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THE IMPORTANCE OF PHARMACOSOMES IN NOVEL TARGETED DRUG DELIVERY SYSTEM: REVIEW

Prof. Dr. S.A. Azeez Basha[1], Amtul Hajera*[2], Md. Abubakar[3] and Afreen Sultana[4]

[1]Principal, Professor and HOD, Deccan School of Pharmacy (Affiliated to OU).

[2]Department of Pharmaceutics, Deccan School of Pharmacy (Affiliation OU).

[3]Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research-Guwahati (NIPER G).

[4]Department of Pharmaceutics, Deccan School of Pharmacy (Affiliation OU).

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***Corresponding Author**
Amtul Hajera
Department of Pharmaceutics, Deccan School of Pharmacy (Affiliation OU).

ABSTRACT

Several issues are encountered in the field of solubility augmentation. Pharmacosomes are a revolutionary technique based on a lipid drug delivery mechanism. Pharmacosomes are colloidal, nanometric-sized micelles, vesicles, or hexagonal assemblies of colloidal drug dispersions covalently bonded to the phospholipid. The drug-phospholipid complex is appropriate for oral delivery since it is biodegradable and non-toxic, allowing it to be used as a solubilizer, emulsifier, and matrix forming excipient for drugs with low solubility and/or permeability. The current review summarises the recent developments about pharmacosomes and the mechanisms by which they improve drug bioavailability. It also includes information on pharmacosome formulation and preparation processes, as well as characterisation techniques. The rising number of recent research addressing the use of drug-phospholipid complexes to improve drug oral bioavailability demonstrates how important this method is for successful oral delivery.

KEYWORDS: Oral bioavailability; phospholipid; drug-phospholipid complex; pharmacomes; preparation; characterization.

INTODUCTION

A drug is dissolved in the gastric fluid (Hydrophilic environment), then penetrated across biological membranes (Lipophilic environment) and ultimately absorbed into the systemic

circulation after oral intake. It is possible that their poor water solubility is responsible for poor absorption. While inadequate permeation may be due to the drug's structural framework or due to poor solubility with oils and other lipids, greatly reducing their ability to pass across the lipid-rich surface membrane of the small intestine enterocytes.[1]

To increase the absorption and penetration of various bioactive compounds of synthetic and natural origin, many techniques have been developed. This includes fabrication of more soluble pro-drug, solid dispersion and complexation with metals, cyclodextrin and phospholipids. Among several other complexations, phospholipids have been demonstarated to increase both absorption and permeation of the bioactive constituent. Therefore designing pharmaceuticals as lipid complexes (also termed as pharmacosomes) could be a potential option for improving solubility, permeability and lessening the GI toxicity.[2,3]

Pharmaacosomes are a type of drug delivery technology that is new. Vaizoglu and Speriser were the first to introduce them in 1968.[4]

The term pharmacosomes is principally used to describe the zwitterionic, amphiphilic, stoichiometric complexes of polyphenolic compounds with phospholipids.[5] These are lipid-based drug delivery systems that are commonly known as colloidal dispersions of drugs with a covalent bond, amphiphilic component that promote membrane, tissue, or cell wall transfer in the organism.[5] They're a potent tool to achieve therapeutic objectives including drug targeting and controlled release. The surface and bulk interactions of lipids with the drug are the criterion for the development of vesicular pharmacosomes. Any drug with an active hydrogen atom (-COOH, -OH, -NH2, etc.) can be esterified to lipids, with or without a spacer chain, results in a amphiphilic derivative.[5]

The amphiphilic properties aid pharmacosomes in reducing interfacial tension and exhibiting mesomorphic behaviour at higher contractions. This decline in interfacial tension results in an increase in contact area, which increases pharmaceutical bioavailability. When phospholipids are immersed in water, they form micelles or lipid bilayers, with the hydrophobic tails aligned against one another on both sides and the hydrophilic head group facing the water. Because of these characteristics, phospholipids are ideal excipients for drugs that are poorly water soluble. As an outcome, enhances the solubility of lipophilic drugs.[6,7]

COMPARISION OF FEW LIPOIDAL PARTICULATE CARRIER AND THEIR APPLICATIONS

Table 1: Omparision of few lipoidal particulate carrier and their applications.

