International Journal of Pharmaceutical and Medicinal Research

Journal homepage: www.ijpmr.org

Review Article

A Review on current scenario of Pharmacosomes

Charanjeet Kaur*, *Vaishali Goel, Rainu Devi, Aman Kuma, Ujjwal Nautiyal*

Himachal Institute of Pharmacy, Paonta Sahib, Distt. Sirmour, HP, 173025

ARTICLE INFO:

Article history:
Received: 20 January, 2017
Received in revised form: 22 February, 2017
Accepted: 25 February, 2017
Available online: 28 February, 2017

Keywords:
Pharmacosomes
Vesicular drug delivery system
Immunology
Genetic Engineering
Membrane biology

ABSTRACT

Limited permeation into the cells and the adverse effects are the major detriments with most of the drugs used in the chronic disorders. So from the past few decades our focus is on the advanced drug delivery system which can vanquish these problems and vesicular drug delivery system can overcome these problems. Encapsulation of the drug in vesicles increases the existence of the drug in the systemic circulation and reduces the toxicity. Vesicular drug delivery system finds application in immunology, membrane biology and genetic engineering. Pharmacosomes are a type of vesicular system which are defined as the colloidal dispersions of drug covalently bound to lipids and may exist as ultrafine vesicular, micellar or hexagonal aggregates. There has been advancement in the scope of this delivery system for a number of drugs used for inflammation, heart diseases, cancer, and protein delivery along with a large number of herbal drugs. Hence, pharmacosomes open new challenges and opportunities for improved novel vesicular drug delivery system. The present review deals with the review of the research done in the field of pharmacosomes.

1. Introduction

Most of the drugs, particularly chemotherapeutic agents, have shown to have narrow therapeutic window, and their clinical use is limited. Thus, their therapeutic effectiveness may be increased by incorporating them in an advantageous manner. In the past few decades, considerable attention had been focused on the development of novel drug delivery system (NDDS). The NDDS should ideally fulfil two requirements. Firstly, it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should deliver the active moiety to the site of action. Unfortunately, at present no available drug delivery system behaves ideally, but sincere attempts have been made to achieve them through various novel approaches in drug delivery. Various approaches have been adapted to achieve this goal, by paying attention either to control the distribution of drug by incorporating it in a carrier system, or by altering the structure of the drug at the molecular level, or to control the input of the drug into the bio-environment to ensure its appropriate profile of distribution[1]. The novel drug delivery system is said to be a rebirth system as it has modified a number of drugs and helped in overcoming several associated problems with these drugs and has thus got us with prolonged acting drugs with controlled action. There has been a tremendous growth in the area of developing various new drug delivery systems. The novel drug delivery system is the most suitable and approachable in developing the delivery system which improves the therapeutic efficacy of new as well as pre-existing drugs thus provides controlled and sustained drug delivery to the specific site and meets the real and appropriate drug demand of the body[2]. 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. Now a day's vesicles as a carrier system have become the vehicle of choice in drug delivery and lipid vesicles were found to be of value in immunology, membrane biology and diagnostic technique and most recently in genetic engineering[3].

1.1 Vesicular drug delivery system

The vesicular systems are highly ordered assemblies of one or more concentric lipid bi layers formed, when certain amphiphilic building blocks are confronted with water. Vesicles can be formed from a diverse range of amphiphilic building blocks[4]. Vesicular drug delivery system is one of the systems that can improve the bioavailability of the drug and can result in the reduction of toxicity by targeting drug to the specific site. Bingham pioneered the biologic origin of vesicular systems in 1965, and hence named them Bingham bodies[5]. Encapsulation of a drug in vesicular structures can be predicted to prolong the existence of the drug in systemic circulation and perhaps, reduces the toxicity if selective uptake can be achieved. Lipid vesicles are one type of many experimental models of bio membranes which evolved successfully, as vehicles for controlled delivery. For the treatment of intracellular infections, conventional chemotherapy is not effective due to limited permeation of drugs into cells. This can be overcomed by the use of vesicular drug delivery systems[6].

