

## PHARMACOSOMES: A NOVEL CARRIER FOR TARGETED AND CONTROLLED VESICULAR DRUG DELIVERY SYSTEM

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Article Received on  
25 May 2014,

Revised on 20 June 2014,  
Accepted on 15 July 2014

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### ABSTRACT

Vesicular drug delivery system showed application in targeted and controlled drug delivery and transport the active agent to the tissue through biological barriers. Novel vesicular drug delivery carrier intend to delivery the drug at a rate directed by the need of body during the period of treatment and channel the active moiety to the site of action providing target. Pharmacosomes are one of the most promising approaches for this system to increase the bioavailability of drug substance, improve drug stability, and prolong the existence of the drug in systemic circulation and target drugs to specific site in the body. Pharmacosomes are amphiphilic, colloidal dispersion prepared

from drug lipid conjugates with or without additional surfactant. Targeted pharmacosomal drug delivery system is very useful in cancer therapy because such pharmacosomes should selectively localize anticancer drug at the tumour site, thus reducing the toxicity of the drug to normal cell and improving their therapeutic activity. The great advantages of pharmacosomes are it may be minimize drug degradation and diminished the toxicity (GIT).

**KEY WORD:** Vesicular system, Concept of targeting, Carrier, Pharmacosomes.

### INTRODUCTION

New drug delivery system development is mostly based on promoting the therapeutic effects of a drug and minimizing its toxic effects by increasing the amount and diligence of a drug in the vicinity of a target cell and reducing the drug exposure of non target cells. This is still largely based on Paul Ehrlich's magic bullet concept. Novel drug delivery systems will be discussed in the general categories of topical, oral, vaginal, implanted, ophthalmic, and parenteral preparations. New drug delivery systems can provide clinical benefits, therapeutic benefits and economic benefits, such as <sup>1</sup>

1. Improvement of patients' compliance.
2. Reduction of adverse effects.
3. Optimization of the duration of action of the drug.
4. Decreasing dosage frequency.
5. Controlling the site of release.
6. Maintaining constant drug levels.
7. Decreasing the number of concomitant medications a patient must take.
8. Decreasing the need for interventions.
9. Simplifying administration regimens.
10. A reduction in the overall use of medicinal resources.
11. An overall reduction of health care costs.
12. Improvement of patients' acceptance of the treatment.
13. Avoidance of costly interventions such as laboratory services.
14. Allowing patients to receive medication as out patients and possibly.

A system that formulates or tool that delivers therapeutic agent to desired body site and provides timely release of therapeutic agent, such a system by which a drug is delivered can have a significant effect on its efficacy. In recent decades, significant advances in drug-delivery systems have enabled more effective drug administration. To minimize drug degradation and loss, to prevent harmful side-effects and to increase drug bioavailability and the fraction of the drug accumulated in the required zone, various drug delivery and drug targeting systems are currently under research and development.<sup>2,3</sup>

The therapeutic effectiveness of a drug molecule mainly depends upon the ability of the dosage form to deliver the medicament to its site of action at a rate and amount sufficient to elicit the desired pharmacological response. This aspect of the dosage form is referred as physiologic availability, biologic availability or simply bioavailability. Thus the term bioavailability is defined as the rate and the extent to which the ingredient or active moiety reaches to systemic circulation and becomes available at the site of action. As per the definition of bioavailability, a drug with poor bioavailability is one with poor aqueous solubility, slow dissolution rate in biological fluids, poor stability of dissolved drug at physiological pH, poor permeation through bio-membrane and extensive pre-systemic metabolism.<sup>4</sup>

Colloid drug-delivery systems are used to increase the bioavailability of drug substances, to improve drug stability, to sustain and control drug-release rates, to target drugs to specific sites in the body, and to stimulate the immune system.<sup>5</sup> Lipid based drug delivery system now a day is experiencing resurgence due to new drug application.<sup>6</sup> They were adopted to achieve many objectives which included targeted drug delivery, enhanced drug transport through various biological membranes or prolonging and controlling drug release.<sup>7</sup>

### **Concept Of Targeting<sup>8</sup>**

The concept of designing specified delivery system to achieve selective drug targeting has been originated from the perception of Paul Ehrlich, who proposed drug delivery to be as a “magic bullet”. It was the very first report published on targeting (Paul Ehrlich 1902) describing targeted drug delivery as an event where a drug-carrier complex /conjugate delivers drug exclusively to the pre selected target cell in specific manner. Bangham’s observation on phospholipids hexagonal liquid crystals, that they are perm-selective to the ions in manner similar to bio-membrane, led to discovery of artificial vesicular system based on phospholipids’ amphiphiles. Gregoriadis, 1981 described drug targeting using novel drug delivery systems as “old drugs in new cloths”.