TYPE	COMPOSITION	FEATURE
Liposomes	Phospholipids: cholesterol: alcohol	The amphiphilic characteristic allows for the solubilization of both hydrophilic and lipophilic medicines, as well as the internalisation and amplification of bioactives.[8]
Transferosomes	Phospholipids: edge activators: alcohols: buffering agent: dye	Vesicles which are ultra deformable can deform and pass through constrictions that are 5 to 10 times smaller than the corresponding diameter without noticeable loss.[9]
Ethosomes	Phospholipids: ethanol	Its use as a combination of high concentrations of ethanol and phospholipids enhances the effect of deeper drug distribution and penetration in the skin.[10]
pharmacosomes	Phospholipids: dicholromethane	Colloidal dispersions of drug covalently bonded to lipids, which boosted entrapment efficiency; no drug loss due to leakage, and no drug incorporation difficulties.[11]

SALIENT FEATURES OF PHARMACOSOMES[12]

As the drug is conjugated with lipids forms vesicles, entrapment efficiency is not only significant, but also predetermined.

1. There is no need to go through the time-consuming and difficult process to remove the unentrapped, free drug from the formulation.
2. As the medicine is covalently bonded, there is no loss owing to drug leakage. Hydrolysis, on the other hand, can result in the loss.
3. Drug incorporation into lipids is not a challenge; Drugs can be delivered straight to the infection site.
4. The entrapment efficiency of pharmocosomes is unchanged by encaptured volume or drug-bilayer intractions
5. The membrane fluidity of pharmacosomes is influenced by the phase transition temperature of the drug lipid complex, but this has no impact on the drug's release rate since the drug is covalently linked to lipids
6. There is much less phospholipid transfer/exchange, and HDL solubilization is limited.
7. The physicochemical stability of pharmacosomes is determined by the drug-lipid complex's physiochemical properties.

8. Following absorption, the size and functional groups of the drug molecule, the chain length of the lipids, and the spacer all play a role in how rapidly they disintegrate into active drug molecules.
9. They can be administered orally, topically, subcutaneous, or intravenously.
10. Hydrolysis regulates drug release from pharmacosomes in most cases (including enzymatic). Therapy costs are lower.

MERITS OF PHARMACOSOMES OVER OTHER CONVENTIONAL VESICULAR SYSTEM[13]

Table 2: Advantages of Pharmacosomes over other conventional vesicular system.

Vesucular system	Feature	Problem	Pharmacosomes
Liposomes	One or more lipid bilayers, separated by water or an aqueous buffer compartment in a microscopic vesicle (25nm to 100m).	Preparation costs are high, and the drug is degraded by oxidation, sedimentation, and leaching. Also there is a lack of purity in natural phospholipids.	Advantages over liposomes: Entrapment efficiency is self-determining and is not dependent on inclusion volume and drug bilayer interactions, covalent bonding prevents drug leakage, oxidation resistance, and the use of pure and natural phospholipids is not required.
Transferosomes	Suitable for both low and high molecular weight drugs, as well as lipophilic and hydrophilic drugs.	Expensive, susceptible to oxidative degradation, and lacking of natural phospholipid purity.	Advantages over tranferosomes: Phospholipids that are less expensive, more resistant to oxidation can be used and use of pure and natural phospholipids is not required.
Niosomes	They are Non- ionic surfactant vesicle	Time consuming, drug leaching, and poor mechanical properties	Advantages over niosomes: More robust and efficient

LIMITATIONS[14]

1. The amphiphilic nature of a compound influences its synthesis.
2. It requires a lipid's surface and bulk interaction with drugs.
3. It requires covalent bonding to prevent drug leaking.
4. Pharmacosomes fusions and aggregates, and undergo chemical hydrolysis, occur upon storage.

