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An Overview on the Advancement of Proniosomal Drug Delivery System over Conventional Drug Delivery

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ABSTRACT
Compared to traditional dosage forms, drug delivery systems that use colloidal particle carriers, such as liposomes and niosomes, have definite advantages. Niosomes are technically more promising than liposomes as drug carriers because of their higher chemical stability and lack of several drawbacks, like high cost and issues with phospholipid purity. Scientists sought to stabilize the marital properties of the niosome drug delivery system without affecting it, which resulted in the establishment of the prospective drug carrier Proniosomes.This review summarizes the advantages of proniosomal drug delivery over the conventional drug delivery system like liposomes and niosomes Proniosomes are a dry formulation of drug carriers that, upon hydration, transform into niosome dispersion. An improved dosage of the medication with better solubility and stability can be administered via dry proniosomal powder. They have a bilayer shape similar to liposomes but have chemical variations in monomer units that make Proniosomes stable. By addressing the instability difficulties with niosomes and liposomes, they have the potential to improve the solubility, accessibility, and uptake of numerous drugs. Furthermore, they provide a versatile mechanism of drug delivery for a wide range of hydrophilic and hydrophobic medications. They can transport pharmaceuticals to the target site of action via a variety of ways, allowing for regulated drug release and a reduction in potentially hazardous side effects. "Proniosome derived" niosome preparation is one of the advances in nanotechnology. Proniosome, a potential drug carrier, has been developed as a result of strategies to stabilize the niosomal drug delivery system without altering its beneficial features.The focus of this review is to bring out different advantages of proniosomes over other conventional nanoparticles such as liposomes and niosomes.

KEYWORDS:proniosome, Niosome, Liposomes, Nanotechnology

I. INTRODUCTION

In recent times, attempts have been made through novel approaches to achieve controlled or targeted drug delivery using various routes of administration. In recent times, attempts have been made through novel approaches to achieve either controlled or targeted delivery, but no single drug delivery system fulfil all the criteria.[1] Novel vesicular drug delivery systems have been developed to deliver drugs at a rate directed by the body's needs during the treatment period and to direct the active substance to the site of action. These vesicles were first reported to have a biologic origin in 1965 by Bingham and have since been given the name "Bingham bodies".[2] Conventional pharmaceutical dosage forms have limitations in controlling drug delivery for a longer period of time in the body. This results in large peaks and valleys in the drug plasma profiles, which can cause problems with dosing intervals. Additionally, patients often struggle with compliance when having to follow multiple dosing regimens and potent drugs can cause adverse effects. These concerns can be addressed by designing controlled and targeted drug delivery systems that can improve treatment efficiency and lower the incidence of adverse effects. However, there are currently very few drug delivery systems that can meet the pharmaceutical and clinical goals.[3]

Proniosomes

Proniosomes are a promising form of drug delivery. They are a dry formulation that, upon hydration, converts into a niosome dispersion. This dry powder can deliver a unit dose of the drug while enhancing its stability and solubility.[4] Proniosomes are vesicular systems in which the vesicles are made up of non-ionic based surfactants, cholesterol, and other additives. Semisolid liquid crystal gel (proniosomes) ready by dissolving the surfactant in a minimal quantity of

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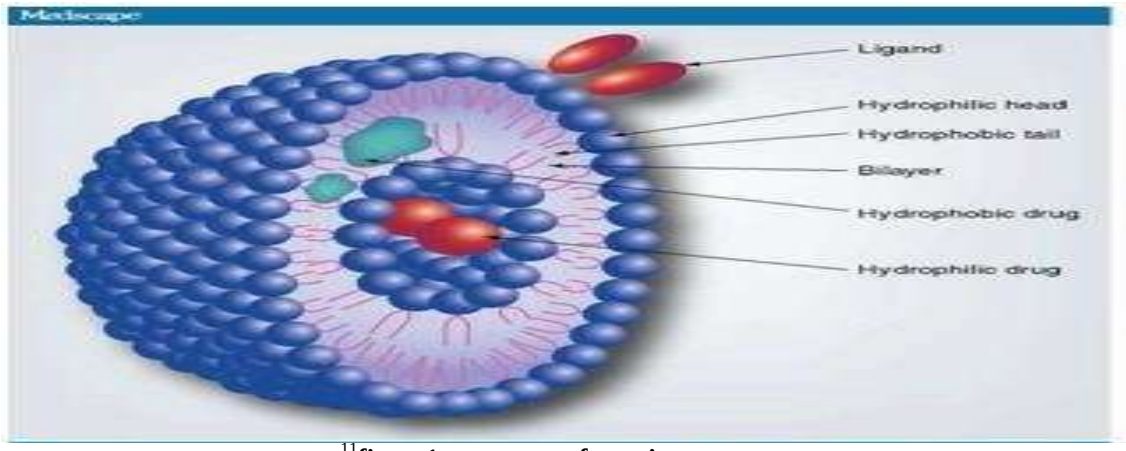
an acceptable solvent, namely ethanol, and then hydration with the slightest amount of water to form a gel.[5] Proniosomes are a recent development in novel drug delivery systems. They are the most advanced drug carriers in the vesicular system, which overcomes the demerits of liposomes and niosomes.[6] Proniosomes, also known as 'dry niosomes', are vesicular structures that are used to encapsulate drugs. These structures maintain the systemic circulation of the drugs, provide controlled release, enhance penetration in targeted areas, and reduce any toxic effects. The surfactant molecules direct themselves in such a way that the hydrophilic ends of the non-ionic surfactant orient outward, while the hydrophobic ends are oriented inward to form a bilayer. Proniosomes are also made up of these bilayer liposomes, where the bilayer is composed of non-ionic surface-active agents.[7]this review is mainly focused on the various advantages of proniosomes over conventional method of drug delivery.

