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NIOSOME: AN UPDATED DELIVERY

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ABSTRACT:

Drugs can be delivered to diseased locations using target-specific drug delivery devices. The vesicular system of niosomes offer the same potential advantages as phospholipid vesicles (liposomes) in that they can accommodate both water and lipid soluble drug molecules while controlling their release, making them adaptable drug delivery devices with a wide range of uses. Niosomes are also more cost-effective, chemically stable, and sometimes physically stable than liposomes. Niosomes can be made from commonly used surfactants in pharmaceutical technology and simple manufacturing methods. This article examines the recent deepening and broadening of interest in niosomes throughout a wide range of scientific disciplines, with a focus on their use in medicine. This article includes covers niosome preparation processes, types of niosomes, characterisation, and uses.

Keyword: Targeted delivery, Non- ionic Surfactant, Structure, Method of preparation, Application.

INTRODUCTION:

Paul Ehrlich developed the "magic bullet" technique of focused administration directly to the afflicted cell without harming healthy cells in 1909.[1]The term "targeted drug delivery system" refers to a method of administering drugs at a predetermined pace in order to generate a therapeutic impact in the target tissue while lowering drug concentrations in non-target areas. Localized pharmacological action improves the medicine's efficacy while reducing systemic tissue toxicity.[2]

Niosomes are vesicular nanocarriers that have gotten a lot of attention in the last 30 years as prospective drug delivery systems due to their unique characteristics.[3] L'Oreal created and patented the first niosome formulations in 1975.[4] Anticancer medications were the first to be delivered via niosomes. [5,6] Niosomes are an exclusive drug delivery expertise that encapsulates the medication in a vesicle. Niosomes are non-ionic surface active bilayer elements. [7] Niosomes have a flexible structure, shape, and size, allowing them to entrap hydrophilic medicines in aqueous compartments or divide lipophilic pharmaceuticals into bilayer domains.[8]

ADVANTAGE:[9]

1. Biodegradable, biocompatible, and non-immunogenic surfactants are utilised.
2. The approach for routine and large-scale niosome manufacture does not necessitate the use of hazardous solvents.
3. Niosomes are easy to handle and store because of their chemical stability.
4. Physicochemical features of niosomes, such as shape, fluidity, and size, can be easily modified by altering their structural composition and manufacturing procedure.
5. Because niosomal diffusion is aqueous, the drug release rate can be regulated by emulsifying it in a non-aqueous phase.
6. Because the structure of niosomes protects medication ingredients from a variety of conditions, they can be employed to deliver labile and sensitive pharmaceuticals.
7. Niosomes improve drug particle therapeutic performance by rescheduling circulatory clearance and restricting effects to target cells.
8. Niosomes can be administered through a variety of methods, including oral, parenteral, and topical.
9. Different dose forms, such as powders, suspensions, and semisolids, improve oral bioavailability and drug permeability when administered topically.
10. Because niosomal diffusion is aqueous, the drug release rate can be regulated by emulsifying it in a non-aqueous phase.
11. Niosomes improve patient compliance and satisfaction, as well as effectiveness, when compared to maketed oily preparations.
12. The vesicles serve as a drug repository, slowly releasing the medication.
13. The structural properties of niosomes are malleable.
14. Because niosomal vesicle suspension is a water-based carrier, it has a higher patient compliance rate than oily dosing formulations.
15. They are stable, osmotically active, improve the drug's stability.

DISADVANTAGE:

1) They are known to be more irritating than liposomes due to the absence of generally recognised as safe (GRAS) components (such as phospholipid).[10]

2) There is a potential that surfactants will not be completely hydrated during the hydration process.[11]

3) Some formulation procedures take a long time and necessitate the use of specialised equipment.[11]

4) Because niosomes are dispersed, there is a potential that the encapsulated medicine will silt, aggregate, fuse, or leak during storage.[12]

STRUCTURE OF NIOSOME:

It is a spherical bilayer made up of nonionic surfactant that is stabilised by cholesterol. The hydrophobic part of the nonionic surfactant faces indoors (toward the lipophilic phase). The hydrophilic portion faces away (toward the aqueous phase), resulting in a closed lipid bilayer that

backgrounds solutes in the aqueous phase, and which looks to be the outer and inner surfaces of the hydrophilic area, squeeze in between them by the lipophilic area.

