INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Review Article

A COMPARATIVE REVIEW ON VESICULAR DRUG DELIVERY SYSTEM AND STABILITY ISSUES

Saurabh Bansal, Chandan Prasad Kashyap, Geeta Aggarwal and SL Harikumar

[1]Department of Pharmaceutics, Rayat and Bahra Institute of Pharmacy, Sahauran, Mohali, Punjab, India.

ABSTRACT

Designing of the drug in the vesicular system has brought a new life to the old pre-existing drugs and thus has improved their therapeutic efficacies by controlling and sustaining the actions. This review mainly focuses on the stability issues associated with vesicular drug delivery. Consequently a number of vesicular drug delivery systems like liposomes, niosomes, transfersomes, pharmacosomes, ethosomes, sphinosomes, colloidosomes, herosomes and cubosomes etc have been developed. Every new system shows one or more advantages over the older vesicular systems. 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 provesicular 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.

Keywords: Vesicles, Stability of Vesicular System.

INTRODUCTION

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[1]. It is capable of providing the drug to particular site of action. Encapsulation of the drug in vesicular structures is one such system, which can be predicted to prolong the existence of the drug in systemic circulation and reduce the toxicity[2]. Advances have since been made in the area of vesicular drug delivery, leading to the development of systems that allow drug targeting and the sustained or controlled release of conventional medicines. The stability of the vesicular system remains the area of interest due to the formation of vesicles. It has also reduced number of toxic, dose related side effects and maintained therapeutic efficacy of drugs for longer time duration by decreasing dosing frequency[3].Vesicular drug delivery reduces the cost of therapy by improved bioavailability of medication, especially in case of poorly soluble drugs. They can incorporate both by hydrophilic and liophilic drugs.

The vesicular systems are highly ordered assemblies of one or several concentric lipid bilayers formed, when certain amphiphillic building blocks are confronted with water. Vesicles can be formed from a diverse range of amphiphillic building blocks. The main aim is to control degradation of drug and loss, prevention of harmful side effects and increase the availability of the drug at the disease site[4].

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 biomembranes 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 overcome by the use of vesicular drug delivery systems. Vesicular drug delivery system has some of the advantages like:

1. Prolong the existence of the drug in 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.
2. Improves the bioavailability especially in the case of poorly soluble drugs.
3. Both hydrophilic and lipophilic drugs can be incorporated.
4. Delays elimination of rapidly metabolizable drugs and thus function as sustained release systems[5].

Along with the number of advantages vesicular system has some serious disadvantages which restrict their use:

Drugs passively, which may lead to low drug loading efficiency and drug leakage in preparation, preservation and transport invivo. Thus the major problem of their stability acts as a barrier and thus limiting their use[6].

Liposomes

Liposomes consist of one or more concentric lipid bilayers, which enclose an internal aqueous volume(s). For drug delivery applications liposomes are usually unilamellar and range in diameter from about 50 - 150 nm[7]. Larger liposomes are rapidly removed from the blood circulation. Liposomes are unique in their ability to accommodate drugs, which differ widely in physicochemical properties such as polarity, charge and size. Sites in liposomes where these drugs can localize include the liposome bilayer with its hydrophobic hydrocarbon chain core, its large polar surface, which can be neutral or charged and the internal aqueous space. The word drug is used as a generic term and refers to conventional drugs.

Liposomes are just hollow spheres of lipids, i.e. some lipids form membranes that close on themselves forming liposomes. The main component of liposome membranes is dipalmitoyl phosphatidil choline (DPPC, PC or EPC- egg phosph... choline). However, some other compunds are added in order to improve stability or other structural properties. Two compunds added are: dipalmitoyl phosphatidil glycerol (DPPG or PG) and cholesterol. Apparently, cholesterol has the effect of making the membrane less permeable by filling up holes or disruptions[8].

Advantages

- Phospholipids are one of the few solubilizers that are well tolerated.
- Liposomes may increase the solubility of insoluble drugs between one hundred to ten thousand fold[9].
- In the small intestine, liposomes are digested in the presence of bile and enzymes. The solubilized compound is liberated and further solubilized in bile and digested lipids.
- Ideal models for biological membranes as well as efficient carriers for drugs, diagnostics, vaccines, nutrients and other bioactive agents.
- Both water soluble and water insoluble compounds can be delivered[10].

