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An updated review on pharmacosomes, a vesicular drug delivery system

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ABSTRACT

Novel drug delivery system mainly consents about achieving the targeted concentration to release the drug at targeted site by using carrier system, altering the structure and microenvironment around the drug. Especially drugs which are having narrow therapeutic window are difficult to formulate, with the advantage of novel drug delivery systems like particulate, polymeric carrier, macromolecular and cellular carriers. They are used to reduce complications as well as release the drug in a determined fusion at targeted site. In vesicular drug delivery system drug binds covalently to the lipid molecule by which the drug release is in a controlled manner and also drugs which are of hydrophilic or lipophilic nature can be delivered by using vesicular drug delivery systems. The release of drug from the vesicles depends on the physicochemical properties of both the drug and carrier. Vesicular drug delivery includes liposomes, niosomes, transferosomes, pharmacosomes, electrosomes, ethosomes etc. Of all these drug delivery systems pharmacosomes are having more advantages like no leakage or loss of drug, stability, high entrapment efficiency etc, pharmacosomes may be hexagonal aggregates , ultrafine vesicular and micellar forms. Both synthetic and natural drugs which are facing difficulties like low solubility and low permeability can be effectively formulated and can achieve required pharmacokinetic and pharmacodynamic parameters. Pharmacosomes are prepared by hand shaking method, ether injection, solvent evaporation method, anhydrous co-solvent lyophilyzation, supercritical fluid approach and other alternative methods they are characterized by complex determination, surface morphology, drug entrapment, solubility, drug lipid compatibility, crystal state measurement, dissolution studies and *in vitro* drug release rate.

Keywords: Pharmacosomes, covalently, vesicular drug delivery system, hexagonal aggregates, micellar, ultrafine.

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INTRODUCTION

Novel drug delivery system (NDDS) primarily focuses on formulation, technologies, and systems for transporting a pharmaceutical compound in the body as needed to safely achieve its desired therapeutic effects. Safely novel drug delivery is far better than the conventional dosage form. Novel drug delivery system should full fill the following requirements:

- Firstly, it delivers specific amount of drug at a rate directed by the needs of the body, over the period of treatment.
- Secondly, it delivers the active drug moiety to the targeted site of action.[1]

Advantages of novel drug delivery systems

- Optimal dose at the right time and right location
- Efficient use of expensive drugs and excipients
- Cost efficient and also show more benefits than other novel drug delivery systems.
- Better therapy and improved comfort and standard of living
- The adverse effects and also toxic effects are minimized

Basic modes of novel drug delivery system are:

1. Targeted drug delivery system.
2. Controlled drug delivery system.
3. Modulated drug delivery system.

Vesicular drug delivery systems

Nowadays vesicular drug delivery is one of the advanced novel drug delivery system. Biological origins of the vesicles were first reported by the Bingham in year of 1965, so they termed as “Bingham bodies”. [2]

From the past few years, vesicles have evolved by the vehicle of choice in novel drug delivery. Vesicular drug delivery has immense worth in genetic engineering, immunological, membrane, biological and diagnostic techniques. Vesicular drug delivery plays a vital role in modeling membrane as well as in the targeting and delivery of active principle. [3] Drug carriers are the substance which used in the process of drug delivery and they help to improve the drug effectiveness, selectivity, and/or safety in administration of drug.

Drug carriers release the drug in systemic circulation in a controlled manner. This can be attained either by slow release of drug over a long period of time or by actuated release at the drug target by some stimulants such as changes in pH, application of heat, and activation by light. Especially, in the case of drugs with poor water solubility and/or membrane permeability, drug carriers are used to improve their pharmacokinetic and the bioavailability. [4]

Liposomes consist of either natural or synthetic phospholipids. [5] They consist of hydrophilic, lipophilic and amphiphilic moieties which help in accommodation of the drug molecule having a wide array of solubility. These vesicles are variable and controllable and their properties can be supervised by modifying the vesicle structure, size, lamellarity, tapped density, surface charge and concentration. It can be a depository and release drug in a controlled way. [6]

The pharmaceutical carriers are classified as particulate type, polymeric, macromolecular and cellular carriers. Particulate types of carriers are also known as colloidal carriers which include lipid particles of low and high density lipoproteins, low density lipoproteins and high density lipoproteins. [7] A wide variety of drug carriers are being studied and each of them has unique benefits and ill effects. More prominent type of drug carriers are niosomes, liposomes, polymeric micelles, microspheres, and nanoparticles. The different methods present in binding the drug with carrier include adsorption, encapsulation and covalent bonding. Different type drug carriers utilize different type of attachment methods. [4]

