

**Review Article**

**SGVU Journal of Pharmaceutical Research & Education**

**ISSN: 2456-4508**

Journal homepage: <http://www.gyanvihar.org/researchjournals/>

**JPRE**

**PHARMACOSOMES: AN EFFECTIVE APPROACH FOR DRUG  
DELIVERY**

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**ABSTRACT**

Pharmacosome is one of the vesicular drug delivery system which is used to decrease the toxicity of drug by minimizing the side effects because of drug targeting to the site specificity and also used to enhance the bioavailability of many drugs. As compare to other vesicular systems pharmacosome shows improved bioavailability due to its good biopharmaceutical properties. One of the best advantages of pharmacosome is its economical technique used for the formulation development. For the preparation of pharmacosome intermediate polarity solvent is used. These formulations basically improve membrane fluidity and enhances the rate of permeation. Pharmacosomes have gain greater interest by enhancing therapeutic effects of many medicine like beta blocker. Both hydrophilic and lipophilic drugs can be used for the manufacturing of pharmacosomes. Pharmacosomes have been prepared for various cardiovascular drugs, proteins, non-steroidal anti-inflammatory drugs & antineoplastic. This review covers the method of preparation, applications, limitations, research update & all about the pharmacosomes.

**Key words:** Pharmacosomes, Amphiphilic Compounds, Carrier Mediated Drug Delivery, glycerylmonooleate, lipid crystal.

**INTRODUCTION:**

The term pharmacosomes is employed to explain the zwitterion, amphiphilic ratio complexes of polyphenolic compounds with phospholipids. it's a kind of vesicle based drug delivery system.<sup>1</sup> The vesicle based drug delivery system is that which improves the bioavailability of the drug and also the reduction in toxicity by drug targeting to the precise website. Pharmacosomes square measure the novel drug delivery system within which medicine square measure covalently guaranteed to lipids and exist as vesicle based, micellar or polygonal shape aggregates, in line with the chemical structure of the drug macromolecule complicated. The pharmacosomes square measure shaped by linking a drug (Pharmakon) to a carrier (soma).<sup>2</sup>Pharmacosomes may be ready to cross the biomembrane expeditiously and having several benefits alternative vesicle based systems like liposomes, niosome and transferosomes. Pharmacosomes possess higher biopharmaceutical properties of the drug leading to improved bioavailability.<sup>3</sup>

Pharmacosomes in the form of prodrug when come in contact with water formulate pharmacosomes and assemble to form multilayers. This method is developed by keeping the surface properties further because the bulk properties of the drug-lipid conjugate in thought. until date numerous pharmacosomes containing formulations of non-steroidal medicament medicine, proteins, vessel and antineoplastic medicine are ready.<sup>4</sup> By the event of pharmacosomes the medicine absorption will improve and gastrointestinal toxicity will minimise. Pharmacosomes will move with biomembranes and perform higher transfer of medicine. By this interaction the natural process temperature of bio membrane will modified, and membrane thinness is improved, resulting in increased permeation. Pharmacosomes will scale back issues related to the defence of polar molecules like low drug incorporation, solubility and outflow.

The carrier mediated drug delivery (CMDD) system may be a useful process for the treatment of many diseases. The therapeutic index (TI) of standard and novel drugs is enhanced by the utilization of drug targeting to a selected cell or inner compartment, the management of release Profile, the chemical agent or a mixture of these.<sup>5</sup>

**The therapeutic benefits of pharmacosomes include:**<sup>3,6</sup>

- ❖ The efficacy of the drug is increased.
  - Drug delivery to the specific site.
  - Side effects may be decreased by decreasing toxicity.
- ❖ Healthcare cost is reduced.
- ❖ Patient compliance will be better.