COMPONENTS OF PHARMACOSOME FORMULATION[15]

The preparation of pharmacosomes requires three essential components.

i. Drugs

Drugs with active hydrogen atoms (-COOH, OH, NH2) can be esterified to lipids with or without a spacer chain, in an amphiphilic compound that aids membrane, tissue, and cell wall transfer in animals.

ii. Solvents

The solvents used in preparation of pharmacosomes should be of high purity and volatile in character. For the preparation of pharmacosomes, an intermediate polarity solvent is selected.

iii. Phospholipids

Phospholipids, they are two major type of phospholipids – Phosphoglycerides ans sphingolipids. are the major structural component of vesicle membrane. The most common phospholipid is phosphotidylcholine molecule, phosphotidylcholine are amphipathic molecules in which a glycerol bridge is linked to a pair of hydrophobic acryl hydrocarbon chain, with a hydrophilic polar head group, phosphocholine. Majority of the commercially available lecithin products contain 20% phosphotidylcholine.

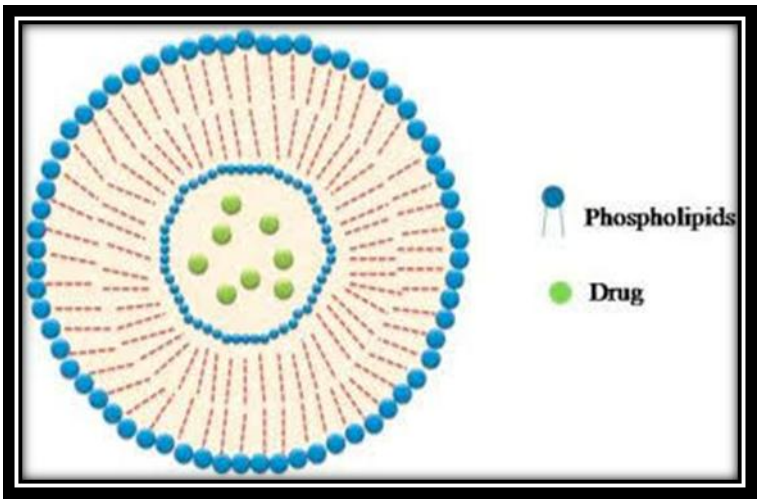

Figure 1: Pharmacosomes.

METHODS OF PREPARATION

1. Solvent Evaporation Technique

i. Hand-shaking method: In this process, the drug-lipid conjugate is combined with an suitable organic solvent, which forms a thin film on the round-bottom flask walls under vacuum and forms a vesicular suspension when hydrated with aqueous medium.[16]

ii. Rotary evaporator: iIn the solvent evaporation method, to prepare pharmacosomes, the drug is first acidified using the solvent so that the active hydrogen is available for complexation. The drug acid is then extracted into chloroform before being recrystallized. Different molar ratios of drug acid and PC are mixed to make the drug-PC complex. Correctly weighed PC and drug acid are dissolved in an appropriate volume of dichloromethane in a 100 mL round bottom flask.[17] The mixture is refluxed for one hour. The solvent is then evaporated under vacuum at 40° C in a rotary vacuum evaporator. After that, the leftovers are collected and dried completely.

2. Ether-Injection Technique

The drug-lipid combination is dissolved in an organic solvent in this method. This mixture is then slowly injected into a heated aqueous agent, which causes vesicles to develop. Amphiphiles condition is determined by their concentration. Amphiphiles introduce a monomer state while the concentration is low, but as the concentration rises, a range of structures, such as round, cylindrical, disc, cubic, or hexagonal structures, can be formed.[18]

3. Supercritical fluid process

This method is known as solution enhanced dispersion by complex supercritical fluid. The drug and lipid complex are mixed in a supercritical carbon dioxide fluid, and then passed through the nozzle mixture chamber to achieve high supersaturation. The rapid mixing of dispersion caused by the turbulent flow of solvent and carbon dioxide contribute to the formation of pharmacosomes.[19]

4. Alternative Approach

Synthesizing a biodegradable micelle-forming drug combination from the hydrophobic drug and a polymer consisting of polyxyethylene glycol and polyaspartic acid is an alternate method for generating pharmacosomes. This method has the benefit that, even if the micelle is diluted, the drugs are unlikely to precipitate due to the water solubility of monomeric drug conjunct.[20]

