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Review Article

Niosomes: Pharmaceutical Novel Drug Delivery System

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ABSTRACT

Niosome is an innovative drug delivery system designed to address the challenges associated with conventional drug administration methods. This system employs advanced nanotechnology to encapsulate pharmaceutical compounds within lipid-based nanovesicles, known as niosomes. Niosomes offer several advantages, including enhanced drug stability, controlled release, and improved bioavailability. This technology holds great promise for improving the efficacy and safety of various drugs, leading to better patient outcomes. This abstract provides a glimpse into the potential of neosomes as a groundbreaking solution in the field of drug delivery.

INTRODUCTION

Paul Ehrlich, in 1909, initiated the era of development for targeted delivery when he envisaged a drug delivery Mechanism that would target directly to diseased cell. We will now study what is drug Targeting[1] . The drug targeting can be elobrated as The ability to direct a therapeutic agent to a desired Specific site to show the action on targeted tissue. Both consist of bilayer, which is made up of non-ionic surfactant in the case of niosomes and phospholipids in case of liposomes. Niosomes are microscopic lamellar structures of size range between 10 to 1000 nm and consists of biodegradable, non-immunogenic and biocompatible surfactant. Niosomes are ampiphillic in nature, meaning that hydrophilic and hydrophobic drugs can be incorporated into them. Hydrophilic drugs can be trapped in the core cavity of the niosome, while hydrophobic drugs can be trapped in the non-polar region of the bilayer. The structure of niosomes is shown in Fig. No. 1 below. [2].

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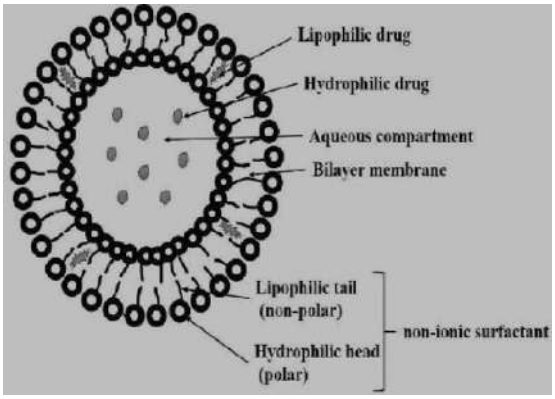

Fig no 1: Niosome structure

Merits Of Niosomes [3]

- The less amount of dose is effective to get the Proper effective effect.
- Niosomes are stable as we use hydrophilic System because of hydrophilic in nature they Are osmotically active .
- Due to hydrophilic in nature the drug that they Entrapped they tend to increase their stability.
- Can enhance the skin penetration of drugs.
- The vesicles present in the suspension are Hydrophilic that's why they show high amount Of patient acceptance over oil based system.
- Vesicles act as depot to release the drug slowly.

Demerits of Niosomes [3]

- May require specialized equipment
- High production cost
- Inefficient drug loading
- Fusion
- Aggregation
- Leaking of entrapped drugs
- The demerits of hydrolysis on the Encapsulated drugs results into limiting the shelf Life of the paticular formulation.[3]

Composition of Niosome: The two major components used for the preparation Of niosomes are [3]

a) Cholesterol

b) Non-ionic surfactants

a. Cholesterol: Cholesterol is a steroid derivative, which is used to Provide rigidity and proper shape, conformation to The niosomes preparations.

b. Nonionic surfactant: following non-ionic surfactants are generally Used for the preparation of niosomes.E.g.Spans ,Tweens ,Brijs . The non-ionic surfactants possess a hydrophilic head And a hydrophobic tail.