Niosomes

Niosomes are formations of vesicles by hydrating mixture of cholesterol and nonionic surfactants. These are formed by self-assembly of non-ionic surfactants in aqueous media as spherical, unilamellar, multilamellar system and polyhedral structures in addition to inverse structures which appear only in non-aqueous solvent. Niosomes are non-ionic surfactant vesicles obtained on hydration of synthetic nonionic surfactants, with or without incorporation of cholesterol or other lipids. They are vesicular systems similar to liposomes that can be used as carriers of amphiphilic and lipophilic drugs[11]. The vesicles are defined to be composed of or relating to small, saclike bodies. In niosomes, the vesicles forming amphiphile is a non-ionic surfactant which is usually stabilized by addition of cholesterol and small amount of anionic surfactant such as dicetyl phosphate. Niosomes and liposomes are equiactive in drug delivery potential and both increase drug efficacy as compared with that of free drug. Niosomes are preferred over liposomes because the former exhibit high chemical stability and economy. One of the reasons for preparing niosomes is the assumed higher chemical stability of the surfactants than that of phopholipids, which are used in the preparation of liposomes. Due to the presence of ester bond, phospholipids are easily hydrolysed[12].

Advantages

- They improve the therapeutic performance of the drug molecules by delayed

clearance from the circulation, protecting the drug from biological environment and restricting effects to target cells[13].

- Handling and storage of surfactants requires no special conditions.
- They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of drugs.
- They can be made to reach the site of action by oral, parenteral as well as topical routes[14].
- They possess an infrastructure consisting of hydrophilic, amphiphilic and lipophilic moieties together and as a result can accommodate drug molecules with a wide range of solubilities.

Pharmacosomes

These 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[15]. The prodrug conjoins hydrophilic and lipophilic properties and therefore acquires amphiphilic characters and was found to reduce interfacial tension and thus at higher concentrations exhibits mesomorphic behavior. Because the system is formed by linking a drug (pharmakon) to a carrier (soma), they are called pharmacosomes. Pharmacosomes bearing unique advantages over liposome and noisome vesicles have come up as potential alternative to conventional vesicles[16].

Advantages

- They are an effective tool to achieve desired therapeutic goals such as drug targeting and controlled release.
- High and predetermined entrapment efficiency as drug and carrier form a stoichiometrically defined unit covalently linked together[17].
- Volume of inclusion doesn't influence entrapment efficiency.
- No need of removing the free, unentrapped drug from the formulation which is required in the case of liposomes.
- Improves bioavailability especially in the case of poorly soluble drugs.
- Drug carriers such as liposomes, nanoparticles, microemulsions which have lead to low drug-loading efficiency, physical stability such as fusion, aggregation, sedimentation and drug leakage during preparation, preservation etc is absent in pharmacosomes[18].

Ethosomes

The vesicles have been well known for their importance in cellular communication and particle transportation for many years. Researchers have understood the properties of vesicles structure for use in better drug delivery within their cavities, which would to tag the vesicle for cell specificity. One of the major advances in vesicle research was finding a vesicle derivative, known as an Ethosomes[19]. Ethosomes are noninvasive delivery carriers that enable drugs to reach the deep skin layers and/or the systemic circulation. These are soft, malleable vesicles tailored for enhanced delivery of active agents. They are composed mainly of phospholipids, (phosphatidylcholine, phosphatidylserine, phosphatitidic acid), high concentration of ethanol and water. The high concentration of ethanol makes the ethosomes unique, as ethanol is known for its disturbance of skin lipid bilayer organization therefore, when integrated into a vesicle membrane it gives that vesicle the ability to penetrate the stratum corneum. Also because of their high ethanol concentration, the lipid membrane is packed less tightly than conventional vesicles but has equivalent stability, allowing a more malleable structure and improves drug distribution ability in stratum corneum lipids[20].

Advantages

- Ethosomes are enhanced permeation of drug through skin for transdermal and dermal delivery.
- Ethosomes are platform for the delivery of large and diverse group of drugs (peptides, protein molecules).
- Ethosome composition is safe and the components are approved for pharmaceutical and cosmetic use.
- High patient compliance. The Ethosomal drug is administrated in semisolid form (gel or cream), producing high patient compliance by is high. In contrast, Iontophoresis and Phonophoresis are relatively complicated to use which will affect patient compliance.
- The Ethosomal system is passive, non-invasive and is available for immediate commercialization.
- Various application in Pharmaceutical, Veterinary, Cosmetic field[21].

Transferosomes

Liposomal as well as niosomal systems, are not suitable for transdermal delivery, because of their poor skin permeability, breaking of vesicles, leakage of drug, aggregation and fusion of vesicles. To overcome these problems, a new type of carrier system called "transfersome" has recently been introduced, which is capable of transdermal delivery of low as well as high molecular weight drugs[22].

