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Niosomes: A review of their structure, properties, methods of preparation, and medical applications

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ABSTRACT:-
A new medicine delivery method called noisome involves encapsulating the drug in a vesicle. A bilayer of non-ionic surfactants makes up the vesicle. Due of their stability and affordability, niosome are generally chosen over liposome. Noisome made of non-ionic surfactant vesicles are made by hydrating a non-ionic surfactant and cholesterol combination. They can be employed as drug carriers for both lipophilic and amphiphilic substances. Noisome are a particular kind of delivery mechanism where drugs are contained within vesicles.
Among the many characteristics of noisome are their flexibility in structure, biodegradability, biocompatibility, and lack of immunogenicity. The reason for writing this review is to shed light on the several ways that niosomes are utilized to treat a variety of illnesses. We will examine several facets of noisome in this review paper.

Keywords:- noisome, advantage, disadvantage, structure , composition of noisome, Types, method of preparation and application.

I. INTRODUCTION:-

Niosomes are non-ionic vesicles based on surfactants. Niosomes are mostly produced as an incipient by the inclusion of cholesterol and non-ionic surfactants. Both liposomes and niosomes are bilayers with structural similarities. However, niosomes are more stable due to the materials utilized in their creation. Both hydrophilic and lipophilic medications have the ability to entrap; for hydrophilic pharmaceuticals, this can happen in an aqueous layer, whereas for lipophilic drugs, it can happen in a lipid-based vesicular membrane.

Paul Ehrlich started the era of targeted delivery development in 1909 when he envisioned a medicine delivery system that would directly target diseased cells. The capacity to focus a therapeutic medication to a specifically intended site of action with little to no interaction with non-targeted tissue is known as drug targeting. A niosome drug delivery system vesicle contains the medicine. Amphiphillic non-ionic surfactants, like span-60, are created by vesicles in niosomes and stabilized by adding a little quantity of anionic surfactant and cholesterol. Dicetyl phosphate is one example.

Because niosomes are a completely novel drug delivery system, they can contain both hydrophilic and hydrophobic tablets. The deliquescent medicine is confined in the hollow region in the middle, and the hydrophobic cure is located inside the non-polar area that contains the different steel layers. Because they are ampiphillic in nature, the medication is encapsulated in an extraordinary sac that is produced using a non-ionic solvent; hence, the term "niosomes."

The niosomes length can be a totally little and microscopic.The number one noisome formulations have been evolved and proprietary via way of means of L'Oreal in 1975.Within the presence of accurate combos of surfactants and fee inducement sellers from thermodynamically strong vesicles. Niosomes are in large part studied as an trade to liposomes due to the alleviate the hazards associated with liposomes. Niosomes conquer the hazards related to liposomes cherish chemical instability.Liposomes' susceptibility to aerophilic breakdown and fluctuating phospholipid purity are the causes of their chemical instability. Chemical stability, biodegradability, biocompatibility, cheap manufacturing costs, ease of storage and handling, and minimal toxicity are the main factors contributing to the growth of niosomal devices. Niosomes can be administered orally, parenterally, or topically, among other ways. Different types of tablets, including synthetic and herbal ones, antigens, hormones, and unique bioactive chemicals, are supplied by niosomes. Along with a description of the educational tactics, this newsletter offers several noteworthy niosome substitutes. It also discusses the latest niosome packages used in the encapsulation and transportation of bioactive substances. Rapid and significant advancements in the use of generation in the diagnosis and treatment of diseases have given