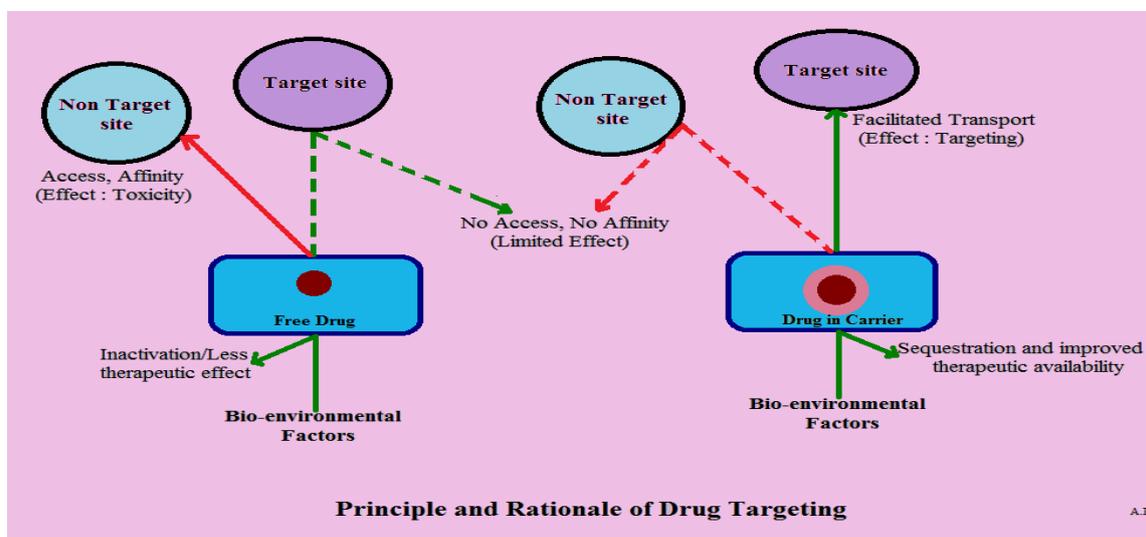
A number of essential aspects which should be considered for the designing of drug delivery systems to achieve this goal include target, carrier, ligands and physically modulated components. Targeting drug delivery implies for selective and effective localization of pharmacologically active moiety at pre-selected targets in therapeutic concentration, while restricting its access to non-target normal cellular linings, thus minimizing toxic effects and minimizing therapeutic index. The targeted delivery to previously in accessible domains e.g. intracellular sites, virus, bacteria and parasites offers distinctive therapeutic benefits.

### **Level Of Targeting**

Targeting drug delivery may be achieved by using carrier system where reliance is placed on exploiting both intrinsic pathway that these carriers follow and the bio-protection that they can offer to drugs during transit through the body. The various approaches of vectoring the drug to the target site can be broadly classified:

1. Passive targeting
2. Inverse targeting
3. Active targeting
4. Dual targeting

5. Double targeting
6. Combination targeting



Drug targeting can improve the therapeutic index of a drug by optimizing the access, amplitude, and nature of interactions with the pharmacological receptor. Drug targeting can also protect the drug and the body from any unwanted and deleterious disposition.<sup>9</sup>

The Food and Drug Administration defines bioavailability as “the rate and extent to which the active ingredient or active moiety is absorbed from a drug product and becomes available at the site of action. The “targeted bioavailability” is a term which extends the idea that the true bioavailability of a drug is the fraction of the administered dose that reaches the site of action.<sup>10</sup> Targeting is the ability to direct the drug-loaded system to the site of interest. Its potential benefits of in drug delivery and drug targeting. Improve efficacy offers great potential benefits to patients, and Improving delivery techniques that minimize toxicity and drug delivery are focused on crossing particular physical barriers, such as the blood brain barrier in order to better target the drug and finding alternative and acceptable routes for the delivery of protein drugs other than via the gastro-intestinal tract, where degradation can occur.<sup>11</sup>

### Vesicular System

Vesicular systems have been employed as drug delivery carriers for many decades. They were adopted to achieve many objectives which included targeted drug delivery, enhanced drug transport through various biological membranes or prolonging and controlling drug release. These included liposomes, niosomes, transfersomes, ethosomes, vesosomes,

colloidosomes, and pharmacosomes.<sup>12</sup> Encapsulation of drug in vesicular structures prolongs the existence of drug in systemic circulation and reduces the toxicity, if selective uptake can be achieved. The phagocytic uptake of the systemic delivery of drug loaded vesicular carriers provides an efficient means for delivery of drug directly to the site of infection, leading to reduction of drug toxicity with no adverse effects. This system reduces the cost of therapy by bioavailability improvement of medication, especially in case of poorly soluble drugs. They can incorporate both hydrophilic and lipophilic drugs. This system delays drug elimination of rapidly metabolizable drugs and functions as sustained release system. Vesicular drug delivery system solves the problem of drug instability, insolubility and rapid degradation.<sup>13, 14</sup>

Novel vesicular drug delivery carriers intend to deliver the drug at a rate directed by the need of body during the period of treatment, and channel the active moiety to the site of action providing target.<sup>15</sup> Thus, the marvellous pharmaceutical research in understanding the causes of low oral bioavailability has led to the development of novel technologies to address these challenges. One of the technologies is to design a prodrug with the required physicochemical properties to improve the oral bioavailability.<sup>16</sup>

Various technologies are in use to enhance the oral bioavailability of drugs, having poor aqueous solubility. These include the use of micronization, nanosizing, crystal engineering, solid dispersions, cyclodextrins, and solid lipid nanoparticles and other colloidal drug delivery systems such as microemulsions, self emulsifying drug delivery systems, self micro emulsifying drug delivery systems and vesicular drug delivery systems. The technology which has the potential to solubilise varying quantities of poorly water soluble drugs with the help of lipids protects the drug from harsh GI environment and prolongs the existence of drug in systemic circulation, is the vesicular drug delivery system.<sup>17</sup>

