World Journal of Pharmaceutical ReseaRch
SJIF Impact Factor 5.045
Volume 3, Issue 6, 1299-1322. Review Article ISSN 2277 – 7105

AN OVERVIEW: THE NOVEL CARRIER FOR VESICULAR DRUG DELIVERY SYSTEM

Dinesh Chandra*[1], Kamlesh Km Yadav[1], Vijay Kumar Singh[1], Anand Patel[1], Shashi Chaurasia

[1]Kamla Nehru Institute of Management and Technology, Sultanpur, India

Article Received on
20 June 2014,

Revised on 15 July 2014,
Accepted on 10 August 2014

***Correspondence for Author**
Dr. Dinesh Chandra
Kamla Nehru Institute of Management and Technology , Sultanpur , India

ABSTRACT

The focus of this review is to development of a novel drug delivery system. Novel drug delivery system aims to deliver the drug at a rate directed by the needs of the body during the period of treatment, and channel the active entity to the site of action. A number of novel drug delivery system has emerged encompassing various routes of administration, to achieve controlled and targeted drug delivery. Encapsulation of the drug in vesicular structure is one such system, which can be predicted to prolong the existence of the drug in systemic circulation, and reduce the toxicity, if selective uptake can be achieved. Consequently a number of vesicular drug delivery system such as liposomes, niosomes, sphinosomes, transferosomes and pharmacosomes are used to improve the therapeutic index of both existing and new drug molecules by encapsulating an active medicament inside vesicular structure in one such system. The era of vesiclular delivery has much to explore by achieving success in various upcoming systems such as aquasomes, cryptosmes, discomes, emulsomes, enzymosome, genosomes, photosomes, virosomes, vesosomes, proteosomes etc. The approaches like pro vesicular drug delivery, coating of vesicles, layerosomes, ufosomes system etc have also been developed which have better stabilities in comparison to simple vesicular drug delivery systems.

KEY WORDS: Vesicles, lipid based drug delivery systems, liposome, pharmacosome, noisome, transferosome.

INTRODUCTION

Novel vesicular drug delivery systems intend to deliver the drug at a time directed by need of body during the time of treatment and the site of action. Biologic origin of these vesicles

was first reported in 1965 by Bingham and has been given the name Bingham bodies[1]. The vesicular drug delivery system is the most approachable in developing the delivery system which improves the therapeutic index of new as well as pre-existing drugs thus provides controlled drug delivery to the specific site and suitable drug demand of the body.The stability of the system remains the area of interest because of formation of vesicles. It has also reduce toxicity, side effects and maintained therapeutic value of drugs .Vesicular drug delivery decreases the cost of therapy by increase bioavailability of medication, especially in case of poorly soluble drugs. They can both hydrophilic and lipophilic drugs.[2] 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.[3,4] Lipid based drug delivery system now a day is experiencing resurgence due to new drug application.[5] 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.[6]

Vesicular system-Carrier for Drug Delivery

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.[7] 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.[8] 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.[9]

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.[10] 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 sysem like liposome, noisome, transferosome, ethosome and pharmacosomes have been suggested to overcome the problems assemblies of one or several concentric lipid bilayers formed.[11] Pharmacokinetics is to be exhaustively studied, in order to exploit more advantage of this system.[12] 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 cast of therapy by improved bioavailability of medication, in case of poorly soluble drugs.[13] The vesicular systems are highly ordered assemblies of one or several concentric lipid bilayer formed, when certain amphiphillic building blocks are confronted with water. Drug carrier can be manufactured to slowly degrade, react to stimuli and specific to site. The ultimate aim is to control degradation of drug and loss, prevention of harmful side effects and enhance the availability of the drug at the disease site . Vesicular drug delivery system has some of the advantages like

1. The drug is in systemic circulation reduces the toxicity and can be achieved because of the indirectly delivery of drug to the site of infection.
2. Improves the bioavailability particularly in the case of poorly soluble drugs.
3. Hydrophilic and lipophilic drugs can be incorporated.
4. Delays elimination of rapidly metabolizable drugs and thus function as sustained release systems .[13]

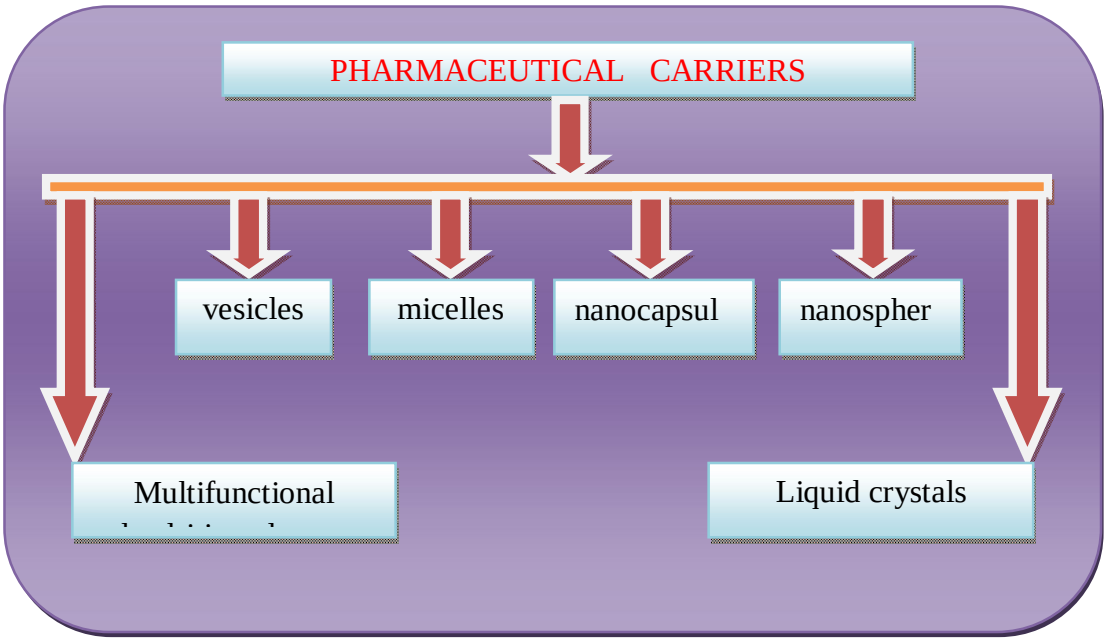
Carriers- [14]

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. 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.

