

Review Article



Ufasomes: An Emerging Vesicular System and A Comparative Study with Other Vesicular Carriers

Navjot Singh¹, Gurjeet Singh^{1*}, Lakhvir Kaur¹, RK Dhawan², Gurpreet Singh Sandhu³, Manu Sharma¹, Manjeet Kaur¹

¹Department of Pharmaceutics, Khalsa College of Pharmacy, Amritsar, Punjab, 143001, India.

²Department of Pharmacology, Khalsa College of Pharmacy, Amritsar, Punjab, 143001, India.

³Department of Pharmaceutical Analysis, Khalsa College of Pharmacy, Amritsar, Punjab, 143001, India.

*Corresponding author's E-mail: sainigurjeet21@gmail.com

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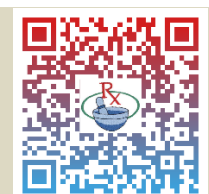
ABSTRACT

In the advanced period, the drug delivery turns out to be more targeted and controlled by the utilization of different Novel drug delivery system (NDDS). In the present time the pace of drug delivery and site of activity can be predetermined by the vesicular drug delivery system for better action and more patient compliance. Liposomes, sphingosomes, cubosomes, ethosomes, niosomes, ufasomes, pharmacosomes etc are the recently evolved vesicular drug delivery system. In this review our focus will be the Ufasomes as the vesicular drug carrier. Ufasomes are the vesicular type of drug delivery system arranged by generally thin layer hydration method at different proportion of surfactant and cholesterol along with the API. Unsaturated Fatty acid and their salts are the primary surfactant utilized in this in the range of 4-7 pH as for the most part given as the topical form of drug delivery. They have the numerous positive considerations among the contenders as the strength, formulation cost and accessibility are significantly more than other vesicular system. The comparison between the mostly used and available carrier has been done to prove the dominance effect of the Ufasomes over them. This review inferred that Ufasomes are the promising vesicular drug delivery system for a scope of conceivable helpful applications.

Keywords: Pharmacosomes, Thin layer hydration, Ufasomes, Fatty acid and Dominance.

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INTRODUCTION

Drug delivery system is the medium to move the drug compound in the body securely and in controlled way to achieve the ideal therapeutic characteristics. The NDDS to be in a perfect condition should satisfy two requirements. firstly, it ought to transfer the drug at a predetermined rate according to the requirements of the body, over the period of treatment. Secondly, it should target the active entity to the site of activity. NDDS have the better impact as the conventional dosage forms does not meet these prerequisites¹. Recently different carrier systems and advancements have been widely determined to control the drug release and working on the adequacy and selectivity of dose. Presently, vesicles as a carrier system have turned into the vehicle of choice in drug delivery and lipid vesicles were utilized in immunology, membrane biology, diagnostic technique and in genetic engineering. Vesicular delivery system gives a productive technique to deliver drug to the site of action, prompting reduction of drug toxicity with less adverse impacts.

Novel drug delivery system endeavors to either support drug activity at a predetermined rate, or by keeping a consistent drug level in the body with attending minimization of undesirable adverse effects. It can likewise restrict drug activity by spatial placement of controlled delivery systems nearby in the diseased tissue or organ and target drug activity by utilizing carriers or chemical derivatization to transfer drug to specific cell. There are few benefits of novel drug delivery systems over conventional drug delivery system that they have the ideal remedial drug concentration in the blood or in tissue might be kept up for prolonged period of time². Duration for short half-life drug might be expanded by focusing on the site of activity and adverse effects might be mitigated. Frequent dosing and leakage of the drug might be decreased or rejected and better persistent consistence might be guaranteed³.

In this review article, an endeavor has been made to examine the vesicular drug delivery system and the attention is primarily on the Ufasomes and furthermore attempted to do an evaluation among them and to demonstrate the overwhelming impact of Ufasomes over liposomes and other carrier based vesicular system.

Vesicular drug delivery system

Novel vesicular drug delivery systems expect to transfer the drug at a rate coordinated by need of body during the time of treatment, and transport the drug to the site of activity. Biologic beginning of these vesicles was first introduced in 1965 by Bingham and has been given the



name Bingham bodies. The designated vesicular drug delivery system was created by Paul Ehrlich, in 1909, which transferred the drug directly to unhealthy cells. From that point forward, quantities of carriers were used to transfer the drug at target site and these incorporate immunoglobulins, serum proteins, engineered polymers etc.