BIOAVAILABILITY ENHANCEMENT USING A PHOSPHOLIPID COMPLEX: A MECHANISTIC OUTLOOK

When taken orally, drugs with low solubility (BCS classes II and IV) or poor permeability (BCS classes III and IV) have shown a relatively low bioavailability.[21] Other factors that contribute to reduced bioavailability include the presence of the P-gp pump, which causes

naked drug efflux, the presence of metabolising enzymes, and ambient pH-mediated degradation.[22] As a result, drug delivery vehicles are required in order for medications to reach a desired level in the systemic circulation.[23] Phospholipid-drug complexes, in which the absorption process is identical to that of triglycerides and essential phospholipids, could be adopted for the very same absorption of drug moiety.

Structurally, the phospholipid is made up of two fatty acid chains connected to a glycerol (diacyl glycerol) molecule, which is hydrolyzed to liberate fatty acid, which causes it to be absorbed. When given orally, the drug-diacyl glycerol complex also undergoes hydrolysis. At a ph of ~ 1.5 in stomachs, some minor hydrolysis occurs, and the majority of it occurs in the small intestine. In the intestine, beginning with the duodenum, secretions from the liver, bile bladder, and pancreas are produced.[24,25]

The presence of phospholipases in the gut causes the hydrolysis of drug-diacyl glycerol, resulting in the release of fatty acid and the formation of drug-monoacyl glycerol. In the presence of phospholipases (especially phospholipase A2) in the intestine, the hydrolysis of drug-diacyl glycerol, resulting in the release of fatty acid and the formation of drug-monoacyl glycerol. Micellar vehicles are formed when the former drug, monoacyl glycerol, is conjugated with bile salts. They are hydrolyzed to form drug-monoacyl phospholipid vesicles, which are then taken up by enterocytes via passive diffusion. Enterocytes' acyl-coA enzymes convert drug-monoacyl phospholipids and endogenous diglycerides to diacyl phospholipids and triglycerides, respectively, in the smooth endoplasmic reticulum.[26]

Additionally, apoportein B-48 is integrated into the phospholipid vesicle in the golgi apparatus to produce nascent chylomicron. The chylomicron leaves the enterocyte via exocytosis and enters the lymph capillary, which takes it away from the intestine and escapes first-pass metabolism. At the thoracic duct link with a left subclavian vein, the chylomicrons transfer the drug complex into systemic circulation.[27] When a nascent chylomicron enters the systemic circulation, apolipoprotein C-II and apolipoprotein E are transferred to the nascent one by high density lipoprotein.[28,29]

The matured chylomicron releases the apolipoprotein C-II after storing the triglycerides, and they are then referred to as chylomicron remnants, which are commonly found in the liver for endocytosis and disintegration.[29] As a result, the drug phospholipid complex reaches the systemic circulation via the chylomicron and avoids first-pass metabolism. The drug-

phospholipid complex's mechanism enables for the absorption of drugs that are either not soluble or have undergone substantial first-pass metabolism.

PHARAMACOSOME CHARACTERIZATION

Pharmacosomes are characterised using the same evaluation approaches that are used to characterise other vesicular delivery systems. Pharmacosome characterisation is divided into two primary stages. The first phase involves characterising the prodrugs that make up the bilayer, while the second involves evaluating the vesicles.

i. Physicochemical characterization

1. Determination of melting point

The melting point of an organic molecule is a crucial parameter for assessing any structural changes. The melting point of prodrugs changes greatly from that of either pure drug or lipid throughout their synthesis. It has been demonstrated that a pharmaceutical molecule can enhance or decrease the melting point of the original drug.[30] The melting points of several of the drugs and their lipid conjugates are listed in Table 3.

Table 3: Melting points of the drugs and their lipid conjugates.