   Different type of pharmaceutical carriers are present. they are polymeric, macromolecular, particulates and cellular carrier.[12]



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.[15] They can be tailored for site-specific delivery of drugs.[25] When developing these formulations, the goal is to obtain systems with optimized drug loading and release properties, long shelf-life and low toxicity.[16] In this review has been made to different

aspects related to the vesicular system, including method of preparation, stabilization, drawbacks, and applications. different types of vesicular systems such as liposomes, niosomes, transfersomes, and pharmacosomes, have been discussed .[17]

Types of vesicles[1]

The targeted vesicles are classified on the basis of their Composition.

1.Lipoidal biocarriers

2. Non-lipoidal biocarriers

1. Lipoidal biocarriers for site specific targeting

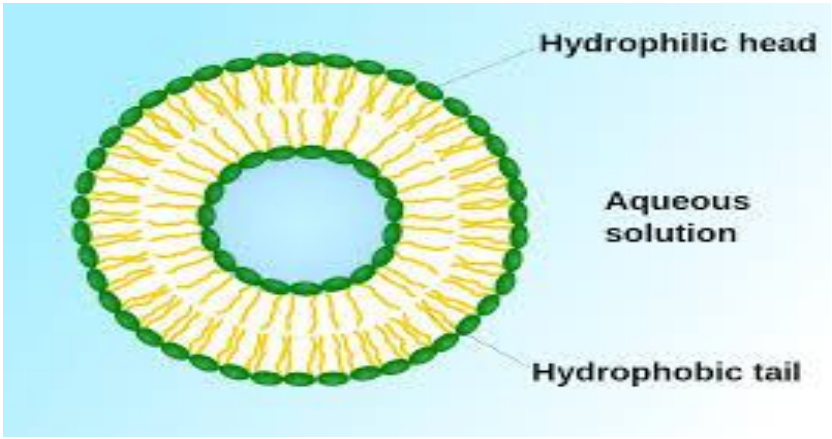
1. Liposomes
2. Emulsomes
3. Enzymosomes
4. Ethosomes
5. Sphingosomes
6. Transferosomes
7. Pharmacosomes
8. Virosomes

2. Non- lipoidal biocarriers for site-specific targeting

1. Niosomes
2. Bilosomes
3. Aquasomes

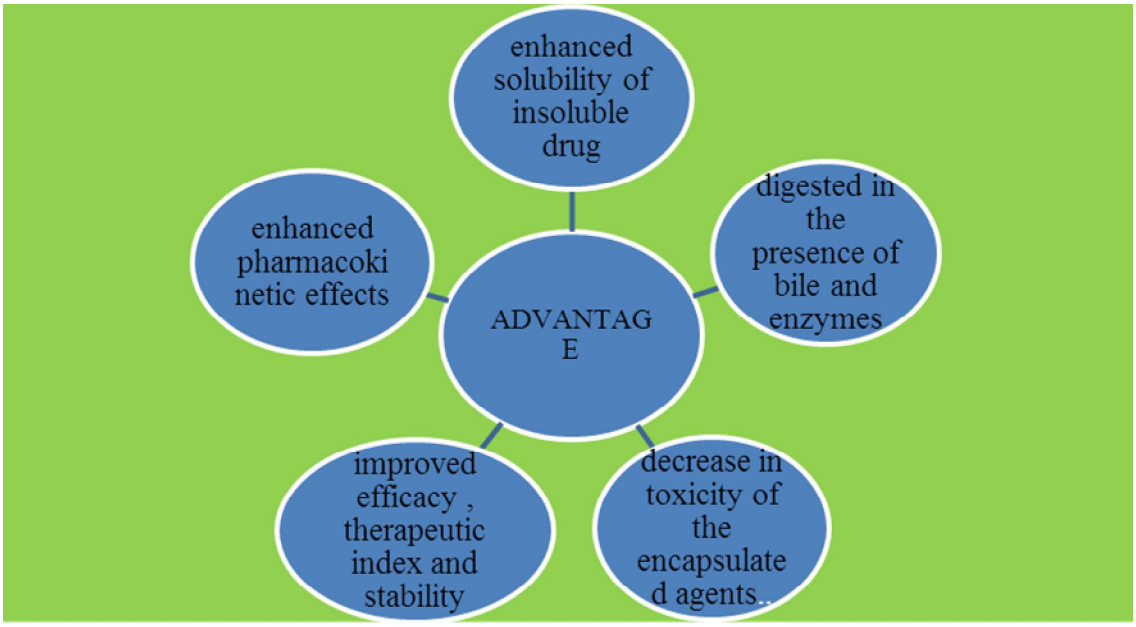
LIPOSOMES

The name liposome is derived from two Greek words: 'Lipos' meaning fat and 'Soma' meaning body. Liposomes are concentric bilayered vesicle in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of synthetic phospholipids[18]. which are molecules that have a hydrophilic head and a hydrophobic tail group. The head is attracted to water, and the tail, which is made of a long hydrocarbon chain, is repelled by water.Liposomes can be filled with drugs, and used to deliver drugs for cancer and other diseases[19].