PREPARATION METHODS OF NIOSOMES

- Ether injection method
- Hand shaking method (thin film hydration Technique)
- Sonication Method
- Micro fluidization method
- Multiple membrane extrusion method
- Reverse Phase Evaporation Technique (REV)
- The Bubble Method

1. The ether injection method:

The ether injection method basically involves slowly injecting niosomal ingredients in ether into a heated aqueous phase that is kept at 60°C using a 14-gauge needle at a rate of about 0.25 ml/min.The formation of larger unilamellar vesicles is likely due to the slow vapourization of the solvent, which creates an ether gradient that extends towards the aqueous-nonaqueous interface. The bilayer structure may have formed as a result of the former. This method's drawbacks include the fact that a tiny amount of ether is usually present in the suspension of the vesicles and is challenging to remove.[4]

2. shaking method (thin film hydration techniques):

In this method the surfactant and cholesterol are dissolved in a volatile organic solvent in a round bottom flask. The organic solvent is removed at room temperature using rotary evaporator leaving a thin layer of solid mixture deposited on the wall of the flask. The dried surfactant film is to be rehydrated with aqueous phase at 0-60°C with gentle agitation to yield multilamellar niosomes.[3]

3. sonication method:

The niosome preparation process involved the use of sonication. Precisely weighed doses of the medication (200 mg), non-ionic surfactants Span40 (200 mg), and cholesterol were dissolved in 10 ml of a solvent mixture consisting of a 2:1 ratio of chloroform (50 ml) to methanol (25 ml) to produce a transparent solution. One pours the resultant solution into a sonicator. After being taken out of the bath, the sonicator was left to return to room temperature. 20 milliliters of distilled water were added to the film while it was being gently stirred in a sonicator at a specific temperature. The resulting niosome suspension was kept in a refrigerator in a container that was tightly closed.[5]

4. Microfluidization method:

The submerged jet principle forms the basis of the microfluidization process. Using this technique, the drug and the fluidized streams of surfactant interact at very high speeds in precisely mapped out microchannels inside the interaction chamber. Niosomes form as a result of the high speed impingement and the energy involved. In the formulation of niosomes, this method provides higher reproducibility, smaller size, unilamellar vesicles, and greater uniformity.[7] [8]

5. Multiple Membrane extrusion method:

A mixture of surfactant, cholesterol and dicetyl phosphate in chloroform is evaporated to a thin film. The film is Hydrated with an aqueous drug solution and the resulting suspension is extruded through polycarbonate membranes that Are placed in series for up to 8 passes. It is a good method to control the size of niosomes.[9]

6. Reverse Phase Evaporation Technique (REV):

The reverse phase evaporation technique is composed of inverted micelles or water-in-oil emulsions in which the water phase contains the interested drugs and the organic phase consists of the lipids to form liposomal bilayer.The clear gel formed is Further sonicated After the addition of a small amount of phosphate Buffered saline.The organic phase Is removed at 40°C at low pressure. Resulting viscous Niosome suspension is diluted with PBS and Heated On a water bath at 60°C for 10 min to yield niosomes.

7. Bubble Method:

It is a new technique for the one-step preparation of liposomes and niosomes without the use of organic solvents. The bubbler unit consists of a round-bottom flask with three necks keep in a water bath for temperature control. A cooled water reflux and thermometer are placed in the first and second ports of the homogenizer and immediately bubbled at 70°C using nitrogen and nitrogen through the third port. Cholesterol and surfactant is dispersed together in this buffer (pH 7.4) at 70 °C, the dispersion is stirred for 15 seconds at high clip.[10]

CHARACTERISATION OF NIOSOMES

1. Measurement of Angle of repose:-

Using a funnel method, the angle of repose of powdered dry niosomes was determined. Pouring the niosome powder into a funnel that was positioned so that its 13mm outlet orifice is 5 cm above a level black surface was done. The angle of repose was then determined by measuring the cone's height and base diameter after the powder flows out of the funnel and forms a cone on the surface.[1]

2. Drug Entrapment efficiency of niosomes:

Entrapment efficiency of niosomes is determined by exhaustive dialysis method. The measured quantity of niosomal suspension is taken into a dialysis tube to which osmosis cellulose membrane was securely attached on one side.The dialysis tube was suspended in 100ml phosphate buffer, which is stirred by a magnetic stirrer.The unentrapped drug is separated from the niosomal suspension into the medium through osmosis cellulose membrane.At every hour entire medium is replaced with fresh medium till the absorbance

reached a constant reading indicating no drug is available in unentrapped form.The niosomal suspension in the dialysis tube was further lysed with propane-1-ol and estimated the entrapped drug by UV spectrophotometric method at 243nm.The entrapment efficiency is calculated using following equation. [11]

$$\text{Entrapment efficiency} = \frac{\text{Amount of entrapped drug}}{\text{Total amount of drug}} \times 100$$

