Review Article

UFASOME: A POTENTIAL PHOSPHOLIPID CARRIER AS A NOVEL PHARMACEUTICAL FORMULATION

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Article Received on: 20/02/14 Revised on: 19/03/14 Approved for publication: 03/04/14

DOI: 10.7897/2230-8407.050453

ABSTRACT

Ufasomes are unsaturated fatty acid vesicles. They are the suspensions of fatty acids and their ionized species (soap) which are arranged as closed lipid bilayer. The molecular arrangement in ufasome is that the hydrocarbon tails are oriented towards interior of the membrane and carbonyl groups are in contact with water. The stability of formulation depends on the selection of fatty acid, pH range, amount of lipoxigenase etc. Film hydration method is used for the preparation of vesicle by using oleic acid as fatty acid principle components. The present article describes about the advantages, disadvantages, method of preparation, *in vitro* evaluation and recent innovations of ufasomes. The present investigation aims at exploring the potential of fatty acid vesicle for the topical delivery of drugs. Earlier ufasomes were considered as the pre-biotic models for cellular compartments. Now, ufasomes are also found as carriers for horizontal transfer of engineered gene from plants to soil microbes or environment.

Keywords: Fatty acid vesicle, topical drug delivery system, amphiphils, liposomes, surfactants

INTRODUCTION

Ufasomes (UFM) are vesicles enclosed by fatty acid obtained from long chain fatty acid by mechanical agitation of evaporated film in the presence of buffer solution. Fatty acid and their ionized species (soap) restricted to narrow pH range from 7- 9 included ufasome which as we all know, are fatty acid vesicle which are colloidal suspensions made up of closed lipid bi layers. Fatty acid vesicles contain non-ionic neutral and ionized form (the negatively charged soap) which are two type of amphiphiles, the fatty acid, which contain carboxyl group are in direct contact with H₂O and the hydrocarbon, tails are directed towards the inferior membrane. Ufasomes are derived from unsaturated fatty acid such as linoleic acid, oleic acid etc (Table 1). But later investigations shown that it can also formed from saturated fatty acid such as octanoic and decanoic acid.^{1,2} The formation of UFM was first put forward in 1973 by Gibicki and Hicks. The vesicle stability is determined by the ratio of non-ionized form, proper selection of fatty, amount of cholesterol, buffer pH range, amount of lipoxigenase and the presence of divalent cations are certain other criteria for the stability of ufasome (UFM) formulation. Phospholipids and the general components used in formulation of liposome, which are chemically heterogeneous even in their natural form and also the reasonable quantities of pure synthetic phospholipids are not available. The ready availability of fatty acid is one of the major advantage of ufasome (Figure 1) over liposome.^{3,4}

Advantages

- Ufasomes are easily available than liposome.
- In case of topical application easy penetration of drug.
- Low cost effective composed to liposome and noisome due to easy availability of fatty acid.
- Appreciable drug entrapment.
- Dose requirement is due to absorption of chief constituents.

- Entrapment efficiency is more over and predetermine because drug itself in configuration with fatty acid are forming vesicles so no problem of drug entrapment.

Disadvantages

- It is readily oxidized creating a stability problem for some fat based drug product.
- Some of the oxidation by product tends to be rather toxic in biological system.
- Atherosclerosis

Method of Preparation

- For the preparation of the ufasomes unoxidised materials are only preferred. 10 % of oleic acid and linoleic acid in chloroform are present in stock solution which is stored at 20°C after preparation. In a test tube 0.02 ml of stock solution was taken and placed in water pump to evaporate the stock solution then it is dried under a steam of nitrogen in a typical preparation. In a 0.2 ml of 0.1M tris-hydroxymethyl amino methane buffer at a pH range of 8-9, the fatty acid film is broke completely by vigorous shaking in vortex mixer. The mixing result in the formation of ufasome suspension, which is stable at least for 24 hours. Ultrasonic generator with a titanium microtip is used in the preparation of particles in some experiments. During irradiation the suspension is blanketed with gas prior to which air is removed from the buffer by a nitrogen stream. Ice water bath is used to maintain constant temperature. Different ratios of oleic acid, drug and surfactant are used for the formulation of different batches of ufasome.
- Film hydration methods are used for the formulation of oleic acid vesicles.
- Accurately weighed oleic acid of strength 80 mM span to 20, dexamethasone were dissolved in methanol which is taken in a clean dry round bottom flask by using rotary evaporator, the solvent is evaporated under vacuum.

- The last traces of organic solvent are removed under reduced pressure at a 40°C. As a result a dried film is form in the rotary evaporator. (Figure 2)

Due to the presents of residual organic solvent formation of emulsion is possible so the formulation is kept over night for the removal of traces of methanol for the formation of uniform size vesicular dispersion sonification is performed, before which dried film was hydrated at ambient temperature for 1 h.⁵

***In vitro* Evaluation of Ufasome for Dermal Administration**

Size Evaluation

Determination of average diameter and size distribution of ufasome suspension are evaluated by photo correlation spectroscopy, using 90 plus practical size analyzer at a fixed angle of 90° and at 25°C. The interference particulate matters are minimized before sizing by filtering it through a 1 m polycarbonate membrane after diluting ufasome suspension with phosphate buffer at pH 7.4.