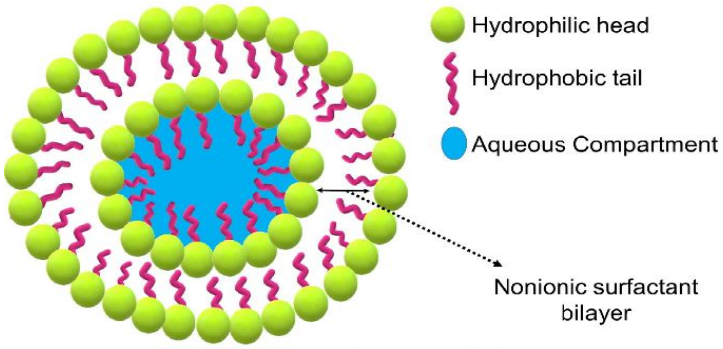

Figure 1:. A typical structure of niosome

Hydrophilic medications are confined within the vesicle's contained region, whereas hydrophobic drugs are incorporated within the bilayer. The production of vesicular assemblies necessitates the application of energy, and all experimental approaches entail the hydration of a surfactant mixture above the system's gel to liquid phase transition temperature, followed by optional size reduction.[7, 13]

COMPOSITION OF NIOSOMES:

The following are the two main ingredients required to make niosomes:

1. Cholesterol: Steroid derivative that provides stiffness and conformation, resulting in fewer leaky niosomes.[14]

2. Surfactants: Nonionic surfactants are recommended since they have a lower risk of irritating the skin. A surfactant's hydrophilic-lipophilic balance (HLB) value is critical, and it should be between 4 and 8 in order to form stable, optimal vesicles.[15,16]Table 1 shows some examples.

3. Charge-inducing agents: These agents give vesicles a charge and make them bigger, enhancing drug entrapment efficiency. They also generate repulsions on the surface of the vesicles, resulting in a larger zeta potential. As a result, it aids in preventing fusion and improving vesicle stability.[17,18] Dicetyl phosphate, dihexadecyl phosphate, and lipoamino acid are negative charge inducers, while dihexadecyl phosphate and lipoamino acid are positive charge inducers.

Non Ionic Surfactants	Examples
Ethers	Brij, decylglucoside, octyl glucoside, lauryl glucoside
Esters	Spans, glyceryl laurate, polysorbates
Fatty alcohols	Cetyl alcohol, cetostearyl alcohol, stearyl alcohol
Black copolymers	Poloxamers

Table 1: Types of surfactants

TYPES OF NIOSOMES: Niosomes are classed based on the amount of bilayer present, the size of the bilayer, or the method of synthesis.

The following are the several types of niosomes:

1. Multilamellar vesicles: This type of vesicle is made up of many bilayers that enclose the aqueous lipid compartment individually. Those vesicles are approximately 0.5-10 m in diameter.

2. Large unilamellar vesicles: The aqueous/lipid compartment ratio is large in these vesicles.

3. Small unilamellar vesicles: These vesicles range in size from 10 to 100 nm in diameter and are made by sonication from multilamellar vesicles.[19]

METHOD OF PREPARATION:

1. Ether injection method: Surfactant is dissolved in diethyl ether before injected. This solution is then injected (with a 14 gauge needle) into a 60°C drug aqueous solution. By vaporising ether, single-layered vesicles (50-1000 m) are generated. The particle size is determined by the operating circumstances.[9]

2. Thin Film Hydration Technique (Hand Shaking Method): Surfactant and cholesterol are dissolved in a round bottom flask using a volatile organic solvent like chloroform or diethyl ether. A rotary evaporator is used to extract the organic solvent, leaving a thin film of solid on the flask's walls. The dried lipid film is then rehydrated with the hydration medium at a temperature above the system's gel to liquid phase transition, with mild agitation, to give multilamellar niosomes.[9]

3. Reverse Phase Evaporation Technique: This approach involves dissolving an equal amount of cholesterol and surfactant in a volatile solvent combination. An aqueous drug solution is added, and the mixture is sonicated at 4-5°C to produce transparent gel. Phosphate buffered saline (PBS) is then added and sonicated again. The organic phase is eliminated by increasing the temperature to 40°C while decreasing the pressure, resulting in a viscous suspension that is diluted with PBS and heated at 60°C for 10 minutes to give niosomes.[9]