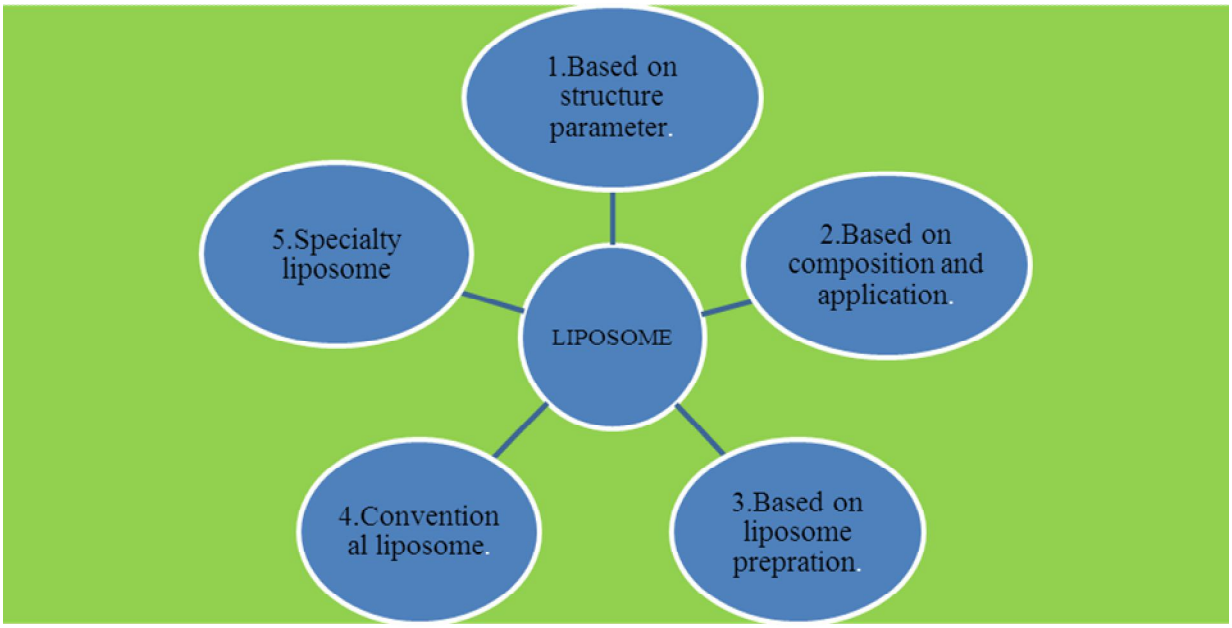


Structure Of Liposomes

Advantage and Disadvantage -[2,9,20]



Classification Of Liposomes-[1, 18, 21]



1. Based on structure parameter

Abbreviation	Vesicle type	Diameter size	No. of lipid bilayer
MLV	Multilamellar large vesicle	More than 0.5 micrometer	5-25
OLV	Oligolamellar vesicle	0.1 – 1 micrometer	5
UV	Unilamellar vesicle	All size ranges	one
SUV	Small sized unilamellar vesicle	20-100 nm	one
MUV	Medium sized unilamellar vesicle	More than 100 nm	one
LUV	Large unilamellar vesicle	More than 100 nm	one
GUV	Giant unilamellar vesicle	More than 1 micrometer	one
MV	Multivesicular vesicle	More than 1 micrometer	Multi compartmental structure

2. Based on liposome preparation

Method of preparation	Vesicle type
DRV	Dehydration rehydration method
MLV-REV	Multilamellar vesicle made by reverse phase evaporation method
FATMLV	Frozen and thawed MLV
SPLV	Stable plurilamellar vesicle
VET	Vesicle prepared by extrution technique
REV	Single or oligolamellar vesicle made by reverse phase evaporation method

1. Based on composition and application

Type of liposome	Composition	Application
Long circulatory liposome	Neutral high Transition temprature liposme	Selective targeting topathological areas
Conventional liposome	Neutral or negatively charged Phospholipid	Targeted delivery of antimicrobial agent to macrophages, vaccination
Fusogenic liposome	Reconstitute sendai virus envelop	

Immuno liposome	Long cerculatory liposome with attached monoclonal antibody	Subject to receptor mediated endocytosis, specific targeting
pH sensitive liposome	Phospholipid like Phosphatidyl ethanolamine	Tumourtargeting, coated pit endocytosis
Cationic liposome	Cationic lipid	Gene delivery

4. Based on conventional liposome

1- Stabilize natural lecithin (PC) mixtures

2- Synthetic identical, chain phospholipids

3- Glycolipids containing liposome

5. Based on specialty liposome

1- Bipolar fatty acid.

2- Antibody directed liposome.

3- Methyl/ Methylene x- linked liposome.

4- Lipoprotein coated liposome.

5- Carbohydrate coated liposome.

6- Multiple encapsulated liposome.

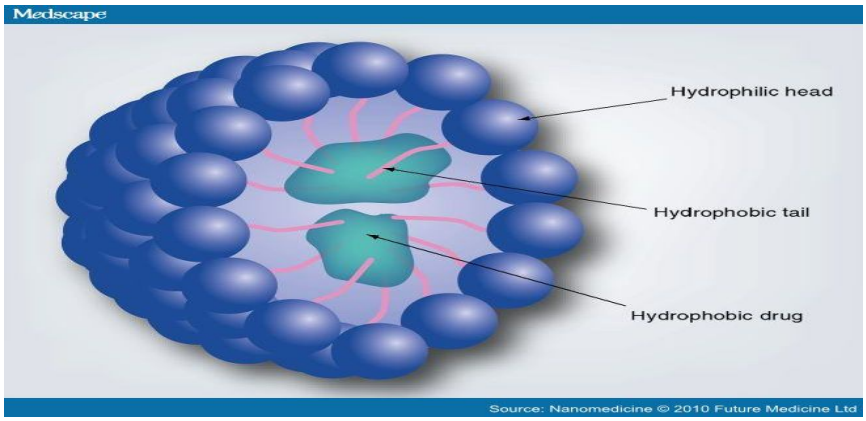
Therapeutic Applications of Liposomes[13]

1. Used in ergosterol membrane.
2. Used in protein synthesis inhibitor.
3. Used in decrease Intra-ocular pressure.
4. Used in inhibiton of Prostaglandin.
5. Used in phosphodiesterase.
6. Used in cyclo-oxygenase enzyme inhibitor.