Entrapment Efficiency

The entrapment efficiency of drug was determined after removing the free drug for determination of amount of drug release the clear solution, and was calculated as % of drug incorporated into liposome, obtained finely was analyzed by HPLC.

Skin Irritation Studies

Due to the presents of free acidic group in oleic acid vesicles they were responsible to cause skin irritation hence their dispersion were used to test skin (Figure 3) irritation studies, but the irritation test showed that the oleic acid vesicle dispersion revealed negligible irritation while the free oleic acid produce irritation.⁶

***In vitro* Release in Ufasome using Non equilibrium Dialysis Method**

The locally fabricated cell system consist a dialysis membrane which separates the donor and receptor compartments of the cell in equal volume. The cell was thermostated at a particular temperature using phosphate buffer as receiving medium. The donor formulation includes drug aqueous solution and liposome suspension. The solution from the receptor compartment was taken out at fixed interval of time; compartment was refilled using fresh phosphate buffer.

Recent Innovations in Conventional Ufasomes

Extension of pH range

A narrow range of pH is suitable for the formation of FA vesicle due to requirement that about half of the carboxylic acid is to be ionized.

Addition of amphiphilic additives

A vesicle are formed between the pH range 6.4 and 7.8 in case of a mixture decanoic acid decanoate, but by addition of sodium dodecylbenzenesulphonate (SDBS) the pH can be lowered to about 4.3 at which the vesicle can be formed.⁷

Synthetically modification in size of hydrophilic group of fatty acid

A fatty acid with an oligo unit intercalated between the hydrocarbon chain and carboxylate head group was reported to be having enhanced stability of the formed vesicle at low pH. The effects of bulky polar group are lowering of the phase transition temperature and lowering of the pH for the formation of vesicle.⁸

Intensity towards divalent cation

Divalent cations like Mg^{2+} , Ca^{2+} etc. even in this small quantity and lower concentration result in the precipitation of the vesicles. The fatty acid vesicles where found to be stabilized by the addition of fatty acid glycerol esters in presence of ionic solutes.⁹ Certain studies like cryogenic transmission electron microscopy studies of the mono oleic sodium oleate-water system showed that uni and multi lamellar vesicles are found from the mixture of mono olein and sodium oleate and the formed vesicles was found to remain stable for a prolonged period of time.

Enhancement of stability

The stability of the vesicles was enhanced by crom linking the fatty acid molecules by chemical

Dynamic nature of ufasome

The fatty acid vesicles are compound of simple chain amphiphiles due to which is one of the important features of fatty acid vesicles. Conventional vesicles are found from double chain amphiphiles and micelles are formed from single chain surfactants and hence the dynamic nature places the fatty acid vesicle in between conventional vesicles and micelles. A change in the ionization ratio of the terminal carboxylic acid result in the formation of a range of fatty acid aggregates. When compared to the micelles; vesicles have greater number of amphiphilic and the formation of fatty acid vesicles posse a higher energy barrier. When compared to the formation of a fatty acid micelles. A fatty vesicle can be prepared by adding an alkali soap sol to a buffer sol of intermediate pH which is one of the convenient methods for the preparation of fatty acid vesicles. When alkaline micelles are added to the buffered vesicle the fatty acid vesicles grow spontaneously.^{10,11}

Figure 1: Optical microscopic view of ufasome

Figure 2: Rotary vacuum evaporator

Table 1: Unsaturated fatty acids

Common name	Chemical structure	C:I
Myristoleic acid	$\text{CH}_3(\text{CH}_2)_3\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	14:1
Palmitoleic acid	$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	16:1
Sapienic acid	$\text{CH}_3(\text{CH}_2)_8\text{CH}=\text{CH}(\text{CH}_2)_4\text{COOH}$	16:1
Oleic acid	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	18:1
Elaidic acid	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	18:1
Linoleic acid	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_7\text{COOH}$	18:2
Arachidonic acid	$\text{CH}_3(\text{CH}_2)_4\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CHCH}_2\text{CH}=\text{CH}(\text{CH}_2)_3\text{COOH}$	20:4
Erucic acid	$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}(\text{CH}_2)_{11}\text{COOH}$	22:1

Figure 3: Layers of skin

CONCLUSION

Ufasomes are fatty acid vesicles obtained using oleic acid. It is a safe surfactant used widely, which can be applied nonocclusively. In delivery of anti-inflammatory drug encapsulation of drug in fatty acid vesicle can act as a potential carrier. Sustained release of drug is a benefit of ufasome. Other benefits are cost effectiveness, therapeutic viability and drug retention in deeper part of skin and their by enhances penetration. They increase the permeation of drug molecule by avoiding the stratum corneum barrier potential. They enhances *in-vitro* skin delivery of drug compared to normal liposome.¹²

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Cite this article as:

Nair Athira J, K Aswathi, George Ashitha, P. P Athira, Nair Sreeja C. Ufasome: A potential phospholipid carrier as a novel pharmaceutical formulation. *Int. Res. J. Pharm.* 2014; 5(4):250-253 <http://dx.doi.org/10.7897/2230-8407.050453>

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