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REVIEW ON NIOSOMES AS A NOVEL DRUG DELIVERY

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ABSTRACT

Targeted drug delivery, also known as smart drug delivery, is a method of administering medication to a patient in such a way that the concentration of the medication insome parts of the body is higher than in others. A targeted drug delivery system's goal is to prolong, localize, target, and have a safe drug interaction with diseased tissue. A niosome is a non-ionic structure. Niosome is based on surfactant. They have a bilayer and are structurally like niosomes; however,the materials used to Preparing niosomes increases their stability, and thus niosomes have many more advantages over liposomes. Using niosomes, various drug delivery methods such as targeting, ophthalmic, topical, parental, and so on are possible.

KEYWORDS: Niosome, Multilamellar, Unilamellar, Structure of niosomes, Methods of niosomes.

INTRODUCTION

Drug targeting is the ability to direct a therapeutic agent to a specific site of action with little or no interaction with non-target tissue.[1] The medication is encapsulated in a vesicle in the niosomes drug delivery system.[2] The vesicle is made up of a bilayer of non-ionic surface-active agents, which gives rise to the name niosomes. The amphiphilic vesicles in niosomes are formed by a non-ionic surfactant such as Span - 60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as diacetyl phosphate.[3] Niosomes are a novel drug delivery system that entraps hydrophilic and hydrophobic drugs in the core cavity. in the core cavity and hydrophobic drugs in the non-polar region present within the bilayer, allowing for the incorporation of both hydrophilic and hydrophobic drugs. Niosomes are amphiphilic in nature, with the medication encapsulated in a vesicle formed by a nonionic surfactant, hence the name. Niosomes are extremely small and microscopic in size.[4] The primary goal of developing a niosomal system is to achieve chemical stability, biodegradability, biocompatibility, chemical stability, low production cost, ease of storage and handling, and low toxicity.[5,6] Niosomes improve the therapeutic performance of encapsulated drug molecules by shielding them from harsh biological environments, causing them to be cleared more slowly.[7]

Niosome Salient Features[8,9]

- Niosomes could entrap solutes.
- Niosomes are stable and osmotically active.
- Niosomes have an infrastructure that is mostly made up of hydrophobic and hydrophilic molecules, which provides the medication atoms with a wide range of dissolvability.
- Niosomes release medication in a controlled manner via their bilayer, which allows for the supported arrival of the encased medication; thus, niosomes serve as medication warehouses in thebody.
- Targeted medication conveyance is also possible with niosomes; the medication is delivered specifically to the body part where the therapeutic effect is required. As a result, the measurement required to achieve the desired impact is reduced.
- They increase the solubility and oral bioavailability of poorly soluble drugs, as well as the permeability of drugs when applied topically to the skin.
- Niosomes have structural characteristics that are flexible (composition, fluidity, and size) and can be designed to fit the situation.
- Niosomes have the potential to improve the performance of drug molecules.
- Niosomes improve drug availability to specific sites simply by protecting the drug from biological environments.

Benefits[10,11]

Bioavailability Enhancement: Bioavailability refers to the portion of a dosage that is available at the site of activity in the body. Niosomes have clear preferences

over conventional plans. Because the vesicles can act as medication stores and protect the sedate from acidic and enzymaticattack, degradation in the gastrointestinal tract, improves bioavailability and expands the capacityto cross the anatomical barrier of the gastrointestinal tract.

- They improve the therapeutic execution of medication particles by delaying their dissemination, shielding the medication from natural conditions, and limiting the effects on target cells.
- To regulate delivery, niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase.
- Rate of drug administration and normal vesicle administration in the nonaqueous phase externally.
- They are osmotically active and stable, and they increase the entrapped drug's stability.
- Surfactant handling and storage do not necessitate any special precautions.
- They increase the oral bioavailability of poorly absorbed drugs and increase drug penetration through the skin.
- They can be delivered to the site of action via oral, parenteral, or topical routes.

Niosome Disadvantages

1. Fusion
2. Compilation
3. Drug entrapment leakage
4. Physical insecurity
5. Encapsulated drug hydrolysis, which reduces the shelf life of the dispersion.