Vesicular drug delivery systems delay drug elimination of rapidly metabolizable drugs, and function as sustained release systems. This system solves the problems of drug insolubility, instability, and rapid degradation.<sup>18</sup> Many technologies and systems have been investigated to evade this barrier and one of most promising technique is to formulate novel vesicular carrier for drug delivery through the skin. These novel drug delivery system bear great potential for dermal delivery. Among them lipidic and non-lipidic vesicular system like liposome, niosome, transferosome, ethosome and pharmacosomes have been suggested to overcome the problems assemblies of one or several concentric lipid bilayers formed.<sup>19</sup>

Pharmacokinetics is to be exhaustively studied, in order to exploit more advantage of this system.<sup>20</sup> Recently different carrier systems and technologies have been extensively studied with the aim of controlling the drug release and improving the efficacy and selectivity of formulation. Vesicular delivery system provides an efficient method for delivery to the site of infection, leading to reduce of drug toxicity with no adverse effects. It may be reducing cost of therapy by improved bioavailability of medication, in case of poorly soluble drugs.<sup>21</sup>

Vesicular drug delivery system has some of the advantage like:<sup>22</sup>

1. Prolong the existence of the drug in systemic circulation and, diminish the toxicity if selective uptake can be achieved due to the delivery of drug directly to the site of infection.
2. Improve the bioavailability in case of poor soluble drug.
3. Both hydrophilic and lipophilic drugs can be incorporated.
4. Delays elimination of quickly metabolizable drugs and thus function as sustained release systems. Suitable drug carriers can help to reach the goal. A suitable carrier should load the drug effectively to protect it against undesired clearance in the skin and the carrier should retain the drug long enough, on, in, and also below the skin barrier.<sup>23</sup>

### Carriers<sup>8</sup>

Carrier is one of the most important entities essentially required for successful transportation of the loaded drug. They are drug vectors, which sequester, transport and retain drug en route, while elute or deliver it within or in the vicinity of target. Carrier can do so either through an inherent characteristic or acquired to interact selectively with biological targets or otherwise they are engineered to release the drug in the proximity of target all lines demanding optimal therapeutic index.

Silent Features of ideal drug carrier

1. It must be able to cross anatomical barriers and in case of tumour chemotherapy tumour vasculature.
2. It must be recognized specifically and selectively by the target cell and must maintain the avidity and specificity of the surface legands.
3. The linkage of the drug and the directing unit should be stable in plasma, interstitial and other bio-fluids.
4. Carrier should be non-toxic, non-immunogenic and biodegradable or macromolecule and after recognition and internalization.
5. The carrier system should release the drug moiety in side the target organs tissues or cells.

6. The bio-modules used for carrier navigation and site recognition should not be ubiquitous otherwise it may cross over the sites, defeating the concept of targeting.

### Carrier system used for targeted drug delivery

Carrier system	Types
Colloidal carriers	Vesicular system: Liposome's, Niosomes, Pharmacosomes, Virosomes, Immunoliposomes Microparticulate system: Microparticules, Nanoparticules, Magnetic microspheres, Nanocapsules
Cellular Carriers	Resealed erythrocytes, serum albumin, antibodies, platelets, leucocytes
Supramolecular Delivery System	Micelles, Reverse micelles, Mixed micelles, Polymeric micelles, liquid crystals, lipoproteins
Polymer Based System	Signal sensitive, Muco-adhesive, Biodegradable, Bioerodible, Soluble Synthetic Polymer carrier
Macromolecular Carrier	Proteins, glycoproteins, Neo glycoproteins, Artificial viral envelopes (AVE) Glycosylated water soluble polymer (poly-L-lysine) Mabs, Immunological Fab Fragments, Antibody enzyme complex and Bispecific Abs Toxins, Immunotoxin and rCD4 toxin conjugates Lectins and Polysacchrids

**Ideal Properties of Drug-Carrier Systems** The drug carrier should accumulate selectively at the required site, achieve sufficient drug loading, be able to release the drug at the appropriate rate at the site of action, be stable in vitro and in transit to the target site in vivo, be biodegradable, be non-toxic and non-immunogenic, be easy and inexpensive to prepare, and be sterile for parenteral use.<sup>24</sup> They can be tailored for site-specific delivery of drugs.<sup>25</sup> When developing these formulations, the goal is to obtain systems with optimized drug loading and release properties, long shelf-life and low toxicity.<sup>26</sup> Carrier-mediated drug delivery has emerged as a powerful methodology for the treatment of various pathologies. The therapeutic index of traditional and novel drugs is enhanced via the increase of specificity due to targeting of drugs to a particular tissue, cell or intracellular compartment, the control over release kinetics, the protection of the active agent or a combination of the above.<sup>27</sup> They can deliver the drug in the target organ using lower drug doses in order to reduce side effects.<sup>28</sup> To pursue optimal drug action, functional molecules should be transported by a carrier to the site of action and released to perform their task, for which the carrier itself should be non toxic ,biodegradable, and of suitable shape and size to accommodate wide variety of substances.<sup>29</sup>