Many researchers have been explained that pharmacosomes may be improved the water solubility of analgesic drugs. These pharmacosomes (phospholipid complex) can be prepared & evaluated for physicochemical testing. The increase in water solubility in pharmacosomes will improve the dissolution & lowering the gastrointestinal toxicity. ketoprofen–phospholipid complex (pharmacosomes) were also prepared by a simple and reproducible method, it shows that ketoprofen converts in a complex with phospholipids, having better dissolution profile & solubility.<sup>7</sup>

The prodrug having amphiphilic properties are regenerated to pharmacosomes upon dilution with water. The drug carrier conjugate forms a compound, amphiphilic in nature. The prodrug conjoins hydrophilic and lipotropic properties thereby having amphiphilic characteristics therefore reduces surface tension, at higher concentrations, it exhibits athletic behaviour.<sup>8</sup> Due to a decrease in surface tension, the area of contact will increase, thus increasing bioavailability. Pharmacosomes outlined as dispersion of mixtures containing medication containing lipids and they occur as ultrafine particles as vesicle, hexangular aggregates and micelle, all dependent on the chemical moiety of drug-lipid system.<sup>9</sup>

Pharmacosome is a novel drug delivery carrier system, within which the dispersions of colloids with drug covalently certain to lipids. This is often a good tool to attain desired therapeutic goals in targeting the drug and controlled release formulation. Drug carrier systems based on colloids are like micellar solutions, liquid dispersions & vesicles.<sup>10</sup>

### **Advantages of Pharmacosomes over other Vesicular Systems<sup>2,5,9</sup>**

- The restrictions of transferosomes are overcome by the pharmacosome.
- The pharmacosomes benefits over noisome & liposome vesicles have come up as potential various to conventional vesicles.
- Pharmacosomes is an economical technique for delivery of drug directly to the infected site.
- The volume of inclusion will not influence the defense efficiency.
- Vesicular systems are now developed for the controlled and targeted drug delivery.
- The drug carrier covalent binding.
- Drug release in pharmacosomes is by chemical reaction in most of the time.
- Reduction in adverse effects.
- Improvement of the bioavailability in case of water soluble medication.
- It can be administered via intravascular, topical & oral route.
- loss because of leak of drug, doesn't occur because drug is covalently bound.
- Drug is directly delivered to the site of infection.

### **Limitations of Pharmacosomes:<sup>3,11,12</sup>**

- a) The synthesis of this compound can depend on both hydrophilic and lipophilic nature of the drug.
- b) It requires both superficial and mass drug-lipid interaction.
- c) The bond like covalent type required to restrict drug leakage.
- d) The Pharmacosomes get fused due to their susceptibility and chemicals on storage gets aggregate or hydrolyse.

### **Material of Pharmacosomes:**

- **Drug:** Any drug possessing (-COOH-OH-NH<sub>2</sub> etc.) is esterified to the lipid, with or without spacer chain, resulting in both hydrophilic and lipophilic complexes. Such type of a compound synthesis they are guided in like how that powerfully lead to both hydrophilic and lipophilic nature of a compound, due to this it can facilitate membrane, tissue, or plasma membrane transfer, within the organism.
- **Lipid:** The lecithin, lipid or phosphatidylcholine is main molecular strength of cell membranes. Phospholipids are the medication form both hydrophilic and lipophilic merchandise that renders phospholipids hydrophilic and also the drug soluble in lipids.<sup>13</sup>
- **Solvents:** For the formation of Pharmacosomes, the solvents help to show more purity and nature is volatile. For pharmacosome preparation the intermediate polarity solvents are select.<sup>14</sup>

### **Method for Preparation of Pharmacosomes:**

In general, there are four methods have been used to formulate pharmacosomes:

- ❖ **Handshaking Method:** In this technique, the drug lipid complicated dried film (with or without egg lecithin) is deposited in a spherical shaped bottom flask and due to this association with medium that is aqueous in nature it forms a vesicular suspension without

any delay. The ether injection technique, the complex of organic resolution of the drug lipid is injected slowly whereby the vesicles are without delay fashioned the injected medium is hot liquid medium. At less concentration the chemical compound exists amphiphilic state.<sup>15</sup>The monomers might cause kind of structures when it increases additional i.e. spherical rod like micelles or formed like disc type or isometric or shape of form. In this two result are compared one is diglycerides prodrug on interfacial surface tension, another one is result created by a standard detergent dodecylamine hydrochloride and both are having exact same results as decrease in surface tension. The prodrug exhibits mesomorphic lyotropic nature, and assembles in supramolecular structures when it reaches to more than critical particle concentration.<sup>10,15</sup>

