A REVIEW ON DIFFERENT METHOD OF PREPARATION OF NIOSOMAL GEL

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Abstract:
The Niosomes is a targeted drug delivery system wherein medication is encapsulated within vesicles composed of a bilayer of non-ionic surface-active agents, hence the name "niosomes." Niosomes are microscopic and small in size, typically in the nanometric scale. They have demonstrated significant advancements in transdermal drug delivery and targeted drug delivery. Niosomes are formed primarily by incorporating cholesterol and surfactants as excipients, where cholesterol is crucial for stability and entrapment efficiency. Other charged molecules are also used to enhance stability, and niosomes can be unilamellar or multilamellar vesicles. They resemble liposomes and can encapsulate both hydrophilic and lipophilic drugs.The components for niosome preparation include cholesterol, non-ionic surfactants (such as spans, tweens, and brij), and charged molecules (like dicetyl phosphate or stearyl amine). Cholesterol's content influences stability, loading capacity, and vesicle formation. The preparation methods for niosomal gels vary, with techniques like Thin-Film Hydration, Ether Injection, Hand-Shaking, Reverse Phase Evaporation, and Microemulsion Template being common. These methods involve steps such as creating a lipid film, hydration, emulsification, and incorporation into a gel matrix.The advantages of niosomal gels include their potential for targeted and controlled drug delivery, improved stability of encapsulated drugs, enhanced penetration through the skin barrier, and the ability to encapsulate both hydrophilic and lipophilic drugs. Additionally, niosomal gels can offer a sustained release of drugs, reduce side effects, and improve patient compliance.Overall, niosomes represent a promising avenue for drug delivery, offering versatility and potential benefits in various medical applications.

Keywords: Niosomes, targeted drug delivery system

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Niosomes is a targeted drug delivery system in which medication encapsulated in a vesicle. Vesicle composed of a bilayer of non-ionic surface active agent hence name as niosomes. Niosomes are microscopic small in size. Their size lies in nanometric scale. Niosomes have recently been shown to greatly increased transdermal drug delivery and also used in targeted drug delivery. It is mostly formed by cholesterol surfactants incorporation as an excipient. Other excipients are also used. Niosomes are unilamellar or Multilamellar vesicles. They are very similar to the liposomes.[1,2,3]

Definition: Niosomes or non-ionic surfactant vesicles are microscopic lamellar structures formed on admixture of non-ionic surfactant like span, tween, alkyl or dialkyl polyglycerol ether class and cholesterol with subsequent hydration in aqueous media. In niosomes the vesicles forming amphiphiles is a non-ionic surfactant such as dicetyl phosphate, Stearyl amine. Both hydrophilic and lipophilic drugs are incorporated. Drug delivery by niosomes is potentially applicable to many pharmacological agents for their action against various diseases. Niosomes have shown potential in the release studies and serve as a better option for drug delivery system.[4,5,6]

Components of niosomes: .[7,8]

There are mainly three types of components are used for the preparation of niosomes:

- Cholesterol, 2.Non-ionic surfactants, 3.Charged molecules
- **Cholesterol:** Most important components of noisome is cholesterol. It forms hydrogen bond with the hydrophilic head of surfactant in the bilayer structure. It can influences some significant vesicular properties like entrapment efficiency, increase stability. It also promotes the stability of bilayer surface by influencing the gel liquid transition temperature. In case of surfactants having HLB >6is essential to form bilayer vesicles and for lower HLB value stability is improved by adding cholesterol. Its content also adjusts the loading capacity which is important factor for niosomal formulation. It has also been showed that incase of more hydrophobic surfactants addition of cholesterol helps ininhibiting the chance of aggregation and helps in vesicles formation.
- **Non-ionic surfactants:** Surfactants play a main role in the formation of niosomes. The following non-ionic surfactants are generally used for the preparation of niosomes the spans(span60,40,20,85,80),tweens (tween20,40,60,80) and Birijs (brij 30,35,52,58,72,76). The non-ionic surfactants have a hydrophilic head and a hydrophobic tail. The choice of non-ionic surfactant depends upon Hydrophilic and Lipophilic balance (HLB), critical micellar concentration (CMC) and critical packing of parameter of amphiphiles