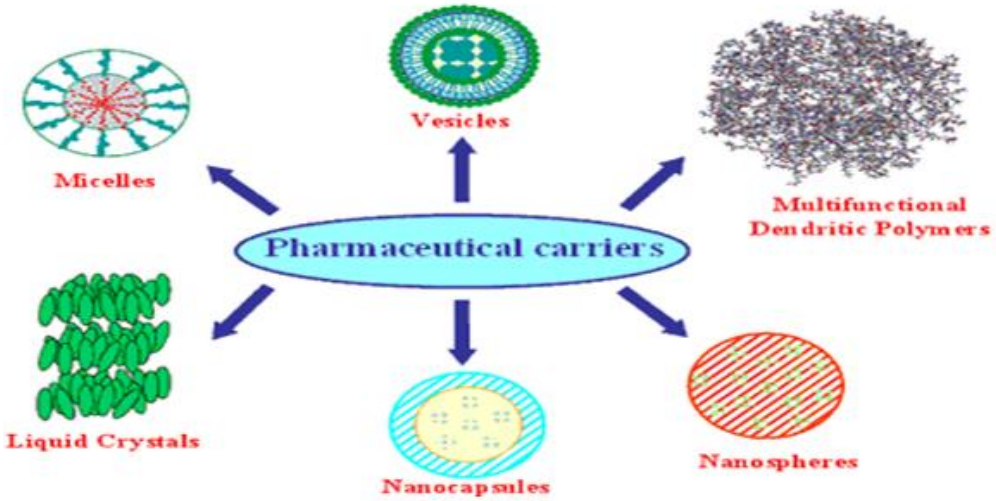

Figure 1: Pharmaceutical carriers of pharmacosomes

Advantages of vesicular drug delivery system

- They extend the presence of the drug in systemic circulation.
- Vesicular drug delivery is an efficacious method for reducing the drug toxicity and targeting to the site of action.
- This system improves the bioavailability principally in case of the poorly aqueous soluble drugs.
- In this systems both the hydrophilic and lipophilic drugs are embodied.
- It sustains the release of drugs by delaying the time of elimination through they are rapidly metabolizable. [8]
- They overcoming the problems regarding stability, solubility and degradation of the drug.
- The limitations of conventional dosage forms can be triumph by acting as drug reservoir by encapsulating the drug.
- The carriers of the vesicular drug delivery system are biocompatible and biodegradable as they are similar to biomolecular functions and structure.
- Vesicular systems are associated with some complications of drug carrier such as particulates and loading of drug passively, which may lead to decrease in drug loading efficiency and leakage of drug during formulation, storage and delivery *in vivo* .[9]

Pharmacosomes:

Pharmacosomes are part of the novel drug delivery system. They were first introduced by vaizoglu and Speriser in 1968. [10] Pharmacosomes are determined as the colloidal dispersions, drugs covalently bound to the lipids, and may exists as ultra fine vesicular, micellar, or hexagonal aggregates, on the basis of the chemical structure of the drug-lipid complex. [10, 11] The system is composed by linking a drug (pharmakon) to a carrier (soma), so they termed as "Pharmacosomes".