Different types of vesicular drug system have arisen to satisfy the need of time as to make it more patient compliance by giving controlled and targeted delivery of drug. The controlled as well as the targeted delivery assists with keeping up with the drug body level for delayed time, decrease the dosing interval, diminish harmfulness and likewise suppresses down the adverse impacts and consequently guard from any harm to the healthy tissue by drug⁴.

In the idea of the vesicle, the chief element to investigate on different parts like it should be biodegradable, inert, nonpoisonous should not show any leakage, entrap both hydrophilic and lipophilic drug and should be highly stable in acidic or natural environment. The vesicular systems are highly ordered assemblies of one or a few concentric lipid bilayers shaped.

Various kinds of drug carriers are available. They are - particulate, polymeric, macromolecular, and cell carrier. Particulate sort carrier otherwise called a colloidal carrier system, incorporates lipid particles (low- and high-density lipoprotein-LDL and HDL, individually), microspheres, nanoparticles, polymeric micelles and vesicular like liposomes, niosomes pharmacosomes, virosomes, etc¹⁰. Furthermore, to study the advanced vesicular carrier system the most practical and stable form of carrier that is Ufasomes is discussed for the better understanding.

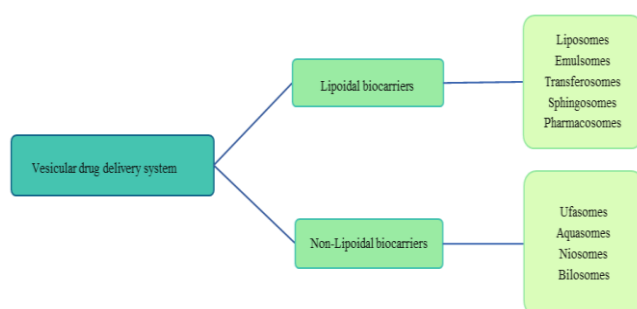


Figure 1: Order of vesicular drug delivery system

UFASOMES - AS VESICULAR DRUG CARRIER

Ufasomes are the vesicular structure comprised of unsaturated long chain fatty acid by the mechanical agitation of evaporated thin film layer of non-lipoidal bilayer. Membrane fatty acid hydrocarbon tails are arranged towards the layer inside, while their carboxyl groups are in touch with water, making a bilayer structure. Ufasomes are soapy suspensions of closed lipid bilayers made primarily of unsaturated fats^{7 8}. They usually prepared under pH range of 7 to 9 in nature. Unsaturated fat present in Ufasomes contains non-ionic impartial and

ionized type of negatively charged soap¹¹. It is reported by the Gebicki and Hicks in 1973 to overcome or to demonstrate the strength or more stable item when compared with other present vesicles like liposomes, ethosomes etc.

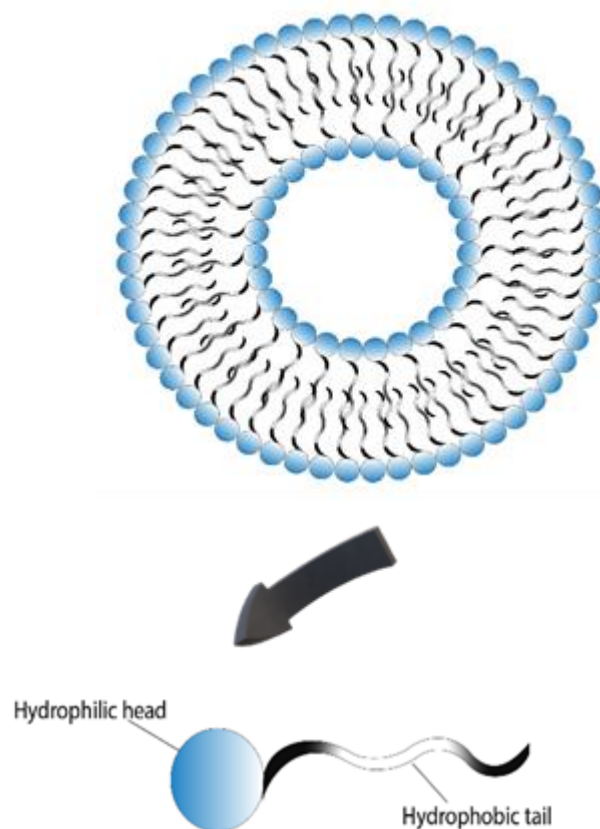


Figure 2: Structure of Ufasomes

Ufasomes is the better approach to improve drug dispersion through the skin. They are made to cross the skin as the normal actual boundary as it is obligatory to cross the shallow layer of skin to show the impact of drug penetration. Ufasomes contains the oleic and linoleic acid that normally acts as the permeation enhancer¹². Along with the surfactant cholesterol is added as the fluidity buffer and these two components along with API dissolved in particular solvent that has the solubility of all present components. The salts and ester of the oleic acid also act as the penetration enhancer that easily cross the subcutaneous layer of skin for the better effect of drug¹¹.

