity with no adverse effects. They also reduce the cost of therapy by improving bioavailability of medication, especially in the case of poorly soluble drugs. This approach as a drug delivery system certainly promises a reliable, safe, selective and precise method of drug delivery. They help in controlled release of drug at the site of action as well as in reduction in cost of therapy, drug leakage and toxicity, increased bioavailability of poorly soluble drugs, and restorative effects. They are mainly prepared by hand-shaking and ether injection method. The Pharmacosomes have evaluated for different parameters such as size, surface morphology and in vitro release rate. This article reviews the potential of pharmacosomes as controlled and targeted drug delivery systems and highlights the methods of preparation and characterization.

**Keywords**: Amphiphilic, biosomes, bioavailability, Pharmacosomes, phospholipids, targeted drug delivery system.

**INTRODUCTION**

Many researchers have been working on novel drug delivery system for the past few decades, with an aim to further develop this system. The main purpose for the development of novel drug delivery systems can be explained in on the basis of clinical advantages of these systems, and their economic aspects\(^1\). An ideal novel drug delivery system should fulfill two prerequisites: firstly, it should deliver the drug at rate directed by the body requirements, secondly; it should channel the active entity to the target site of action\(^2\). One of the approaches to modify the original biodistribution of drugs is to entrap them in submicroscopic drug carriers such as liposomes, transferosomes, niosomes, polymeric nanoparticles, serum proteins, immunoglobulins, microspheres, erythrocytes, reverse micelles, monoclonal antibodies, and pharmacosomes\(^3\).

In the recent years, lipid vesicles were found to be of importance in the field of immunology, membrane biology, diagnostic techniques and most recently genetic engineering\(^4\). Vesicular structures are such system that prolong the duration of the drug in systemic circulation, and reduce the toxicity by selective uptake\(^5\). These vesicles were first reported in 1965 by Bingham, and were given the name “Bingham bodies” which play a major role in modeling biological membranes, and in the transport and targeting of active agents\(^6\).

These are defined as colloidal dispersions of drugs covalently bound to lipids and may exist as ultrathin vesicular, micellar or hexagonal aggregates, depending on the chemical structure of drug-lipid complex\(^7\). These systems are formed by linking a drug (pharmakon) to a carrier (soma), so they are called pharmacosomes. After absorption, their velocity of degradation into active drug molecule depends to a
great extent on the size and functional groups of drug molecule, the chain length of the lipids and the spacer.

**Advantages**

Since the drug is covalently linked to the carrier, no leakage of drug takes place.
1. Entrapment efficiency is high and not affected by encaptured volume and drug-bilayer interactions.
2. Suitable for both hydrophilic and lipophilic drugs.
3. No problem is associated with drug incorporation.
4. The physicochemical stability of the pharmacosomes depends upon the physicochemical properties of the drug-lipid complex.
5. Drug can be delivered directly to the site of action.
6. It improves bioavailability especially in case of poorly soluble drugs.
7. No need of removing the free unentrapped drug from the formulation as needed in case of liposomes.
8. There is reduction in adverse effects and toxicity.
9. There is reduction cost of therapy.

**Limitations**

Synthesis of a compound depends upon its amphiphilic nature.
1. It requires surface and bulk interaction of lipids with drugs.
2. It requires covalent bonding to protect the leakage of drugs.
3. On storage, there is fusion and aggregation, as well as chemical hydrolysis.

**Components of pharmacosomes**

For this delivery system the three components are drugs, solvent and carriers (lipid).

1. **Drugs**
   Any drug having an active hydrogen atom (COOH, OH, NH2 etc) can be esterified to the lipid, with or without spacer chain resulting into amphiphilic complexes. These synthesized amphiphilic complexes (pharmacosomes), facilitate membrane, tissue, or cell wall transfer, in the organism.

2. **Lipids**
   Phospholipids are principal molecular building block of cell membranes. Two type of phospholipids generally used are phosphoglycerides and sphingolipids. The most common phospholipid is phosphotidyl choline molecule.

3. **Solvent**
   Organic solvent of analytical grade and intermediate polarity is used in development of pharmacosomes. It must be of high purity and volatile in nature. The phospholipids and the drug must be dissolved in the selected solvent. The selection of solvent depends on polarity of the drug and the lipid.

**METHODS OF PREPARATION**

1. **Ether injection method**
   In this method solution containing drug-lipid complex is mixed properly and is slowly injected into a hot aqueous medium through gauze needle and vesicles form readily.

2. **Solvent evaporation method/ hand shaking method**
   Mixture of drug and lipid is dissolved in a volatile organic solvent. Thereafter solvent is evaporated using rotatory evaporator in round bottom flask which leaves a thin film of solid mixture deposited on the walls of flask. The dried film hydrates with aqueous medium and readily gives a vesicular suspension.

3. **Anhydrous co-solvent lyophilization method:**
   First of all drug and phospholipids are dissolved in solution of dimethyl sulfoxide containing glacial acetic acid. Then mixture is agitated to get clear liquid and then freeze-dried overnight at condenser temperature. The resultant complex is flushed with nitrogen and stored at 4°C.