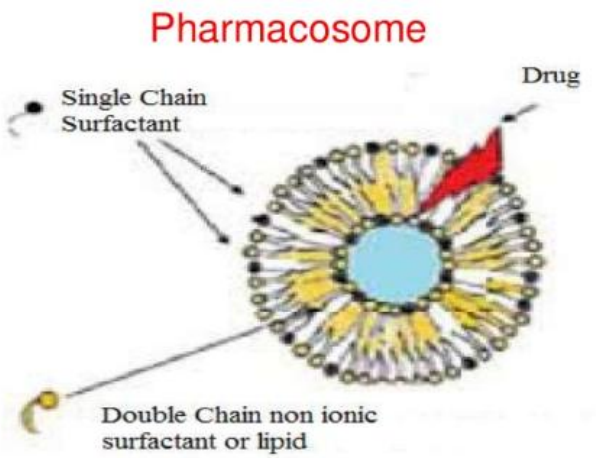

Figure 2: Pharmacosomes

- Pharmacosomes assist in drug targeting and controlled release of drug to achieve desired dose.
- They bearing unique advantage over liposome and niosome vesicles and are serve as an altering to conventional vesicles.
- Problems like drug incorporation, leakage, or insufficient shelf life of drug can be avoided in pharmacosomes.
- The concept of creation of the vesicular pharmacosomes is in accordance with bulk interaction and surface of lipids with drug substances.
- Drugs occupying an active hydrogen atom (-COOH, -OH, $-NH_2$, etc.) can be esterified into the lipid form, with or without spacer chain that results in formation of an amphiphilic compounds, which helps in the permeation into the target site.
- The prodrug amalgamates have both hydrophilic and lipophilic properties, so they acquire amphiphilic nature and therefore found to decrease the interfacial tension, and mesomorphic behavior at elevated concentrations. [7,11]

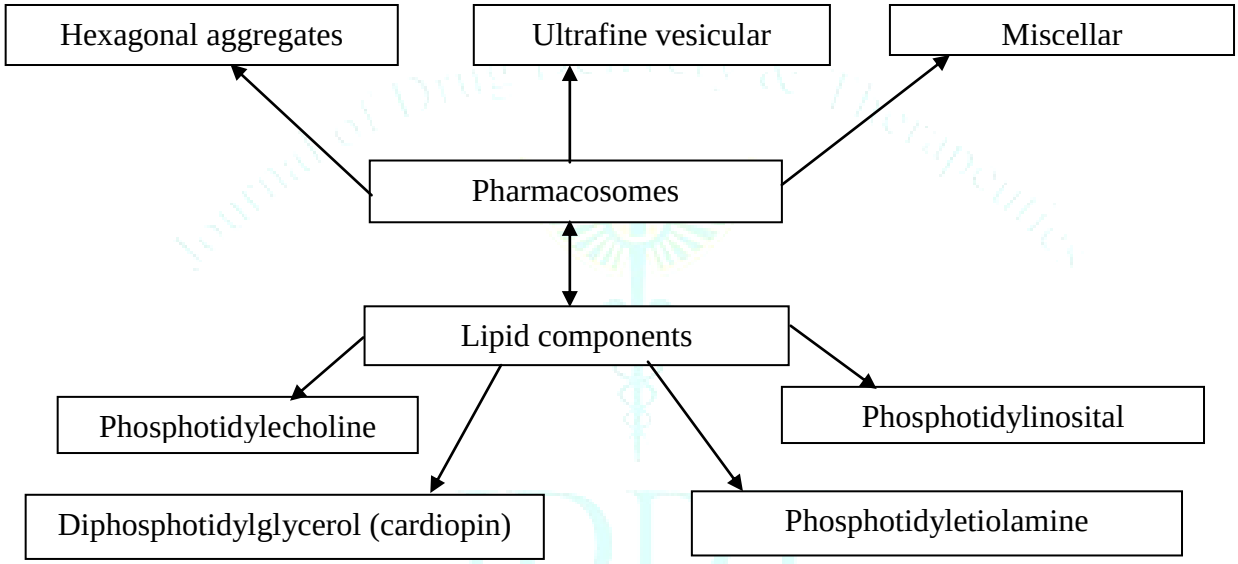

Figure 3 Components of pharmacosomes

Advantages of pharmacosomes:

- When compared with other categories of lipid based delivery systems, pharmacosomes exhibit better results in many ways.
- The drug-lipid complex depends upon the phase transition temperature but independent on rate of release as it is covalently bounded to the lipid.
- No leaching will occur as drug is bounded to the lipid by covalent bonding.
- Delivers drug at the specific site and site targeted.
- By enzymatic methods like hydrolysis drug is released from the lipid polymer.
- The metabolism of the drug depends on the spacer, length of chain in lipid, functional groups and size of the drug during its absorption.
- They reduce the cost of therapy.
- They are suitable for the both lipophilic and hydrophilic drugs.
- The aqueous solution of the amphiphiles exhibits concentration dependant aggregation.
- The drug and carrier are covalently linked together so, entrapment efficiency is high and predetermined.
- Drug release of pharmacosomes is by hydrolysis.
- They improves the bioavailability majorly incase of poorly soluble drugs.
- They reduce the adverse effects and toxicity.
- In pharmacosomes, there is no need to remove the unentrapped drug when compared to liposomes where the free drug should be removed
- Drugs like bupranolol hydrochloride, pindolol maleate, acyclovir, taxol, etc by using of pharmacosomes drug delivery has therapeutic performance has been improved.[9,10]