They are versatile drug carriers, which can be used to control retention of entrapped drug in the presence of biological fluids, controlled vesicle residence in the systemic circulation or other compartment in the body and enhanced vesicle uptake by target cells.<sup>30</sup> Carrier mostly used for topical / transdermal drug delivery in the pharmaceutical fields.<sup>31</sup> In the formulation of topical dosage forms, attempts are being made to utilize drug carriers that ensure adequate localization or penetration of drug within or through the skin in order to enhance the local and minimize the systemic effects or to ensure adequate percutaneous absorption.<sup>32</sup> Topical preparations are formulae which are applied directly to an external body surface by spreading, rubbing, spraying or instillation. The topical route of administration has been utilized either to produce local effect for treating skin disorder or to produce systemic drug effects.<sup>33</sup>

The penetration rate of a topical agent may be influenced by drug-vehicle, drug-skin, and vehicle-skin interactions.<sup>34</sup> Advantages associated with particulate carriers are (a) high drug payload, (b) possibility of both covalent and ionic association between the drug and the carrier, and (c) high degree of protection available to drug after encapsulation.<sup>35</sup> Advantage of colloidal carriers is that they can be tailored for site-specific delivery of drugs. The physicochemical properties of a drug carrier need to be optimized for a targeted drug therapy.<sup>36</sup>

#### Pharmacosomes

Pharmacosomes are amphiphilic, colloidal dispersions of drugs covalently bound to lipids, and may exist as ultra fine vesicular, micellar, or hexagonal aggregates, depending on the chemical structure of the drug lipid complex. These are the lipid based drug delivery systems that are appropriately elaborated as the colloidal dispersions of drugs having a covalent, electrostatic or hydrogen bonding with lipid. They are rightly termed as “pharmacosomes” due to the linking of a drug (pharmakon) to a carrier (soma).<sup>37, 38</sup> Pharmacosomes are amphiphilic lipid vesicular systems that have shown their potential in improving the bioavailability of poorly water soluble as well as poorly lipophilic drugs.<sup>39</sup>

These amphiphilic drug-lipid complexes are stable and more bioavailable with low interfacial tension between the system and the GI fluid, thereby facilitating membrane, tissue, or cell wall transfer, in the organism. The salient features of pharmacosomes are, increased entrapment efficiency, easy removal of untrapped drug from the formulation, no loss of drug due to leakage, no problem of drug incorporation and no influence of uncaptured volume and

drug-bilayer interaction on entrapment efficiency.<sup>40</sup> A part from other methods used for modifying the solubility, the complexation with phospholipids has been found to show improvement in both absorption as well as permeation of the active constituent.<sup>41</sup>

Phospholipids play major role in drug delivery due to its amphiphilic nature that can modify the rate of drug release for the enhancement of drug absorption across biological barriers. Developing of amphiphilic drug-lipid complex or pharmacosomes may prove to be a potential approach for improving the bioavailability.<sup>42</sup> Water insolubility of many drugs is often manifested in poor gastrointestinal absorption and bioavailability, intra- and interindividual bioavailability variations, and food interaction in their absorption after oral administration. A phospholipid-based drug delivery system use for water-insoluble drugs.<sup>43</sup>

Drug targeting will ensure high therapeutic efficacy. But may be even more important it will reduce side effects. The reduction or even prevention of side effects can also be achieved by controlled release. Drug carriers such as particulates and externally triggered carriers have widely been explored. Vaizoglu and Speiser used the word 'pharmacosomes' to describe the colloidal dispersions prepared from drug-lipid conjugates with or without additional surfactants. Pharmacosomes have been not deeply studied, possibly because no appropriated theory supports the new dosage form and no appropriated drugs and lipids are selected.<sup>44</sup>

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, also reduce the cost of therapy by improved bioavailability of medication especially in case of poorly soluble drugs. Pharmacosomes are suitable for incorporating both hydrophilic and lipophilic drugs to improve their solubility, bioavailability and minimize the gastrointestinal toxicity of various drugs. So, developing the drugs as pharmacosomes may prove to be a potential approach to improve the bioavailability of drugs and also to minimize the GI toxicity.<sup>45</sup> Pharmacosomes being amphiphilic compounds facilitate membrane, tissue, or cell wall transfer in the organism. The amphiphilic characters help pharmacosomes to reduce interfacial tension and at higher concentrations exhibit mesomorphic behaviour. This decrease in the interfacial tension leads to an increase in the contact area thereby increasing bioavailability of drugs.<sup>46</sup>

**MERITS**<sup>47</sup>

1. Suitable for both hydrophilic and lipophilic drugs.
2. The aqueous solution of these amphiphiles exhibits concentration dependent aggregation.
3. High and predetermined entrapment efficiency as drug and carrier form a stoichiometrically defined unit covalently linked together.
4. Volume of inclusion doesn't influence entrapment efficiency.
5. No need of removing the free, untrapped drug from the formulation which is required in the case of liposomes.
6. As drug is covalently bound, membrane fluidity has no effect on release rate, but in turn depends upon the phase-transition temperature of the drug-lipid complex. No leakage of drug takes place as the drug is covalently linked to the carrier.
7. Drug can be delivered directly to the site of infection.
8. Drug release from pharmacosomes is by hydrolysis (including enzymatic).
9. Their degradation velocity into active drug molecule, after absorption depends very much on the size and functional groups of the drug molecule, the chain length of the lipids, and the spacer.
10. Improves bioavailability especially in the case of poorly soluble drugs.
11. Reduction in adverse effects and toxicity.
12. Reduced cost of therapy.