4. **Supercritical fluid process**
   Drug and lipid complex are dissolved in a supercritical fluid of CO2, then mix into nozzle mixing chamber.

**Evaluation of pharmacosomes**

1. **Complex Determination**
   The formation of complex and conjugate can be determined by the correlation spectrum observed in complex sample with that of discrete constituents and also with their mixture with the help of FTIR spectrum.

2. **Surface morphology**
   With the help of scanning electron microscopy (SEM) or transmission electron microscopy (TEM), the surface morphology can be observed. Purity grades of phospholipid affected to shape and size of pharmacosome and the process variables such as speed of rotation, vaccum applied or the method used.

3. **Drug content**
   To determine the drug content in drug-pc complex, coplex equivalent to drug weighed and added into volumetric flask with suitable solvent. The solution is mixed by means of magnetic stirrer. After 24 hrs suitable dilution drug content is determined UV spectrophotometrically.

4. **Differential scanning calorimetry (DSC)**
   This thermal analytical technique is used to determine the drug-excipients compatibility or interactions. The interaction can be concluded by the elimination endothermic peaks, appearance of peaks and change in peak shape and its onset, peak temperature /melting point and relative peaks area or enthalpy.

5. **X-ray power diffraction (XRPD)**
   It is performed to determine the degree of crystallinity by using the relative integrated intensity of reflection peaks. The integrated intensity is given by the area under curves of the XRPD patterns and it represents the specimen characteristics.

6. **Fourier transforms infrared spectroscopy (FTIR)**
   With the help of IR spectroscopy the formation of complex can be confirmed by comparing the spectrum of complex with the spectrum of individual components and their mechanical mixture.

7. **In-vitro Study**
   Depending upon the expected therapeutic activity of biologically active constituents, model of in–vivo and in-vitro evaluation is carried out.
Table 1: Comparison of conventional vesicular systems and pharmacosomes

| Vesicular system | Limitations | Pharmacosomes |
|------------------|-------------|---------------|
| Niosomes         | Drug leaching, time consuming, less stable | More stable, more efficient |
| Liposomes        | Expensive, degradation by oxidation, sedimentation, leaching of drug | Cheaper to prepare, entrapment efficiency is independent of inclusion volume and drug bilayer interactions, covalent linkage prevent drug leakage, oxidation resistant and pure and natural phospholipids not needed |
| Transfersomes    | Expensive, oxidative degradation, lack of purity of natural phospholipids | Cheaper, oxidation resistant, pure and natural phospholipids not needed |

Application of pharmacosomes
Pharmacosomes demonstrate a wider stability profile and greater shelf life. They have the capacity to augment drug absorption and its transport. Pharmacosomes can improve the rate of permeation by improving the membrane fluidity. The transition temperature of vesicles in the form of vesicles and micelles might pose an evident effect on vesicular interaction with biomembrane, hence improving the transfer of drug across membrane. This approaches has been successfully used by many researchers to improve the therapeutic performance of various drug. Such as pindolol diglyceride, amoxicillin, taxol, cytarin, dermatsulfate, bupranolol hydrochloride etc. In a study Yue et al., optimized the formulated geniposide pharmacosomes and examined their attributes. Pharmacosomes have greater degree of selectivity for action on specific target cells. In a study Raikhman et al., described pharmacosomes as building particles capable of transporting biologically active substances including nucleic acids and proteins. Semalty et al., developed and evaluated diclofenac pharmacosome, and it was found that solubility was enhanced in pharmacosomes (22.1 g/mL) as compared to diclofenac (10.5 g/mL). Drug release was also improved from 60.4% of diclofenac to 87.8% of diclofenac pharmacosomes after 10 hrs of dissolution study. Zhang et al., developed and evaluated pharmacosomes of 3’, 5’-didoctanoyl-5-fluoro- 2’-deoxyuridine using central composite design, and observed good targetting efficiency of pharmacosomes in vivo and improved drug potential to pass through blood brain barrier. In a study Yi-Guang et al., prepared acyclovir pharmacosomes and observed that the plasma proteins in blood absorbed pharmacosomes and interfered with the interactions of erythrocytes and hence reduced haemolytic reaction.

CONCLUSION
There are many limitations that are associated with vesicular drug delivery systems, like other vesicular system pharmacosomes plays an important role in the selective targeting and the controlled delivery. Pharmacosomes have immense potential, and advantages over other vesicular systems. The influence of spacer groups and linkages should be observed more rigorously for further improvement in drug fate and biological activity of the drug to achieve the therapeutic goal. The system requires greater efforts towards investigating the non-bilayer phases and exploring the mechanism of action. Pharmacosomes do not have only high entrapment efficiency but delivery can be predetermined, because drug itself in conjuction with lipids forms vesicles. Since pharmacosomes have immense potential, there is need of more work to be done on this system to get more fruitful results.

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