STRUCTURE

Niosomes are spherical and consist of microscopic lamellar (unilamellar or multilamellar) structures (Figure 1). The bilayer is formed by non-ionic surfactants, with or without cholesterol and a charge inducer[8] A typical niosome vesicle would consist of a vesicle forming amphiphile i.e. 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, which also helps in stabilizing the membrane. [9] Hydrophilic heads are attracted to aqueous solutions, while hydrophobic heads are attracted to organic solutions. Bilayer vesicles are available in two types, uniflagellar and multilamellar vesicles. Multilamellar vesicles consist of concentric circles formed by at least 2 bilayer vesicles or a large vesicle containing one or more small vesicles. Therefore, multilamellar vesicles are generally larger than unilamellar vesicles. For unilamellar sorbitan monostearate (C18-sorbitan monoester)-cholesterol niosomes, X-ray scattering data revealed a bilayer spacing of 15 nm and a thickness of 3.3–3.4 nm. Niosomes are typically in the sub-micron (colloidal) size range. The particle sizes of small unilamellar vesicles range from 10–100 nm, large unilamellar vesicles range from 100–3000 nm, and multi-lamellar vesicles are greater than 5 μm, while a few "giant" (> 15 um) vesicles have also been reported.[10]



[11]**figure1: structure of proniosome**

Composition of proniosomes

Non-ionic surfactants: such as the Tween series (Tween 20, Tween 80, etc.) and Span series (Span 60, Span 80, etc.), are the primary components of proniosomes. These surfactants have a hydrophilic head and lipophilic tail and are capable of self-assembling into a bilayer structure under aqueous conditions. The concentration of non-ionic surfactant may vary depending on the application and type of surfactant used for proniosomes.[12]

Membrane stabilizer: When cholesterol is added to the bilayer composition of proniosome, it stabilizes the membrane and reduces membrane leakiness. This leads to an increase in the entrapment efficiency of the proniosome. Additionally, the incorporation of cholesterol reduces the permeability of the vesicle bilayer to 5,6-carboxyfluorescein (CF) by 10 times.[13] Cholesterol and lecithin are primarily used to stabilize cell membranes. Steroids, which are important components of cell membranes,

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significantly affect the stability, fluidity, and permeability of the bilayer. Cholesterol, a naturally occurring steroid, is added to the membrane to prevent aggregation by including molecules that stabilize the system against the formation of aggregates through repulsive steric or electrostatic effects.[14]

Carrier: The use of the carrier in proniosomes preparation allows for flexibility in the ratio of surfactant and other components, resulting in increased surface area and more efficient loading.. The carriers should be safe, non-toxic, free-flowing, have poor solubility in the loaded mixture solution and good water solubility for ease of hydration. Commonly used carriers include sorbitol, mannitol, glucose, lactose, and sucrose stearate.