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rise to a new field called nanomedicine and related subfields, such as pharmaceutical nanocarriers, which are referred to as new clinical science branches.Lipid-based businesses (liposomes), wetter-based businesses (niosomes), and nanogel. Reducing the size of pharmaceutical companies to the nanoscale has many benefits, including improving the pharmacology and biodistribution of therapeutic agents, reducing toxicity through drug accumulation at the target site, facilitating drug passage between cells, and extending retention times in organic structures, all of which increase the drug's efficacy.Polymers, metals, steel oxides, nanogel, lipid-based companies (liposomes), and wetter-based companies (niosomes) are some examples of the various materials that can make up nanostructures. Reducing the size of pharmaceutical companies to the nanoscale has many benefits, including improving the pharmacology and biodistribution of therapeutic agents, reducing toxicity through drug accumulation at the target site, facilitating drug passage between cells, and extending retention times in organic structures, all of which increase the drug's efficacy.The creation of new drug-transport architecture is crucial. The drug unharness profile, absorption, distribution, and tablet elimination are all reinforced by this generation. Two requirements should be taken into account while creating a replacement drug-transport device: The medication must first be released at a predetermined rate. Second, it must unleash a significant amount of the dynamic element at the destination; doses of old documentation cannot achieve those objectives.As a medication delivery system, vesicles with a bilayer membrane and a crater interior have garnered more attention.

SALIENT FEATURES OF NIOSOMES:-

- Solutes can be trapped by niosomes.
- Niosomes are stable and osmotically active.
- Since niosomes' primary structural components are hydrophobic and hydrophilic, they also provide the drug atoms with a comprehensive level of dissolvability.
- Niosomes function as the body's pharmaceutical repository since they release the drug in a regulated manner thanks to their bilayer, which facilitates the drug's encapsulated arrival.
- Niosomes can also be used as a vehicle for targeted drug delivery, which delivers the medication precisely to the area where the desired remedial effect is needed.
- When administered topically, they increase the permeability of the skin and improve the oral bioavailability and solubility of poorly soluble medications.
- Niosomes' structural properties are flexible, and their design should be tailored to the specific circumstance.
- Niosomes may improve the way the drug's molecules function.
- Improved accessibility to the genuine location just by shielding the medication from the biological surroundings.
- Niosomes make the medicine that is entrapped more stable.

ADVANTAGES:-

- Enhanced duration of action and decreased adverse effects more patient compliance when compared to alternative administration methods.
- Very little medication is needed to provide the intended effect.
- The preparation's active ingredient or constituent is shielded from a variety of internal and external influences by a bilayer.
- The medication is shielded from gastrointestinal breakdown and first-pass metabolism.
- Niosomes can be administered parenterally, topically and orally.
- serve as a depot formulation, allowing for a regulated release of the medication.

DISADVANTAGE:-

- Time consuming procedure.
- Processing calls for specialized equipment.
- Short shelf life as a result of:-

1) Fusion
2) Congregation
3) Drug leakage from confined individuals
4) Drugs in capsules are hydrolyzed.

- Unstable in terms of body

COMPOSITION OF NIOSOMES:-

The vital components used in the niosome formulation are:

- Non-ionic surfactants
- Cholesterol
- Charge inducer
- Hydration medium

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➢ **Non ionic surfactants:-**

Niosomes are non-ionic surfactant unilamellar or multilamellar vesicles formed from synthetic non-ionic surfactants. Non-ionic surfactant possesses hydrophilic head group and hydrophobic tail. As HLB value increases therefore alkyl chain increases, the size of niosome increases. Hence HLB value 14-17 is not suitable for niosome formulation. HLB values 8 have highest entrapment efficiency. Nonionic surfactants are as follows,

Ether linked surfactant: These are surfactants contain hydrophilic and hydrophobic moieties which are linked by ether, polyoxyethylene alkyl ethers with the general formula (CnEOm), where n; i.e. number of carbon atoms varies between 12 and 18 and m; i.e. number of oxyethylene unit varies between 3 and 7. Di-alkyl chain surfactant: Surfactant was used as a principal component of niosomal preparation of stibogluconate and its potential in delivering sodium stibogluconate in experimental marine visceral leishmaniasis has been explored.