Drug	Melting point of drug	Drug derivative	Melting point of derivative
Chlorambucil	64-69	Dipalmitoyl prodrug	69-71
Flufenamic acid	133-134	Cholesteryl Flufenamate	145-148
Ganciclovir	250-252	Valaric acid prodrug	224-226
Pioglitazone	183-184	Butyroyloxymethyl prodrug	60-61
Propanolol	92.9	Palmitoyl propanolol prodrug	49
Theophylline	270-274	Acetyloxymethyl prodrug	163-166

2. Thin layer chromatography

TLC (thin layer chromatography) is a chemical characterisation technique that uses a simplified planar chromatographic technique.[31] This method can be used to verify the quality of raw materials and finished products, as well as the progress of drug-phospholipid conjugate synthesis. Compared to TLC32, complex technologies such as high performance thin layer chromatography (HPTLC) and high performance liquid chromatography (HPLC) provide faster separation, better resolution, and more accuracy[32]. When lipids are attached to a drug molecule, the parent drug's lipophilic character is increased, resulting in a change in retention time.

Table 4: Chromatographic analysis of drug's and their derivatives.

Drug	Mobile phase	drug	drug derivatives	Mobile phase	drug derivatives
Azauridine	Water-methanol (12:88)	2.50	3'-O-Stearoyl-6- azauridine	Water-methanol (12:88)	18.88
Butyric acid	Methanol (100%)	2.16	1 -butanoyl- 2-palmitoyl	Methanol (100%)	4.84
Paclitaxel	Methanol-water (80:20)	6	paclitaxel	Methanol-water (80:20)	7.5
Trifluridine TFT	Water-methanol (20:80)	2.33	5'- Hezanoyl TFT	Water-methanol (20:80)	3.60
zidovudine	Acetonitrile- 0.025 M phosphate buffered pH3 (15:85)	5.3	Butyrate ester prodrug	Acetonitrile- 0.025 M phosphate buffered pH3 (15:85)	8.8

3. Acyclovir Determination of solubility

The creation of a drug-phospholipid derivative is bound to have an impact on the drug's solubility profile. Drug conjugation with hydrophilic moieties improves the parent drug's water solubility, whereas conjugation with lipophilic moieties improves membrane permeability. Conjugation with amphiphilic moiety increases both absorption and permeability of the drug.[33] Solubility tests are carried out in water and buffer solutions with variable pH values. An excess amount of sample is introduced in various solvents in vials and allowed to equilibrate for 24 hours at regulated rpm in a shaker bath at 30ºC A known volume of sample is taken after saturation, and the amount of drug solubilized is measured using spectroscopic or chromatographic methods.[34]

Table 5: Solubility studies of drug and their derivatives.

Drug	Solubility in given solvent
Acyclovir	methanol (Freely soluble) Octanol (0.212 mM)
Mitomycin C	water (2.73 mM) sesame oil (0.0180 mM) IPM (0.0193 mM)
Propanolol	Aq.phase (392mM) Octanol(941mM)
Pioglitazone	Ethyl acelate (<30 M)
Thalidomide	Aq.phase (0.24mM) Octanol (0.27mM)

4. Determination of partition coefficient

When determining whether a drug is lipophilic or hydrophilic, the partition coefficient is the most commonly utilized quantitative factor. Determined using the shake flask method, generator column method, or high performance liquid chromatography.[35] SFM is the most extensively utilized method. To make up the stock solution, a precise amount of drug derivative is dissolved in an appropriate buffer solution. Aliquots of the solution are divided

and presaturated overnight in 1-octanol-aqueous systems. The two phases are vigorously shaken to ensure even distribution, and then kept in constant motion on the shaker at room temperature for 24 hours. Both phases are separated after centrifugation, and the amount of drug in each phase is determined using an appropriate analytical technique. In addition to experimental approaches, C logP® (biobyte Corp.), SlogP (Chemical Computing Group), VlogP (Accelrys Software), and other programmes can be used to measure partition coefficient. The addition of a phospholipid moiety to a drug frequently boosts its effectiveness.[36] The prodrug has a higher log P value than the drug itself, indicating lipophilicity. The differences in partition coefficient generated by conjugation of medications with different derivatives are summarised in Table 6.

Table 6: Partition coefficient of drug and their derivatives.

