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Niosomes as target drug delivery system: A Review

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ABSTRACT

The formulation of vesicles as a way of improving the delivery of drugs over the past several years has generated a lot of concern among scientists working in the field of drug delivery systems. The vesicular niosomal system is capable of increasing the bioavailability of a product. When its bilayer structure is constructed by non-ionic surfactants, the bioavailability of products to a specified region for an extended period. Niosomes and liposomes are equative in drug delivery capacity, and both have decreased drug usefulness regarding free drug use. Niosomes are contrasted with liposomes when the high chemical stability and efficacy of the substitute are considered. For medicines and therapeutic purposes, the implementation of vesicular (lipid vesicles and non-ionic surfactant vesicles) devices can give many benefits. They strengthen drug molecules ' clinical efficiency by delaying clearance from circulation, safeguarding the drug from the genetic atmosphere, and limiting target cell impacts. This study focused on recent developments in the distribution for niosomal medicines, possible benefits above other delivery systems, methods of construction, characterisation methods, and current niosome studies. Niosome seems to be a system of choice of drug delivery over liposome as a stable and economical niosome. Niosomes often have tremendous potential for nanotechnology to achieve focused non-cancer, non-infective agents. Niosome's potential for drug delivery can be improved using new ideas such as proniosomes, discomes, and aspasome. Niosomes are also useful for diagnostic testing and as an active ingredient to the vaccine. Such areas, therefore, need additional study and development to products available in the market niosomal preparations.

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INTRODUCTION

Paul Ehrlich began the history of controlled distribution in 1909 when he foresaw a method for the delivery of drugs that would specifically target diseased cells. Drug directing can be characterised as the capacity to precisely guide a beneficial product to the target location of operation with next to no non-target tissue interference.

The medicine is encompassed in a vesicle in the drug delivery process of niosomes (Baillie *et al.*, 1985; Madhav and Saini, 2011). The lipid membrane consists of a bilayer of active non-ionic surface elements and therefore the designation of niosomes. (Allen, 1998)

Niosomes are also among the strongest between these reservoirs. Structural niosomes are comparable to liposomes and are equating in the capacity of nanotechnology, but strong chemical stability and economy make niosomes preferable to liposomes. All comprise of the bilayer, however, in the case of liposomes is composed of non-ionic surfactant and phospholipids. Niosomes were lamellar microscopic complexes varying from 10 to 1000 nm and composed of environmentally friendly surfacts, non-immunogenic and biodegradable. (Handjani-Vila *et al.*, 1979).

The niosomes are amphiphilic, which also allows the caging of hydrophilic drugs in the underlying membrane and the introduction of hydrophobic drugs in the non-polar region into the bilayer. (Priyanka *et al.*, 2019). Niosomes or non-ionic surfactant vesicles seem to be microscopic lamellar constructions created by an admixture of alkyl or dialkyl polyglycerol ether class non-ionic surfactant as well as cholesterol subsequently hydrated in aqueous media. For Niosomes, amphiphile vesicles are anion-ionic surfactants like Span – 60, which would be usually balanced by adding cholesterol and a small proportion of anionic surfactant like dicetyl phosphate (Buckton and Harwood, 1995)

Advantages of niosomes

1. Depend entirely on the condition, the properties of the vesicle, including size, lamellarity etc. can differ.
2. The vesicles may behave as a warehouse to gradually release the drug and provide a controlled release.
3. The niosome composition provides a place for lipid-soluble, lipophilic and amphiphilic drug moods. They could be used for a lot of drugs.
4. These have a network that consists of hydrophilic, amphiphilic and lipophilic molecules and can, therefore, handle drug compounds with a wide variety of solubilities. (Gandhi *et al.*, 2014)

Type of Niosomes

Niosomes are defined as either a variable of bilayer number (e.g. MLV, SUV) or size function. (LUV, SUV, for example) or as a component of the preparing technique (REV, DRV, for example).