Transfersomes are specially optimized, ultradeformable (ultraflexible) lipid supramolecular aggregates, which are able to penetrate the mammalian skin intact. Each transfersome consists of at least one inner aqueous compartment, which is surrounded by a lipid bilayer with specially tailored properties, due to the incorporation of "edge activators" into the vesicular membrane. Surfactants such as sodium cholate, sodium deoxycholate, span 80 and Tween 80, have been used as edge activators. It was suggested that transfersomes could respond to external stress by rapid shape transformations requiring low energy. These novel carriers are applied in the form of semi-dilute suspension, without occlusion. Due to their deformability, transfersomes are good candidates for the non-invasive delivery of small, medium and large sized drugs[23]. They have been used as drug carriers for a range of small molecules, peptides, proteins and vaccines, both in vitro and in vivo. Transfersomes penetrate through the pores of stratum corneum which are smaller than its size and get into the underlying viable skin in intact form. This is because of its deformable nature[24]. Multiliter quantities of sterile, well-defined transfersomes containing drug can be and have been prepared relatively easily. Materials commonly used for the preparation of transferosomes are phospholipids (soya phosphatidyl choline, egg phosphatidyl choline), surfactant (tween 80, sodium cholate) for providing flexibility, alcohol (ethanol, methanol) as a solvent, dye for confocal scanning laser microscopy (CSLM) and buffering agent (saline phosphate buffer pH 7.4), as a hydrating medium.

Advantages

- Delivery of peptides by transfersomes provides a very successful means for the noninvasive therapeutic use of such large molecular weight drugs on the skin.
- They are used as a carrier for protein and peptides like insulin, bovine serum albumin, vaccines, etc. The delivery of these large biogenic molecules into the body is difficult. When given orally, they are completely degraded in the GI tract[25].

Colloidosomes

Colloidosomes are the hollow shell microcapsules consisting of coagulated or fused particles at interface of emulsion droplets. Colloidosomes have exciting potential applications in controlled release of drugs, proteins, vitamins as well as in cosmetics and food supplements. Colloidosomes have a great encapsulation efficacy with a wide control over size, permeability, mechanical strength and compatibility[26]. Colloidosomes is a novel class of microcapsules whose shell consists of coagulated or fused colloid particles at interface of emulsion droplets. The particles self assemble on the surface of droplets in order to minimize the total interfacial energy forming colloidosomes. Such structures were produced for first time by templating latex particles adsorbed on the surface of octanol-in-water emulsion drops and subsequent removal of oil after fusing the particles monolayers. Similar structures have also been obtained by templating water-in-oil emulsions and templated solid nanoparticles on the surface of solid sacrificial microparticles based on electrostatic attraction and layer by layer assembly of multilayer shells consisting of alternating positively and negatively charged nanoparticles or polyelectrolytes. The final hollow shells are obtained by removal of central, sacrificial colloidal particles[27]. Colloidosomes assemble polymer latex colloidal particles into shells around water-in-oil emulsion drops followed by partial fusion of shell and centrifugal transfer into water to yield stable capsules in which the shell permeability can be controlled by adjustment of partial fusion conditions. Hairy colloidosomes whose shell consists of microrod particles, are designed and fabricated novel colloidosome capsules that consist of aqueous gel core and shells of polymeric microrods. This has been achieved by templating water-in-oil emulsions stabilized by rod like particles followed by gelling of the aqueous phase, dissolution of oil phase in ethanol and redispersion of obtained colloidosome microcapsules in water.

Advantages

- Control of the size allows flexibility in applications and choice of encapsulated materials[28].
- Colloidosome membrane offer great potential in controlling the permeability of the entrapped species and allow the selective and time release.
- Control of the mechanical strength allows the yield stress to be adjusted to withstand varying of mechanical loads and to enable release by defined shear rates[29].

Herbosomes

The term "herbo" means plant, while "some" means cell-like. Over the past century, phytochemical and phyto-pharmacological sciences established the compositions, biological activities and health promoting benefits of numerous botanical products[30]. Most of the biologically active constituents of

plants are polar or water soluble molecules. However, water soluble phytoconstituents (like flavonoids, tannins, glycosidic aglycones etc) are poorly absorbed either due to their large moleculer size which cannot absorbed by passive diffusion, or due to their poor lipid solubility, severely limiting their ability to pass across the lipid-rich biological membranes, resulting poor bioavailability. Phytomedicines, complex chemical mixtures prepared from plants, have been used for health maintenance since ancient times. But many phytomedicines are limited in their effectiveness because they are poorly absorbed when taken by mouth. Herbosomes are also often known as phytosomes. Herbosomes exhibit better pharmacokinetic and pharmacodynamic profile than conventional herbal extracts[31]. Molecular layer consisting of PC and other phospholipids provides a continuous matrix into which the proteins insert.