Disadvantages of pharmacosomes:

- Water insoluble drugs are encapsulated relatively in a less hydrophobic region within membrane bilayer rather than relatively large surface area.
- The storage of pharmacosomes undergoes fusion and aggregation as well as chemical hydrolysis.[12]

Salient features of pharmacosomes:

- Pharmacosomes can be administered in various route such as orally, extra vascular and intravascular.
- The drug conjugates with lipids and results in high entrapment efficacy in predetermined fashion.
- There is no problem when the drug is incorporated into the lipid.
- They consist of both hydrophilic and lipophilic properties so they can easily pass through the cell membrane, walls, or tissues either by action of endocytosis or exocytosis.
- The physicochemical characters of the drug-lipid complex affect the stability of pharmacosomes.

Limitations of pharmacosomes:

- Amphiphilicity is required in the compound.
- Both the surface and bulk interaction may be observed.
- Drug should be covalently bounded to the lipid.

Components of pharmacosomes:

The components for pharmacosomes preparation are: Drug, Solvent and Lipid.

Drugs

Any drug containing active hydrogen atom (-COOH, -OH, -NH_2, etc) can be esterified with the lipid, with or without spacer chain. Facilitates membrane, tissue, cell wall transfer in the organisms is due to its amphiphilic nature.

Solvents

They should be high pure and volatile in nature, and should be selected based on the intermediate polarity for their preparations.

Lipids

- Phospholipids are the major components of biological membrane; majorly two types of phospholipids are used namely phosphoglycerides and sphingolipids.
- The most common type of phospholipids is Phosphotidylecholine moiety.
- Phosphotidylecholine is an amphiphilic molecule in which a glycerol bridges links a pair of hydrophobic acylhydrocarbon chains with hydrophilic polar head group phosphocholine.[13]

Applications of phosphotidylecholine

- Phosphotidylecholine place a vital role in supporting cell membrane integrity and basic biological process.
- Impairment of cell membrane and its repair which results in liver disorders can be managed and also acts as a hepato-protective agent by acting as supplement source of choline.
- It can also promote breakdown of collagen and prevent fibrosis and cirrhosis.
- It also shows protection against hepatitis A, B & C.
- It can acts as supplement in treatment of Alzheimer's disease.
- It also have therapeutic role in cancer patients.
- It shows reduction of serum cholesterol level by which it can shows as anti-hyper lipidimic.

Preparation of pharmacosomes:

There are two methods which have been employed to prepare pharmacosomes;

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.[13]

2) Ether injection method

- The drug-lipid complex is dissolved in specified volume of ether.
- Then the above mixture is slowly injected into a heated buffer solution, resulting in the formation of the vesicles.
- The nature of vesicle especially the shape depends on the concentration.
- The variety of structures may be formed that are, round, cylindrical, disc, cubic, or hexagonal type depending on the amphiphilic state.[9,14,15]

3) Anhydrous co-solvent lyophilyzation method

- Drug and phospholipids are dissolved in solution of dimethyle sulfoxide containing glacial acetic acid.
- Then the above mixture is agitated to get clear liquid and then freeze-dried overnight at condenser temperature.
- The complex obtained is flushed with nitrogen and stored at 4°c.[16]

4) Supercritical fluid process

- This method is known as solution enhanced dispersion by complex supercritical fluid. Drug and lipid complex are premixed in a supercritical fluid of carbon dioxide, then high super saturation is obtained by passing through the nozzle mixture chamber.
- The turbulent flow of solvent and carbon dioxide results in fast mixing of dispersion leading to the formation of pharmacosomes.

5) Solvent evaporation method

- In the solvent evaporation method of preparing the pharmacosomes, the drug is first acidified so that the active hydrogen might be available for complexation.
- The drug acid is then extracted into chloroform and subsequently recrystallized. The drug-PC complex is prepared by associating drug acid with PC in various molar ratios.

- The accurately weighed PC and drug acid are placed in a 100 ml round bottom flask and dissolved in sufficient amount of dichloromethane.
- The mixture is refluxed for one hour. Then the solvent is evaporated off under vacuum at 40 ° C in a rotary vacuum evaporator.
- The dried residues are then collected and placed in vacuum desiccator for complete drying.