**ADVANTAGES**<sup>48</sup>

1. They are an effective tool to achieve desired therapeutic goals such as drug targeting and controlled release.
2. High and predetermined entrapment efficiency as drug and carrier form a stoichiometrically defined unit covalently linked together.
3. Volume of inclusion doesn't influence entrapment efficiency.
4. No need of removing the free, untrapped drug from the formulation which is required in the case of liposomes.
5. Improves bioavailability especially in the case of poorly soluble drugs.
6. Drug carriers such as liposomes, nanoparticles, microemulsions which have led to low drug-loading efficiency, physical stability such as fusion, aggregation, sedimentation and drug leakage during preparation, preservation etc is absent in pharmacosomes.

## MATERIALS FOR PHARMACOSOMES<sup>49</sup>

There are three essential components for pharmacosome preparation.

### 1. Drugs

Drugs containing active hydrogen atom (-COOH, OH, NH<sub>2</sub>) can be esterified to the lipid, with or without spacer chain and they forms amphiphilic complex which in turn facilitate membrane, tissue, cell wall transfer in the organisms.

### 2. Solvents

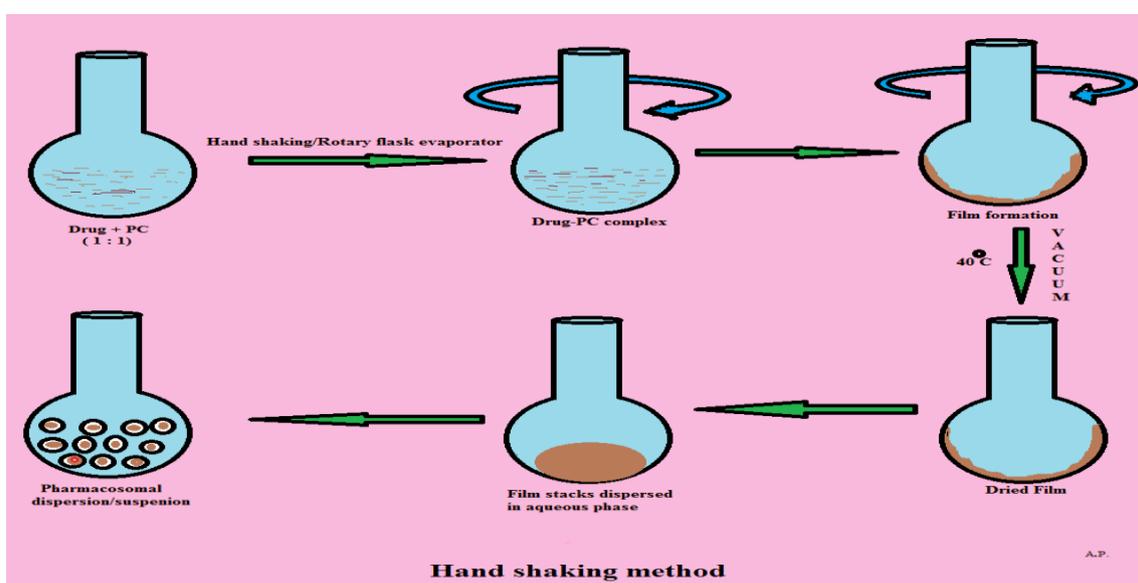
For the preparation of Pharmacosomes, the solvents should have high purity and volatile in nature. A solvent with intermediate polarity is selected for pharmacosome preparations.

### 3. Lipid

Phospholipids are the major structure component of biological membranes, where two type of phospholipids generally used- phosphoglycerides and spingolipids. The most common phospholipid is phosphotidyl choline molecule. Phosphotidylcholine is an amphipathic molecule in which a glycerol bridges links a pair of hydrophobic acyl hydrocarbon chains, with a hydrophilic polar head group, phosphocholine.

## FORMULATION OF PHARMACOSOMES<sup>50,51</sup>

1. Solvent evaporation method / Hand shaking method : Firstly a mixture of drug and lipid are dissolved in a volatile organic solvent such as dichloromethane .Thereafter solvent is evaporate using rotatory evaporator in round bottom flask which leaves a thin film of solid mixture deposited on the walls of flask. Then dried film hydrated with aqueous medium & readily gives a vesicular suspension.



2. Ether injection method: In this method solution containing drug-lipid complex is slowly injected into a hot aqueous medium through gauze needle and vesicle is formed readily.
3. Supercritical fluid process (Solution enhanced dispersion by complex supercritical fluid) - Drug and lipid complex are dissolved in a supercritical fluid of CO<sub>2</sub>, then mix into nozzle mixing chamber.
4. Anhydrous co-solvent lyophilisation method: Drug powder and phospholipids dissolved in 1 ml of Dimethyl sulfoxide (DMSO) containing 5% glacial acetic acid, after that agitates the mixture to get clear liquid. Freeze-dried overnight at condenser temperature. Then resultant complex flushed with nitrogen & stored at 4°C.
5. Other approach: Another approach for producing pharmacosomes was recently developed in which a biodegradable micelle forming drug conjugate was synthesized from the hydrophobic drug dexamethasone and a polymer composed of polyoxyethylene glycol and polyaspartic acid. This method has the benefit that although it may be possible to dilute out the micelle, the drug will probably not precipitate because of the water solubility of the monomeric drug conjugate. Approaches have been done to attach drugs to various glyceride-like groups, and the resulting amphiphilic molecules have been spontaneously dispersed. They were labelled pharmacosomes because of their tendencies to form unilamellar vesicles. It was suggested that these molecules should enhance lymph transport.