Advantages

Ufasomes prolongs the presence of the drug in systemic circulation and decreases the harmfulness. Particular take-up of the drug can be accomplished because of the delivery of drug directly to the site of action. Further develops the bioavailability particularly in the event of ineffectively dissolvable drugs. Both hydrophilic and lipophilic drugs can be entrapped in Ufasomes⁷. It Delays the end of quickly metabolizable drugs and in this way work as supported delivery systems. The drug can enter effectively in the skin and used as topical applicable drug delivery. Because of the simple accessibility of unsaturated fats, Ufasomes are

practical contrasted with liposomes and niosomes. Entrapment effectiveness of the drug is considerable⁹.

Drawbacks

Ufasomes are oxidized prompting stability issues in fat based product. A few products created during oxidation might be poisonous for body healthy cell. Colloidal uncertainty of Ufasomes influences their application in food added substances and drug delivery¹³.

DIFFERENT TECHNIQUES FOR THE PREPARATION OF UFASOMES

Thin layer hydration technique

Thin layer hydration technique used in vesicle development occurs across a narrow pH range. In a flask with a circular rim, unsaturated fatty acid is joined with organic solvent. In the production of the Ufasomes oleic acid acts like unsaturated fat alongside surfactant and cholesterol are prepared in chloroform and methanol like solvent. In the wake of mixing all these contents in single compartment, this combination transferred to round bottom flask of Rota evaporator. The apparatus then at that point set for a fix rpm and temperature and starts rotating under vacuum. Finally, a thin fatty acid layer is made and hydrated utilizing a pH-appropriate buffer^{8,10}.

General technique

Stock solution is prepared which contains 10 % oleic acid and linoleic acid in chloroform and stored under 20°C. In the preparation, test tube containing 0.02 ml of the stock solution is taken and the stock solution is evaporated in a water pump and with the nitrogen gas and continued until dried. The film unsaturated fat is completely broken in 0.2 ml of 0.1 M tri-hydroxymethyl aminomethane buffer at 8 to 9 pH range, on a vortex blender by gentle shaking. Subsequently, the Ufasomal suspension formed because of blending and kept for 24 hours. In certain investigations, particles are ready by ultrasonic generator with a microtip. Steam of nitrogen, air is first taken out from the buffer and the suspension is overlaid with the gas during irradiation. Utilizing ice bath, reliable temperature is kept up^{8,10}.

Addition of alcohol

This is the new technique where addition of alcohol (having same chain length as that of fatty acid) prompts the development of vesicles. Unsaturated fatty acid vesicles arranged by this technique show great stability over a wide pH range. This is a time-consuming cycle. To keep away from this time utilization, vesicles are prepared based on the helpful guideline known as matrix effect. This strategy includes triggering the pace of vesicle development within the sight of pre-added fatty acid vesicles in the system^{7,8}.

CHARACTERIZATION OF UFASOMES

Size and Vesicle Charge

Vesicle size and charge are the prerequisites of every formulation that need to be entrapped or controlled. Zeta

analyzer is used for the characterization of vesicle's size and shape and its further factors like stability etc. Zeta potential analyzer is used to determine the charge of the molecule, as lesser the charge more will be the stability. So, for the great stability we consider that surfactant and excipients having less zeta potential. Vesicle size is determined by optical microscopy technique utilizing adjusted optical magnifying lens (By Ocular and Stage micrometer). For the most part the size is considered by repulsion powers that act between the bilayers^{9,16}.

Photo microscopy

Vesicle scattering were portrayed by photograph microscopy for vesicle arrangement and morphology. Ufasomal suspension were analyzed under optical magnifying lens through fitted camera and captured at amplification of 40 to 100X¹¹.

Entrapment efficiency

To get the highest entrapment productivity, a few variables, including the incorporation of cholesterol, the structure of the surfactant and the strategy of preparation, were studied and optimized. To study the entrapment efficiency the difference between the entrapped and untrapped drug are determined by using different strategies like centrifugation, gel filtration etc^{10,14}.