The Structure of Niosomes

Niosomes are spherical structures made up of microscopic lamellar structures (uniflagellar or multilamellar). Nonionic surfactants, with or without cholesterol, and a charge inducer form the bilayer.[12,13] Niosomes are made up of various types of surfactants in various combinations and molar ratios,[14] The amphiphilic vesicles of niosomes are non-ionic surface-acting agents such as span -60 that are stabilized by the addition of cholesterol and an adequate amount of anionic surfactant such as diacetyl phosphate that is used to stabilize the niosomes vesicles.[15]

Niosome Composition[16]

The following are the various components used in the preparation of niosomes.

1. LDL cholesterol
2. Surface-acting non-ionic agent

- Cholesterol: This is a steroid derivative that is used to provide flexibility, rigidity, andappropriate shape.
- Surfactants: That are not ionic Non-ionic surfactants such as the ones listed below are commonly used in the preparation of niosomes. Spans, for example (span 60, 40, 20, 85, 80) Tweens (tween 20, 40, 60, 80) (tween 20, 40, 60, 80) The hydrophilic head of nonionic surfactants is followed by a hydrophobic tail.

Niosome Types[17]

The surfactant used in bola surfactant containing niosomes is made of omega hexadecyl bis-(1- aza-18 crown-6) (bola surfactant): span- 80/cholesterol in a 2:3:1 molar ratio.

Proniosomes: Proniosomes are formed from a carrier and surfactant mixture. Niosomes are formed following the hydration of proteasomes.

Apasomes: Acorbylpalmitate, cholesterol, and exceptionally charged lipid diacetyl phosphate are combined to form acorbylpalmitate, which prompts the formation of vesicles. To obtain niosomes, liposomes are first hydrated with a water/fluid arrangement and then subjected to sonication. Aspasomes can be used to increase medication transdermal saturation. Aspasomes, which have innated cell reinforcement properties, have also been used to reduce scatter caused by reactive oxygen species.

Niosomes in carbopolgel: Niosomes were made from drug, spans, and cholesterol and then incorporated into a carpool-934 gel (1%w/w) base containing propylene glycol (10% w/w) and glycerol (30% w/w).

Vesicles in water and oil (v/w/o): Aqueous niosomes are incorporated into an oil stage frame vesicle in water in oil emulsion (v/w/o) in this strategy. This can be accomplished by transferring a niosome suspension composed of sorbitol monostearate, cholesterol, and solulan C24 (Poly-24- Oxyethylene cholesteryl ether) to an oil stage at 60 0C. This produces a vesicle in water in oil (v/w/o) emulsion, which when cooled to room temperature forms a vesicle in water in oil gel (v/w/o gel). The resulting v/w/o gel can entrap proteins drugs while also protecting them from enzymatic degradation after oral administration and controlled release.

Niosomes of hydroxyl propyl methyl cellulose: Niosomes were added to a base containing 10% glycerin of hydroxyl propyl methyl cellulose. Deformable niosomes are formed by a mixture of non-ionic surfactants, ethanol, and water. These are smaller vehicles that can easily pass through the pores of the stratum corneum, increasing penetration efficiency. It is suitable for topical preparation.[18,19] Niosomes are also classified based on the number and size of bilayers, which are as follows:

1. Multi Lamellar Vesicles (MLV): MLVs are the most used niosomes. It is made up of several bilayers. Vesicles range in size from 0.5 to 10 m in diameter. It is simple to make and mechanically stable when stored for long periods of time.
2. Large Unilamellar Vesicles (LUV): These are large unilamellar vesicles with a highaqueous/lipid compartment ratio that can entrap larger volumes of bioactive materials.
3. Small Unilamellar Vesicles (SUV): These small unilamellar vesicles are typically prepared from

multilamellar vesicles via sonication, French press, or extrusion.