Corresponding Author: *Charanjeet Kaur* *, Himachal Institute of Pharmacy, Paonta Sahib, Distt.Sirmour, HP, 173025; E-mail: charanjeetk00@gmail.com

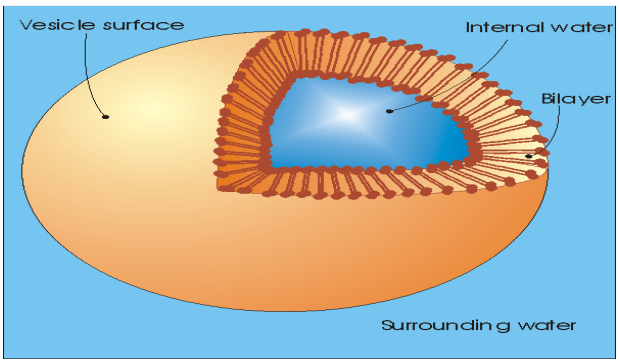

Figure No. 1: Image of a vesicle

1.2 pharmacosomes

Pharmacosomes are defined as colloidal dispersions of drugs covalently bound to lipids and may exist as ultrafine vesicular, micellar or hexagonal aggregates, depending on the chemical structure of drug-lipid complex[7,8]. Some of the limitation which has been encountered in transferosomes is because of their predisposition to oxidative degradation & purity of natural phospholipids, which can be overcomed by pharmacosomes[8,9]. In the pharmacosomes, the prodrug conjoins hydrophilic and lipophilic properties, and therefore acquires amphiphilic characters. Similar to other vesicle forming components, it was found to reduce interfacial tension and at higher concentrations exhibits mesomorphic behaviour[10-12]. The term pharmacosomes is explicitly used to describe the zwitterionic, amphiphilic, stoichiometric complexes of polyphenolic compounds with phospholipids[10,11,8]. Pharmacosomes is derived from the word "Pharmakon "which means drug and "soma "meaning carrier. It means a vesicular system in which the drug is associated with the carrier. These lipid conjugated vesicles may exist as colloidal, nanometre size micelles, vesicles or may be in the form of hexagonal assembly enjoying a functional hydrogen atom banking upon the architecture of the complex. The drug molecule with a free carboxylic or functional hydrogen atom like amino, hydroxyl groups is converted to an ester with the help of the hydroxyl moiety of the lipid, resulting in the formation of a prodrug. A spacer chain may or may not be used for this purpose. The prodrug possesses both hydrophilic and lipophilic properties. Despite these properties, prodrugs have the capability to reduce interfacial tension, increase the area of contact, and hence improve bioavailability. They aid the deportation through the cell membrane, cell wall, and tissues. If the concentration is increased beyond a level, it may exist in an intermediate state between the liquid and the crystal[13].

1.3 Advantages of pharmacosomes

Pharmacosomes have certain advantages such as they are suitable for hydrophilic as well as lipophilic drugs[11], show high and predetermined drug loading, reduce side effects and toxicity, are stable and efficient due to covalent linkage, Amphiphilicity leads to improved bioavailability of poorly lipid and water soluble drugs[10], leakage of drug does not take place because the drug is covalently linked to the carrier[7]. Pharmacosomes can intact with bio membranes enabling a better transfer of active ingredient[11].

1.4 Disadvantages of pharmacosomes

Certain draw backs are also reported such as synthesis of a compound depends upon its amphiphilic nature, require surface and bulk interaction of lipids with drugs, require covalent bonding to protect the leakage of drugs and on storage, undergo fusion and aggregation, as well chemical hydrolysis[14].

1.5 Components of pharmacosomes

There are three essential components for Pharmacosomes preparation.

Drugs : Drugs containing active hydrogen atom (-COOH, OH, NH_2) 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.

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

Lipid: Phospholipids are the major structure component of biological membranes, where the two types of phospholipids generally used phosphoglycerides and sphingolipids. 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[15, 16]. The components are shown in table 1.

Table No. 1: Components of pharmacosomes[17]

Component	Requirements
Drugs	Functional hydrogen atom from amino, carboxyl, or hydroxyl group that can be esterified.
Solvents	High purity, volatile, and intermediate polarity
Lipids	Phospholipids-phosphoglycerides or Sphingolipids

2. Method of preparation of pharmacosomes

Initially for the formation of pharmacosomes, there is a need of drug-lipid conjugate. For this purpose, the salt form of the drug is converted into the acidic form to expose the functional hydrogen atom to form a complex. There are generally four methods of the preparation of pharmacosomes which are solvent evaporation method, ether injection method, super critical fluid process and anhydrous solvent lyophilisation as shown in figure 2. In the research done on pharmacosomes solvent evaporation method and ether injection methods are frequently followed.