4. Drug Uptake Using a Transmembrane pH Gradient (Remote Loading): In organic solvent, surfactant and cholesterol are dissolved (chloroform). The solvent is evaporated under low pressure, giving a thin film on the flask's wall. The film is then vortex mixed to hydrate it with a citric acid solution. Three freeze-thaw cycles and sonication are then applied to multilamellar Niosome vesicles. A drug-containing aqueous solution is added to the suspension and vortexed. To obtain niosomes, the pH of the sample is raised to 7.0-7.2 using disodium phosphate, and the mixture is heated at 60°C for 10 minutes.[9]

5. Bubbling method: The bubble approach eliminates the need of organic solvents in the manufacture of niosomes. It's a brand-new technique. Three necks are placed around the bottom flask in the water bath to create the bubbling unit. The first, second, and third necks each have a water-cooled reflex, thermometer, and nitrogen supply. In the buffer (7.4) at 70°C, the cholesterol and surfactant are added. The mixture is homogenised using a high shear homogenizer for 15 seconds before being bubbled at 70°C with nitrogen gas.[20]

6. Heating method: In this process, a precisely weighed quantity of medication, surfactant, and cholesterol was heated at a specific temperature before being added to the aqueous phase. The mixture was heated at a low pace while stirring until vesicles formed. To make uniform sized vesicles, sonicate the formed vesicles for 2 minutes.[20]

7. Probe sonication: An aliquot of aqueous drug solution is added to the lipid mixture in a 10 ml glass container in this procedure. To obtain tiny lamellar niosomes, the mixture is probe sonicated for 3 minutes at 60°C with a titanium probe.[9]

8. Microfluidization: Microfluidization is a new technology for making unilamellar vesicles. It works on the principle of a submerged jet. Within the interaction chamber, two fluidized streams interact at extremely high velocities. The Impact of a Thin Liquid Layer in Micro Channels. Niosomes are generated with a smaller size and improved reproducibility.[9]

9. Multiple Membrane Extrusion Method: This is a fantastic way to adjust the size of niosomes. In chloroform, surfactant, cholesterol, and dicetyl phosphate are dissolved. Evaporation creates a thin film. The film is hydrated with an aqueous polycarbonate membranes solution containing medication and then extruded as a suspension.[9]

10. Supercritical carbon dioxide fluid: It's a one-step procedure that doesn't involve the use of an organic solvent. This method is both cost-effective and non-harmful to the environment.[20]

Method	Drug	Surfactant	Result/Outcome	Reference
Thin film hydration	Diacerein	Tween 40 Tween 60	The study has suggested that different niosome formulations can provide consistent and prolonged release of diacerein. in this way, the entrapped drug will stay in the body for a longer period of time, which lessens any potential side effects and magnifies the medication's positive effects.	21
	Tenofovir Disoproxil Fumarate (Tdf)	Span20 Span40 Span60 Span 80	Niosomes could be a promising delivery for tdf with improved oral bioavailability and prolonged release profiles	22
	Morusin	Span 60	The findings show that the morusin- the niosome system is a promising technique for improving anti-cancer activity against a variety of cancers, and it could be a key component of future tailored chemotherapeutic regimens.	23
	Herbal Medicine (thdc3-2615rd)	Span20 Span40 Span60	Niosomes are a potential new type of protein. for transdermal drug delivery, there is a drug delivery module. A higher penetration rate was attained, which aided in the localised delivery of drugs and, as a result, enhanced drug availability. medication at their place of action, lowering the dose and reducing	24