PREPARATION OF METHOD

Method of handshaking (Thin film hydration techniques)[20] Surfactant and cholesterol are dissolved in an extremely round bottom flask with a volatile organic solvent such as diethyl ether chloroform, or methanol. At a temperature (of 20°C), the natural dissolvable is removed using a turning evaporator, leaving a thin layer of the strong blend on the mass of the jar. The dried surfactant is frequently rehydrated with a watery stage at 0-60°C with delicate fomentation to yield multilamellar niosomes.

The micro fluidization method[21] is a new technology for preparing unilamellar vehicles with a well-defined size distribution. The micro fluidization strategy is based on the principle of two fluidized streams interacting with each other at ultra-high velocity. The impingement of the thin liquid sheet along a conventional front is arranged in such a way that the energy supplied to the system remains within the realm of niosome formation. The result could be greater uniformity, smaller size, and better reproducibility of formed niosomes.

REV (Reverse Phase Evaporation) Technique[22] The cholesterol and surfactant mixture are dissolved in a 1:1 ratio in a mixture of the same organic materials, chloroform, and ether. The drug is dissolved in the aqueous phase and added to the above mixture, which forms two phases that are sonicated at 4-5°C. After the addition of phosphate-buffered saline, a transparent gel is formed and sonicated. There is an organic phase present, which is removed at 40°C, resulting in low pressure. The Niosomes solution is now in viscous form and is diluted with phosphate buffer. The diluted solution is also heated in a water bath for 10 minutes at a temperature.

Slow injection of surfactant: Cholesterol (150 micromoles) in 20ml ether through a 14-gauze needle (25ml/min.) in preheated 4ml aqueous phase maintained at 600c.[23] The ether solution was evaporated using a rotary evaporator; after the organic solvent was evaporated, it formed single- layered vesicles.

Sonication [24]: Prepared niosomes using the sonication method. Surfactant: cholesterol (150 micromoles) mixture was dispersed in a 2ml aqueous phase in a vial in this method. The dispersion is probe sonicated for 3 minutes at 600°C. This method entailed the creation of MLVs that were then subjected to ultrasonic vibration. There are two types of sonicators: probe sonicators and bath sonicators. When the sample volume is small, a probe sonicator is used, and when the sample volume is large, a bath sonicator is used.

The Bubble Method[25]: The foaming unit is a round-lined flagon with three necks that will be placed in an extremely hot water shower to regulate the temperature. The thermometer and water- cooled reflux are placed in the primary and second necks, and the nitrogen supply is provided in the third neck. Within the buffer (PH 7.4), cholesterol and surfactant are dispersed together. At 70°C, the dispersion was mixed for 15 seconds with a high-shear homogenizer and immediately bubbled with nitrogen gas to yield niosomes.[26]

Method of micro fluidization:[27] Micro fluidization is a current strategy for planning unilamellar vesicles of characterized estimate circulation. This strategy, based on the submerged jet principle, connects two fluidized streams at ultrahigh speeds in properly characterized smaller-scale channels inside the interaction chamber. The impingement of a thin liquid sheet along a common front is configured in such a way that the energy supplied to the system remains within the niosome formation area. The result is a more noticeable consistency, smaller size, and better reproducibilityof shaped niosomes.

Factors affecting niosome physicochemical properties
Surfactant amount and type[28]: Because the surface free energy of a surfactant decreases with increasing hydrophobicity, the mean size of niosomes increases proportionally with increasing HLB of surfactants such as Span 85 (HLB 1.8) to Span 20 (HLB 8.6). The vesicle bilayers are either in the supposed fluid state or in the gel state, depending on the temperature, the type of lipid or surfactant, and the proximity of different segments, such as cholesterol. Alkyl chains are available in an all-around requested structure in the gel state, but the structure of the bilayers is more confused in the fluid.

Cholesterol content and charge:[29,30] Cholesterol increases the entrapment efficiency and hydrodynamic diameter of niosomes. It promotes membrane stabilization and reduces membrane leakiness. If the cholesterol content of the bilayer increases, the release rate of the encapsulated material may decrease, resulting in an increase in the rigidity of the bilayers obtained. In a multilamellar vesicle structure, the presence of charge increases the interlamellar distance between successive bilayers, resulting in a greater overall entrapped volume.