2.1. Solvent evaporation method

Solvent evaporation method involves the removal of the solvent either by the hand shaking method or by the use of rotatory evaporator. In this method, firstly a mixture of drug and lipid are dissolved in a volatile organic solvent such as dichloromethane .Thereafter the solvent is evaporated 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 as shown in figure 3**[18, 19].**

2.2. Ether injection method

Ether injection method is a frequently used method in the preparation of pharmacosomes. In the ether-injection method, an organic solution of the drug lipid complex is injected slowly into the hot aqueous medium, and the vesicles are readily formed**[16].**

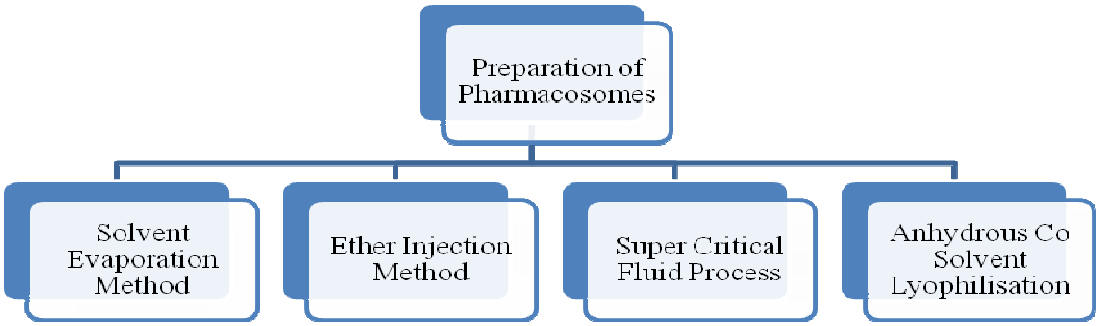

Figure No. 2: Method of preparation of Pharmacosomes

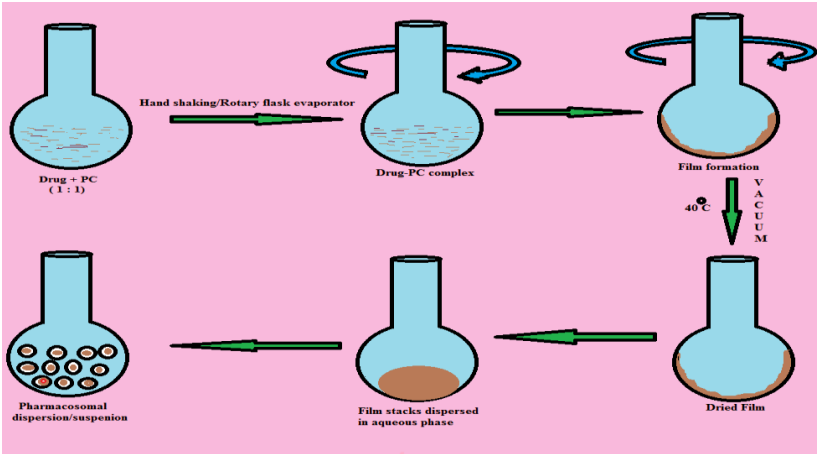

Figure No. 3: Solvent Evaporation method[20]

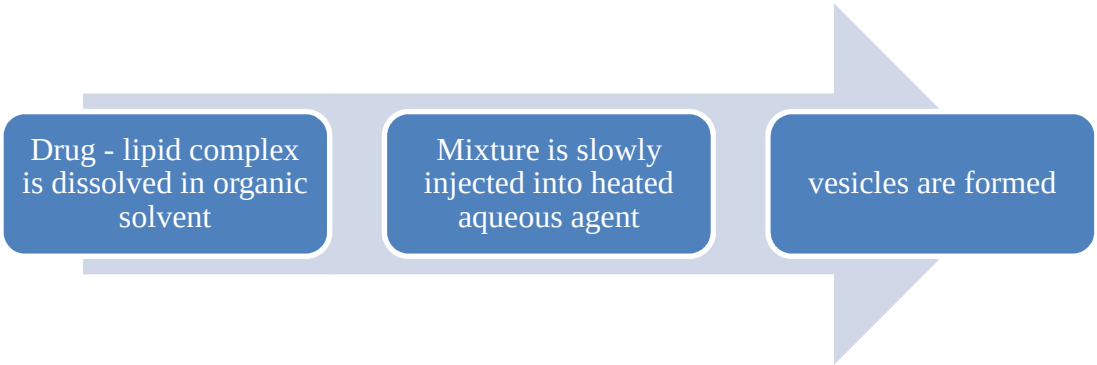

Figure No. 4: Ether injection method

2.3. Super critical fluid process

Two different techniques of super critical fluid process are used. Gas anti solvent (GAS) and solution enhanced dispersion by the supercritical fluid (SEDS). Drug and lipid complex are dissolved in a supercritical fluid of CO_2 and then mixed into the nozzle mixing chamber**[18, 19]**. The general scheme is shown in the figure 5.