C16H33CH-O[-CH2-CH-O]7-H
| |
CH2 CH2OH
|
C12H25-O (mol. Wt. 972)

Ester linked: These surfactants have ester linkage between hydrophilic and hydrophobic groups; hence it is also called as Ester linked surfactants.

C15H31CO[O-CH2-CH-CH2]2-OH
|
OH (mol. Wt. 393)

This surfactant was also studied for its use in the preparation of stibogluconate bearing niosomes and in delivery of sodium stibogluconate to the experimental marine visceral leishmaniasis.

This surfactant was also studied for its use in the preparation of stibogluconate bearing niosomes and in delivery of sodium stibogluconate to the experimental marine visceral leishmaniasis.

Sorbitan esters: These are the ester linked surfactants. The commercial sorbitan esters are mixtures of the partial esters of sorbital and its mono and di-anhydrides with oleic acid

CH2
|
H-C-OH
|
RCOO- C-H
|
H-C-OH
|
H-C-OOC-R
|
CH2OOC-R

Where, R is H or an alkyl chain.

These have been used to entrap wide range of drugs viz doxorubicin.

Fatty acid and amino acid compounds:-In certain niosome preparations that result in "Ufasome" vesicles, long chain fatty acids and amino acid moieties have also been utilized.

➢ **Cholesterol:-**

Cholesterol is an amphiphilic molecule; it orients its OH group towards aqueous phase and aliphatic chain towards surfactant's hydrocarbon chain. Cholesterol a waxy steroid metabolite is usually added to the non-ionic surfactants to provide rigidity Cholesterol is also known to prevent leakage by abolishing gel to liquid phase transition.

Charge inducer :-

Positive and negative charge inducers are the two categories of charged inducers. By introducing a charge onto the prepared vesicles' surface, it makes them more stable. It works by giving larger zeta potential values and prevents vesicles with the same charge from fusing together due to repulsive forces. Sterylamine and cetylpyridinium chloride are frequently used positive charge inducers, while lipoamine acid, dicetyl phosphate, and dihexadecyl phosphate are frequently used negative charge inducers.

➢ **Hydration medium**:-

Phosphate buffer is the most widely utilized hydration medium while making niosomes. At different pHs, these phosphate buffers are employed. The solubility of the medication being encapsulated determines the hydration medium's actual pH.

TYPES OF NIOSOMES:

The different types of niosomes can be classified as follows: (Figure).

1) Multilamellar vesicles (MLV)
2) Large unilamellar vesicles (LUV)
3) Small unilamellar vesicles (SUV)

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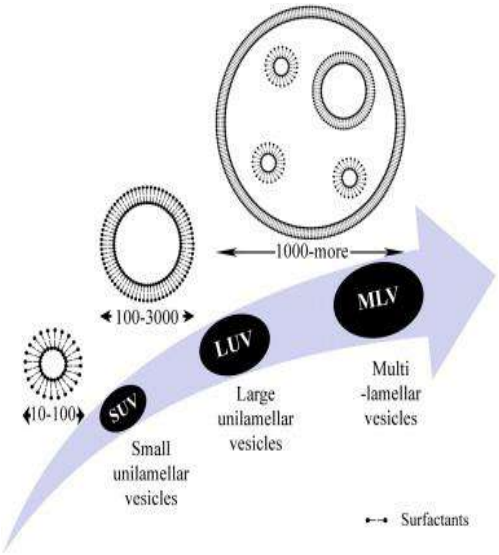


Figure: - Types of Niosomes

1)Multilamellar vesicles (MLV):-

Niosomes are the most common type of multilamellar vesicles. The vesicles have a diameter of roughly 0.5 to 10 µm. The vesicles are simple to prepare and maintain their mechanical stability throughout extended storage. The aqueous lipid component is often surrounded by a number of bilayers. For lipophilic substances, these miltilamellar vesicles are ideal drug carriers.