Charged molecule: Are mainly added to increase stability by providing charged groups to the bilayer surface. Dicetyl phosphate is mostly used as charged molecules which impart negative charged molecules on the bilayer surface are mainly added to increase stability of the vesicles and to prevent aggregation by providing charged groups to the bilayer surface. Dicetyl phosphate is mostly used charged molecules which impart a negative charge on the bilayer surface. Usually added in an amount of 2.5-5 mol%. Even so increasing the amount of charged molecules can suppress niosome preparation. Examples: Dicetyl phosphate (DCP)-inducing negative charge, Stearyl amine (SA) inducing positive charge..[9,10,11]

Structure of Niosomes: Niosome vesicles would consists of a vesicle forming amphiphilic i.e. Surfactant such as span 20,40,60,80 which is stabilized by the addition of cholesterol and a small amount of anionic surfactant such as Dicetyl phosphate which also helps in stabilizing the vesicles. These are microscopic lamellar structures which are formed on the admixture of non-ionic surfactant of alkyl or dialkyl polyglycerol ether class and cholesterol with hydration in aqueous media..[12,13]

There are several methods for preparing niosomal gels, each with its own set of advantages and considerations. Here are some common methods of niosomal gel preparation:

Thin-Film Hydration Method:

The Thin-Film Hydration Method is a commonly used technique for preparing niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are similar in structure to liposomes but are composed of non-ionic surfactants instead of phospholipids. The Thin-Film Hydration Method involves several key steps to create niosomal vesicles within a gel matrix. Here's a detailed explanation of the process:.[14,15,16]

Ingredients and Materials:

Non-ionic surfactant: The primary component responsible for forming the niosomal bilayers.

Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.

Volatile organic solvent: Used to dissolve the surfactant and drug, and later evaporated to form a thin lipid film.

Aqueous phase: Contains the gelling agent and other necessary components to create the gel matrix.

Gelling agent: Responsible for creating the gel structure within which the niosomes will be dispersed.

Steps:

Preparation of Organic Phase:

The non-ionic surfactant and the drug are dissolved in a volatile organic solvent (e.g., chloroform, ether, or a mixture of solvents).

The drug can either be dissolved in the organic solvent or added to the surfactant solution.

Evaporation of Organic Solvent:

The organic solvent is then evaporated using methods such as rotary evaporation or vacuum drying, leaving behind a thin lipid film on the walls of the container.

The lipid film contains the surfactant and the drug, forming a layer that will serve as the basis for niosome formation.

Hydration and Niosome Formation:

The thin lipid film is rehydrated by adding an aqueous phase containing a gelling agent.

Gentle agitation, such as magnetic stirring or sonication, is applied to facilitate the hydration process and encourage the formation of niosomal vesicles.

The surfactant molecules arrange themselves into bilayers to encapsulate water and drug molecules, forming niosomal vesicles suspended in the aqueous phase.

Gel Formation:

The aqueous phase also contains the gelling agent, which starts to gel upon contact with water or by adjusting the pH if necessary.

The niosomal dispersion is incorporated into the gel-forming aqueous phase, resulting in the creation of a niosomal gel.

Homogenization (Optional):

In some cases, additional homogenization or mixing steps might be applied to ensure uniform distribution of niosomes within the gel matrix.

Final Formulation:

Once the niosomal gel is formed, it can be transferred to suitable containers for storage and application.

Ether Injection Method:.[17,18,19]

The Ether Injection Method is a technique used for the preparation of niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are similar in structure to liposomes but are composed of non-ionic surfactants instead of phospholipids. The Ether Injection Method involves the injection of an aqueous phase into an organic phase containing the surfactant and the drug. This method facilitates the self-assembly of niosomes in the presence of water, and these niosomes can be subsequently incorporated into a gel matrix. Here's a detailed explanation of the Ether Injection Method:

Ingredients and Materials:

Non-ionic surfactant: The primary component responsible for forming the niosomal bilayers.

Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.

Organic solvent: Used as a dispersion medium for the surfactant and drug.

Aqueous phase: Contains water and other necessary components for niosome formation.

Gelling agent: Used to create the gel structure within which the niosomes will be dispersed.