### **Evaluation Of Pharmacosomes**<sup>52</sup>.

**These are evaluated for the following parameters**

#### **Solubility**

To determine the change in solubility due to complexation, solubility of drug acid and drug-PC complex was determined in pH 6.8 phosphate buffer and n-octanol by the shake-flask method. Drug acid (50 mg) (and 50 mg equivalent in case of complex) was placed in a 100-mL conical flask. Phosphate buffer pH 6.8 (50 mL) was added and then stirred for 15 minutes. The suspension was then transferred to a 250 mL separating funnel with 50 mL n-octanol and was shaken well for 30 minutes. Then the separating funnel was kept still for about 30 minutes. Concentration of the drug was determined from the aqueous layer spectrophotometrically.

### **Drug Content**

To determine the drug content in pharmacosomes of drug (e.g: diclofenac-PC complex), a complex equivalent to 50 mg drug was weighed and added into a volumetric flask with 100 mL of pH 6.8 phosphate buffer. Then the volumetric flask was stirred continuously for 24 h on a magnetic stirrer. At the end of 24 h, suitable dilutions were made and measured for the drug content by UV spectrophotometrically

### **Scanning Electron Microscopy (SEM)**

To detect the surface morphology of the pharmacosomes, SEM of the complex was recorded on a scanning electron microscope.

### **Differential Scanning Calorimetry (DSC) <sup>53</sup>**

Differential scanning calorimetry (DSC) experiments were performed with differential scanning calorimeter. Samples of pure drug, mixture of soya lecithin and drug-loaded multilamellar pharmacosomes were subjected to DSC analysis. The analyses were performed on 5 mg samples sealed in standard aluminum pans. Thermograms were obtained at a scanning rate of 10°C/min. Each sample was scanned between 0°C to 250°C. The temperature of maximal excess heat capacity was defined as the phase transition temperature.

### **X-Ray Powder Diffraction (XRPD)**

The crystalline state of drug in the different samples was evaluated using X-ray powder diffraction. Diffraction patterns were obtained on a Bruker Axs-D8 Discover Powder X-ray diffractometer. The X-ray generator was operated at 40 kV tube voltages and 40 mA tube current, using lines of copper as the radiation source. The scanning angle ranged from 1 to 60° of 2 $\theta$  in the step scan mode (step width 0.4°C/ min). Drug acid, phosphatidylcholine 80% (Lipoid S-80) and the prepared complex were analyzed.

### **Dissolution Study**

*In vitro* dissolution studies of drug PC complex as well as plain drug were performed in triplicate in a USP six station dissolution test apparatus, type II at 100 rpm and at 37°C. An accurately weighed amount of the complex equivalent to 100 mg of drug acid was put into 900 mL of pH 6.8 phosphate buffer. Samples (3 mL each) of dissolution fluid were withdrawn at different intervals and replaced with an equal volume of fresh medium to maintain sink conditions. Withdrawn samples were filtered (through a 0.45-mm membrane filter), diluted suitably and then analysed spectrophotometrically.

## CONCLUSION

Vesicular carriers proved that they are very promising novel drug delivery system with respect to biocompatibility, reduced toxicity and also reduce dose frequency and provide the targeted and controlled release quality that would be essential for oral, topical and parenteral rout of drug administration. Pharmacosomes followed all above significance for therapeutic effectiveness in terms of duration of action. Its amphiphilic nature produces greater advantage for both lipohilic and hydrophilic drug. It may be increase the bioavailability of drug, improve drug solubility and stability prolongs existence of the drug in systemic circulation. Further research in this area will allow better control over drug release in vivo and long term safety data allow in the therapy more effective.

## REFERENCES

1. Loyd V. Allen, Jr., Nicholas G. Popovich, Howard C. "Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems" Wolters Kluwer & Lippincott Williams & Wilkins Publication, 9th edition, Page no. 646-650
2. Mahammad Rafi Shaik, Madhuri Korsapati and Dinakar Panati "Polymers in Controlled Drug Delivery Systems" International Journal of Pharma Sciences vol. 2, No. 4 (2012): 112-116 ISSN: 2320-6810
3. Priyanka R Kulkarni, Jaydeep D Yadav, Kumar A Vaidya, "Liposomes: A Novel Drug Delivery System" International Journal of Current Pharmaceutical Research, Vol 3, Issue 2, 2011, ISSN- 0975-7066
4. Bhatt D.A., Pethe A.M., Lipid Technology-A Promising Drug Delivery System for Poorly Water Soluble Drugs, International Journal of Pharmaceutical Research and Development, 2(7), 2010, 1-11.
5. James Swarbrick, "Encyclopedia of pharmaceutical technology" 3rd edition Vol.1 Informa Healthcare USA,
6. Atmaram Pawar, Anuprita Lange, et al, 2013, "Investigation of cochleates as carrier for topical drug delivery" International journal of pharmacy and pharmaceutical science vol.5 Issue2, ISSN-0975-1491
7. Ibrahim A. Alsarra, Amel y, K.K.Jain, et al 2010, "Vesicular systems for Intanasal drug delivery" Chapter 8 Drug delivery to the central nervous system, Human Press a part of springer science business media, llc
8. S.P.Vyas, R.K.Khar, "Targeted and Controlled Drug Delivery" Novel Carrier System, CBS Publisher and Distributers, 1st edition 2002, Page no. 39-42