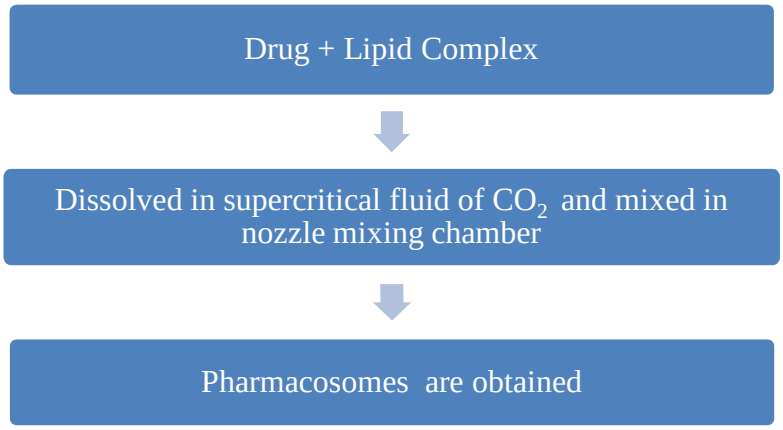

Figure No. 5: Super critical fluid process

2.4. Anhydrous co-solvent lyophilisation method

This approach involves the dissolution of drug powder and phospholipids in Dimethyl sulfoxide (DMSO) containing 5% glacial acetic acid, after that agitates the mixture to get clear liquid and freeze dried overnight at condenser temperature. Then resultant complex is flushed with nitrogen & stored at 4° C**[18,19]**.

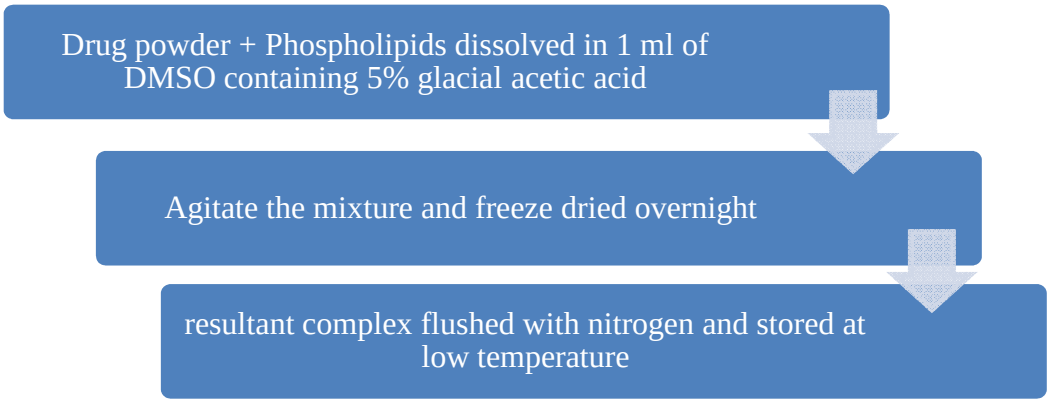

Figure No. 6: Anhydrous co solvent lyophilisation

3. Evaluation of pharmacosomes

3.1. Complex determination

With the help of FTIR spectrum, the formation of the complex or the conjugate can be determined by correlating spectrum observed in complex sample with that of discrete constituents and also with their mixture**[21]**.

3.2. Stability of pharmacosomes

Correlating the spectrum of complex at various points of time in the solid state with spectrum of dispersion in water consisting of small particles, once the product has been lyophilized, is used to evaluate the stability of the system.

3.3. SEM/TEM

These techniques can be utilized for studying the surface order of pharmacosomes. The purity grades of the lipid being used and few variables observed during operation (method of preparation, vacuum assigned and rotational speed) alter the shape and size of pharmacosomes. Pharmacosomes are formed of greasy nature if prepared using lower purity grades of lipids resulting in large aggregate formation and those fabricated using lipids of more than 90% purity grade show susceptibility to degradation due to oxidation, which affects complex stability. So, 80% purity grade is the commonly used phospholipid grade**[13]**.

3.4. 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 at 276 nm**[22]**.