The encapsulated drug's nature:[31] The charge and unbending nature of the niosome bilayer areinfluenced by the physical-synthetic properties of the typified medicate. The medication works with surfactant head groups to build up the charge, which causes shared aversion between surfactant bilayers and, as a result, expands vesicle size. The charge development on the bilayer prevents vesicle aggregation. Some drug is entrapped in the long PEG chains in Polyoxyethylene Glycol (PEG) coated vesicles, reducing the tendency for the size to increase.

Surfactant structure:[32] The geometry of the vesicle formed from surfactants is influenced by the structure of the surfactant, which can be characterized by basic pressing parameters. The geometry of the vesicle to be

formed can be based on the basic pressing parameters of surfactants.The following equation can be used to define critical packing parameters: CPP =V/lc a (Critical Packing Parameters) Where V denotes the volume of the hydrophobic group, lc denotes the critical length of the hydrophobic group, and a0 denotes the area of the hydrophilic head group. Important packing parameter the value type of micellar structure formed can be determined as follows: If CPP 12 results in the formation of spherical micelles, If CPP is less.

Resistance to osmotic stress: The diameter of the niosome suspension is reduced by adding a hypertonic salt solution.

Hydration Temperature: The temperature of hydration influences the shape and size of niosomes.

Niosome Characterization

%EE (percent drug entrapment efficiency) studies: The efficiency of fusidic acid entrapment in niosomes was determined using the previously described cooling centrifuge. The niosomal formulations were centrifuged at 12,000 rpm for 30 minutes at 4°C. The supernatant was decanted,and the free drug content was determined using a UV/visible spectrophotometer set to 210 nm. The %EE was then calculated using the formula: 14 Total drug entrapment % Total drug in supernatant x10.[33]

Morphology and Dimension: The most used methods for determining niosome sizes and morphology are dynamic light scattering (DLS),[34] scanning electron microscopy (SEM),[35] transmission electron microscopy (TEM) (36), freeze-fracture replication electron microscopy (FF-TEM), and transmission electron microscopy (cryo-TEM) (37). DLS provides both cumulative information on particle size and valuable information on solution homogeneity. A single sharp peak in the DLS profile indicates the presence of a single scatterer population. In this regard, the PI is useful. For colloidal systems, less than A homogeneous population is represented by a value of 0.3 Microscopic methods are commonly used to characterize niosome morphology.

Potential Zeta: Niosome surface zeta potential can be determined using zeta Sizer and DLS instruments. The surface charge of a niosome is very important in its behavior. Charged niosomes are more resistant to aggregation than uncharged vesicles. Bayindir and Yuksel created paclitaxel- loaded niosomes and investigated the physicochemical properties of niosomes such as zeta potential. They discovered that negative zeta potential values ranging from 41.7 to 58.4 mV are sufficient for niosome electrostatic stabilization.[38]

Characterization of Bilayers: The bilayer properties of niosomes are important for drug entrapment efficiency. AFM, NMR, and small angle X-ray scattering (SAXS) can all be used to determine the number of lamellae in multilamellar vesicles.[39] The mobility of a fluorescence probe as a function of temperature can be used to measure the membrane rigidity of niosomal formulations.[40] DPH (1,6 diphenyl1,3,5-hexatriene) is the most used fluorescent probe in niosomal dispersion. DPH is normally found in the bilayer membrane's hydrophobic region. Fluorescence polarization determines the micro viscosity of the niosomal membrane. High fluorescence polarization indicates a high membrane micro viscosity. Furthermore, the bilayer thickness can be determined using the latter method in conjunction within situ energy-dispersive X-ray diffraction (EDXD).

Entrapment Effectiveness: Entrapment efficiency (EE%) is the percentage of the applied drug that is entrapped by the niosomes. Centrifugation,[41] dialysis,[42] or gel chromatography[43] can be used to remove the unencapsulated free drug from a niosomal solution. Following this step, the loaded drug can be released from niosomes via vesicle destruction. Niosomes can be destroyed by adding 0.1% Triton X-100 or methanol to the suspension. A spectrophotometer. [44] or high-performance liquid chromatography (HPLC),[45] can be used to determine the loaded and free drug concentrations.