2)Large unilamellar vesicles (LUV):-

Large unilamellar niosomes can entrap higher amounts of bioactive compounds with a very cost-effective utilization of membrane lipids because of their high aqueous/liquid compartment ratio. Large unilamellar vesicles range in length from 100 to 3000 nm.

3)Small unilamellar vesicles (SUV):-

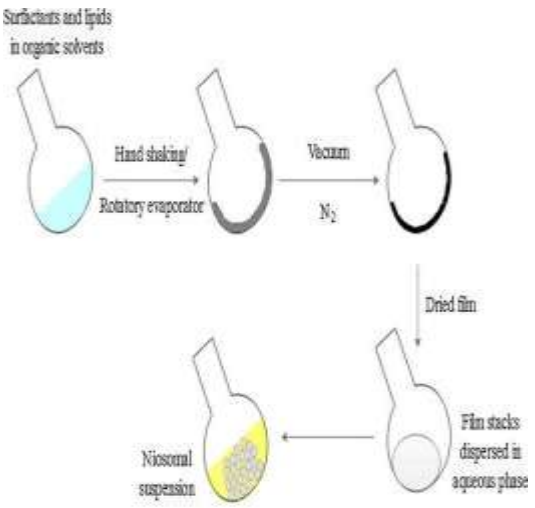
The sonication process is typically used to create small unilamellar vesicles from multilamellar vesicles. According to reports, the tiny unilamellar vesicles range in size from 10 to 100 nm.

METHOD OF PREPARATION: -

1) Hand shaking method (Thin film hydration technique)
2) Micro fluidisation
3) Reverse Phase Evaporation (REV)
4) Ether Injection Method
5) Trans-membrane pH-gradient (inside acidic)
6) The Bubble Method
7) Sonication
8) Multiple extrusion method
9) Formation of niosomes from proniosomes

1)Hand shaking method (Thin film hydration technique):-

The hand shaking method involves dissolving cholesterol and non-ionic surfactant in a volatile organic solvent (such as methanol, diethyl ether, or chloroform) in a round-bottom flask. A thin coating of solid mixture is left on the flask wall after the organic solvent is eliminated using a rotary evaporator set to room temperature (20°C). The drug-containing aqueous phase is added to the dry surfactant film at 50–60°C while being gently stirred. Multilamellar niosomes are created using this technique.



{ Figure Of Hand shaking method}

2) Micro fluidisation:-

One method for creating unilamellar vesicles with a certain size distribution is micro-fluidization. Its foundation is the submerged jet principle, which describes how two fluidized streams interact in precisely specified microchannels inside an interaction chamber at extremely high velocities (100 ml/min). Thin liquid sheets are impinged along a shared front in a way that keeps the energy entering the system inside the region where niosomes form. This process produces niosomes that are more consistent, smaller, and more reproducible.

3)Reverse Phase Evaporation (REV):-

The cholesterol and surfactant are consumed in a 1:1 ratio during reverse phase evaporation. Ether and chloroform are used to dissolve the aforementioned combination. The

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aqueous phase dissolves the drug. The temperature range for sonicating both mixtures is 4-6°C. The niosomes are obtained by diluting the niosome solution in PBS at 60°C using a water bath for ten minutes. PBS is added to the final product once again, and it is sonicated at low pressure while maintaining a temperature of 40 to 45°C, which eliminates the organic phase. To produce niosomes, the resulting solution is heated on water at 60°C for 10 minutes after being diluted with PBS.

4)Ether injection method:-

By adding a solution of surfactant dissolved in diethyl ether (a volatile organic solvent) to warm water that is kept at 60°C, the ether injection method creates niosomes. A 14-gauge needle is used to inject the surfactant mixture in ether into an aqueous solution of material. Ether (a volatile organic solvent) is vapourized to create single-layered vesicles.