Advantages

- It enhances the absorption of lipid insoluble polar phytoconstituents through oral as well as topical route showing better bioavailability, hence significantly greater therapeutic benefit[32].
- As the absorption of active constituent(s) is improved, its dose requirement is also reduced.
- Phosphatidylcholine used in preparation of herbosomes, besides acting as a carrier also acts as a hepatoprotective, hence giving the synergistic effect when hepatoprotective substances are employed.
- Herbosome permeates the non-lipophilic botanical extract to be better absorbed in intestinal lumen.
- Unlike liposome, chemical bonds are formed between phosphatidylcholine molecule and phytoconstituent, so the Herbosomes show better stability profile[33].

Sphinosomes

Liposome stability problems are of course much more severe so it is very important task to improve the liposomal stability. Liposomal phospholipid can undergo chemical degradation such as oxidation and hydrolysis either as a result of these changes or otherwise liposome maintained in aqueous suspension may aggregate, fuse, or leak their content. Hydrolysis of ester linkage will slow at pH value close to neutral. The hydrolysis may be avoided altogether by use of lipid which contains ether or amide linkage instead of ester linkage (such are found in sphingolipid) or phospholipid derivatives with the 2- ester linkage replaced by carbomoyloxy function**.** Thus sphingolipid are been nowadays used for the preparation of stable liposomes known as sphingosomes[34]. 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.

Sphingosomes are administered in many ways these include parentral route of administration such as intravenous, intramuscular, subcutaneous, and intra-arterial. Generally it will be administered intravenous or some cases by inhalation. Often it will be administered into a large central vein, such as the superior vena cava and inferior vena cava to allow highly concentrated solution to be administered into large volume and flow vessels. Sphingosomes may be administered orally or transdermally. In simple way we can say sphingosome is liposome which is composed of sphingolipid.

Advantages

- Provide selective passive targeting to tumor tissue.
- Increase efficacy and therapeutic index.
- Increase stability via encapsulation.
- Reduction in toxicity of the encapsulated agent.
- Improve pharmacokinetic effect (increase circulation time).
- Flexibility to couple with site specific ligands to achieve active targeting[35].

Cubosomes

Bicontinuous cubic liquid crystalline materials are active ingredients because they give the unique structural ends to controlle release applications. Amphiphilic molecules form bicontinuous water and oil channels, where “bicontinuous” refers to two distinct (continuous, but non-intersecting) hydrophilic regions separated by the bilayer. Cubosomes are discrete, sub micron, nanostructured particles of bicontinuous cubic liquid crystalline phase[36]. Cubosomes possess the same microstructure as the parent cubic phase but have much larger specific surface area and their dispersions have much lower viscosity than the bulk cubic phase. The ability of cubic phases to exist as discrete dispersed colloidal particles or cubosomes is perhaps the most intriguing. Whereas most concentrated surfactants that form cubic liquid crystals lose these phases to micelle formation at high dilutions, a few surfactants have optimal water insolubility[37]. Their cubic phases exist in equilibrium with excess water and can be dispersed to form cubosomes. Cubosomes are

typically produced by high-energy dispersion of bulk cubic phase, followed by colloidal stabilization using polymeric surfactants. After formation of the cubosomes, the dispersion is formulated into a product and then applied to a substrate of interest, usually bodily tissue.

Advantages

- Cubic phase materials can be formed by simple combination of biologically compatible lipids and water and are thus well suited for use in treatments of skin, hair, and other body tissue.
- With respect to liposome, cubosome possesses a larger ratio between the bilayer area and the particle volume and a larger breaking resistance[38].