Stability: Niosome stability can be determined by measuring mean vesicle size, size distribution, and entrapment efficiency over a period of several months at various temperatures. The niosomes are sampled at regular intervals during storage, and the percentage of drug retained in the niosomes is determined using UV spectroscopy or HPLC methods.[46]

In Vitro, Fermentation: Dialysis tubing is a commonly used method for studying in vitro release. Distilled water is used to clean and soak a dialysis bag. The drug-loaded niosomal suspension is transferred into this bag after 30 minutes. The vehicles are immersed in buffer solution with constant shaking at 25 C or 37 C. Samples were removed from the outer buffer (release medium) at regular intervals and replaced with the same volume of fresh buffer. An appropriate assay method is used to determine the drug content of the samples.[47]

Drug content: The drug content of all sixteen formulations was determined using UV spectroscopy at 271 nm.[48]

Niosomes as Drug Transporters

Anticancer: Niosomes are extremely promising carriers for a wide range of pharmacological and diagnostic agents. Several papers have been published that describe the preparation, characterization, and use of niosomes as drug carriers. They have excellent biocompatibility and low toxicity due to their nonionic nature. Anticancer Drug Delivery. The current treatment for cancer is usually chemotherapy. The therapeutic efficacy of many anticancer drugs is limited by their poor penetration into tumor tissue and by their severe side effects on healthy cells.

Breast cancer: Breast cancer is a serious disease. Cosco et al. created 5-FU-loaded polyethylene glycol (PEG-) coated and uncoated bola-niosomes and tested them on breast cancer cell lines. In comparison to the free drug, both bola-noisome formulations increased the cytotoxic effect. After30 days of treatment, in vivo, experiments on MCF-7 xenograft tumor SCID mice models revealed that PEGylated niosomal 5-FU at a concentration ten times lower (8 mg/kg) was more effective against tumors than the free solution of the drug (80 mg/kg).[49] The optimized niosomal formulation of tamoxifen demonstrated significantly increased cellular uptake (2.8-fold) and cytotoxic activity on the MCF-7 breast cancer cell line. In vivo, studies revealed that niosomal tamoxifen reduced tumor volume more effectively than placebo.[50]

Cancer of the ovaries: doxorubicin-loaded niosomes were prepared. Doxorubicin activity was investigated in hexadecyl diglycerol ether (C16G2) and Span 60 niosomes against a human ovarian cancer cell line and its doxorubicin-resistant subline. When the drug was encapsulated in Span 60 niosomes, the IC50 against the resistant cell line was reduced slightly when compared to the free drug in solution.[51]

Cancer of the lungs: encapsulated Adriamycin into the noisome using a Mono alkyl tri glycerol ether, and the activity of niosomal Adriamycin was compared to that of free Adriamycin solution on human lung tumors cells grown in monolayer and spheroid culture, as well as tumor xenografted nude mice. It is possible that administering Adriamycin in niosomal form will improve its therapeutic ratio even more.[52]

Targeted Distribution: Active targeting for tumor therapy can improve the efficiency and specificity of cellular targeting of niosomal drug delivery systems by using a ligand coupled to the surface of niosomes, which can be actively taken up, for example, via receptor-mediated endocytosis. To enable cell-specific targeting, niosome surfaces can be conjugated with small molecules and/or macromolecular targeting ligands.[53]

Codrug Distribution: Nanoparticles have emerged as a promising class of carriers in the codelivery of multiple drugs for combination therapy in recent years.[54] Combination therapies improve therapeutic efficacy and reduce dosage while maintaining or increasing efficacy and reducing drug resistance.[55]

Niosome Applications

The niosome as a hemoglobin carrier Niosomal suspension has a visible spectrum that is superimposed on that of free hemoglobin and can thus be used as a hemoglobin carrier. Vesicles are also oxygen permeable, and the hemoglobin dissociation curve can be modified in the same way that non-encapsulated hemoglobin can.[56]