Drug	Log P (Drug)	Derivatives	Log P (Derivatives)
Doxorubicin	0.6	Acetyl doxorubicin derivative	1.67
Mitomycin C	-0.386	Pentyloxycarbonyl	2.053
Paclitaxol	3.20	Squalenoyl- paclitaxel prodrug	7.30
Thalidomide	0.49	Thalidomide methyl derivative	1.15
Propanolol	0.38	Acetyl- propanolol	0.62

5. Ultravoilate-visible spectroscopy

Ultraviolet-visible spectroscopy is a preliminary spectroscopic technique for determining absorption peak alterations caused by molecule structure changes. For pure drug, phospholipid, physical combination, and prodrug, the UV-visible spectrum is presented. Pure drugs and phospholipids show absorption peaks at the same wavelength as physical combinations. The formation of new bonds and the introduction of new neighbouring groups cause the peaks to move, confirming the synthesis of the prodrug.

6. Infrared spectroscopy

The production of prodrug is confirmed by comparing the infrared spectra of conjugate with individual components and physical combinations. The spectrum of conjugates differs significantly from that of individual components or physical mixtures due to chemical interactions between the drug and the phospholipid, which result in the formation of new bonds. If there is no substantial change in corresponding IR bands37, there is no interaction between the pure medication and the lipid.[37]

7. Nuclear Magnetic Resonance (NMR)

NMR is also useful for validating conjugate formation by examining the magnetic properties of various nuclei, such as hydrogen, carbon, and phosphorus. The shielding or deshielding effect of neighbouring nuclei in the phospholipid derivative can be related to the upfield or downfield shift in the NMR signals of separate nuclei.[38] In contrast to phosphoric acid at 0 ppm, the chemical shifts of 31P NMR are determined. Varied 31P-NMR spectral line forms result from the different degrees of motional freedom that occur in different phases of phospholipids.[39]

8. X-ray diffraction

X-ray diffraction can demonstrate drug-phospholipid conjugate formation. Crystalline drugs have distinctive concentrated peaks in X-ray diffraction pattern, where as phospholipids, which are amorphous, have wide peak. The physical mixtures contain both sharp and wide peaks due to the presence of both free drug and phospholipids. The absence or reduction in intensity of sharp peaks indicates the emergence of a drug-phospholipid conjugate.[40]

9. Differential Scanning Calorimetry (DSC)

DSC is a thermoanalytical technique for assessing drug-lipid compatability that provide most information about the possible interaction. The eradication of endothermic peak(s), development of new peak(s), change in peak shape and its onset, peak temperature/melting point, and relative peak area or enthalpy are all indication of interaction between drug-lipid.[41]

ii. Evaluation of vesicles

1. Surface morphology

In order to study the surface morphology of drugs, phospholipids, physical mixtures, and prodrugs scanning electron microscopy (SEM) or transmission electron microscopy (TEM) can be utilized. The purity of lipid used as well as form and as well as process including preparation method, rotational speed size , and vacuum applied determines the shape and size of pharmacosomes.[42]

2. Size distribution

Fraction and flow field flow fractionation (FFFF) coupled with refractive index, size exclusion chromatography (SEC), Photon co-relation spectroscopy (PCS), hydrodynamic chromatography, and static or dynamic light scattering detector can all be used to determine

the particle size distribution of pharmacososmes.[43,44] The combination of FFFF with multi angle light scattering (MALS) and dynamic light scattering (DLS) is a influential method for determining the exact particle size distribution in complicated heterogeneous and polydispersed mixtures is. Electron microscopy techniques such as SEM and TEM techniques in addition to quantitative data in the form of number of particles, it also provides qualitative information on vesicle size and shape. It also displays information exactly on thickness of the bilayer and how far apart the bilayers exist.[45]

3. Transition temperature

Amphiphilic molecules are notable for undergoing thermo tropic phase at temperatures well below their melting point. This phase behavior of vesicles membranes uncovers crucial features such as protein binding, fusion, permeability, and aggregation, all of which influence vesicle stability.[46] Differential scanning calorimetry, confocal fluorescence microscopy, and ultrasonic spectroscopy can all be used to detect the transition temperatures of amphiphilic substances.[47]

4. Lamellarity

Lamellarity of vesicle i.e. the number of consecutive lipid bilayers within a vesicle, is particularly important. Electromicroscopy (frozen fracture and cryo-electromicroscopy), spin-labelled lipids, epifluorescence microscopy, small angle x-ray scattering, trapped volume measurement, and 31P-NMR are methods used to determine vesicles lamellarity.[48]