Stability Comparison of Some Effective Vesicular Systems

Liposomes	Liposomes have proved to be the good candidates for increasing the solubility of poorly soluble drugs. But the stability issue of liposomes remains an area which is surrounded by a number of problems due the formation of ice crystals in liposomes, the subsequent instability of bilayers leads to the leakage of entrapped material. The physical instability is another problem faced by liposomes. The oxidation of cholesterol and phospholipids also leads to the formulation instability. Chemical instability primarily indicates hydrolysis and oxidation of lipids. Hydrolysis detaches the hydrophobic chains of ester bonds. Oxidation is more likely due to the presence of unsaturated chains. Adding antioxidants to the liposome formulation can usually protect the lipids from oxidation. The cationic liposomes can be stable at 4 degree centigrade (refrigerator) for a long period of time if they are properly sterilized. Liposomes in plasma are prone to aggregation and exhibit leakage. The destabilization of liposomes is due to the lipid exchange between the liposomes and HDLs[8].
Niosomes	The niosomes even being superior than liposomes have various stability problems associated with them such as physical stability of fusion, aggregation, sedimentation and leakage on storage. The Hydrolysis of encapsulated drugs which limits the shelf life of the dispersion is also an issue for nisomes[39].
Pharmacosomes	Encaptured volume and drug-bilayer interactions do not influence entrapment efficiency, in case of pharmacosomes. Entrapment efficiency is not only high but predetermined, because drug itself in conjugation with lipids forms vesicles. It has no time-consuming steps for removing the free, unentrapped drug from the formulation. Since the drug is covalently linked, loss due to leakage of drug, does not take place[40].
Ethosomes	Ethosomes has initiated a new area in vesicular research for transdermal drug delivery which can provide better skin permeation and stability than liposomes. Application of ethosomes provides the advantages such as improved entrapment and physical stability[41].
Transferosomes	Transferosomes are chemically unstable because of their predisposition to oxidative degradation. Purity of natural phospholipids is another criterion militating against stability of transferosomes as drug delivery vehicles. These are more elastic than the standard liposomes and therefore are used as a novel carrier for effective transdermal drug delivery. Transfersomes are chemically unstable because of their predisposition to oxidative degradation, lack of purity of the natural phospholipids comes in the way of adoption of transfersomes as drug delivery vehicles[42].
Colloidosomes	Colloidosomes have a great, encapsulation efficacy with a wide control over size, permeability, mechanical strength and compatibility. Allows encapsulation of fragile and sensitive ingredients such as biomolecities and cells. Major problem in the colloidosome manufacture is the poor yield of particles. If the shell locking is inefficient then the colloidosomes simply coalesce and fall apart on transfer into water. In addition a large proportion of the colloidosomes seem to be lost on the transfer from organic to water media[43].
Herbosomes	Chemical bonds are formed between phosphatidylcholine molecule and phytoconstituent, so the herbosomes show better stability profile with appreciable drug entrapment[44].
Sphingosomes	Sphingolipid are been nowadays used for the preparation of stable liposomes known as sphingosomes. Higher cost of sphingolipid hinders the preparation and use of these vesicular systems. They show better stability as compared to liposomes though they have low entrapment efficacy[35]. Sphingosomes solve the major drawback of vesicle system (liposomes, niosomes) like less stability, less in vivo circulation time, low tumor loading efficacy in case of cancer therapy[45].
Cubosomes	Cubosomes posses the simple production procedure and have better chemico-physical stability. They are the good option with many advantages over liposomes, manufacture of cubosomes on a large scale embodied difficulty because of their viscosity[37].

Approaches for improvement of vesicular system

Pro-vesicular Drug Delivery

Pro vesicular drug delivery developed to overcome the stability problems associated with vesicular drug delivery systems composed of water soluble porous powder as a carrier drug is dissolved in organic solvent to produce free-flowing granular product. It can avoid many of the problems associated with aqueous vesicular dispersions[46].

Types of pro vesicular drug delivery systems:

Proliposomes, Proniosomes

Comparision between liposomes and proliposomes.

Liposomes-Unilamellar or multilamellar spheroid structures composed of lipid molecules, often phospholipids. They show controlled release and increased solubility. But have tendency to aggregate or fuse, susceptible to hydrolysis or oxidation.

Proliposomes-an alternative forms to conventional liposomal formulation Composed of water soluble porous powder as a carrier,

phospholipids and drugs dissolved in organic solvent. Lipid and drug are coated on to a soluble carrier to form free-flowing granular material[47]. Show controlled release, better stability, ease of handling and increased solubility.

Comparision between niosomes and proniosomes

Niosomes-are non-ionic surfactant based multilamellar or unilamellar vesicles, aqueous solution of solute is entirely enclosed by a membrane of surfactant macro-molecules as bilayers. They are cheap and chemically stable but posses' problems related to physical stability such as fusion, aggregation, sedimentation and leakage on storage.

Proniosomes-approach minimizes the problems associated with niosomes as it is a dry and free flowing product which is more stable during sterilization and storage[48]. Ease of transfer, distribution, measuring and storage make it a versatile delivery system. Proniosomes are water-soluble carrier particles that are coated with surfactant.