3. Size:

Since niosomal vesicles are thought to have a spherical shape, a number of methods, including laser light scattering, electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy, and freeze fracture electron microscopy, can be used to determine their mean diameter.[12][13][14]

4. In vitro release studies:

a) Dialysis: Dialysis tubing can be used to facilitate in vitro release rate studies. A dialysis sac was cleaned and allowed to soak in purified water. The vesicle suspension was pipetted into a tubing-filled bag, sealed, and kept in a 250 ml beaker with 200 ml of buffer solution at 25°C or 37°C while being constantly shaken. Using the proper assay technique, the buffer was examined for drug content at different time intervals.[15]

b) Reverse Dialysis:

This method involves putting niosomes in several tiny dialysis tubes with 1 mL of dissolution medium, and then removing the niosomes from the dissolution medium.[16]

c) Franz diffusion cell:

The cellophane membrane serves as the dialysis membrane in a Franz diffusion cell. At room temperature, the niosomes are dialyzed through a cellophane membrane against an appropriate dissolving medium. The samples are taken out at appropriate intervals and their drug content is examined.[17]

5. in vivo release study:

Using the proper disposal syringe, niosomal suspension was administered intravenously (through the tail vein) to the albino rats for the in vivo study. These rats were separated into several groups.[16]

Application of Niosome:

1. Niosomes as a drug carriers:

Niosomes have also been employed as delivery systems for the diagnostic drug iobitridol, which is used in X-ray imaging. Topical niosomes can act as a solubilization matrix, a local depot for the sustained release of compounds that are dermally active, penetration enhancers, or a membrane barrier that limits the rate at which drugs are absorbed systemically[18].

2. Leishmaniasis:

When treating diseases where the pathogenic organism resides in a reticulo-endothelial system organ, niosomes can be used to target the drug. One such illness where a parasite invades the liver and spleen cells is leishmaniasis. Antimonials, a class of drugs related to arsenic, are frequently prescribed medications that harm the kidney, liver, and heart at high concentrations. Hunter et al.'s investigation into the distribution of antimony in mice revealed elevated liver levels following intravenous injection of the drug's carrier forms. The effectiveness of the niosomal formulation in increasing sodium stibogluconate was reported by Baillie et al. Additionally, the two doses administered on different days had an additive effect.[19]

3. Delivery of peptide drugs:

The stability of the peptide increased significantly when Yoshida et al. studied oral delivery of 9-desglycinamide, 8-arginine vasopressin entrapped in niosomes in an in-vitro intestinal loop model.[19]

4. To Increase Oral Bioavailability:

According to Ismail A. et al., the oral bioavailability of griseofulvin and acyclovir was

enhanced by the niosome formulation when compared to the medication alone. Similar to this, when given as micellar solution alongside POE-24-cholesteryl ester in the common bile duct of rats, the absorptivity of poorly absorbed peptide and ergot alkaloid is frequently increased.[20]

5. Other Applications: [1]

i. It has been used to study the immune response Provoked by antigen.
ii. It is widely used to study the Drug targeting.
iii. We can use it as anti-neoplastic Treatment that Is in treatment of cancer.
iv. Niosomes can be used as Carriers for Hemoglobin.
v. Nowadays it can be used as delivery of peptide Drugs .
vi. It can give good therapeutic effect on Opthalmic drug delivery.
vii. It widely can used as diagnostic agent.