Differential Scanning Calorimetry

Differential Scanning Calorimetry is used to determine the physical condition of the material contained inside the oleic acid vesicles. The vesicles were put in a traditional aluminum pan and filtered at a pace of 2°C/min⁸. From the DSC curve we analyses the enthalpy and melting behaviour of oleic acid and other excipients which constitute the vesicles along with that it also depicts the compatibility of the entrapped drug with their excipients.

Zeta Potential-Charge Repulsion Measurement

Zeta potential is a measure of the magnitude of the electrostatic or charge repulsion/attraction between particles. Zeta potential depends on the properties of the liquid as well as on properties of the particles. It plays an important role in determining the aggregative stability of the solution or emulsion. The greater the zeta potential, the more robust the repulsion, and more stable the system⁸.

In-Vitro Drug Release

The objective of this study is to sort out how quick a drug delivery from Ufasomes and what its release kinetics are. This is performed by utilizing Franz diffusion cell. There are two compartments in the Franz diffusion cell: one is the donor and other is receptor. A polycarbonate layer with pore sizes of 50 nanometers isolates these two compartments. The donor compartment contained 1 ml of Ufasomal dispersion, though the receptor compartment contained phosphate buffer saline (PBS) pH 7.4, which was kept at 37°C and stirred at a steady rate utilizing magnetic stirrer. Aliquots of tests are removed and replaced with



equivalent amounts of PBS (pH 7.4) at predetermined intervals¹³.

COMPONENTS OF UFASOMES

Solvent: Organic solvents like chloroform/methanol mixtures are normally used to disperse lipid layer and release the vital proteins and subcellular parts. They form blended micelles of the different parts of the film and the detergent. The techniques depend on chloroform and methanol to shape a monophasic solvent system to extract and disintegrate the lipids. The components that are used should be dissolve in the selected solvent that allows the kinetic control in the process.

Surfactant: Surfactant, also called surface-active agent, substance such as a detergent that, when added to a liquid, reduces its surface tension, thereby increasing its spreading and wetting properties. Fatty acid vesicles acts as the surfactant and made up of colloidal suspensions of closed lipid bilayers that are composed of unsaturated fats and their ionized species (soaps)¹⁴. Fatty acid vesicles develop immediately when soluble micelles are added to buffered vesicles. The oleic acid-based surfactant containing a double bond in the hydrophobic oleyl tail showed a greater capability to reduce the surface tension of an aqueous solution¹⁵.

Cholesterol: Cholesterol acts as a bidirectional controller of membrane fluidity on the grounds at high temperatures, it stabilizes the layer and raises its melting point, while at low temperatures it intercalates between the phospholipids and prevents them from grouping together and solidifying. On the biophysical front, cholesterol altogether expands the request for the lipid pressing, brings down the layer porousness, and keeps up with film smoothness by shaping fluid arranged phase lipid rafts^{7,13}. Cholesterol goes about as a smoothness cradle against non-ideal temperatures and permits our films to reestablish the best liquid organization. At the point when it is cold, cholesterol builds smoothness, preventing the layer from freezing. At the point when it is hotter, cholesterol reduces fluidity⁶.

COMPARISON OF UFASOMES WITH OTHER VESICULAR SYSTEMS

Liposomes

Liposomes are bilayer concentric Structure comprised of the phospholipids as surfactant along with solvent. They are ended up being the wide examined vesicular drug delivery system starting around 1970 as firstly found by the Bangham and his associates. They are loaded with the lipid bilayer dispersed in the aqueous media that give inside aqueous environment. The lipid utilized can be of natural or synthetic origin. Different parts utilized alongside lipid are the cholesterol and hydrophilic polymer conjugates¹⁶. However, liposomes-based drug formulations have an incredible potential but numerous limitations emerges when the examinations upgraded. Lipid is the center part of liposomes and when utilized in greater amount can be

harmful for body and chances to have go through oxidation of unsaturated acyl chains or hydrolysis of ester bond. The expense of formulation is high and entrapment efficiency is low^{19, 21}. Other instability might happen causes drug leakage and change in liposomes size in case of non-optimized formulations. While comparing with Ufasomes, Ufasomes have the better entrapment efficiency for hydrophilic and lipophilic drugs. The formulation cost of fatty acid vesicles is low as fatty acids are inexpensive, readily available and have greater stability than that of lipids. Surfactants (Fatty acid) acts as penetration enhancer, Ufasomes possess better penetration when contrasted with liposomes⁹.