Coated vesicles

Improving the stability of vesicular systems is of great concern. A number of attempts have been made to improve the stability of vesicles by preparing polymerizable vesicles such as polymer-izable liposomes[49]. Increasing the circulation half-life of liposomes by coating of nonionic surfactant and by using polyethylene glycol. Recently, a method to produce stable, discrete, polymer-coated niosomal vesicles for controlled delivery of the contents has been reported. Among the various methods employed for increasing the stability of niosomes, microencapsulation technique has gained wide attention[50]. Polymer coating of the vesicle can be achieved by interfacial polycondensation. The polymer-coated vesicles are slightly larger in size as compared to their uncoated counterparts. The release of drug from polymer-coated vesicles is retarded as compared to plain vesicles. This may be attributed to the effective double barrier produced by the polymeric coat[51]. In order to obtain a stable and protective vesicular system, this system paves way for a newer dimension in vesicular carrier system stability.

Layerosomes

The layer-by-layer coating concept is one of the strategies used for the preparation or the stabilization of nanosystems[52]. The layersomes are conventional liposomes coated with one or multiple layers of biocompatible polyelectrolytes in order to stabilise their structure. The formulation strategy is based on an alternative coating procedure of positive poly(lysine) (pLL) and negative poly(glutamic acid) (pGA) polypeptides on initially charged small unilamellar liposomes. The major drawback of liposomes is their instability during storage or in biological media which is related to surface properties. This surface modification stabilized the structure of the liposomes and led to stable drug delivery systems. Oral administration or their incorporation in biomaterials are among potential fields of application[53]. Thus the concept of layerosomes has brought forward the stable nanosystem.

Ufosomes

The formation of fatty acid vesicles are named "ufasomes," ufosomes are unsaturated fatty acid liposomes. Fatty acid vesicles are colloidal suspensions of closed lipid bilayers that are composed of fatty acids and their ionized species (soap). They are observed in a small region within the fatty acid-soap-water ternary phase diagram above the chain melting temperature (Tm) of the corresponding fatty acid-soap mixture[54]. Fatty acid vesicles always contain two types of amphiphiles, the nonionized neutral form and the ionized form (the negatively charged soap). The ratio of nonionized neutral form and the ionized form is critical for the vesicle stability. Fatty acid vesicles are actually mixed "fatty acid/soap vesicles". Ufasome membranes are much more stabilized in comparison to liposomes[55].

Future prospectives for betterment of vesicular delivery

Aquasomes

Three layered self assembly compositions with ceramics carbon nanocrystalline particulate core coated with, glassy cellobiose specific targeting and molecular shielding[56].

Cryptosmes

Lipid vesicles with a surface coat composed of pc and of suitable polyoxoyethylene derivative of phosphotidyl ethanolamine[57]. Capable of ligand mediated drug targeting.

Discomes

Niosomes solublized with non ionic surfactant solutions (polyoxyethylene cetyl ether class). Show ligand mediated drug targeting[41].

Emulsomes

Nanosize Lipid particles (bioadhesives nanoemulsion) consisted of microscopic lipid assembly with apolar core[18]. Parenteral delivery of poorly water soluble drugs.

Enzymosomes
Liposomal constructs engineered to provide a mini bioenvironmental in which enzymes are covalently immobilized or coupled to the surface of liposomes. Targeted delivery to tumor cell[58].

Genosomes
Artificial macromolecular complexes for functional gene transfer .Cationic lipids are most suitable because they possess high biodegradability and stability in the blood stream[59]. Cell specific gene transfer.

Photosomes
Photolysase encapsulated in liposomes, which release the content photo-triggered charges in membrane permeability characteristics[60].

Virosomes
Liposomes spiked with virus glycoprotein, incorporated into the liposomal bilayers based on retro viruses' derived lipids[61].

Vesosomes
Nested bilayer compartment in vitro via the inter digested bilayer phase formed by adding ethanol to a variety of saturated phospholipids[62]. Multiple compartments of the vesosomes give better protection to the interior contents in serum.

Proteosomes
High molecular weight multi-submit enzyme complexes with catalytic activity, which is specifically due to the assembly pattern of enzymes. Better catalytic activity turnover than non associated enzymes[63].

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. The significance of the system lies in controlling and sustaining of drug action. Though there are number of shortcomings associated with vesicular delivery, still they play an important role in bringing new life to the old pre-existing drugs. The upcoming new systems are predicted to bring forward the new era of drug delivery. The approaches at pro-level and coating etc are other prospectives in vesicular delivery.