NIOSOME

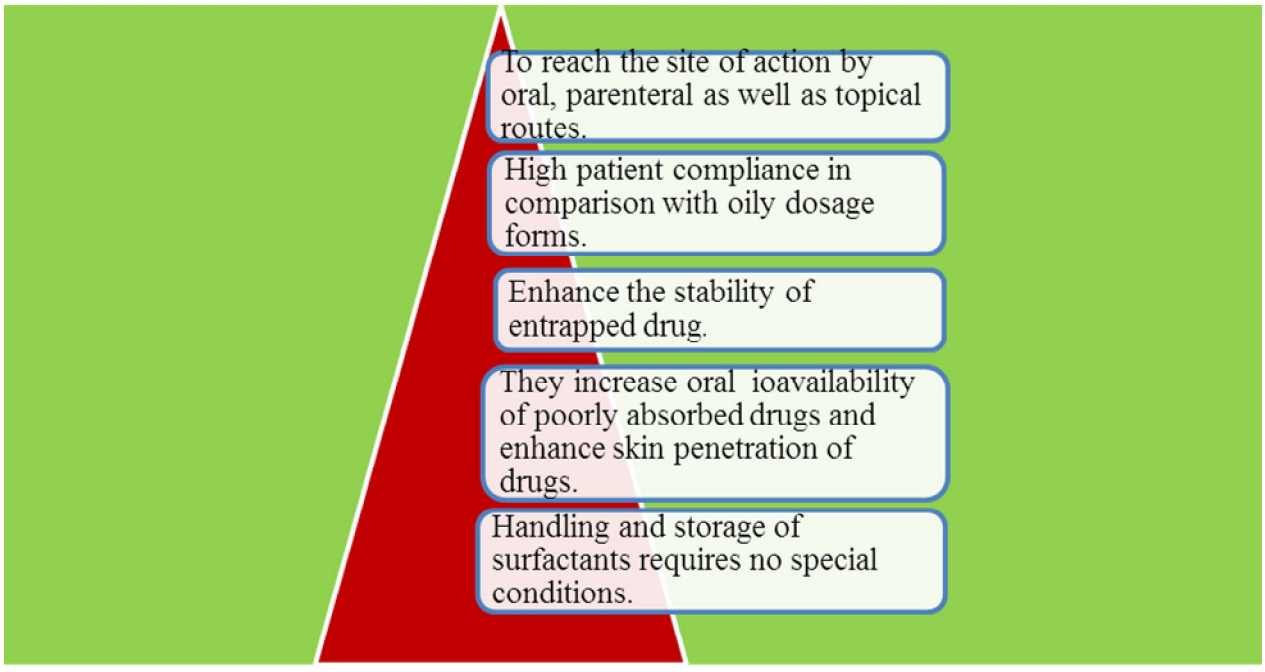
Niosomes were first introduced as a feature of cosmetic industry. Nonionic surfactants are chosen due to less irritation power which decreases in order of cationic>anionic>ampholytic>non-ionic.[22] Niosomes are microscopic lamellar structures of size range between 10 to 1000 nm and mainly composed of biodegradable, and biocompatible surfactants. The niosomes are ampiphillic in nature, which allows trap of hydrophilic drug in the core cavity and hydrophobic drugs in the non-polar region.[23] The two basic components of niosomes are non-ionic surfactant and cholesterol, non-ionic surfactants used due to their capability to increase solubility are used to enhance bioavailability of poor

water soluble drugs and increases both permeability and fluidity of biological membranes . The presence of the cholesterol increase the inflexibility of the bilayer and affects bilayer fluidity, enzymatic activity, ion permeability, elasticity, fusion processes , size and shape. This carrier system protects the drug molecules from the premature degradation and inactivation due to excess pharmacological and immunological effects.[24]

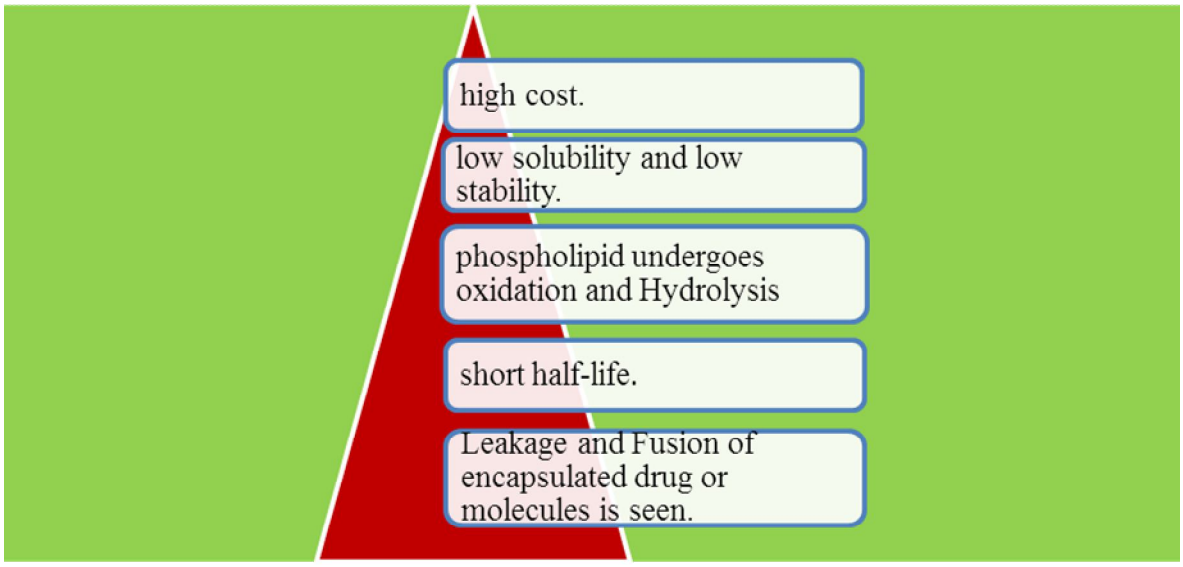


Struture Of Niosome

Advantage-[25]



Disadvantage-[26]



Types of Niosome-[27]

Niosomes can be divided into three groups on the basis of their vesicles size:

TYPE	VESICLE SIZE
Small Unilamellar Vesicles (SUV)	0.025-0.05 µm
Multilamellar Vesicles (MLV)	>0.05 µm)
Large Unilamellar Vesicles (LUV)	>0.10 µm).