Ethosomes

Ethosomes are principally utilized for the transdermal drug delivery system. They are delicate and malleable vesicles that arrives at deeper in skin because of the use of alcohol i.e. ethanol that act about as the permeation enhancer. They are comprised of phospholipids (phosphatidylcholine, phosphatidylserine, phosphatidic acid), alcohol (ethanol, isopropyl alcohol) in relatively high concentration and water²³. Ethosomes have high transdermal transition than the liposomes. The high ethanol concentration makes the ethosomes prepared to do better permeation through the skin. Different components are mostly same as the liposomes, for example, cholesterol, phospholipid and so forth. As the utilization of lipid in the formulation can cause the instability and that causes the poor yield¹⁹. In the incident of excess of components, the ethosomes may coalesce and self-destruct on move into water and loss of product during transfer from organic to water media. On contrary Ufasomes components are promptly available and are of stable nature in their natural environment. The solvent utilized are easily evaporated when used in hydration technique and parts are formed in a uniform layer²².

Transferosomes

Transferosomes have high vesicle deformability which is its unique property and gives better permeation of intact vesicle and have both hydrophilic and hydrophobic properties. They are the ultra-deformable lipid aggregates made out of lipids and biocompatible membrane softeners. Different kind of lipids are considered while making this like soya phosphatidylcholine, dipalmitoyl phosphatidylcholine, surfactants like tweens, span etc. The solvent which is utilized is alcohol with the appropriate pH phosphate as buffer. They are pretty much as comparable as the liposomes however shows the deformability and the better film integrity. On comparison with Ufasomes they are costly to make and material is hard to store due to the instability issues. The lipids that are consumed should be in exceptionally unadulterated structure to stick deformable property. On other hand Ufasomes are most economically useful vesicular based drug formulation which is effectively accessible and stable in nature. There is no such necessity of ultrapure of synthetics as the



property of adherence for the most part not revealed at this point²¹.

Niosomes

Niosomes is a bilayer vesicle made out of non-ionic surface-active agents. Its surfactant shows the hydrophilic tail of monomers. By adding cholesterol as fluidity buffer a well stable bilayer is framed. For the most part nonionic surfactant that are used are polyglycerol alkyl ethers, glucosyl diacyl ethers tweens etc. It has most attractive characteristics of better stability and non leakage of drug.²⁰ Entrapment efficiency of niosomes is increased by the addition of non-ionic surfactant that additionally builds the size of the vesicle and furthermore gives a charge to the vesicle. They are used as it causes less irritation and are economically useful. If these surfactants are used in over a limited value can causes the toxicity and enzymatic corruption of ester sort of surfactant²³. The components used require more shelf life the essential directions. On other hand Ufasomes includes the unsaturated fatty acid surfactant like the oleic acid and their salt sodium oleate are non harmful in nature and also act as better penetration enhancer. There is no enzymatic corruption due to no usage of ester linkage¹¹.

Sphingosomes

Sphingosomes are the concentric, bilayer vesicular design which comprise of aqueous center is enclosed inside a lipid film which is comprised of normal or synthetic sphingolipid. They overcome the burden of liposomes and the niosomes due to its high stability to acid hydrolysis and have better impact on body by improving the maintenance period²¹. Sphingosomes are generally comprises of amide and ester linkage and they can be regulated into the body from parenteral, inhalation, oral, transdermal route etc. The formulation cost of the sphingosomes is higher than niosomes but their drug leakage and entrapment efficiency values are less as compared with other vesicular structure²⁴. On contrasting Ufasomes are promptly accessible and formulation cost is less. Whenever the cholesterol is utilized in specific proportion the drug leakage is nearly negligible and Ufasomes are the promising vesicles in matter of drug entrapment²¹.

CONCLUSION

Vesicular drug delivery systems are acquiring popularity in the vesicular field due to its site specifically targeted drug delivery and different benefits. The appropriate determination of unsaturated fat, measure of cholesterol, structure, pH range etc are a portion of the components that decide the stability of Ufasomal formulation. Fatty acid vesicles have also been proven to be especially useful in the treatment of skin disorders and illnesses like AIDS due to the controlled release of the medicine. Ufasomes are regarded a superior option to liposomes for topical drug administration due to their cheaper cost, rapid penetration capacity, and excellent entrapment performance

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