REFERENCES

1. Robinson JR and Lee VHL. In Controlled Drug Delivery:Fundamental Applications, 1987; 2(N4):7.
2. Kao GY, Change LJ and Allen TM. Gene Ther, 1996; 3(4):250-260.
3. Goldberg EP. Eds, In Targeted Drugs, Wiley, NY, 1983; 2:312.
4. Gregariadis G. Nature, 1977; 265:407.
5. Post G, Krisch R and Koestler T. In Gegoriadis G Eds,Liposomes Tech, CRC Press Inc, 1983; F1:29.
6. Breimer DD and Speiser R. Topics in Pharmaceutical Sciences, Flsevier Science Publishers, New York, USA, 1985; 57:291.
7. Yatvin MB and Lelkes PI. Med. Phys, 1982; 9:149.
8. Allen TM, Ahmed I, Lopes De Menezes DE and Moase EH. Biochem. Soc. Trans, 1995; 23:1073.
9. Kirpotin DB and Lasic DD. Papahadjobpoulos, D.Eds, Medical Applications of Liposomes, Elsevier, 1998; 4:325.
10. Deamer DW and Lister PS. Liposome Prep:Methods and Mechanism in Liposomes, Marcel Dekker, 1983; 1:27.
11. Hunter CA. Vesicular System (Niosomes and Liposomes) J.Pharm.Pharmacol, 1988; 33:161.
12. Uchegbu FI and Vyas PS, Nonionic Surfactant Based Vesicles in Drug Delivery Int., J.Pharm., 1998; 7:33.
13. Manosroi A, Characterization of Vesicules Prepared with Various Nonionic Surfactant Mixed with Cholesterol., Colloids and Surfaces, Biointerfaces, 2003; 30:129.
14. Handjani VRM. Dispersion of Lamellar Phases of Nonionic Lipids in Cosmetic Products, Int J Cosmetic Sc., 1979; 30:212.
15. Mantelli S, Speiser P and Hauser H. Chem. Phys. Lipids, 1985; 37:329.
16. Leo A and Hansche FD. Chem. Rev., 1971; 71:525.
17. Yadav JB. Advanced Practical Physical Chemistry, Goel Publishing House Meeruth India, 1990; 1:74.
18. Vyas SP, Jaitely V and Kanuja P. Indian J.Exp. Biology, 1997; 35:212.
19. Joke A, Bouwstra, Loan Honeywell-Nguyen, P.Vesicles as a Tool for T.D.D.S. Drug Discovery Today: Technologies, Drug Delivery From Nanotech, 2005; 2(1):67-74.
20. Gangwar S, Singh S and Garg G. Ethosomes: Novel Tool for Drug Delivery Through The Skin. J.Pharm Res, 2010; 3(4):688-691.
21. Dubey V, Mishra D, Jain NK, Dutta T, Nahar M and Saraf DK. T.D.D of