Therapeutic Application of Niosomes[13]

1. Used in anticancer .
2. Used in antiinfective Agent.
3. Used in antiinflammatory Agent.
4. Used in opthalmic Drug Delivery.
5. Used in niosomal in Oral Drug Delivery.
6. Used in transdermal Drug Delivery.
7. Used in Brain Targeted Delivery Sytem for the Vasoactive Instestinal peptide.

Pharmacosomes

Pharmacosomes are amphiphilic, colloidal dispersions of drugs covalently bound to lipids, and may exists 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).[28,] 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.[29] 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 unentraped 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.[30] 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.[31] Phaspholipids 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.[32] 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.[33]

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.[34]

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.[35] 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.[36]

Advantage

1.High and predetermined drug loading.

2.drug can be Delivered drug directly to the site of infection.

3.Reduction in adverse effects ,cost of therapy and toxicity.

4. improved bioavailability of poorly lipid and water soluble drugs.

5. Stable and efficiency due to covalent linkage.[36]

6.Suitable for both hydrophilic and lipophilic drugs.

7.Volume of inclusion doesn't influence entrapment efficiency.

8.No leakage of drug take place as the drug is covalently linked to the carrier.

9.Drug release from pharmacosomes is by hydrolysis.[37]

10. No need of removing the free un-entrapped drug from the formulation which is required in case of liposomes .

11.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 lipids and the spacer. [38]

Advantages of Pharmacosomes over Liposomes -[38]

1. In case of pharmacosome, volume of inclusion does not influence entrapment efficiency. On the other hand in case of liposomes, the volume of inclusion has great influence on entrapment efficiency.
2. In pharmacosomes membrane fluidity depends upon the phase transition temperature of the drug lipid complex but it has no effect on release date because the drug is covalently bound. In liposomes, the lipid composition decides its membrane fluidity, which affects the rate of drug release and physical stability of the system.
3. Drug release from pharmacosomes is by hydrolysis (including enzymatic) unlike liposomes the release of drug is by diffusion through bilayer, desorption from the surface or degradation of liposomes.
4. Unlike liposomes in pharmacosomes there is no need of following the tedious, time consuming step for removing the free, un-entrapped drug from the formulation.

5. In liposomes there are chances of sedimentation and leaching of drug but in pharmacosomes the leakage of drug does not take place because the drug is covalently linked to the carrier.

Demerits of Pharmacosomes[36]

1. Synthesis of a compound depends upon its amphiphilic nature.
2. Required surface and bulk interaction of lipids with drugs.
3. Required covalent bonding to protect the leakage of drugs.
4. On storage, undergo fusion and aggregation, as well as chemical hydrolysis.

Therapeutic Application of Drugs After incorporation with Pharmacosomes[13]

Drug	Efffect after Incorporation in Pharmacosomes
Pindolol diglyceride	Three to five fold increase in plasma concentration Lower renal clearance
Dermatan sulphate ,Taxol , Cytarbin	Improved biological activity
Bupranolol hydrochloride	Enhanced effect on intraocular pressure Enhance lymph transport
Amoxicillin	Improved cytoprotection and treatment of H.pylori infections in male rats

TRANSFERSOME

Transfersomes is latest novel drug delivery system and are special types of liposomes, consist of phosphatidylcholine and an edge activator. They are ultra flexible membrane, which deliver the drug reproducibly either into or through the skin. The system delivers the drug with high efficiency depending on the choice of administration or application. This system has several order magnitude of elasticity and flexibility over liposomal drug delivery which makes it favourable for efficient skin penetration and hence for the novel drug delivery system.[39] Transferosomes is a highly adaptable and optimized mixed lipid complex aggregates. The transferosomes crossvarious transport barriers efficiently and then act as a drug carrier for non invasive targeted drug delivery and sustained release of therapeutic agents. Transferosomes are super molecular entities that can pass through a permeability barrier and there by transport material from the site of application to the destination. The transferosomes enhance the permeation of most of low as well as high molecular weight drugs.The entrapment efficiency can reach upto 90%. the transferosomes penetrate the stratum corneum by either intracellular or transcellular. Transferosomes" was introduce for the effective transdermal delivery of number of low and high molecular weight drugs. It consist of both hydrophilic and hydrophobic properties, high deformability gives better

penetration of intact vesicles. Transferosomes have been developed in order to take advantage of phospholipids vesicles as transdermal drug carrier.[40]

Salient Features Of Transfersomes-[41]

1 Transfersomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubilities.

1. Transfersomes can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without significant loss.
2. High deformability of this system gives better penetration of intact vesicles.
3. They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anaesthetic,corticosteroids, sex hormone, anticancer, insulin and albumin.
4. They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes.
5. They have high entrapment efficiency, in case of lipophilic drug near to 90%.
6. They protect the encapsulated drug from metabolic degradation example: protein and peptides .
7. They act as depot, releasing their contents slowly and gradually.
8. They can be used for both systemic as well as topical delivery of drug.
9. Easy to scale up, as procedure is simple, and avoid unnecessary use or pharmaceutically unacceptable additives.

Application of Transfersome

Transfersomes as drug delivery systems have the potential for providing controlled release of the administered drug and increasing the stability of labile drugs.[41]

Ethosomes

Ethosomal drug delivery system is non-invasive and delivers the drug to the deep skin layers to systemic circulation. Ethosomes are soft, malleable vesicles composed mainly of phospholipids (phosphatidylcholine, phosphatidylserine, and phosphatitidic acid), ethanol (relatively high concentration) and water having a size range from tens of nanometres to microns. Size of ethosomes depends upon the method of preparation and application of techniques like sonication. These “soft vesicles” represents novel vesicular carrier for enhanced delivery through skin. The soft, malleable vesicles tailored for enhanced delivery of active agents[42,43] Drug delivery can be modulated by altering alcohol: water or alcohol-

polyol: water ratio. Some preferred phospholipids are soya phospholipids such as Phospholipon 90 (PL-90).[44] High concentration of alcohol (20-45%) in the formulation provides soft, flexible characteristics and stability to the vesicles and it also disrupts lipid bilayer structure of the skin results in an increase in the membrane permeability. Examples of alcohols, which can be used, include ethanol (commonly used) and isopropyl alcohol. Glycols can also be used in preparations as a penetration enhancer. Among glycols propylene glycol and Transcutol are generally used. For providing further stability to ethosome vesicles cholesterol at concentrations ranging between about 0.1-1% can also be incorporated.[45]

Therapeutic application

Ethosomes, the high ethanol containing vesicles are able to penetrate the deeper layers of the skin and hence appear to be vesicles of choice for transdermal drug delivery of hydrophilic and impermeable drugs through the skin.[46]

1. Treatment of Herpetic Infection.
2. Treatment of AIDS.
3. Treatment of Parkinsonian Syndrome.
4. Treatment of Diabetes.