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. [13]
- Diluting lyotropic liquid crystals of amphiphilic drug by Muller-Goymann and Hamann.[17]
- 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.[18]

Characterization of pharmacosomes

1) Complex determination

Using correlation spectrum the formation of both conjugate and complex can be contingent upon inspecting with that of discrete constituents and also with their mixture using FTIR spectrum. [19]

2) Surface morphology

The surface morphology can be predicted using Scanning Electron Microscopy (SEM) or Transmission Electron Microscopy (TEM). The shape and size of pharmacosomes are prone to variations by some variables such as rotation speed, vaccum applied, Purity grade of phospholipids or the method used.

3) Drug entrapment

To know the amount of drug present in the drug complex estimated quantity of pharmacosomes were transferred into a suitable flask containing known volume of solvent in which drug is soluble. Mix the above contents thoroughly or sonicate, leave the contents for 24 hrs without disturbing and estimate the dug present by using UV spectroscopy or HPLC.

4) Solubility

Solubility is determined by placing the known amount of phospholipid complex in a screw caped penicillin bottle containing aqueous phase buffer solution of varying pH (2-7.4) and organic phase like 1- Octonol with continuous shaking at a temperature of 37^{o}c for 24hrs. Then both the layers will be separated and samples were analyzed using HPLC or UV spectrophotometer [20]

5) Drug lipid compatibility

Differential scanning electron microscopy is a thermo analytical technique used to determine drug-lipid compatibility and their interactions. Thermal response is studied by using separate sample and heating them in a sample pan, which is closed. The nitrogen gas is plugged, and the temperature is maintained in a definite range with a specific heating rate.

6) Crystal state measurement

The crystal nature of the drug can be determined by using X-ray diffraction technique. The tube voltage and tube current can be regulated in the X-ray generator. Copper lines may be used as the source of radiations. The overall integrated intensity of all reflection peaks are projected by area under curve of X-ray diffraction pattern that specifies the specimen characteristics. [21]

7) Dissolution studies

Dissolution studies *in vitro* are done by using various models available using different buffers, then the results obtained are estimated on the basis of activity of the drug. [22]

8) *In vitro* drug release rate

The *in vitro* drug release rate is estimated by reverse dialysis bag technique. In this method pharmacosomes are introduced inside the dialysis bag and the receiver phase is placed outside. Dialysis bag containing the continuous phase and they are suspended in a vessel containing the donor phase and stirred at predetermined time intervals, each dialysis bag is removed and the contents are analyzed for drug release. An advantage of this technique is increase in the membrane surface area available for transport from the donor to receptor compartment. Another advantage of this technique is the increased efficiency in terms of staffing as a consequence of reduction in number of steps. [21]

Applications of pharmacosomes

- Pharmacosomes possess better stability and shelf life compared to other vesicular drug delivery systems.
- Absorption and permeation of the drug can be enhanced formulating in to pharmacosomes.
- The transportation of drug across the biological membranes is due to the vesicular formation as they have the capacity to interact with the membranes, due to their transitions from vesicle to micelle by altering the transition temperature
- By altering the temperature at the targeting site pharmacosomes have the capacity to deliver the drug in the targeted site especially in the case of cell specific drug vehicles.
- Pindolol diglyceride, Amoxicillin, Taxol, Cytrabine, Dermatansulfate, Bupranolol hydrochloride etc showed increase in pharmacological action by formulating into pharmacosomes.
- The mechanism of action of drugs and non bilayer phases can be studied by using pharmacosomes.
- PEGylation and biotinyzation are used in current research in the production of pharmacosomes.
- Ophthalmic drug delivery with a modified corneal drug transport and release by diluting with tears where the drug should be of amphiphilic in nature
- Phytoconstituents such as flavonoids, glycosides, xanthones etc, shows both increase in pharmacokinetic and pharmacodynamic actions.
- The ability of transportation of biological components like proteins and amino acids by using pharmacosomes[23]
- Optimizing the preparation of 20(S)-protopanaxadiol pharmacosomes showed encapsulation efficiency of pharmacosomes.[25]