9. James Swarbrick, "Encyclopedia of pharmaceutical technology" 3rd edition Vol.1, Informa Healthcare USA,
10. Binghe Wang, Teruna Siahaan, Richard Soltero, "Drug Delivery :Principles and Applications", A John Wiley & Sons Inc. Publication, page no.75-76
11. Priyanka R Kulkarni, Jaydeep D Yadav, Kumar A Vaidya,. "Liposomes: A Novel Drug Delivery System" International Journal of Current Pharmaceutical Research, Vol 3, Issue 2, 2011, ISSN- 0975-7066
12. Ibrahim A. Alsarra, Amel Y. Hamed, Fars K. Alanazi, and Gamal M. El Maghraby. K.K. Jain (ed.), Drug Delivery to the Central Nervous System, Neuromethods Chapter 8 Vesicular Systems for Intranasal Drug Delivery A Humana Press, a part of Springer Scienc Business Media Page no. 182
13. Kumar R., Kumar S., Jha S.S., Jha A.K., Vesicular System-Carrier for Drug Delivery, Der Pharmacia Sinica, 2(4), 2011, 192-202.
14. Gupta S., Singh R.P., Lokwani P., Yadav S., Gupta S.K., Vesicular System as Targeted Drug Delivery System: An Overview, International Journal of Pharmacy and Technology,3(2), 2011, 987- 1021.
15. Biju S.S., Talegaonkar S., Mishra P.R., KharR.K., Vesicular Systems: An Overview, Indian Journal of Pharmaceutical Sciences,68(2), 2006, 141-153ed and controlled release of drug.
16. Ettmayer P., Amidon G.L., Clement B., Testa B., Lessons Learned from Marketed and Investigational Prodrugs, Journal of Medicinal Chemistry, 47, 2004, 2393-2404
17. Bajaj H., Bisht S., Yadav M., Singh V., Bioavailability Enhancement: A Review, International Journal of Pharmacy and Biological Sciences, 2(2), 2011, 202-216
18. Stuti Gupta, Ravindra Pal Singh, Priyanka Lokwani, Sudhir Yadav, Shivjee K. Gupta International Journal Of Pharmacy&Technology IJPT June-2011 Vol. 3 Issue No.2 987-1021 Page 989 ISSN: 0975-766X
19. Gyati shilakari et al., 2013 ,. "Novel vesicular carrier for topical drug delivery and their application's" International Journal of pharmaceutical sciences and research , ISSN0976-044x
20. Mayank Gangwar, Ragini Singh, RK Goel, Gopal Nath "Recent advances in various emerging vescicular systems: An overview" Asian Pacific Journal of Tropical Biomedicine (2012)S1176-S1188
21. Amit Kumar Jha, Ravi Kumar, et al 2011,. "Vesicular system – Carrier for drug delivery" Pelagia Research library coden (USA) ISSN:0976-8688

22. Saurabh Bansal, Chandan Prasad Kashyap, Geeta Aggarwal and SL Harikumar “A Comparative Review on Vesicular Drug Delivery System And Stability Issues” International Journal of Research in Pharmacy and Chemistry, 2012, 2(3) ISSN: 2231-2781
23. G. Cevc, U. Vierl, S. Mazgareanu Functional characterisation of novel analgesic product based on self-regulating drug carriers, International Journal of Pharmaceutics 360 (2008) 18–28
24. James Swarbrick, “Encyclopedia of pharmaceutical technology” 3rd edition Vol.1 Informa Healthcare USA
25. Xiaoling Li, Bhaskara R. Jasti, “Design of Controlled Release Drug Delivery Systems” McGraw-Hill eBooks Page no. 315-357
26. P. Dwarakanadha Reddy, D. Swarnalatha, “Recent Advances in Novel Drug Delivery Systems” International Journal of Pharm Tech Research Vol.2, No.3, pp 2025-2027, July-Sept 2010, CODEN (USA) ISSN : 0974-4304
27. Dimitrios Missirlis, Development of a novel drug delivery system based on polymeric, thermoresponsive, hydrogel nanoparticle, Page no.3-4
28. Jose Juan Escobar-Chavez<sup>1</sup>, Isabel Marlen Rodriguez-Cruz and Clara Luisa Dominguez-Delgado Chemical and Physical Enhancers for Transdermal Drug Delivery Pharmacology Edited by Dr. Luca Gallelli InTech Published online page no.415 14, March, 2012 Published in print edition March, 2012 ISBN 978-953-51-0222-9
29. Dr. Rakesh P. Patel, Hardik Patel and Ashok H. Baria, Formulation and evaluation of liposomes of ketoconazole” International journal of drug delivery technology, 2009.1(1)16-23.
30. Parveen Goyal, Kumud Goyal et al., “Liposomal drug delivery system: Clinical application”, Acta Pharm. 55(2005), 1- 25.
31. Jose Juan Escobar-Chavez<sup>1</sup>, et al, [www.intehopen.com/download/pdf/32136](http://www.intehopen.com/download/pdf/32136) Mar 14, 2012
32. C.R. Kokare, K.R. Mahadik et al., “Formulation and evaluation of topical liposomal gel for fluconazole”, Indian Journal of Pharmaceutical Education and Research, 2010,
33. Doaa A. Helal et al Formulation and evaluation of fluconazole topical gel”, International Journal of Pharmacy and Pharmaceutical Science 2012, ISSN-0975-1491.
34. H.M. El Laithy and K.M.F. El-Shaboury., 2002, “The development of cutaneous lipogels and gel microemulsion for topical administration of fluconazole” AAPS Pharm sci tech.