			dose-dependent adverse effects such as discomfort.	
	Streptomycin sulfate	Span 60 Tween 60	Controlled drug release and antibacterial activites were seen in optimised niosomal formulation against gram positive and gram negative bacteria. Niosomes showed lower toxicity to normal cells than free streptomycin sulphate, in addition to greater antibacterial activity.	25
	Curcumin	Span 80	The pH-dependent release of the niosomal formulation was observed, with a slow-release profile at physiological ph (7.4) and a higher release rate at acidic ph (3.0)	26
	Glipizide	Tween 80	With enhanced bioavailability and a longer drug release profile, the niosomal formulation for glipizide could be a potential delivery strategy	27
	Paclitaxel	Span 40	the results of this study suggest that niosomal formulation could be a suitable drug delivery strategy for intravenous paclitaxel administration.	28
	Melittin	Span 60 Tween 60	due to improved targeting, encapsulation efficiency, pdi, and release rate, melittin-loaded niosomes are a good replacement in breast cancer treatment and demonstrate a high anticancer effect on cell lines, according to this study.	29
Probe sonication method	Rifampicin and ceftriaxone sodium	Pluronic l121 Span 60	Pluronic l121 and span 60 were used to make ceftriaxone and rifampicin-loaded niosomes that were stable, tiny, and had high drug entrapment efficiencies and improved drug release profiles.	30
Ether injection method	Glimepiride	Span 60	Glimepiride is a loud and palatable form of suitable surfactant that has the advantages of lowering dosage, reducing dosing frequency, and overcoming resistance to conventional single-drug regimen therapy with greater stability.	31
	Ciclopirox olamine (cpo)	Span 40 and Span 60	All the formulations prepared by ether injection method using non-ionic surfactant are showed sustain drug release rate for 24 h.	32
	Albendazole	Span 60	The spherical pegylated niosomes have a diameter of 296.390.62 nm. potential for zeta 3.44 mv, 98.97 percent w/v, and 92.93 percent in-vitro release were the results. w/v the t90 of pegylated niosomes was discovered to be twice as high as that of non-pegylated niosomes (1440.8 min) as if it were dug up for free (720.2 min). as a result, the release of pegylated niosomes was prolonged. albendazole.	33
	Tamoxifen citrate (tam) and doxorubicin hcl	Span 20	Tamoxifen-containing dual-drug-loaded niosomes to create a synergistic effect, doxorubicin was entrapped in a mixture. on the mcf-7 breast cancer cell line, there was a significant effect. Basic physicochemical properties of the niosomes were good. in vitro and ex	34

			vivo studies on cytotoxicity and drug absorption revealed that when they were used together, they were able to achieve better tumour suppression and localization. Nation is superior to either of the individual formulations. this combo therapy could be a potential approach for breast cancer treatment.	
Heating method	Testosterone	Tween 80	The development of a niosomal-based gel formulation could be a promising alternative to steroid-based drug delivery. molecule to reduce skin-related adverse effects while also increasing the rate of permeation transdermal medication delivery is used to provide steroids	35
Reverse phase evaporation (rpe) method,	Isoniazide	Span 20 and Span 60	The niosomes were able to stay in the treated area for up to 30 hours and sustain constant medication concentrations. the drug-loaded niosomes were taken up by macrophage cells in a similar way. as high as 61.8 percent, a level capable of efficient tuberculosis therapy..	36
Supercritical carbon dioxide fluid technique(scco2)	Theophylline	Span 80 and Tween 80	The release period of theophylline was increased by nearly 5-fold by putting this active chemical in niosomes made with the highest surfactant to water ratio.	37

Table 2: Niosome method with Applications

CHARACTERIZATION OF NIOSOMES:

1. Morphology, size, and shape: The size of a niosome can be used to estimate its biodistribution and plasma pharmacokinetics. Optical microscopy and dynamic light scattering are two methods for determining size (DLS). Niosomes have been found to have a spherical form using electron microscopy techniques such as TEM and SEM.[38,39]

2. Surface charge: Vesicle charge is measured by measuring the zeta potential. The method of dynamic light scattering has two functions: it estimates average particle size and zeta potential.[40]

3. Bilayer formation and lamellae number: NMR spectroscopy, electron microscopy, and small angle X-ray scattering are utilised to characterise the bilayer formation and number of lamellae.[5]

4. Membrane rigidity and homogeneity: A fluorescent probe measures the rigidity of niosomal solution as a role of temperature. Membrane homogeneity is measured using P-NMR, differential scanning calorimetry (DSC), and Fourier transform-infrared spectroscopy (FTIR).[41]

5. Encapsulation efficiency: The amount of drug entrapped can be carried out using centrifugation, gel filtration, and dialysis, among other methods.

Centrifugation: The niosomal dispersion is centrifuged for 30 minutes. The entrapped drug is detected using a UV or HPLC technique after the supernantant is decanted.

Gel filtering: Niosomal diffusion is passed over a Sephadex G-50 column and eluted with normal saline after gel filtration.