- Pharmacosomes found to increase solubility and permeability of drug than conventional dosage forms in Diclofenac and Aceclofenac. [21] [24]
- Pharmacosomes employed to prepare Tetrahydrofuran injection method and studied in the *in-vitro* behavior in rats for didanosine, by which they observed that pharmacosomes possess prolonged action in both targeted site and liver. [26]
- Pharmacosomes formulated using 3, 5-dioctanoyl-5-fluro-2-deoxyuridine with a central composite design resulted in formation of regulated pharmacosomes, shows a great targeting efficiency in both *in-vitro* and enhanced drug capacity to pass through blood brain barrier. [27]
- The suppression in hemolytic reaction of pharmacosomes of acyclovir by noticing the interaction of pharmacosomes with erythrocytes and plasma proteins after absorption. [28]
- Improved bioavailability and reduced gastrointestinal toxicity in aspirin was predicted by preparing aspirin phospholipid complex. [29]

CONCLUSION

In pharmacosomes drug is bound to the polymer by covalent, van der Waal and hydrogen bonding. The drug will be released will by hydrogen bonding. Pharmacosomes achieve desired dose by drug targeting in controlled release. The pro-drugs can be amalgamated acquiring amphiphilic in nature. Both the lipophilic and hydrophilic drugs can be suitable candidates, by covalent bonding with the polymer shows increase in entrapment efficiency. Pharmacosomes reduce toxicity and can improve therapeutic performance of drug. A biodegradable micelle forming drug conjugates increasing hydrophilicity of drug, Whereas change in the ratio of polymers show enhance cytoprotection by formulation of "vesicular constructs "using aqueous domain .

Table 1: Comparing various methods and their outcomes of drugs using pharmacosomes [21, 24, 26, 30-39]

S. no	Drug	Polymers	Solvents	Bonding	Technique used	Results	Final product
1	Geniposide	Phospholipids	Tetrahydrofuran	Hydrogen, van der waal forces	Vaccum evaporation method	Lipid solubility character of Geniposide was increased	Dry powdered pharmacosomes
2	Naproxen	Soya lecithin	Diethyl ether, ethanol, acetone	Covalent bond	Ether injection method	Solubility enhanced and achieved controlled drug release	Pharmacosomes gel
3	Aspirin	Soya phosphotidylecholine	Dichloromethane	Covalent bond	Solvent evaporation	Improved drug delivery controlled drug delivery	Pharmacosomes
4	Aceclofenac	Soya phosphotidylecholine	Dichloromethane	Covalent bond	Solvent evaporation	Enhancement of solubility and dissolution profile and improved bioavailability	Pharmacosomes
5	Furosemide	Soya phosphotidylecholine	Methyl alcohol	Hydrogen bond	Vaccum evaporation	Release and permeation increased	Pharmacosomes
6	Ketoprofen	Soya phosphotidylecholine	Dichloromethane	-	Solvent evaporation	Improved solubility, dissolution profile	Pharmacosomes
7	Etodolac	Soya lecithin	Acetone, dichloromethane, methanol	-	Thin film hydration	Increased solubility, entrapment efficiency and sustained relaese	Pharmacosomes gel
8	Rosuvastatin	Soya lecithin	Chloroform, dichloromethane	-	Solvent evaporation	Sustained drug release and improved bioavailability	Pharmacosomes

9	Losartan	Soya lecithin	Dichloromethane, hydrochloric acid, chloroform	Covalent bond	Solvent evaporation	Increased solubility, dissolution profile and bioavailability	Pharmacosomes
10	Acyclovir	Phosphotidylecholine	-	-	Tetrahydrofuran injection method	Increased solubility and also hemolytic reaction	Pharmacosomes gel
11	Bupranolol	Soya lecithin	-	Covalent bond	-	Enhanced effect on intraocular pressure and enhance lymph transport.	Pharmacosomes
12	Pindolol	Soya lecithin	-	-	Film and ether injection method	Increased bioavailability	Pharmacosomes
13	Ibuprofen	Phosphotidylecholine	Dichloromethane, chloroform	-	-	Increased bioavailability	Pharmacosomes
14	Didanosine	Soya lecithin	Chloroform, acetone, methanol	-	Tetrahydrofuran injection method	Increased solubility, dissolution profile and bioavailability	Pharmacosomes
15	Diclofenac	Phosphotidylecholine	Dichloromethane	Covalent bond	Solvent evaporation	Improved solubility and drug loading	Pharmacosomes

Table 2: Comparison of various vesicular drug delivery systems [41-48]