Steps:

Preparation of Organic Phase:

The non-ionic surfactant and the drug are dissolved in an organic solvent, such as chloroform or ether.

The drug can either be dissolved in the organic solvent or added to the surfactant solution.

Formation of Organic Phase:

The surfactant and drug solution, along with the organic solvent, forms the organic phase.

This phase will serve as the dispersion medium for the surfactant and drug when the aqueous phase is injected.

Preparation of Aqueous Phase:

An aqueous phase is prepared by dissolving the gelling agent and other necessary components in water.

Ether Injection:

The organic phase is slowly injected into the aqueous phase under continuous and gentle stirring.

As the organic phase is injected, small droplets of the organic solution disperse in the aqueous phase due to the difference in polarity between the two phases.

Self-Assembly of Niosomes:

In the presence of water, the non-ionic surfactant molecules in the organic droplets self-assemble into niosomal vesicles.

The hydrophilic heads of the surfactant molecules face outward, while the hydrophobic tails face inward, forming a bilayer structure that encapsulates water and drug molecules within the vesicles.
Gel Formation:
The niosomal dispersion, which contains the self-assembled niosomes, is incorporated into the aqueous phase containing the gelling agent.
The gelling agent starts to form a gel structure, and the niosomal vesicles become embedded within the gel matrix.

Hand-Shaking Method:.[20,21,22]
The Hand-Shaking Method is a relatively simple technique used for the preparation of niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are structurally similar to liposomes but are made from non-ionic surfactants rather than phospholipids. The Hand-Shaking Method involves mechanical mixing of the surfactant, drug, and an aqueous phase to form niosomal vesicles. These niosomes can then be incorporated into a gel matrix for various applications. Here's a detailed explanation of the Hand-Shaking Method:
Ingredients and Materials:
Non-ionic surfactant: The main component responsible for forming the niosomal bilayers.
Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.
Aqueous phase: Contains water and other necessary components for niosome formation.
Gelling agent: Used to create the gel structure within which the niosomes will be dispersed.
Steps:
Preparation of Aqueous Phase:
An aqueous phase is prepared by dissolving the drug and any necessary components in water.
The drug can either be dissolved directly in the aqueous phase or added later to the surfactant solution.
Surfactant Solution:
The non-ionic surfactant is dissolved in a separate container using an appropriate solvent, creating a surfactant solution.
Hand-Shaking:
The aqueous phase and the surfactant solution are mixed together by shaking vigorously using hand shaking or mechanical stirring.
The mechanical agitation leads to the formation of niosomal vesicles as the surfactant molecules self-assemble in the presence of water, encapsulating water and drug molecules within the vesicles.
Gel Formation:
The niosomal dispersion, containing the self-assembled niosomes, is combined with an aqueous phase containing the gelling agent.
The gelling agent starts to form a gel structure, and the niosomal vesicles become incorporated within the gel matrix.
Final Formulation:
Once the niosomal gel is formed, it can be transferred to suitable containers for storage and application.

Reverse Phase Evaporation Method:.[23]
The Reverse Phase Evaporation Method is a technique used for the preparation of niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are similar in structure to liposomes but are made from non-ionic surfactants instead of phospholipids. The Reverse Phase Evaporation Method involves creating a water-in-oil (W/O) emulsion followed by the addition of water to form a water-in-oil-in-water (W/O/W) emulsion. This method leads to the encapsulation of water-soluble substances within the niosomal vesicles. The resulting niosomes can then be incorporated into a gel matrix for various applications. Here's a detailed explanation of the Reverse Phase Evaporation Method:
Ingredients and Materials:
Non-ionic surfactant: The main component responsible for forming the niosomal bilayers.
Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.
Organic solvent: Used as a dispersion medium for the surfactant and drug.
Aqueous phase: Contains water and other necessary components for niosome formation.
Gelling agent: Used to create the gel structure within which the niosomes will be dispersed.
Steps:
Preparation of Organic Phase:
The non-ionic surfactant and the drug are dissolved in an organic solvent, such as chloroform or ether.
The drug is dissolved in the organic solvent, creating a drug-surfactant mixture.
Formation of Organic Phase:
The surfactant and drug solution, along with the organic solvent, forms the organic phase.
Emulsification (Water-in-Oil Emulsion):
The organic phase is added to an aqueous phase containing water and other components.
The mixture is subjected to mechanical agitation (e.g., using a homogenizer or mixer) to form a water-in-oil (W/O) emulsion.
The surfactant molecules in the organic phase stabilize the emulsion by forming a layer around the water droplets.
Addition of Water (Water-in-Oil-in-Water