5. Solubility

To determine the saturated solubility of pharmacomes in distilled water and phosphate buffer pH6.8 excess amount of preparation was added in a 100ml conical flask contatining respective solvent system. Each flask was closed with a stopper. These flasks were shaken at 50rpm in a rotary shaker. Then, at a certain interval of time, test samples were obtained, filtered, and diluted with the same solvent; the drug's absorbance was measured with a UV Visible Spectrophotometer at a specific λmax. The absorbance was then converted into concentration.

6. Entrapment efficiency

The centrifugation method was used to measure the entrapment efficiency of Pharmacosomes. A aliquot of Pharmacosomal dispersion was centrifuged at 5000 rpm for 35 minutes at 4°C in a laboratory centrifuge. The unentrapped medication was carefully

separated from the clear supernatant, and the absorbance was measured. The sediment in the centrifuge tube was rinsed three times with suitable solvent and diluted to 5 mL with same solvent, absorbance measured. Different concentrations of suitable solvents (1 g/mL-10 /10 mL) were used to create a calibration curve. The total amount of drug in a 1 mL dispersion was calculated from the supernatant and sediment.[49]

The following formula was used to determine the percentage of drug entrapment:

7. *In-Vitro* drug release studies

A 0.5 ml concentrated pharmacosomal suspension was placed in a test tube with a 20 mm opening diameter. A semi-permeable dialysis membrane was used to cover the open end, which was then fastened with a thread. Inverted, the test tube was placed over the surface of 100 mL water in a 250 mL beaker, with the membrane just touching the water surface. The test tube was held in place by a clamp attached to a stand. A magnetic stirrer was used to swirl the water in the beaker, ensuring that no vortex formed. The temperature was kept at 37˚c. The drug released from the pharmacosomes passes through the membrane and into the medium of the receptor chamber. The absorbances were measured using a UV-spectrophotometer against a blank of fresh media. Samples of 2 ml were obtained from the receptor chamber medium. To keep the volume of the medium constant in the beaker, 2 ml of new medium was introduced at the same time.[50,51]

8. Stability of pharmacosomes

Although pharmacosomes do not undergo destabilisation of lipid bilayer membrane as that of liposomes beause the drug is covilently bound to the phospholipid but the two major degradation pathway i.e. oxidation and hydrolysis results in reduction of shelf life of phospholipid based vesicles. In comparison to saturated fatty acids, unsaturated fatty acyl chains are more susceptible to oxidation. Phospholipid peroxidation can be reduced by utilizing pure form of phospholipids, storing them at a lesser temperature, protecting them from exposure to light and oxygen, and adding antioxidants.[50] Matrix-assisted laser-desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS), liquid chromatography mass spectrometry (LCMS), and HPLC were used to study the degradation of the drug-phospholipid combination. The appearance phospholipid due to hydrolysis of prodrug indicates that the prodrug has been subjected to enzymatic degradation.[52]

APPLICATIONS OF PHARMACOSOMES.[53,54]

Table 7: Applications of pharmacosomes in various drugs.

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.
Acyclovir	Solubility is increased, as is the hemolytic reaction.
Pindolol	Bioavailability has improved.
Diclofenac	Solubility and drug loading have both improved.

Conclusion and Future Prospective

Despite the limitations of being fused and aggregated, vesicular systems remain an important tool for targeted and sustained drug release in the pharmaceutical industry. In the case of both natural and synthetic active ingredients, pharmacosomes can lower toxicity and offer a huge potential for increasing drug delivery. Based on the research findings, it could be deduced that by enhancing solubility, permeability, and metabolic stability, this technology can help improve bioavailability in the GIT. Because of these characteristics, it qualifies as a good delivery vehicle for pharmaceuticals with restricted solubility (BCS class II), permeability (BCS class III), or both (BCS class IV). This technique also has advantages of being less expensive, easier to formulate, and upgrade than other lipid-based drug delivery systems. However, more effort must be put into understanding the mechanism of action and investing in non-belayed phases.

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