Dialysis: A dialysis bag with phosphate buffer is used to extract free medication from niosomal dispersion.[42]

6. Osmotic shock: Incubate the niosomal formulation for 3 hours with hypotonic, isotonic, and hypertonic solutions. Optical microscopy is used to examine changes in the size of vesicles.

7. Study of stability: Niosomes were kept in airtight sealed vials at various temperatures to test their stability. Niosome stability is also affected by the amount and type of surfactant used, as well as cholesterol. The niosomes were sampled at regular intervals (0,1,2, and 3 months), inspected for colour change, surface properties, and evaluated for the percentage drug retained and checked for drug leakage, then assessed using appropriate analytical procedures.[43,44]

7. In vitro drug release of niosomes: The following procedures can be used to perform in vitro drug release of niosomes: Dialysis is the first step, followed by the Franz diffusion cell. Dialysis in the reverse direction.

1) Dialysis: The dialysis bag is pre-washed and pre-soaked before being filled with niosomal dispersion. The dialysis bag is immersed in a 37 °C buffer solution that is constantly stirred. At a regular interval, aliquotes are withdrawn and replaced with new medium. The amount of drug in question is determined.[45]

2) Franz diffusion cell: The donor and receptor compartments are separated by a cellophane membrane or a dialysis membrane. The sample is placed in the donor compartment, and the buffer is placed in the receptor compartment, which is kept at 37°C and stirred continuously using a magnetic stirrer. At regular intervals, the samples are removed, replaced with fresh medium, and evaluated for drug content.[46]

3) Reverse dialysis: proniosomes are filled with tiny dialysis containing 1ml of dissolving medium. After that, the proniosomes are pushed into the dissolving media. This approach allows for direct dilution of the proniosomes, however it does not allow for the quantification of rapid release.[43,44]

APPLICATION OF NIOSOMES: [47-62]

1) Niosomes have been effectively used to target drugs to many organs such as the skin, brain), liver ,lung, ocular systems, tumor etc.

2) Niosomes have a greater bioavailability than other dose forms.

3) Niosomes have been used to provide controlled and sustained medication release.

4) Niosomes have been shown to improve medication permeation through the skin.

5) Noisy increases the stratum corneum's qualities by lowering transepidermal water loss and improving skin condition.

6) Administration by a variety of methods, including oral, parenteral, and topical.

7) Non-immunogenic, biodegradable, and biocompatible with the body.

8) It's simple to handle, store, and transport.

9) It can protect the medication against enzymatic and acid attack, hence improving its stability.

10) It can be employed in ocular drug delivery without causing tissue irritation or penetration enhancer harm.

11) To improve the efficacy of medications used in cancer treatment.

12) Using carrier radiopharmaceuticals in diagnostic imaging.

CONCLUSION:

Scientists generally embrace niosomes. Niosomes are employed to help the medicine reach the right tissue. Single-chain uncharged surfactant molecules make up niosomes. Toxic medications that require greater doses may be safely administered by niosomal delivery. Lancome's formulation is based on niosomal technology. A few cosmetics are also being investigation. Researchers and academicians agree that integrating drugs into niosomes allows for precise medication targeting at specific tissue sites. Niosomes have a structure that is similar to that of liposomes, however they have some advantages over liposomes, such as cost and stability. They also have the ability to encapsulate a variety of medications, such as anti-infectives and anti-cancer therapies. Niosomes are also useful as diagnostic imaging agents and vaccination adjuvants. These areas should be investigated further. Niosomes can be used for a variety of drug delivery methods, including ocular, parenteral, targeted. One of the best instances of significant progress in drug delivery technologies and nanotechnology is the niosomal drug delivery system. Because niosomes are very stable in nature and cost effectively, they appear to be a popular medication delivery mechanism over other dosage forms. As a result, more comprehensive analysis and study are needed in these areas in order to develop economically viable niosomal preparations. Incorporating the drug is a novel notion. Due to many reasons such as cost, stability, and other considerations, niosomes are regarded to be a better alternative for drug administration than liposomes. Niosomes play a critical part in a variety of drug delivery methods, including targeted, topical, ophthalmic, and parenteral. Niosomes will be highly important in the pharmaceutical industry in the future. Only animal experimentation of this targeted drug delivery system has been reported so far, but more clinical studies in human volunteers, as well as pharmacological and toxicological studies in animals and human volunteers, may help to exploit niosomes as efficient drug carriers for treating cancer, infection, and AIDS, among other diseases.

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