5) Trans-membrane pH gradient (inside acidic):-

Using this approach, the cholesterol and surfactant are combined in a round-bottom flask and then dissolved in chloroform. The chloroform evaporates at a lower pressure, forming a thin layer on the flask wall. By vortex mixing with 300 mM citric acid (pH 4.0), the film is hydrated. An aqueous solution containing 10 mg/ml of the medication is added to the niosomal suspension mentioned previously and vortexed. After adding 1M disodium phosphate to bring the sample's pH down to 7.0–7.2, the mixture is heated for ten minutes at 60°C. This process creates multilamellar vesicle.

6) The Bubble method:-

An innovative method for creating niosomes without the use of organic solvents is the bubble method. This approach makes use of the bubbling unit. This apparatus consists of a round-bottom flask with three necks that are submerged in a water bath to regulate the temperature. The first neck contains water-cooled reflux, the second contains a thermometer, and the third contains nitrogen. At 70°C, cholesterol and surfactant are combined in a buffer solution (pH-7.4). After 15 seconds of mixing with a high shear homogenizer, the solution is instantly bubbled at 70°C using nitrogen gas. (Figure 4).

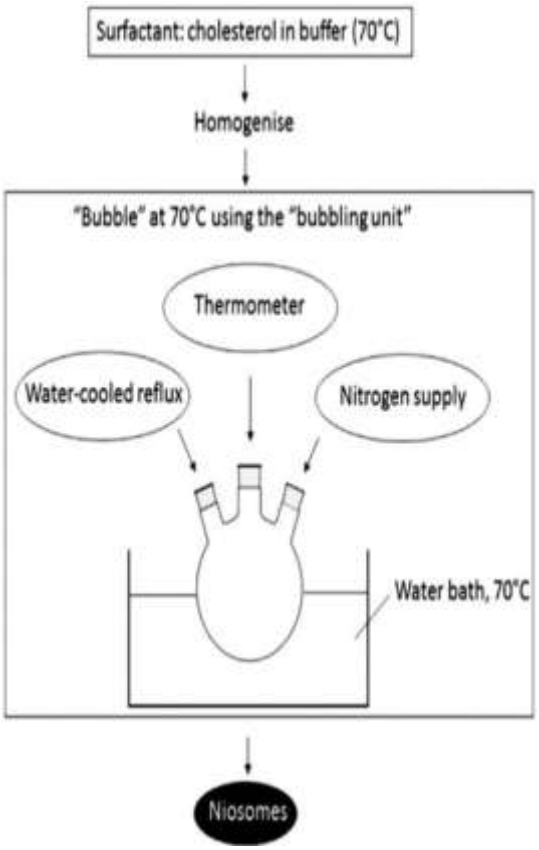

Figure 4: The bubble method

7) Sonication:-

One of the traditional methods for making niosomes is sonication. This approach involves dissolving the drug in a buffer to create the drug solution. The non-ionic surfactant mixture is then added to this buffer drug solution in an ideal ratio. The combination is sonicated at a particular frequency, temperature, and time to produce the desired niosomes. It is one of the simplest methods for regulating the niosomes' particle size. Niosomes having a narrow size distribution can have their diameters reduced using this technique. Although they take a lot of energy, probe sonicators can also be utilized. As a result, titanium is released and the temperature rises abruptly

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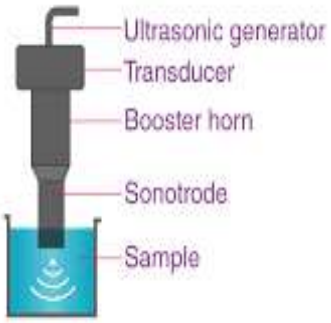

8) Membrane Extrusion Method:-

This process involves mixing diacetyl phosphate, cholesterol, and surfactant with chloroform. The thin film is then obtained by evaporating this chloroform combination. The aqueous drug polycarbonate membrane is used to hydrate the thin film. This membrane, which has eight passages, is used to extrude the solution and the resulting suspension. This technique also yields the niosomes' required size.