Efficient healing of S. aureus -induced deep dermal infections.[11]

Advantages of Ethosomes: [47]

1.Enhanced permeation of drug molecules to and through the skin to the systemic circulation

2. Contrary to deformation liposomes, ethosomes improve skin delivery of drugs both under occlusive and non-occlusive conditions .

3. Since composition and components of ethosomes are safe, they have various applications in pharmaceutical, veterinary and cosmetic field**.**

4. Better patient compliance.

5. Better solubility and stability of many drugs as compared to conventional vesicles.

7. Relatively smaller size as compared to conventional vesicles.

Limitations of Ethosomes [48]

1. Poor yield.

2. In case if shell locking is ineffective then the ethosomes may coalescence and fall apart on transfer into water.

3. Loss of product during transfer form organic to water media.

Sphingosome

Sphingosome may be defined as "concentric, bilayered vesicle in which an aqueous volume is entirely enclosed by a membranous lipid bilayer mainly composed of natural or synthetic sphingolipid". Liposomal formulation based on sphingo myelin based cholesterol has several advantages when compared to other formulation. The Sphingosomes are much more stable to acid hydrolysis, have better drug retention characteristics. Sphingosomes are administered in many ways these include parental route of administration such as intravenous, intramuscular, subcutaneous, and intraarterial. Generally it will be administered intravenous or some cases by inhalation. Sphingosomes may be administered orally or transdermally**.** Sphingosome are comprised of sphingolipid (sphingomyelin) and cholesterol and have an acidic intra liposomal pH ratio of sphingomylin and cholesterol varies in the range of 75/25 mol%/mol% (55/45 mol%/mol% most preferably).[49]

Advantages over the phospholipid liposomes-[50]

It is more stable than the phospholipid liposome because a Sphingolipid built up by only amide and ether linkage. They are more resistant to hydrolysis then ester linkage of lecithin. They also contain less double bond then lecithin and thus less subject to rancidity. . They also absorb less oil then lecithin which in consequence change in geometry and diameter.

Disadvantage

1. Higher cost of sphingolipid hinders the preparation and use of these vesicular systems.
2. Low entrapment efficacy.

Theuraputic application of Sphingosome-[51]

Cancer therapy

1. Used in non-Hodgkins lymphoma.
2. Used in large B-cell lymphoma66.
3. Used in non-small cell lung cancer, metastatic breast cancer.
4. Used in non-small cell lung cancer, breast cancer.
5. Used in relapsed small-cell lung cancer, relapsed ovarian cancer.

Tumor therapy

1. Used in colonic tumour.
2. Used in colon cancer and melanoma.

Antifugal therapy

Used in treating infectious disease.

Gene therapy

Used in radiation-induced lung injury (RILI).

Aquasome

Aquasomes are nanoparticulate carrier system but instead of being simple nanoparticles these are three layered self assembled structures, comprised of a solid phase nanocrystalline core coated with oligomeric film to which biochemically active molecules are adsorbed with or without modification.[52]Aquasomes are like “bodies of water" and their water like properties protect and preserve fragile biological molecules, and this property of maintaining conformational integrity as well as high degree of surface exposure is exploited in targeting of bioactive molecules like peptide and protein hormones, enzymes, antigens and genes to specific sites. These three layered structures are self-assembled by non covalent and ionic bonds. These carbohydrate stabilize nanoparticles of ceramic are known as “aquasomes”. The pharmacologically active molecule incorporated by co-polymerization, diffusion or adsorption to carbohydrate surface of pre formed nanoparticles. Aquasomes discovery comprises a principle from microbiology, food chemistry, biophysics and many discoveries including solid phase synthesis, supramolecular chemistry, molecular shape change and self assembly.[53]

Advantages

1.Aquasomes increases the therapeutic efficacy of pharmaceutically active agents and protects the drug from phagocytosis and degradation.

2. These systems act like a reservoirs to release the molecules either in a continuous or a pulsatile manner, avoiding a multiple-injection schedule.

3. These nanoparticles offer favorable environment for proteins thereby avoiding their denaturalization. This property is due to the presence of inorganic cores, which are coated with polyhydroxyl compounds and these are responsible for their hydrophilic behavior.

4. Multilayered aquasomes conjugated with bio recognition molecules such as antibodies, nucleic acid, peptides which are known as biological labels can be used for various imaging tests.

5. Enzyme activity and sensitivity toward molecular conformation made aquasome as a novel carrier for enzymes such as DNAses and pigment/dyes.

6. Aquasomes-based vaccines offer many advantages as a vaccine delivery system. Both cellular and humoral immune responses can be elicited to antigens adsorbed onto the surface of aquasomes.[54]

Emerging Vesicular Drug Delivery System-[55,56]