Multilamellar vesicles (mlv)

It consists of many bilayers, which correspond to the aqueous lipid compartment separately. Such vesicles are approximately 0.5-10 μm in size. Multilamellar vesicles were the most commonly used niosomes. All such vesicles are suitable for lipophilic substances as a drug transporter.

Large Unilamellar Vesicles (LUV)

The type of niosomes has a high percentage of the aqueous / lipid container, and maybe in a somewhat economical need to have membrane lipids, larger quantities of bioactive substances might be obtained.

Small Unilamellar Vesicles (SUV)

Such Small Unilamellar Vesicles are often formed by sonication approach through multilamellar vesicles. At the same time, the electrostatic stabilisation of French press deformation is the inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) charged niosomes based on Span 60. (Gadhiya and Shukla, 2012).

Niosome components

Niosomes comprise the types of elements mentioned above

Non-ionic surfactants

Surfactant selection must be based on HLB quality. Because Hydrophilic Lipophilic Balance (HLB) is a reliable indicator of any surfactant's ability to establish vesicles, it has been found that the HLB number between 4 and 8 is consistent with vesicle development. Due to increased aqueous solubility, this is also recorded that the hydrophilic surfactant. On hydration, in allowing free hydrated devices to occur aggregates as well as to type a lamellar structure, they may not attain a nation of concentrated technologies.

Alkyl esters

Within this group of surfactants, sorbitan esters are by far the most favoured surfactant who used it to prepare niosomes. Vesicles formed by the monolaurate of polyoxyethylene sorbitan are more soluble than most other vesicles of surfactant. For illustration, polyoxyethylene was used to encapsulate diclofenac sodium (polysorbate 60).

Alkyl amide

Alkyl amide (e.g. galactosides and glucosides) was being used to produce fatty acid and amino acid compounds in the niosomal vesicles (d): Long-chain fatty acids and molecules of amino acids were also used in the production of certain niosomes.

Cholesterol

Steroids are critical elements of the cell membrane and influence the fluidity and permeability of both the bilayer through their inclusion in the layer.

Cholesterol is a steroid variant which is used primarily for the niosome methodology. It may have no position in bilayer formulation, its significance in niosome structure and the control of layer properties could not be dismissed. In particular, the introduction of cholesterol affects the compounds of niosomes such as membrane permeability, inflexibility, the effectiveness of encapsulation, easiness of rehydration of freeze-dried niosomes and their toxic effects.

Niosomes in comparison with liposomes

Niosomes are conclusively disproved as an alternative for liposomes that have certain disadvantages. They are expensive, their parts, including phospholipids, are chemically unstable owing to their susceptibility to oxidative decay, require extra storage and processing, and varying natural phospholipid quality. (Baillie *et al.*, 1986)

METHODS OF PREPARATION

Handshaking method (Thin film hydration technique)

Another round bottom flask dissolves in a volatile organic solvent the mixture of vesicles that shape ingredients including surfactant and cholesterol. At room temp (20 °C), the organic solvent is collected and use a rotary evaporator that leaves a surface layer of solid mixture accumulated on the flask rim. To gentle agitation, its dried surfactant film could be rehydrated at 0-60 °C to the aqueous phase. Standard multilamellar niosomes form this system. (Rogerson *et al.*, 1988; Lohumi, 2012)

Micro fluidisation

Micro fluidisation is a current strategy used only to make specified size production unilamellar vesicles. This approach is based on the concept of the submerged jet where two fluidised streams communicate at ultra-high velocities inside the interaction chamber in discrete microchannels. The impingement on a popular full view thin liquid layer is configured in a very way that perhaps the energy delivered to the device persists inside the niosome formulation region. (Khandare *et al.*, 1994)

Reverse Phase Evaporation Technique (REV)