Antipsoriatic agent via ethanolic Liposomes J.Control, 2007; 123:148-154.
22. Cevc G, Schatlein A and Blume G. J.Control Release, 1995; 36:3.
23. Jain S, Jaio N, Bhadra D, Tivari AK and Jain NK. Current Drug Delivery, 2005; 2(3):223.
24. Vinod KR, Kumar MS, Anbazhagan S, Sandhya S, Saikumar P, Rohit RT, Banji D. Critical issues related to transfersomes-novel vesicular system Acta Sci Pol Technol Aliment 2012; 11(1):67-82.
25. Nanda A, Nanda S, Dhall M and Rao R; Transferosomes A Novel Ultradeformable Vesicular Carrier for T.D.D.S, 2005; 5:395.
26. Biju SS, Talegoankar S, Mishra PR and Khar RK, Vesicular System An Overiew. Ind. J.Pharm. Sci., 2006; 68:141-153.
27. Lee D and Weitz DA. Double Emulsion Templated Nanoparticle Colloiodosomes with Selective Permeability. Adv. Mater, 2008; 20:3498-3503.\
28. Rawat M and Saraf S. Liposphere Emerging Carriers in The Delivery of Protein and Peptides, Int J.Pharm. Sci. Nanotechhnol, 2008; 1:207-214.
29. Dinsmare AD and Weitz DA. Colloidosomes: Selectively Permeable Capsules Composed of Colloidal Particles. Science, 2002; 298:1006-1009.
30. Mukherjee PK and Wahile A. Integrated Approaches Towards Drug Development from Ayurveda and Other Indian System Of Medicine. J.Ethanopharmaol, 2006; 103:25-35.
31. Facino RM, Carini M and Aldini G. Free Radicals Sea Action Arzneim. Forsch., 1994; 44: 592-601.
32. Filburn CR, Kettenacker R and Griffin DW. Bioavailability of Silybin-Pc Complex in Dogs J.Vet Pharmacol.Ther., 2007; 30:132-138.
33. Gabetta B, Zini GF. Spectroscopic Studies, Planta Med., 1989; 55:615.
34. Bangha AD, Standish MM, Watkins JG and Carini M. Diffusion of Univalent Ions Across The Lamellae of Swollen Phospholipid, 1965; 13:238.
35. Hunt C and Tsang S. Int J.Pharm, 1981; 8(2):101.
36. Andersson S, Jacob M. Structure of Cubosomes-A Closed Lipid Bilayer Aggregate Zeitschrift fier Kristallographie., 1995; 210:315-318.
37. Boyd BJ. Character Of Drug Release from Cubosomes Using The Pressure Ultrafiltration Method. Int J.Pharmaceutics, 2003; 260:239-247.
38. Luzzate V and Husson F. The Structure of the Liquid Crystalline Phases of Lipid Water System J.Cell, 1962; 12:209-219.
39. Ballie AJ, Florence AT, Hume LK, Muirhead GT and Rogerson A. The Prep. And Prop. Of Niosomes Non-ionic Surfactant Vesicles, J.Pharm.Pharmacol., 1995; 37:863-868.
40. Khopade AJ, Jain S and Jain NK. Int.J.Pharm.,2002; 241:145.
41. Braunfalco O, Kortung HC and Maibach HI. Gries Bach Conference: Liposomes Dermatitis. Springerverlag. Berlin, 1992; 201:19-23.
42. Vara B, Khopade AJ and Jain NK. Proniosome Based T.D.D, J.Control Rev., 1998; 54:149-165.
43. Chanchal D and Swarnlata S. Novel Approaches in Herbal Cosmetics: J.Cosmet.Dermatol, 2008; 7:89-95.
44. Murray D. Phytosomes- Increase The Absorption of Herbal Extract, 2008; 122:212-215.
45. Swarnlata S, Deepankar G, Chanchal Deep K, Shailendra S. Int J Cur Sci Res. Sphingosomes a novel approach to vesicular drug delivery, 2011; 1(2):63-68.
46. Ijeoma FV and Vyas SP. Int. J.Pharm., 1998; 172:33-70.
47. Kim S. Drugs, 1993; 46:618-638.
48. Fang JY, Yusy WU, Haung YB and Tsai YH. Int. J.Pharm, 2001; 215:91-99.
49. Johnston DS, Sanghera S, Pons M, Chapman D. Phospholipid polymers synthesis and spectra. Biochem. Biophys. Acta, 1980; 602:57–69.
50. Yeung YW, Nixon JR. Preparation of microencapsulated liposomes I. J. Microencapsulation, 1988; 5:331–337.
51. Vyas SP and Venkatesan N. Pharmaceutica Acta Helvetiae,1999; 74:51–58.
52. Sukhorukov G, Fery A, Mohwald H. Intelligent micro- and nanocapsules. Prog. Polym. Sci., 2005; 16:885–897.
53. Ciobanu M, Heurtault B, Schultz P, Ruhlmann C, Muller CD, Frisch B. International Journal of Pharmaceutics, 2007; 344:154–157.
54. Morigaki K, Walde P. Fatty acid vesicles. Curr Opin Colloid Interface Sci 2007; 12(75):80

55. Vinod KR, Kumar MS, Anbazhagan S, Sandhya S, Saikumar P, Rohit RT, Banji D. Critical issues related to transfersomes-novel vesicular system Acta Sci Pol Technol Aliment 2012; 11(1):67-82
56. Godin B, Touitou E. Crit.Rev.Ther.Drug Carrier Syst, 2003; 20:63.
57. Kretschmar M, Amselem S , Zawoznik E and Mosbach K. Mycoses, 2001; 44:281.
58. Huckriede A, Bungener L, Daemen T and Wilschut J. Methods Enzymol, 2003; 373:74.
59. PetitFree C, Clingen PH, Arlett CF and Green MH. J.Invest.Dermatol, 1998; 111:354.
60. Cuppoletti J, Mayhew E, Zobel CR and Jung CV. Proc.Natil.Acad.Sci.USA, 1981; 78:37-86.
61. Babizhayev MA. Arch. Biochem. Biophys, 1988; 266:466.
62. Kisak ET, Coldren B, Evans CA and Zasadzinski JA. Curr.Med.CheM, 2004; 279:11696.
63. Krishnan L, Patil S, Patil GB and Sprott GB, J.Immunol., 2001; 166:1885.