3.5. Drug – lipid compatibility

Differential scanning calorimetry is a thermo analytical technique utilized to determine drug-lipid compatibility and their interactions, if any. The thermal response is studied using separate samples and heating them in a sample pan which is closed. The nitrogen gas is purged, and the temperature is maintained in a definite range with a specific heating rate.

3.6. Crystalline state measurement

The crystalline nature of drug can be determined using X-ray diffraction technique. The tube voltages and tube current can be regulated in the X-ray generator. Copper lines may be used as the source of radiation. The scan angle can be regulated. The overall combined intensity of all reflection peaks is projected by area under curve of X-ray powder diffraction pattern that specifies the specimen attributes**[13].**

3.7. Dissolution studies

Dissolution studies, in vitro are done using various models available for the purpose. The results are assessed on the basis of apprehended activity of the active constituent's therapeutically[23]. *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**[24].**

3.8. *In- vitro* release

In the bulk, equilibrium reverse dialysis bag technique described here, emulsion is introduced inside the dialysis bag and the continuous (receiver) phase is placed outside. Dialysis bags containing the continuous phase (receiver phase) alone are suspended in a vessel containing the donor phase (diluted emulsion) and the system is stirred. At predetermined time intervals, each dialysis bag is removed and the contents are analyzed for released drug. An advantage of this technique is the increase in the membrane surface area available for transport from the donor to the receiver phases. Another advantage of this method is the increased efficiency in terms of staffing as a consequence of the reduction in the number of steps**[13].**

3.9. 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 hours on a magnetic stirrer. At the end of 24 hour, suitable dilutions were made and measured for the drug content by UV spectrophotometrically**[25].** The evaluation parameters of the pharmacosomes in brief are enlisted in the table 2.

Table No. 2: Evaluation of pharmacosomes

S. No.	Evaluation parameter	Technique and instrument employed	Reference
1.	Complex determination	Fourier Transform Infra Red Spectroscopy	**[21]**
2.	Stability	Ultra Violet Spectroscopy	**[13]**
3.	Surface Morphology	Scanning electron microscopy and transmission electron microscopy	**[13]**
4.	Solubility	Shake flask method and Ultra Violet Spectroscopy	**[22]**
5.	Drug lipid compatibility	Differential scanning calorimetry	**[13]**
6.	Crystalline state measurement	X Ray diffraction technique	**[13]**
7.	Dissolution studies	Dissolution test apparatus	**[23, 24]**
8.	*In – vitro* release	Equilibrium bag dialysis technique	**[13]**
9.	Drug content	Ultra Violet Spectroscopy	**[25]**

4. Review of current research on pharmacosomes

In the research by Semalty *et al.* pharmacosomes of diclofenac were prepared by the solvent evaporation method in which Diclofenac salt was converted into the acid form to provide an active hydrogen site for complexation. The pharmacosomes were collected as the dried residue and then subjected to characterization such as drug content, solubility, scanning electron microscopy, infra red spectroscopy analysis, differential scanning calorimetry, X ray diffraction analysis, dissolution study and statistical analysis. The pharmacosomes obtained were irregular shaped, confirmed by SEM; Drug content came out to be 96.2 ± 1.1 %. Water solubility of the complex was found to be 22.1 mg mL^{-1} and water solubility of diclofenac was 10.5 mg mL^{-1}. This improvement in water solubility in may result in improved dissolution and lower gastrointestinal toxicity. Pharmacosomes showed 87.8 % while the free diclofenac acid showed a total of only 60.4 % drug release at the end of 10 h of dissolution study**[23]**.Aspirin- Phospholipid complex for improved drug delivery was prepared by the solvent evaporation method. The dried residues were collected in vacuum desiccator overnight and subjected to characterization for instance drug content, solubility, scanning electron microscopy, infra red spectroscopy analysis, differential scanning calorimetry, x ray diffraction analysis, dissolution study and statistical analysis. Aspirin phospholipid complex obtained were disc shaped having rough surface which was confirmed by the use of SEM, drug content was 95.6%, Aspirin complex showed the release of

90.93% and Aspirin showed the release of 69.42% at the end of 10 hours in pH 1.2 acid buffer**[26]**.

In an attempt made by Semalty *et al.* the pharmacosomes of Aceclofenac were prepared by the solvent evaporation method. In this method aceclofenac sodium, was acidified first so that active hydrogen might be available for complexation. The dried residues were collected and placed in vacuum desiccator overnight and then subjected to characterization which included drug content, solubility, scanning electron microscopy, x ray powder diffraction and dissolution studies. Pharmacosomes obtained were disc shaped, confirmed by the use of SEM. Drug content for aceclofenac- phospholipid complex (1:1) was 91.88% (w/w) and for aceclofenac- phospholipid complex (2:1) was 89.03% (w/w), solubility and dissolution profile of the complex was much better than aceclofenac**[27]**.