- ❖ **Ether Injection Technique:** In this method, by the drug lipid advanced and organic solvent are dissolved together. This mixture forms the vesicles when it slowly injected into the heated liquid agents. The concentration show nature of amphiphilies introduced a chemical compound state when it is at low concentration however because the concentration is inflated, form of structures could be show different shaped, that is spherical cylindrical, disc, cubic, or hexagonal type. Then check the comparative impact on the interfacial surface tension of prodrug of diglyceride a customary wetting agent, dodecylamine hydrochloride.<sup>11</sup> It is higher than the critical micellar concentration when it absolutely finished, the hexagonal arrangement was ascertained by long cylinders, and prodrug exhibited liquid crystalline part, exhibiting massive molecular structures.
- ❖ **Supercritical Fluid Process:** The complex supercritical fluid helps to increase dispersion in solution), it combines into nozzle intermixture chamber before this Drug and lipid complicated are dissolved in a very supercritical fluid of carbon dioxide.<sup>15</sup>
- ❖ **Anhydrous Co-Solvent Evaporation Method:** Explained at that time the mixture is agitates with concerns glacial acetic acid to form clear liquid. At condenser temperature it is freely dried after this resultant complex flushed with nitrogen and store at 40° C.<sup>11,16</sup>
- ❖ **Other Approaches:** There is another approach for manufacturing pharmacosomes is to include mix the hydrophobic drug into a polymer made up of glycol & aspartic acid by-product this will always help to the formation of a biodegradable micelle drug conjunct.<sup>16</sup>The possibilities of precipitation of drug on dilution are reduced due to water soluble conjunct of drug. The diluted lyotropic liquid crystals of amphiphilic medication were employed for developing nonsteroidal anti-inflammatory drug based mostly pharmacosomes from charged techniques.<sup>16,17</sup>

#### **Characterisation of Pharmacosomes**

- ❖ **Complex Determination:** The assistance of Fourier transforms infrared spectroscopy, by correlating spectrum discovered in complicated sample the formation of the complex or the conjugate will be determined there additionally with their mixture and there +with of separate constituents.<sup>16,17</sup>
- ❖ **Stability of Pharmacosomes:** In this correlation of the spectrum in solid state it is show varied point of time with spectrum of dispersion in water consisting of tiny particles were examined, it is help to evaluate the steadiness of the system when the product has been lyophilized.<sup>16-18</sup>