Sr.No	Carriers	Description	Application
1.	Enzymosomes	Liposomal construct engineered to provide a mini bio environment in which the enzyme covalently immobilized to the surface of liposomes	Targeted delivery to tumor cell
2.	Virosomes	Liposomes spiked with virus glycoprotein's, incorporated in the liposomal bilayer based on retrovirus based lipids	Immunological adjuvants
3.	Ufasomes	Vesicles enclosed by fatty acids obtained by long chain fatty acids by mechanical agitation of evaporated film in the presence of buffer solution	Ligand mediated drug targeting
4.	Cryptosomes	Lipid vesicle with surface coat composed of PC and of suitable polyoxyethylene derivative of phosphatidyl ethanolamine	Ligand mediated drug delivery
5.	Emulsomes	Nanosized lipid particles consisted of lipid assembly and a polar group	Parenteral delivery of poorly water soluble drugs
6.	Discosomes	Niosomes coupled with non-ionic surfactants	Ligand mediated drug targeting
7.	Genosomes	Artificial macromolecular complex for functional gene transfer	Cell specific gene transfer
8.	Photosomes .	Photolyase encapsulated in liposomes, which release the contents by photo triggered charges in membrane permeability characteristics	Photodynamic therapy
9.	Erythrosomes	Liposomal system in which chemically cross-linked human erythrocytes cytoskeletons are used as to which a lipid bilayer is coated	Targeting of macromolecular drugs
10.	Hemosomes	Heamoglobin containing liposomes engineered by immobilizing heamoglobin with polymerizable phospholipids	High capacity oxygen carrying
11.	Archaeosomes	Vesicles composed of gylcerolipids of archaea with potent adjuvant activity	Poor adjuvant activity

CONCLUSION

The above article gives an outline about the various vesicular systems depicting their importance, the system provides flexibility for drug design thus overcoming various bioavailability and solubility problems. Inspite of certain drawbacks, the vesicular delivery

systems still play an important role in the selective targeting and controlled delivery of various drugs. Drugs can be successfully delivered using lipoidal biocarriers such as liposomes, enzymosomes, ethosomes, transferosomes, pharmacosomes, sphingosomes, virosomes, emulsomes and non lipoidal biocarriers such as niosomes, bilosomes and aquasomes as per the convenience of therapy. All these biocarriers have been reported for their successfully site specific targeting.

REFERENCES

1. Sunil Kamboj, Vipin Saini, Nancy Magon, Suman Bala , Vikas Jhawat.2013. Vesicular drug delivery systems: A novel approach for drug targeting International Journal of Drug Delivery 5; 121-130
2. Saurabh Bansal, Chandan Prasad Kashyap, Geeta Aggarwal and SL Harikumar . 2012. A Comparative Review on Vesicular Drug Delivery System and Stability Issuse . International Journal Of Research In Pharmacy and Chemistry ;ISSN:2231-2781
3. 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
4. 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
5. 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
6. IbrahimA. 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
7. 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.
8. Ettmayer P., Amidon G.L., Clement B., Testa B., Lessons Learned from Marketed and Investigational Prodrugs, Journal of Medicinal Chemistry, 47; 2004:2393-2404
9. Bajaj H., Bisht S., Yadav M., Singh V., Bioavailability Enhancement: A Review, International Journal of Pharmacy and Biological Sciences, 2(2); 2011: 202-216

10. 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
11. Gyati Shilakari, Davinder Singh, Abhay Asthana 2013 Novel vesicular carriers for topical drug delivery and their application's. International Journal of Pharmaceutical Sciences Review and Research, ISSN 0976 – 044X
12. Mayank Gangwar, Ragini Singh, RK Goel, Gopal Nath 2012. Recent advances in various emerging vescicular systems: An overview. Asian Pacific Journal of Tropical Biomedicine. S1176-S11188
13. Amit Kumar Jha, Ravi Kumar, et al 2011,. "Vesicular system – Carrier for drug delivery" Pelagia Research library coden (USA) ISSN:0976-8688
14. 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
15. Xiaoling Li,Bhaskara R. Jasti, "Design of Controlled Release Drug Delivery Systems" McGraw-Hill eBooks Page no. 315-357
16. 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
17. Chiranjeevi G, M Muthukumaran, and B Krishnamoorthy. 2013 . A Review on Potency of Vesicular Systems in Targeting Drug Delivery Research Journal of Pharmaceutical, Biological and Chemical Sciences (RJPBCS) Volume 4 Issue 2 Page No. 156
18. Mansoori M. A., Agrawal S., Jawade S.,. Khan M. I. 2012.A Reviw on Liposome ,International Journal Of Advanced Research in Pharmaceutical & Bio Sciences(IJARPB),Volume 4 Page No.454
19. J.S. Dua, Prof. A. C. Rana2, Dr. A. K. Bhandari3.2012. Liposome: Method Of Preparation and Applications. International Journal of Pharmaceutical Studies and Research.E-ISSN 2229-4619
20. Murgesan senthil kumar,Ashwani singh rawat,Bharat khurana, Nanjaian mahadevan.2011. Proniosome Gel: A Novel Topical Delivery System. International Journal of Recent Advances in Pharmaceutical Research ISSN:2230-9306
21. Chauhan Tikshdeep, Arora Sonia, Parashar Bharat and Chandel Abhishek.2012. Liposome Drug Delivery: A Review, International Journal Of Pharmaceutical and Chemical Sciences,Volume3,Page No.762,ISSN:2277-5005

22. Rajesh Asija, Avinash Gupta, Hitesh Sharma.2014. Niosome – Vesicular Drug Delivery System International Research Journal for Inventions in Pharmaceutical Sciences, Vol 2 Issue 1, ISSN- 2321-7855
23. Lohumi Ashutosh, Rawat Suman, Sarkar Sidhyartha, Sipai Altaf bhai., Yadav M. Vandana.2012. A Novel Drug Delivery System: Niosome Review, Journal of Drug Delivery & Therapeutics.
24. Adel A. Alia, Randa M. Zakia, Shahira F. El Menshawea and Ahmed Abdel Baryab.2013. Formulation and in vitroEvalution of Diacerein Loaded Niosome, International Journal of Pharmacy and Pharmaceutical Sciences, Vol 6, Suppl 2.
25. Shivendra Kumar Dwivedi, Chanchal Patil, Manoj Nagar,.2013. Niosomes as a Drug Delivery System - An Overview, International Journal of Pharmaceutical &Research Sciences, Vol. 2, Issue 8, ISSN No: 2278-9464.
26. Rutvik P. Parmar1, Ramesh B. Parmar2 S.J. Thakkar Pharmacy College, Rajkot. Conceptual Aspects of Vesicular Drug Delivery System with Special Reference to Niosome. 2013. Asian J. Pharm. Tech.Vol. 3; Issue 2
27. Sonia Dhiman, Harsimran Kaur, Sandeep Arora.2012. Niosomes: A novel drug delivery system, International Journal of Pharmaceutical Sciences Review and Research, ISSN 0976 – 044X
28. De Pintu Kumar , De Arnab, “Pharmacosomes : A Potential Vesicular Drug delivery system” International Research Journal of Pharmacy; 2013: 3(3) ISSN 2230-8407
29. 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.
30. 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
31. 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
32. 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 Nanotechology, Vol. 3;Issue 2; 2010