Hari Kumar *et al.* prepared the pharmacosomes of Ketoprofen by solvent evaporation method. Ketoprofen-PC complex was prepared by associating ketoprofen with an equimolar concentration of PC (80 % purity grade of soya-phospholipids). The dried residues were collected and placed in vacuum desiccators overnight and then subjected to characterization which include drug content uniformity, solubility, vesicle size and distribution analysis, vesicle shape determination, drug excipient interaction studies, differential scanning calorimetry, x ray powder diffraction analysis, *in-vitro* dissolution studies, drug release kinetic data analysis, in vitro diffusion studies and stability studies. In vitro dissolution profile and solubility of pharmacosomes was much better than ketoprofen, drug content came out to be 99.8%, in vitro diffusion rate of the pharmacosomes was higher, and After 24 h, maximum drug was released from formulation PC4 is 55.3%. The release experiments clearly indicated sustained release of ketoprofen from pharmacosomal formulations**[28]**.

The pharmacosomes of Furosemide were developed by the solvent evaporation method. After collecting the pharmacosomes, they were subjected to evaluation parameters such as drug content, solubility, partition coefficient, *in-vitro* dissolution studies, *ex-vivo* permeation studies, drug release kinetics, FTIR, differential scanning calorimetry, SEM, x ray powder diffraction and stability studies. Prepared pharmacosomes were confirmed by the differential scanning calorimetry, FTIR and x ray powder diffraction. The pharmacosomes had enhance aqueous as well as n-octanol solubility as compared to pure drug also the furosemide release behaviour from pharmacosomes showed excellent sustained release property. The prepared molecule not only showed biological activity, but also amphiphilic nature. The release and permeation mechanism of furosemide pharmacosomes follows the Ritger-Peppas model**[29].**

In another research, the pharmacosomes of Rosuvastatin were prepared by the solvent evaporation method. Various evaluation parameters were performed such as drug content, solubility studies, vesicle shape determination, drug excipient interaction studies, x ray powder diffraction analysis, *in-vitro* dissolution studies and in vitro diffusion studies. The prepared pharmacosomes were more soluble than the parent drug which was Rosuvastatin. Drug content came out to be 90.4±0.52% to 94.4±0.61% in all batches of pharmacosomes. FTIR and x ray powder diffraction, confirmed the formation of complex, pharmacosomes obtained were irregular shaped which was confirmed by the SEM. The maximum drug release from the formulation F1 after 24 hours was 66.93% and maximum drug permeated by diffusion through egg membrane from formulation F1 was 49.50% in the diffusion study**[30]**.

JIN Yi-Guang *et al.* did the preparation of the pharmacosomes of Acyclovir succinyl glyceryl monostearate by the tetra hydro furan injection method. Various evaluation techniques were employed such as transmission electron microscopy, laser scattering method. Very weak effect of centrifugation and heating were found on the stability of the pharmacosomes whereas freezing and lyophilization disrupted the pharmacosomes structure. In vivo, pharmacosomes were found absorbed by the plasma proteins in the blood thereby reducing the haemolytic reaction**[31]**.

An attempt was made by Ping *et al.* in the preparation of the pharmacosomes of 5′-cholesterylsuccinyl-dideoxyinosine (CS-ddI) by the tetra hydro furan injection method. HPLC was used to determine drug concentration of the complex in plasma and tissues. Half life of CS-ddI in plasma of rat was found to be 7.64 min, CS-ddI got concentrated in liver quickly after iv administration, there was also some concentration in lung and spleen; its elimination from target tissues was found slow as the half-life of CS-ddI in liver was 10 days.[32]

The preparation of pharmacosomes of 3’, 5’-dioctanoyl-5-fluoro-2’-deoxyuridine was done in a scientific research. Mean particle size of the pharmacosomes came out to be 76 nm with the drug loading of 29.02 % and entrapment efficiency of 96.62 %**[33]**.

Han and colleagues optimized the preparation of 20(S)-protopanaxadiol pharmacosomes and observed the encapsulation efficiency of pharmacosomes, which was 80.84 ± 0.53 for a diameter of 100.1 nm and 72.76±0.63 for the diameter of 117.3nm**[34].** Table 3 gives the brief summary of all the research work done.