S. no	Type	Ingredients	Method	Advantages	Disadvantages
1	Liposomes	Phosphotidylecholine, cholesterol, sphingolipids, steroids, polymeric materials.	Sonication method French pressure cell Freeze-thawed liposomes Lipid film hydration by hand shaking or freeze drying	Suitable for delivery of hydrophilic, hydrophobic drugs. Biocompatible suitable for controlled drug delivery localized action in particular tissue	High production cost leakage (or) fusion of encapsulated drug phospholipid undergo hydrolysis (or) oxidation reaction short half life and low solubility
2	Niosomes	Surfactants, cholesterol, alkyl amides, fatty acids and amide acid compounds	Sonication Microfluididation Hand shaking Ether injection Reverse phase evaporation Bubble method Active transport	Stable, increase the stability of entrapment drug Improved oral bioavailability of poorly absorbed drugs PEG-glucose conjugates on the surface of niosomes significantly improved tumor targeting of an encapsulated paramagnetic agent	Time consuming In efficient drug loading Requires specialized equipments
3	Pharmacosomes	Solvents, phospholipids	Sonication Hand shaking method Ether injection Anhydrous co-solvent lyophilyzation	No leaching will occur as drug bounded to the lipid by covalent bonding Delivers the drug at the site specific and site targeted They reduces the cost therapy Reduces the adverse effects and toxicity	The storage of pharmacosomes undergoes fusion, aggregation and hydrolysis Water insoluble drugs are encapsulated relatively in a less hydrophobic region within membrane bilayer or relatively large surface are

4	Phytosomes	Phospholipids, commercial products, flavonoids	Solvent evaporation Salting out lyophilyzation Rotary evaporation Anti solvent precipitation	As the efficacy increases the dosage requirement is also reduced They have better stability By increasing solubility of bile to herbal origin Phytoconstituents Phytosomes enhance the liver targeting Time period of action is increased	Duration of action is short Phytoconstituents is rapidly eliminated from Phytosomes
5	Transferosomes	Phospholipids, surfactants, alcohols, dye, buffering agents	Thin film hydration method Modified hand shaking method Vortexing-sonication method Suspension homogenization process Aqueous lipid suspension process Centrifugation process	High entrapment efficiency in case of lipophilic drugs They protect the encapsulated drug from metabolic degradation	They are chemically unstable because of prediosition to oxidative degradation Their formulation and manufacturing expensive
6	Aquasomes	Polymers, ceramic core	Preparation of core Carbohydrate coating Immobilization of drugs	Aquasomes preserves the conformational integrity and biochemical stability of bioactive molecules Aquasomes exhibit physical properties of colloids Aquasomes avoids reticuloendothelial clearance or degradation by other environmental challenges Aquasomes suspensions contain colloidal range biodegradable nanoparticles, they are more concentrated in liver and muscles	--
7	Virosomes	Unilamellar phospholipid membrane, proteins	Selection of virus Selection of antigen Reconstituted of Virosomes	Biodegradable , biocompatible and non-toxic No disease transmission risk Applicable for drugs(anti-cancer, proteins, peptides, antibiotics, fungicides) Drug delivery into cytoplasm of target cell Noautoimmunogenity or anaphylaxis	Shorter shelf life Non availability of data related to the chronic use of virosomal carrier system Poor quality of raw materials Manufacturing problems
8	Bilosomes	Non-ionic surfactants, bile salts, charge inducers	Hot homogenization Thin film hydration	They allow small quantities of antigen to be effective and also increase efficacy of antigen which are weak when injected Less toxicity envelop suitable for a wide range of therapeutic agents They removes cold chain requirement for preparation such as vaccine	-
9	Emulsomes	Lipid core, antioxidants, negatively charged particles, surfactants, phospholipids, cholesterol	Lipid film formation Reverse phase evaporation High-pressure extrusion technique Sonication method Cast film Ethanol injection Detergent removal technique	Emulsomes increase the solubility and bioavailability of poorly aqueous soluble drugs Hydrophilic head-group facing the water on both sides They are composed of lipid core, lipids are used to develop oral controlled drug They provide significantly modify the pharmacokinetics of drugs	-

10	Ethosomes	Phosphotidylecholine, phosphotidic acid, phosphotidyle serine, cholesterol, alcohol, non-ionic surfactants	Cold method Hot method	It contains non-toxic raw materials in formulation Ethosomes drug delivery can be applied widely in pharmaceutical, veterinary, cosmetic field Simple method for drug delivery in comparison to iontophoresis and phonophoresis and other complicated method	Poor yield If shell looking is ineffective then the coalescence of ethosomes may occur and fall apart on transfer into water Leakage of product during transfer from organic to water media

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