- ❖ **Solubility:** As this process results complexation and this is due to the change in solubility that may evaluate by shake flask technique. In this process, two phase are used in this one is octanol and aqueous phase is used, at a temperature of 37°C for one day and constant shaking is require in this time period. The concentration is determined using ultraviolet of high performance liquid chromatography technique by using liquid section which is separated by solution.<sup>17</sup>
- ❖ **Drug Lipid Compatibility:** To observed the drug lipid compatibility and their interactions some thermos analytical technique like differential scanning measurement are used, heating the them in an exceedingly sample pan that is closed this is when if any thermal response is studied exploitation separate samples. The temperature is maintained in an exceedingly definite vary with a selected heating rate when the gas is purged.<sup>18</sup> For increase drug absorption with the help of increasing solubilization, lipid-based formulations may be used. Due to this permeability is increased, metabolism of loss of drug by inhibition of hepatic enzymes & enhancement of transport though the inhibition of transporters & increased production of particles. The evaluation of drug-lipid complexes in many lipid based nanoparticles is implicated in both pharmaceutical and medicine.<sup>16</sup> The drug (solute) and excipients (solvent) both are responsible for interaction between drug and excipients this interaction helps miscibility which is dependant process. For the formulation stability of (solid lipid nanoparticles) SLN the miscibility will be the important part. Mixed glycerides, like glycerylmonooleate (GMO), helps to form a well-liked solvent for poorly water soluble medication. For formulating liquid dosage forms GMO helps due to their waxy and long-chain glyceride nature. The Sorbitan fatty acids (Spans) and GMO both show similar physical properties. For co-surfactants polar oils are mainly referred, which helps to promote miscibility because of the presence of radical teams. The interfacial surface tension decrease between two immiscible elements with the help of co-surfactant due to this both thermodynamic stability and miscibility is increase.<sup>17,18</sup>
- ❖ **Crystalline State Measurement:** Mainly present solids are possessing definite crystalline shapes that can be recognized easily. They are show massive size as a result of these are shaped terribly slowly, due to this, particles have enough time to induce correct position within the crystal structure. Some lipidic crystals are so tiny that show amorphous nature. When we examine by the help of hard microscope in additionally they also show some explicit crystalline form. Such types of solids are called as small crystalline solids.<sup>11</sup> The crystalline nature of drug may be determined with the help of X-ray diffraction technique. The general combined intensity of all reflection peaks is projected by space beneath curve of X-ray powder diffraction pattern that specifies the specimen attributes.<sup>17</sup>
- ❖ **Scanning Electron Microscopy/Transmission Electron Microscopy:** These techniques are used to finding out the pharmacosomes surface order. In lipids the purity grades being employed and some variables discovered throughout in the operation (vacuum appointed, method of preparation, move speed) change the size and shape of pharmacosomes discussed by many researchers that nature of pharmacosomes are greasy if they prepared by the help lipids that show low purity grades and resulting in formation of massive aggregates and those fabricated by using high grade purity lipids i.e. over 90% purity

grade show status to degradation because of oxidation, that complicated stability. Therefore, 80% purity grade is that the usually used phospholipid grade.<sup>9,18</sup>

- The pharmacosomes drug delivery system has potential for prolonged result in liver targeting and tissue.
- In case of diclofenac it showed increase solubility in the form of diclofenac pharmacosomes and but in additionally it improved drug release.
- The phase transition temperature in case pharmacosomes in their micellar state & vesicular system might have important influence at the time of interaction with biomembranes sanctioning a stronger transfer of active ingredient. This interaction helps to results in modification of phase transition temperature of biomembranes therefore due to this it improves the thinness of membrane result as a permeations enhancer.<sup>18,19</sup>
- Pharmacosomes helps to improving the membrane fluidity due to this may improve the permeation speed.
- The transition temperature of vesicles within the kind of vesicles and micelles may cause an apparent impact on vesicular interaction with biomembrane, thus helps to improve the transfer of drug across the membrane.
- Pharmacosomes are amphiphilic lipid core system due to this nature it may also be used for the novel ophthalmic dosage forms. In this prodrug of amphiphilic nature once diluted with tear, it improves the drug release profile and tissue layer drug transport.<sup>15,18</sup>
- Pharmacosomes have achieved a new level by enhancing therapeutic effects of many medicines like beta blocker pindolol, taxol, bupranolo acid derivative, cytarabin, Amoxicillin and dermatan sulphate etc.
- Pharmacosomes have high selectivity for the target cells and highest stability. They are act as building particles of capable in transporting of biological substances.
- Plasma protein in blood absorbs pharmacosomes and interfere interaction with erythrocytes and help to reduce hemolytic method.
- Pharmacosomes may be also used for increase the solubility within the gall salts and acts as a liver targeting. In this drug dose is decrease because of greater absorption of therapeutic phytoconstituents.<sup>19</sup>
- As carrier pharmacosomes shows synergistic hepatoprotective effect of phytosomes. Pharmacosomes have many advantages in cosmetology because of their better skin penetration and lipid profile.<sup>19,20</sup>

### CONCLUSION:

Pharmacosomes are having varies advantages over many novel drug delivery systems. It has high entrapment potency as it combined with lipids and form vesicles. It also plays major role in drug targeting for many diseases. In pharmacosomes delivery of drug can be predetermined, as the drug itself is combined with lipids and forms vesicles. So it can be concluded that pharmacosomes have high potential to improve the drug delivery for synthetic & natural active constituents.

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