Table No. 3: Current research work done on Pharmacosomes

S. No.	Active ingredient	Other ingredients	Method employed	Effect	Reference
1.	Diclofenac	Soya phosphatidyl-choline	Ether Injection	Improved Solubility	**[23]**
2.	Aspirin	Soya phosphatidyl-choline	Ether Injection	Improved drug release	**[26]**

3.	Aceclofenac	Soya phosphatidyl-choline	Ether Injection	Improved solubility and Dissolution profile	**[27]**
4.	Ketoprofen	soya-phospholipids	Ether Injection	Improved solubility and Dissolution profile	**[28]**
5.	Furosemide	Soya phosphatidyl-choline	Ether Injection	Improved solubility	**[29]**
6.	Rosuvastatin	Soya- lecithin	Ether Injection	Sustained release and Improved solubility	**[30]**
7.	Acyclovir succinyl glyceryl monostearate	Phospholipid	Tetra hydro furan injection method	Reduced haemolytic reaction	**[31]**
8.	5′cholesterylsuccinyl-dideoxyinosine (CS-ddI)	phospholipid	Tetra hydro furan injection method	Half life in rat was found to be 7.64 minutes	**[32]**

5. Conclusion

Pharmacosomes are the novel vesicular drug delivery system. They reduce side effects and toxicity Pharmacosomes prolong the existence of the drug in the systemic circulation, and perhaps, reduces the toxicity if selective uptake can be achieved due to the delivery of drug directly to the site of infection. They also improve the bioavailability especially in the case of poorly soluble drugs. These are cheaper to prepare and more stable and efficient as compared to niosomes, liposomes and transferosomes. Both hydrophilic and lipophilic drugs can be incorporated into the pharmacosomes. Pharmacosomes delay the elimination of rapidly metabolizable drugs and thus function as sustained release systems. These are the advantages of Pharmacosomes which make them the most suitable vesicular system. Although some research is done in this particular field, still a lot more can be done.

Refernces

[1]. Vaizoglu MO., Speiser PP., Pharmacosomes-A novel drug delivery system, Acta Pharmacetica Sinica 1986; 23:163-172.

[2]. Balasubramanian J., Narayanan N., Pharmacosomes: A Novel Method of Colloidal Dispersions in Drug Delivery, Discovery Pharmacy, Vol.4, No. 10, 2013;2278-5418.

[3]. Chiranjeevi G., Muthukumaran M., Krishnamoorthy B., A Review on Potency of Vesicular Systems in Targeting Drug Delivery, Research Journal of Pharmaceutical Biological and Chemical Sciences 2013;4:2: 156-162.

[4]. Biju SS., Talegaonkar S., Mishra PR., Khar KR., Vesicular System: An overview, Indian Journal of Pharmaceutical Sciences 2009;71:4:421-427.

[5]. Saraf S., Rathi R., Kaur CD., Saraf S., Colloidosomes and advanced vesicular system in drug delivery, Asian Journal of Scientific Research 2011;4:1:1–15.

[6]. Post G., Krisch R., Koestler T., In Gegoriadis G Eds, Liposomes Tech, CRC Press Inc. 1983;F1:29.

[7]. Kavitha D., Naga SJ., Shanker P., Pharmacosomes: An Emerging Vesicular System, International Journal of Pharmaceutical Sciences Review and Research 2010;5:3:168-171.

[8]. Jitendra LP., Praful DB., A review on: pharmacosomes as a novel vesicular drug delivery system, World Journal of pharmaceutical research 2012;1:3:456-469.

[9]. Gupta S., Singh RP., Lokwani P., Yadav S., Gupta SK., Vesicular system as targeted drug delivery system: an overview, International journal of pharmacy and technology 2011;3:2:988-1021.

[10]. Goyal T., Ashwini SR., Meenakshi C., Pharmacosomes: opening new doors for drug delivery, International Journal of Pharmacy and Pharmaceutical Sciences 2012;4:3:25-29.

[11]. De Pintu K., De Arnab., Pharmacosomes: A potential vesicular drug delivery system, International Research Journal of Pharmacy 2012;3:3:102-105.

[12]. Sangwan S., Dureja H., Pharmacosomes: a potential alternative to conventional vesicular systems, Pharmaceutical technology 2009;33:6:62-65.

[13]. Semalty A., Rawat BS., Singh D., Rawat MSM., Pharmacosomes: the lipid-based new drug delivery system, Expert Opinion on Drug Delivery 2009;6:6:599-612.