ROUTE OF APPLICATION OF NIOSOMES DRUGS:

Route of administration	Examples of drug
Ocular route	Timolol maleate, cyclopentol
Nasal route	Sumatriptan, influenzaviral vaccines
Intravenous route	comptothecin, insulin, zidovudine, cisplatin, rifampicin
Inhalation	All trans-retonic acids
Transdermal route	Piroxicam, estradiol, nimesulide

Mechanism of action of niosomes as permeation enhancer:

The ability of niosomes to increase drug transfer through the skin cannot be explained by a single mechanism; instead, a number of them have been put forth. These include: changing the stratum corneum's barrier function due to reversible disruption of lipid organization; reducing transepidermal water loss, which hydrates the stratum corneum and loosens its densely packed cellular structure; and adsorbing and/or fusing niosomes on the skin's surface, as demonstrated by small angle X-ray scattering and freeze fracture electron microscopy. This results in a high thermodynamic activity gradient of drug at the interface, which is what drives drug penetration.

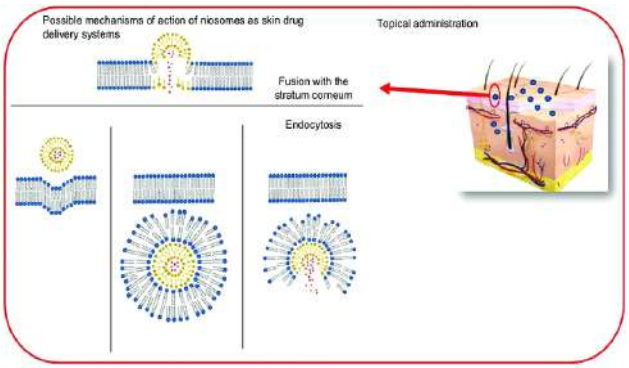

Figure: Mechanisms of action of niosomes as skin drug delivery systems.

Niosome adsorption onto the cell surface happens with little to no internalization of lipid or aqueous components; it can happen because of physical forces drawing in the niosomes or because certain receptors bind to ligands on the vesicle membrane, allowing the drug to be transferred from the vesicles directly to the skin. However, niosomes have the ability to fuse with the cell membrane, which would completely mix the cytoplasm with the contents of the niosomes. Ultimately, the cell may absorb niosomes through a process known as endocytosis, in which case lysozymes present in the cytoplasm break down or digest the niosome's membrane, releasing the material that had been trapped into the medium.[21]

FACTORS AFFECTING NIOSOMES FORMULATION

1. Drug:

Drug entrapment in niosomes affects the noisome bilayer's stiffness and charge. The medication's hydrophilic-lipophilic balance influences the degree of entrapment. [1]

2. Nature and type of surfactant:

When HLB surfactants such as (HLB 1.8) span 85 to span 20 (HLB 8.6) are added, the mean size of niosomes increases correspondingly because the surface as the surfactant's hydrophobicity rises,

free energy falls. Both a hydrophilic head and a hydrophobic tail are necessary for a surfactant. One or more alkyl or perfluoroalkyl groups, or in certain situations, a single steroidal group, can make up the hydrophobic tail. [1]

3. Temperature of hydration:

The size and form of the niosome are determined by the temperature of hydration. It should be above the system's gel to liquid phase transition temperature for optimal conditions. The niosomal system's temperature changes have an impact on surfactant vesicle assembly and cause vesicle shape transformation.When C16G2:solulan C24 (91:9) is heated to 25°C, it forms a polyhedral vesicle that becomes a spherical vesicle at 48°C. However, when the vesicle cools from 55°C, it forms a cluster of smaller spherical niosomes at 49°C and then transforms back into polyhedral structures at 35°C. On the other hand, when heated or cooled, the vesicle made of C16G2:cholesterol:solulan C24 (49:49:2) does not change shape. The hydration medium volume and niosome hydration time, in addition to the previously listed variables, are also crucial. If these factors are not chosen carefully, drug leakage issues or the development of fragile niosomes may arise.[4]

CONCLUSION

Niosome, as a novel drug delivery system, holds great promise in the field of pharmaceuticals. Its ability to encapsulate and efficiently transport drugs to target sites, while minimizing side effects, represents a significant advancement in drug delivery technology. The potential for improved patient compliance, reduced dosing frequency, and enhanced therapeutic outcomes make Niosome a valuable addition to the pharmaceutical landscape. Further research and clinical trials are needed to fully realize its potential, but the preliminary results are encouraging, and Niosome has the potential to revolutionize drug delivery for the betterment of patient health and well-being.

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