Emulsion):
Additional water is added to the W/O emulsion while continuing the agitation.
The water causes the internal water droplets to expand and rupture the outer lipid layer, resulting in the formation of water-in-oil-in-water (W/O/W) emulsion droplets.
Evaporation of Organic Solvent:
The organic solvent is then evaporated, either under reduced pressure or by allowing it to evaporate at room temperature, leaving behind niosomes encapsulating water and the drug.
Gel Formation:
The niosomal dispersion, containing the self-assembled niosomes, is incorporated into the aqueous phase containing the gelling agent.
The gelling agent starts to form a gel structure, and the niosomal vesicles become incorporated within the gel matrix.
Once the niosomal gel is formed, it can be transferred to suitable containers for storage and application.

Microemulsion Template Method:[24]
The Microemulsion Template Method is a technique used for the preparation of niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are structurally similar to liposomes but are made from non-ionic surfactants rather than phospholipids. The Microemulsion Template Method involves using a preformed microemulsion as a template to create niosomal vesicles. The microemulsion serves as a platform for the self-assembly of surfactant molecules into niosomal structures. These niosomes can then be incorporated into a gel matrix for various applications. Here's a detailed explanation of the Microemulsion Template Method:
Ingredients and Materials:
Non-ionic surfactant: The primary component responsible for forming the niosomal bilayers.
Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.
Oil phase: Contains oil and non-ionic surfactants to form the microemulsion.
Water phase: Contains water and other necessary components to form the microemulsion.
Gelling agent: Used to create the gel structure within which the niosomes will be dispersed.
Steps:
Preparation of Oil Phase:
the non-ionic surfactant is combined with an oil phase (e.g., vegetable oil, mineral oil) to form a mixture.
The oil phase should be selected based on its compatibility with the niosomal formulation and desired properties.
Preparation of Water Phase:
The aqueous phase is prepared by dissolving the drug and any other necessary components in water.
Formation of Microemulsion:
The oil phase and the water phase are mixed together under continuous and vigorous stirring.
The surfactant molecules in the oil and water phases self-assemble at the oil-water interface, forming a stable microemulsion.
Drug Incorporation:
The drug can be dissolved in either the oil phase or the aqueous phase, depending on its solubility.
The drug is incorporated into the microemulsion, becoming part of the template for niosome formation.
Niosome Formation in Microemulsion:
The microemulsion serves as a template for the self-assembly of surfactant molecules into niosomal structures.
In the presence of the microemulsion, the surfactant molecules spontaneously form bilayer structures to create niosomal vesicles.
Gel Formation:
The niosomal dispersion, containing the self-assembled niosomes, is incorporated into an aqueous phase containing the gelling agent.
The gelling agent starts to form a gel structure, and the niosomal vesicles become incorporated within the gel matrix Once the niosomal gel is formed, it can be transferred to suitable containers for storage and application.

Hydration Method:.[25]
the Hydration Method is a simple and straightforward technique used for the preparation of niosomal formulations, which are lipid-based vesicles composed of non-ionic surfactants. Niosomes are structurally similar to liposomes but are made from non-ionic surfactants rather than phospholipids. The Hydration Method involves the direct mixing of the surfactant and the drug with an aqueous phase to form niosomal vesicles. These niosomes can then be incorporated into a gel matrix for various applications. Here's a detailed explanation of the Hydration Method:
Ingredients and Materials:
Non-ionic surfactant: The primary component responsible for forming the niosomal bilayers.
Drug: The active pharmaceutical ingredient that will be encapsulated within the niosomes.
Aqueous phase: Contains water and other necessary components for niosome formation.
Gelling agent: Used to create the gel structure within which the niosomes will be dispersed.
Steps:
Preparation of Aqueous Phase:

An aqueous phase is prepared by dissolving the drug and any other necessary components in water.
Surfactant and Drug Mixing:
The non-ionic surfactant and the drug are directly mixed with the aqueous phase.
The drug can either be dissolved directly in the aqueous phase or added to the surfactant solution.
Formation of Niosomes:
The surfactant molecules in the mixture self-assemble to form niosomal vesicles in the presence of water.
The hydrophilic heads of the surfactant molecules face outward, while the hydrophobic tails face inward, creating bilayer structures that encapsulate water and drug molecules within the vesicles.
Gel Formation:
the niosomal dispersion, containing the self-assembled niosomes, is incorporated into an aqueous phase containing the gelling agent.
The gelling agent starts to form a gel structure, and the niosomal vesicles become incorporated within the gel matrix.
Homogenization (Optional):
Additional homogenization or mixing steps might be applied if needed to ensure uniform distribution of niosomes within the gel.
Once the niosomal gel is formed, it can be transferred to suitable containers for storage and application.
The Hydration Method is particularly useful for small-scale preparations and is relatively quick and simple. However, compared to other methods, it might offer less precise control over vesicle size and distribution. Like any niosomal formulation technique, optimizing factors such as surfactant concentration, drug-to-surfactant ratio, and choice of gelling agent is important to achieve the desired characteristics and performance of the niosomal gel.

Advantages of niosomal gel:.[26,27,28,29]
Niosomal gel formulations offer several advantages due to their unique combination of niosomes (lipid-based vesicles composed of non-ionic surfactants) and gel matrices. These advantages contribute to their potential as advanced drug delivery systems for various applications. Some of the key advantages of niosomal gel formulations include:
Enhanced Drug Delivery:
Niosomes facilitate the encapsulation of both hydrophilic and hydrophobic drugs, allowing for the delivery of a wide range of therapeutic agents. The gel matrix helps to retain the niosomes at the application site, enabling controlled and sustained drug release.
Targeted Delivery:
Niosomal gels can be designed to release drugs in a targeted manner, ensuring that the drug is delivered specifically to the intended site. This can improve drug efficacy while minimizing systemic side effects.
Improved Bioavailability:
Niosomes protect drugs from degradation and enhance their stability, leading to improved bioavailability. The lipid bilayer structure of niosomes is similar to cell membranes, potentially aiding in drug absorption.
Controlled Release:
The combination of niosomes and gel matrices provides a controlled release profile for the encapsulated drugs. This is particularly useful for drugs requiring sustained release over an extended period.
Enhanced Stability:
Niosomal gels protect drugs from environmental factors, such as light and oxygen, that can lead to degradation. This is especially beneficial for drugs that are sensitive to degradation.
Reduced Frequency of Administration:
The controlled release and prolonged drug retention provided by niosomal gels may allow for less frequent administration, improving patient compliance and convenience.
Minimized Irritation:
The gel matrix can help reduce irritation or discomfort that may arise from the application of niosomes alone, especially on sensitive skin or mucosal surfaces.
Versatility:
Niosomal gels can accommodate a wide range of drugs, including poorly water-soluble compounds, peptides, and proteins. They can be adapted for topical, transdermal, oral, or mucosal administration.
Enhanced Penetration:
Niosomes can enhance the penetration of drugs through biological barriers, such as the skin or mucous membranes, improving their therapeutic effects.
Tailored Release Profiles:
By manipulating the composition of the niosomal gel, including the type of surfactant and gelling agent, it's possible to design formulations with specific release profiles, such as immediate release, sustained release, or triggered release.
Flexibility in Formulation Design:
The choice of non-ionic surfactants, lipid composition, and gel-forming agents offers flexibility in designing niosomal gels with desired properties.
Conclusion:
Niosomal gels represent a promising and versatile approach in the field of drug delivery. By

combining the benefits of niosomes and gel matrices, these formulations offer enhanced drug delivery, controlled release, improved stability, and the potential for targeted administration. Their applicability to various routes of administration and a wide range of drug types makes niosomal gels a valuable tool for improving therapeutic outcomes and patient experiences in the realm of pharmaceuticals and medical treatments

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