In a combination of ether and chloroform, cholesterol and surfactant (1:1) are diluted. In addition to that, an aqueous phase comprising a drug is sonicated at 4-5°C. The aqueous phase forms into two phases. With the introduction of a low amount of phosphate-buffered saline (PBS), the clear gel produced will further be sonicated. The organic phase is extracted at 40 ° C at lower pressure. The resulting vicious niosome suspension is mixed with PBS and raised for 10 minutes in a water bath to develop niosomes at 60 °C. The production of Diclofenac Sodium niosomes using Tween 85 was recorded by using this process. (RajaNaresh *et al.*, 1994)

Ether injection method

This approach offers the possibility of producing niosomes by progressively introducing a compound of the surfactant submerged in diethyl ether at 60 ° C in warm water. This surfactant mixture in ether is injected via a 14-gage needle into an aqueous substance solution. Ether vaporisation contributes to single-layered vesicles being formed. The vesicle's size ranges between 50 to 1000 nm, based on the circumstances utilised. (Baillie *et al.*, 1986)

Trans-membrane pH gradient (inside acidic) Drug Uptake Process (remote Loading)

Through chloroform, surfactant and cholesterol are consumed. Under lower pressure, the solvent will then dissolve and establish a thin layer on the ground of the round bottom flask. A power mixing citric acid (pH 4.0) moisturises the film.

The MLV is frozen and reheated three times and then sonicated. Aq. Sol. of 10 mg/ml of medicine is added to this niosomal suspension and vortexed to it. The sample pH would then be doubled to 7.0-7.2 including 1 M of disodium phosphate. The mixture then heats up for 10 mins to niosomes at 60 C. (Khan *et al.*, 2011)

The "Bubble" Method

This "Bubble" Method is an innovative strategy to prepare liposomes and niosomes in one phase through the use of organic solvents. A bubbling machine comprises of a round-bottomed flask and several necks to measure temperature in the water bath. Water-cooled reflux and thermometer are inserted via the 3rd neck of the first and second neck and nitrogen supply. Throughout this buffer (pH 7.4) cholesterol and surfactant are spread at 70 ° C, the dispersion combined with a higher shear homogeniser for 15 seconds and then instantly "bubbled" with nitrogen gas at 70°C. (Yasam *et al.*, 2014)

Sonication

A standard technique of vesicle development is by solution sonication as described in Cable. In this technique, a substance solution aliquot in the buffer is introduced in a 10-ml glass vial to the surfactant / choleste mixture. The solution is sonicised for 3 minutes at 60^0C, using just a sonicator with a titanium sample to generate niosomes. (Blazek and Rhodes, 2001)

Comparison of Niosomes and Liposomes

Niosomes are already debated widely as a substitute to liposomes. Liposomes have those drawbacks, i. they are costly, ii. their components - phospholipids are chemically unstable due to their predisposition to oxidative degradation, require additional storage and care, and iii. the quality of natural phospholipids differs. (Azmin *et al.*, 1985)

CHARACTERISATION AND FACTORS AFFECTING FORMATION OF NIOSOMES

Nature of surfactants

A surfactant with a niosome composition will have a hydrophilic head and hydrophobic tail. In certain situations, the hydrophobic tail can consist of either or two areas of alkyls or perfluoroalkyl, or a single classification of steroids. (Uchegbu and Florence, 1995) The ester-type surfactants are chemically least safe than ether-type surfactants as well as the former may be less hazardous than the others because of esterase-linked surfactants deteriorated to triglycerides and in vivo fatty acids. (Hunter *et al.*, 1988) The C12-C18 alkyl chain width surfactants are appropriate to noisome preparing. (Ozer, 1991)

Structure of surfactants

This composition, which would be connected to essential loading variables, influences the shape of the vesicle to be constructed from surfactants. Based on important surfactant packaging variables, vesicle geometry can be predicted to be developed. (Bhaskaran and Panigrahi, 2002)

Membrane composition

That stable niosomes could be formulated along with surfactants and drugs with the introduction of various additives.

Niosomes shaped to get a variety of morphologies, and its permeability and stability qualities could be modified by using various additives to modify membrane behaviours.