35. Patrick J. Sinko, Yashveer Singh “Martin’s physical pharmacy and pharmaceutical sciences: physical chemical and biopharmaceutical principles in the pharmaceutical sciences”, Sixth Edition, 2011, 2006 Lippincott Williams & Wilkins, a Wolters Kluwer business, page .594-624
36. Xiaoling Li, Bhaskara R. Jasti, Design of Controlled Release Drug Delivery Systems McGraw-Hill Companies. 2006 Page no. 316-318
37. De Pintu Kumar , De Arnab, “Pharmacosomes : A Potential Vesicular Drug delivery system” International Research Journal of Pharmacy, 2013, 3(3) ISSN 2230-8407
38. Meenakshi Chauhan, Tanu Goyal, Ashwani Singh Rawat, Pharmacosome: “Opning new doors for drug delivery system”, International Journal of Pharmacy and Pharmaceutical Sciences, Vol 4, Suppl 3, 2012, ISSN- 0975-1491
39. Ajay Semalty, Mona Semalty, Devendra Singh, M.S.M. Rawat Development and physicochemical evaluation of pharmacosomes of diclofenac, Acta Pharm. 59 (2009) 335–344.1.
40. Amandeep Kaur, Neha Sharma and S.L. Harikumar Design and development of ketoprofen Pharmacosomes for oral delivery, Pharmacophore (An International Research Journal) 2013, Vol. 4 (4), 111-119 USA CODEN: PHARM7 ISSN 2229-5402
41. Balasubramanian J, Narayanan N , Pharmacosomes: A novel method of Colloidal dispersions in Drug Delivery Discovery Pharmacy, Volume 4, Number 10, April 2013 ISSN 2278 – 5426 EISSN 2278 – 5418
42. A.Semalty, M.Semalty, D. Singh, M.S.M. Rawat, “Development and characterization of Aspirin-Phospholipid complex for improved drug delivery” International Journal of Pharmaceutical Science and Nanotechnology, Vol. 3, Issue 2, 2010
43. Technology Michael J. Rathbone, Jonathan Hadgraft, Michael S. Roberts, “Modified-Release Drug Delivery” Marcel Dekker, Inc. 2003 ISBN: 0-8247-0869-5 Page. 151- 154
44. Yiguang Jin, Li Tongc, Ping Ai , Miao Li , Xinpu Houb Self-assembled drug delivery systems . Properties and in vitro in vivo behavior of acyclovir self-assembled nanoparticles (SAN) International Journal of Pharmaceutics 309 (2006) 199–207
45. Sunil Kamboj\*, Vipin Saini, Nancy Maggon, Suman Bala, Vikas Chander Jhawar Novel Vesicular Drug Carriers for Bioavailability Enhancement International Journal of Pharmaceutical Sciences Review and Research Rev. Res., 22(1), Sep – Oct 2013; n 19, 92-97 ISSN 0976 – 044X

46. Tanu Goyal, Ashwani Singh Rawat, and Meenakshi Chauhan, “ Pharmacosomes : opning new doors for drug delivery” International Journal of Pharmacy and Pharmaceutical Sciences ISSN- 0975-1491 Vol 4, Suppl 3, 2012
47. Kavitha D, Naga Sowjanya J, Shanker Panaganti, Pharmacosome : An emerging vesicular system” International Journal of Pharmaceutical Sciences Review and Research Volume 5, Issue 3, November – December 2010; Article-030 ISSN 0976 – 044X
48. Saurabh Bansal, Chandan Prasad Kashyap, Geeta Aggarwal and SL Harikumar “A Comparative Review on Vesicular Drug Delivery System And Stability Issues” International Journal of Research in Pharmacy and Chemistry, 2012, 2(3) ISSN: 2231-2781
49. Jitendra L Patel, Praful D Bharadia, A Review on: Pharmacosome As novel vesicular drug delivery system World Journal of Pharmaceutical research Volume 1, Issue 3, 27 June 2012 456-469. Review Article ISSN 2277 – 7105
50. Ujjwala Bhingare, Dr.S.S.Khadabadi, Nita Shinde, Pharmacosomes: A Novel Drug Delivery System International Journal of Pharmaceutical Research & Allied Sciences Volume 3, issue 1 (2014),14-20 , ISSN 2277-3657
51. Mugdha Karde, Harshal Pawar , Rachel Geevarghese, Jaikisan Khatri,. Development and Validation of RP-HPLC Method for estimation of Valproic acid in dissolution study of its formulation International Journal of Pharmacy and Pharmaceutical Sciences ISSN- 0975-1491 Vol 4, Suppl 5, 2012
52. Sreedevi.A, A.Swetha, Ch.Meenakshi, B.Rohit, Pharmacosomes – A Review International Journal of Pharmaceutical Sciences Review and Research Volume 12, Issue 1, January – February 2012; Article-020 ISSN 0976 – 044X
53. Mansoori M.A., Jawade S., Agrawal S., Khan M.I., Formulation Development of Ketoprofen Liposomal Gel, IJPI’s Journal of Pharmaceutics and Cosmetology, Vol 2: 10.2012 ISSN 2229 – 6832