33. 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
34. 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
35. Sunil Kamboj, Vipin Saini, Nancy Maggon, Suman Bala, Vikas Chander Jhawat 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
36. Meenakshi Chauhan ,Tanu Goyal, Ashwani Singh Rawat.2012.Pharmacosomes: Opening new doors for drug delivery , International Journal of Pharmacy and Pharmaceutical Sciences, Vol 4, ISSN- 0975-1491
37. Sreedevi.A, A.Swetha, Ch.Meenakshi and B.Rohit. 2012. Pharmacosomes a review International Journal of Pharmaceutical Sciences Review and Research volume 12, Page 114 Issue 1, ISSN 0976 – 044X
38. Shipra Duggal and Kapil Kanwar. 2012. Development and characterization of self assembeled nanoparticles :A review, International Journal of Pharmaceutical Sciences and Research, Vol. 3 (2), ISSN: 0975-8232
39. Suresh. D. Kumavat, Yogesh S. Chaudhari, Priyanka Borole, Pallavi Duvvuri, Nikita Bubera, Khushbu Shenghani, Pankit Shah, Preetesh mishra. 2013 Transferosomes: A Promising approach for transdermal drug delivery system, Asian Journal of Pharmaceutical Sciences and Research, volume 3 issue 5, ISSN 2249 - 4898
40. Pranay Patel , Urvish Patel.2012. review on transferosome, World Journal Of Pharmacological Research and Technology, ISSN 2347 - 4882
41. Avninder Kaur, Dr. Bharat Parashar, Nisha Gupta, Baljit Singh, Brajesh Maurya,Virendra Yadav. 2012. Transferosomes- An approch for Vesicular drug delivery system, Internationale Pharmaceutica ScienciaVol. 2 Issue 2, ISSN 2231-5896
42. Usha Rai, Dinesh Chandra, Shaundarya Kumar. 2013 .Ethosomal gel: A novel tool for Topical drug delivery, International Journal of Universal Pharmacy and life Sciences vol3 (2) ISSN: 2249-6793
43. Vivek Dave, Ashutosh Pareek, Sarvesh Paliwal .2012. Ethosome: A Novel Approach of Transdermal Drug Delivery System, IJARPB, Vol.2 (4):439- 452, ISSN2277 – 6222,

44. R rakesh, Kr Anoop.2012. ethosomes for transdrmal and topical drug delivery, International Journal of Pharmacy and Pharmaceutical Sciences ,ISSN- 0975-1491 Vol 4, Suppl 3, 2012
45. P. Anitha, S. Ramkanth, K. Uma Sankari, M. Alagusundaram, K. Gnanapraksah, P. Devaki Devi, R. Indira Prasanna. Ethosomes - A noninvasive vesicular carrier for transdermal drug delivery , International Journal of Review in Life Sciences ,vol1(1)
46. Seema M. Jadhav, Pournima Morey, Mrs. Manisha Karpe, Vilasrao Kadam. 2012.novel vesicular system:an overview, Journal of Applied Pharmaceutical Science 02 (01), 193-202
47. Nikalje Anna Pratima, Tiwari Shailee.2012 . Ethosomes: A Novel Tool for Transdermal Drug Delivery, International Journal of Research in Pharmacy and Science vol 2(1), ISSN: 2249–3522
48. Hiraman P. Nandure, Dr Prashant Puranik, Prabhanjan Giram, Vidya Lone.2013. Ethosome: A Novel Drug Carrier, International Journal of Pharmaceutical Research & Allied Sciences; Volume 2: Issue 3 ISSN 2277-3657
49. K.Ashok, A. rajendra kumar Sreekanth nama, B.brahmaiah prasanna kumar desu, chandu babu rao.2013.Sphingosomes:Anovel vesicular drug delivery system, International Journal Of Pharmaceutical Research & bio -Sciences, Volume 2(2); ISSN: 2277-8713
50. Swarnlata Saraf , S. Paliwal, Shailendra Saraf. 2011.Sphingosomes a novel appoach to vesicular drug delivery, International Journal of Current Scientific Research, vol 1(2)
51. Srinivas Lankalapalli and Madhupriya Damuluri.2012. Sphingosomes: Applications in targeted drug delivery, International Journal of Pharmaceutical,Chemical and Biological Sciences, vol 2(4); ISSN: 2249-9504
52. Patel Ravi, Thakkar Dhadhich, Shah Hiral,Shah kinjal, Chaudhary Sunita &shah Ragin.2013. A self assembled nanotechnology system – Aquasome , International Journal of Pharmacy and Integrated Life Sciences, Volume 1 – Issue 4, ISSN : 2320 - 0782
53. Sanjay S. Jain, Pramod S. Jagtap, Neha M. Dand, Kisan R. Jadhav and Vilasrao J. Kadam. 2012. Aquasomes: A novel drug carrier, Journal of Applied Pharmaceutical Science,vol 02 (01); ISSN: 2231-3354
54. Vivek P. Chavda, Moinuddin M. Soniwala, Jayant R. Chavda.2013. Aquasomes: An Attractive Niche as Peptide and Protein Carrier, PhTechMed, Vol-2/Issue-6, ISSN: 2278-1099

55. Shukla Ajay, Pandey Vikas, Shukla Rajesh, Bhatnagar Punit, Jain Suchit.2012. Herbosomes: A Current Concept of Herbal Drug Technology, An Overview, Journal of Medical Pharmaceutical And Allied Sciences,vol 01, ISSN NO. 2320 - 7418
56. Imran K. Tadwee, Sourabh Gore, Prashant Giradkar.2012. Advances in Topical Drug Delivery System: A Review, International Journal of Pharmaceutical Research & Allied Sciences, Volume 1; issue1: ISSN 2277-3657