The structure of polyhedral niosomes remains unchanged throughout the cases of polyhedral niosomes developed with C16G2. The stable structure of such polyhedral niosomes may be by the addition of low solulan C24 (cholesteryl poly-24-oxyethylene ether) that inhibits the aggregation attributable to steric hindrance development. (Arunothayanun *et al.*, 2000)

Temperature of hydration

Temp of hydration tends to affect the noisome's the size and weight. For the optimal condition, the liquid phase development temp of the scheme is above the gel. Changing the temperature of the niosomal structure impacts surfactant installation in and out of vesicles as well as stimulates the transformation of the shape of the vesicle. (Manosroi *et al.*, 2003)

Bilayer formation

Installation of non-ionic surfactants to construct a bilayer vesicle through light polarised microscopy is distinguished by X-cross creation

The number of lamellae

The number of lamellae is established by the use of NMR spectroscopy, X-ray microscopy and electron microscopy (Shahiwala and Misra, 2002; Balasubramaniam *et al.*, 2002)

Membrane rigidity

The stiffness of the membrane could be calculated using the fluorescence probe flexibility as a feature of temperature (Baillie *et al.*, 1985)

Entrapment Efficiency (EE)

The entrapment efficiency (EE) is expressed as EE= quantity trapped / total quantity added' 100. After removal of unentrapped material, full vesicle disruption is calculated by the use of approximately 1ml of 2.5% sodium lauryl sulfate, instantly homogenised and centrifuged and supernatant drug-assayed after sufficient dilution. Following factors influence the efficacy of trapping. (Rogerson, 1987)

Surfactants

The chain length and hydrophilic head of non-ionic surfactants affect the efficiency of trapping, as stearyl chain C18 non-ionic surfactant vesicles result in higher efficiency of trapping than non-ionic surfactant vesicles C12 lauryl chain. The tween sequence of surfactants with such a long alkyl chain and an upper hydrophilic moiety in comparison with 1:1 ratio of cholesterol get the maximum trap capacity for soluble in water drugs. The HLB level of surfactants influences the efficiency of trapping, as the HLB level of 14 to 17 is not appropriate for niosomes, but the HLB value of 8.6 has the maximum efficiency of trapping, and the efficacy of trapping reduces as the HLB level falls between 8.6 to 1.7. (Shahiwala and Misra, 2002)

Cholesterol contents

The introduction of cholesterol through niosome's bilayer formulation promotes membranes stabilising behaviour and reduces membrane leakage. Therefore, cholesterol introduction into the bilayer reduces the productivity of trapping (Weissmann *et al.*, 1975)

Application of Niosomes

1. Niosomes for haemoglobin as a transporter.
2. It will be used as the source of peptide products.
3. Niosomes may be used as a haemoglobin carrier.
4. It is used in Immune Response research.
5. Transdermal niosome delivery methods.
6. It used in the delivery of ophthalmic medicines.
7. Use of the niosomal method as diagnostic agents (RajaNaresh *et al.*, 1994)

CONCLUSION

Niosome tends to become a system of choice of drug delivery over liposome as secure and economical is evident. Niosomes also have significant drug discovery ability for targeted delivery of non-cancer, non-infective agents. Niosomal drug delivery ability can be enhanced by the use of new techniques such as proniosomes, discomfort and aspasome. Niosomes also represent a more substantial clinical aid and as an adjuvant to the vaccine. These regions, therefore, need more research and exploration to produce commonly available niosomal preparedness. Scientists and academics widely understand the notion of integrating the drug into liposomes or niosomes to good target the medicine at the correct tissue location. These display a liposome-like design and can, therefore, reflect alternate vesicular mechanisms concerning liposomes combined with the ability of the niosome to encompass various types of drugs throughout their non-environmental structure. Niosomes are ideas for better drug delivery candidates, particularly in comparison to liposomes due to different variables such as price, stability, etc. Niosomes such as focusing, ophthalmology, oral, parenteral can be used to distribute different types of drugs.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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