9)Formation of niosomes from proniosomes:-

The formulation of niosomes from maltodextrin-based preniosomes has been described by Blazek-Walsh A.I. et al. This formulation provides rapid reconstitution of niosomes with the minimal left over/remaining carrier. The formulation was obtained as a free-flowing powder by drying the slurry of maltodextrin and surfactant, which could be rehydrated by adding warm water. The niosomes are formed by adding an aqueous phase with drug to the preniosomes with brief agitation at a temperature higher than the mean transition phase temperature of the surfactant .

Application of Niosomes:-

❖ **Niosomes as hemoglobin carriers :-**

Niosomal solution can be employed as a hemoglobin carrier since it exhibits a visible spectrum that is superimposable onto that of free hemoglobin.

In addition to being oxygen permeable, vesicles can alter the hemoglobin dissociation curve in a manner akin to that of non-encapsulated hemoglobin.

❖ **Niosomes as transporters of drugs :-**

Additionally, iobitridol, a symptomatic operator used in X-ray imaging, has been transported by niosomes. Topical niosomes can act as an entrance booster, a neighborhood station for the continuous delivery of dermally dynamic mixes, a solubilization grid, or a rate-restricting layer obstruction to modify the fundamental intake of drugs.

❖ **Ophthalmic drug delivery:-**

Because of tear formation, corneal epithelial impermeability, nonproductive absorption, and short residence duration, it is challenging to obtain high bioavailability of drugs from ocular dosage forms such as ophthalmic solution, suspension, and ointment. But niosomal vesicular systems have been suggested as a way to improve medication bioavailability [29]. In contrast to a basic sodium stibogluconate solution, Carter et al. showed that serial treatment with sodium stibogluconate-loaded niosomes was effective against parasites in the liver, spleen, and bone marrow.

❖ **Delivery of peptide drugs:-**

Yoshida et al. looked into the stability of the peptide that niosomes increased. In an in vitro intestinal loop model, Yoshida et al. used niosomes to entrap 8-arginine vasopressin for oral delivery of 9-desglycinamide and found that noisome improved the stability of the peptide.

Numerous pharmacological substances may be useful for noisome medication delivery due to their ability to combat a range of illnesses.

II. CONCLUSION:-

In conclusion, the aforementioned study demonstrated that noisome had superior therapeutic effectiveness in comparison to traditional dosage forms that were administered via the same method. The biggest obstacle to topical medication distribution is the skin's barrier function, which prevents most medications from entering the body. According to the available evidence, noisome' nanometer-scale size and elastic nature made them the ideal vesicles for cutaneous drug administration. Due to the distinct lipid components, they improved penetration into the stratum corneum and subsequently disrupted the intercellular lipid layers inside that layer of the skin, acting as drug carriers to distribute drug molecules trapped in or through the skin. In vivo tests revealed an intriguing relationship between the improved therapeutic efficacy at the site of injury at lower dosages of medications included in the noisome gel formulation and the superior

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penetration capabilities of noisome in comparison to other traditional dosage forms. Niosomal gel outperformed acne gel in comparative in vivo trials of TRA and BPOs because it raised a drug's therapeutic index, which led to a 4.16-fold lower BPO dosage than acne gel. According to MIC and antimicrobial susceptibility studies, 28. µg/mL BPO exhibits strong antibacterial activity against microorganisms that cause acne, including Staphylococcus epidermidis. Niosome gels have the best retention of BPO and TRA in the afflicted skin, according to exvivo skin retention experiments. It is kept on the skin as long as possible to prevent the spread of acne-causing germs. Furthermore, because of the niasome gel, the iosome's "reservoir mechanism" enables the MIC to remain at the target region for an extended amount of time. The aforementioned research suggests that the dosage form based on nanovesicles, or niosomes, created here has superior therapeutic effects at lower doses than traditional dosage forms.

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