Niosomes as drug delivery systems: Niosomes have also been used as transporters for iobitridol, a symptomatic agent used in X-ray imaging. Topical niosomes can act as a solubilization grid, a neighborhood station for the continued arrival of dermally dynamic mixes, entrance enhancers, or rate-restricting layer obstruction for the modification of foundational medication ingestion.[57]

Drug administration in the eye Because of tear production, corneal epithelial impermeability, nonproductive absorption, and transient residence time, it is difficult to achieve excellent drug bioavailability from ocular dosage forms such as ophthalmic solution, suspension, and ointment. However, to improve drug bioavailability, noisome vesicular systems have been proposed.[58] Multiple dosing with sodium stibogluconate-loaded niosomes was found to be more effective against parasites in the liver, spleen, and bone marrow than a simple solution of sodium stibogluconate.[59]

The stability of peptides increased by niosomes was investigated in the delivery of peptide drugs. Yoshida et al used an in-vitro intestinal loop model to deliver 9-desglycinamide, and 8-arginine vasopressin entrapped in niosomes and found that niosomes increased peptide stability.[60]

Use in immunological research.[61] Because of their immunological selectivity, low risk, and higher solidity, niosomes are being used to investigate the concept of the immune reaction induced by antigens. Nonionic surfactant vesicles have clearly demonstrated their ability to function as an adjuvant after parenteral administration of various distinct antigens and peptides.

Anti-inflammatory medications.[62] When compared to the free drug, the niosomal formulation of Diclofenac sodium with 70% cholesterol has greater anti-inflammatory activity. Nimesulide and flurbiprofen niosomal formulations have higher anti-inflammatory activity than the free drug.

Sharma et al. (2009) created a fluconazole span-60 niosomal oral suspension to treat fungalinfections. It is more effective than capsules and tablets.[63]

Table 1: Recent niosome drug delivery research.

The drug'stype	The drug'sname	Composition	Model for experimentation	Year	Reference
Angiotensin converting enzyme inhibitors	Ciexetil candesartan	Maltodextrin,Span 60, cholesterol, diacetyl phosphate	Proniosomal tablet in vitro dissolution test, proniosomal tablet in vivo evaluation, pharmacokinetic analysis	2016	[64]
Anti-inflammatory	Naproxen	cholesterol,tween 80, tween 20,	Preformulatingstudy, in vitro drug release study	2016	[65]
Anti-inflammatory	Dexamethasone	60-span, cholesterol	Niosome characterization,in vitro release studies, and stability testing	2015	[66]
Antibacterial	Moxifloxacin	Tween 60 and cholesterol	Antimicrobial activity, in vitro release studies	2016	[67]
Antibacterial	Cefixime	Surfactant derived from C-glycosides,cholesterol	Experiment animals were used in in vitro release, biocompatibility, and bioavailabilitystudies	2016	[68]
Anticancer	Doxorubicin	N-lauryl glucosamine, Span 60, cholesterol, diacetyl phosphate	Pharmacokineticand tissue distribution studies, as well as formulation studies	2016	[69]
Antiviral	Nevirapine	Cholesterol,Tyloxapol	Drug diffusion kinetics, micro viscosity studies,and in vitro release studies	2015	[71]
Anticancer	Paclitaxel	Span 40, cholesterol,and diacetylphosphate are all ingredients	Pharmacokineticand tissue distribution studies, as well as formulation studies	2015	[72]

CONCLUSION

The niosomal drug delivery system is an excellent example of the rapid advancement of drug delivery technologies and nanotechnology. The niosome appears to be a well-favored drugdelivery system over other dosage forms because the niosome is mostly stable in nature and economical. There is a lot of potential in encapsulating toxic anti-cancer drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory drugs, anti-viral drugs, and so on in niosomes and using them as promising drug carriers to improve bioavailability and targeting properties while reducing toxicity and side effects. As a result, these areas require additional systemic consideration and research to produce a commercially valuable available niosomal preparation.

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