[14]. Volkering F., Influence of non ionic surfactants on bioavailability and biodegradation of polycyclic aromatic hydrocarbons, Applied and Environment Microbiology1995;61:5:1699-1705.

[15]. Seema MJ., Pournima M., Manisha K., Vilasrao K., Novel vesicular system: an overview, Journal of Applied Pharmaceutical Science 2012;2:1:193-202.

[16]. Lawrence MJ., Surfactant Systems: Their Use in Drug Delivery, Chemical Society Reviews 1994;23:6: 417–424.

[17]. Pandita A. & Sharma P., Pharmacosomes: An emerging novel vesicular drug delivery system for poorly soluble

[18]. synthetic and herbal drugs, International Scholarly Research Network 2013;1-10.

[19]. Bhingare U., Khadabadi SS., Shinde N., Pharmacosomes: A Novel Drug Delivery System, International Journal of Pharmaceutical Research & Allied Sciences 2014;3:1:14-20.

[20]. Karde M., Pawar H., Geevarghese R., Khatri J., 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 2012;4:5:201-206.

[21]. Singh VK., Patel A., Chandra D., Yadav KK., Pharmacosomes: a novel carrier for targeted and controlled vesicular drug delivery system, World Journal of pharmaceutical research 2014;3:5:1221-1238.

[22]. Bombardelli E., Spelta M., Phospholipidpolyphenol complexes: a new concept in skin care ingredients, Cosm Toil. 1991;106:3: 69-76.

[23]. Semalty A., Semalty M., Singh D., Rawat MSM., Preparation and characterization of phospholipid complexes of naringenin for effective drug delivery, Journal of inclusion phenomena and macrocyclic chemistry 2010;67:3-4:253-260.

[24]. Semalty A., Semalty M., Singh D., Rawat MSM., Development and physicochemical evaluation of Pharmacosomes of diclofenac, Acta Pharm. 2009;59:3:335-344.

[25]. Mansoori MA., Jawade S., Agrawal S., Khan MI., Formulation Development of Ketoprofen Liposomal

[26]. Gel, IJPI's Journal of Pharmaceutics and Cosmetology 2012;2:10:23- 29.

[27]. Sreedevi A., Swetha A., Meenakshi C., Rohit B., Pharmacosomes – A Review, International Journal of Pharmaceutical Sciences Review and Research, 2012;12:1:114-116.

[28]. Semalty A., Semalty M., Singh D., Rawat MSM., Development and characterization of Aspirin Phospholipid complex for improved drug delivery, International Journal of Pharmaceutical Sciences and Nano technology 2010;3:2:940-947.

[29]. Semalty A., Semalty M., Singh D., Rawat MSM., Development and evaluation of pharmacosomes of Aceclofenac, Indian Journal of Pharmaceutical Sciences 2010;576-581.

[30]. Kaur A., Sharma N., Harikumar SL., Design and development of ketoprofen pharmacosomes for oral delivery, Phamacophore 2013;4:4:111-119.

[31]. Patil SD., Patil PL., Chatap VK., *In-vitro*, *ex-vivo* characterization of furosemide bounded pharmacosomes for improvement of solubility and permeability, Advances in Pharmacology and Pharmacy 2014;2:5:67-76.

[32]. Kumar PT., Mishra J., Podder A., Design, Fabrication and evaluation of Rosuvastatin pharmacosome- a novel sustained drug delivery system, European Journal of Pharmaceutical and medical research, 2016;3:4:332-350.

[33]. Yiguang Ji., Tong cL., Ping A., Miao L., Houb X., Self assembled drug delivery systems- properties and *in-vitro* and *in- vivo* behaviour of Acyclovir self assembled nano particles (SAN), International journal of pharmaceutics 2006;309:199-207.

[34]. Ping A., Jin Y., Da-wei C., Preparation and *in-vivo* Behaviour of Didanosine Pharmacosomes in Rats, Chinese Journal of Pharmaceutics 2005;3:227-235.

[35]. Zhang ZR., Wang JX., Study on Brain Targeting 3',5'-dioctanoyl-5-fluoro-2'-Deoxyuridine Pharmacosomes, Yao Xue Xue Bao. 2001;36:771–6. 21.

[36]. Han M., Chen J., Chen S., Wang X., Preparation and study *in-vitro* of 20(S) protopanaxadiol pharmacosomes, China Journal of Pharmaceutics 2010;35:842–846.

Source of support: Nil, Conflict of interest: None Declared

All © 2017 are reserved by International Journal of Pharmaceutical and Medicinal Research