Solvent. The choice of alcohol used in Proniosomes greatly affects the size of the vesicles and the rate of drug permeation [1]. Different alcohols result in vesicles of different sizes, with the order being Ethanol > Propanol > Butanol > Isopropanol. The largest vesicles are formed with ethanol, likely due to its greater solubility in water, while the smallest vesicles are formed with isopropanol, possibly due to the presence of branched chains.[15]

ADVANTAGES OF PRONIOSOMES OVER CONVENTIONAL DRUG DELIVERY SYSTEMS

a) Bioavailability refers to the amount of a drug that is available at the site of action in the body. Proniosomes have advantages over traditional formulations because the vesicles can act as drug reservoirs and protect the drug from acidic and enzymatic degradation in the gastrointestinal tract. This leads to an enhancement in bioavailability.[16] Extensive research has been conducted on drug delivery systems, which play a crucial role in enhancing the bioavailability of poorly water-soluble drugs. Among these systems, proniosomes have garnered significant attention due to their similar structure to liposomes but with higher stability and lower cost.[17] "Drug delivery with improved bioavailability and reduced adverse effects."[18]

b) proniosomes are currently being extensively researched as a substitute for liposomes, which have certain drawbacks. Liposomes can be expensive, and their ingredients, such as phospholipids, are chemically unstable due to their propensity for oxidative degradation. They require specific storage and handling, and the purity of natural phospholipids is inconsistent.[19] proniosomes have certain advantages over liposomes in terms of stability and circulation half-life. Liposomes, due to the presence of phospholipids, are phagocytosed more quickly than niosomes that contain surfactants. Additionally, the phospholipids used in liposome manufacturing are expensive and tend to degrade easily.[20]

c) proniosomes are similar to liposomes in their behaviour in living organisms. They increase the circulation time of the drug trapped within them and modify the drug's distribution in the body as well as its metabolic stability. Studies have shown that encapsulating different anticancer drugs in niosomes helps to reduce the drug's toxic side effects while maintaining or even increasing its effectiveness against tumors.[19]. Niosomes can be administered via oral, parenteral, or topical routes, and they improve the therapeutic performance of drugs by altering circulatory clearance and targeting specific cells.[21]

d) The properties of niosomes are determined by both the composition of the bilayer and the method of their production, similar to liposomes. Baillie et al10 observed that the intercalation of cholesterol in the bilayers reduces the entrapment volume during formulation, leading to reduced entrapment efficiency. This effect becomes more pronounced as the concentration of cholesterol increases.[19]

e) Niosomes are a type of drug carrier that have been extensively studied in recent years. They have several advantages, including biodegradability, biocompatibility, and no immunogenicity. Additionally, they have a long shelf life, exhibit high stability, and allow for the controlled and/or sustained delivery of drugs to a target site. Niosomes can be formed using various types of non-ionic surfactants and can entrap a large number of drugs with a wide range of solubility.[22]

f) This medication delivery system was designed to distribute drugs in a controlled manner through the skin into the bloodstream, while

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maintaining consistent efficacy and reducing the dosage and associated side effects. Although oral administration is the most popular route and provides faster relief, it is more likely to cause hepatic first-pass metabolism, which requires a higher dose of medication. The main challenge in including surfactants in lipid-based formulations is that they can cause additional gastrointestinal irritation. It is also important to note that when medication is administered throughout the body simultaneously, it may lead to unavoidable adverse effects.[23]

[23]**figure 2: benefits of proniosomes at various body organs**

MECHANISM OF ACTION:

The precise method by which a drug penetrates vesicles and enters the skin has not been fully explored yet. The extent of penetration depends on various factors such as the type and properties of the drug used, the formation of vesicles, and the temperature at which the proniosomes are converted to Niosomes. The lipids used in the preparation of proniosomes act as a carrier that forms a depot at the site of action, thereby prolonging the drug's effect.[24] It is clear that proniosomes need to be hydrated to form niosomal vesicles before the drug can be released and permeate across the skin. Numerous scientists have proposed various theories and mechanisms. Vesicle skin interaction.[25] There are various ways to enhance the absorption of hydrophobic drugs through the skin. These include:

1. Disrupting the lipid bilayer of the stratum corneum - by modifying the lipid bilayer of the SC, the extracellular spaces can be filled up and the permeation rate can be increased.
2. Using nano-sizing to enhance transdermal permeation.
3. Changing the drug's partition into skin layers.
4. Hydrating the skin and dilating the SC intercellular channels - niosomes can alter the barrier properties of the stratum corneum, leading to hydration and loosening of the tightly packed structure. This allows lysozyme to lyse the membrane and release the entrapped drug into the system.
5. Changing the permeation pathway of lipophilic permeants to follicular delivery.

Non-ionic surfactants are an important part of this process as they act as penetration enhancers, entering the intercellular lipids through endocytosis.[26]

That's an interesting point. Non-ionic surfactants play a crucial role in improving the permeation of proniosomes compared to conventional drug delivery systems. Their presence enhances the stability and solubility of the proniosomes, making them a more efficient drug delivery option.

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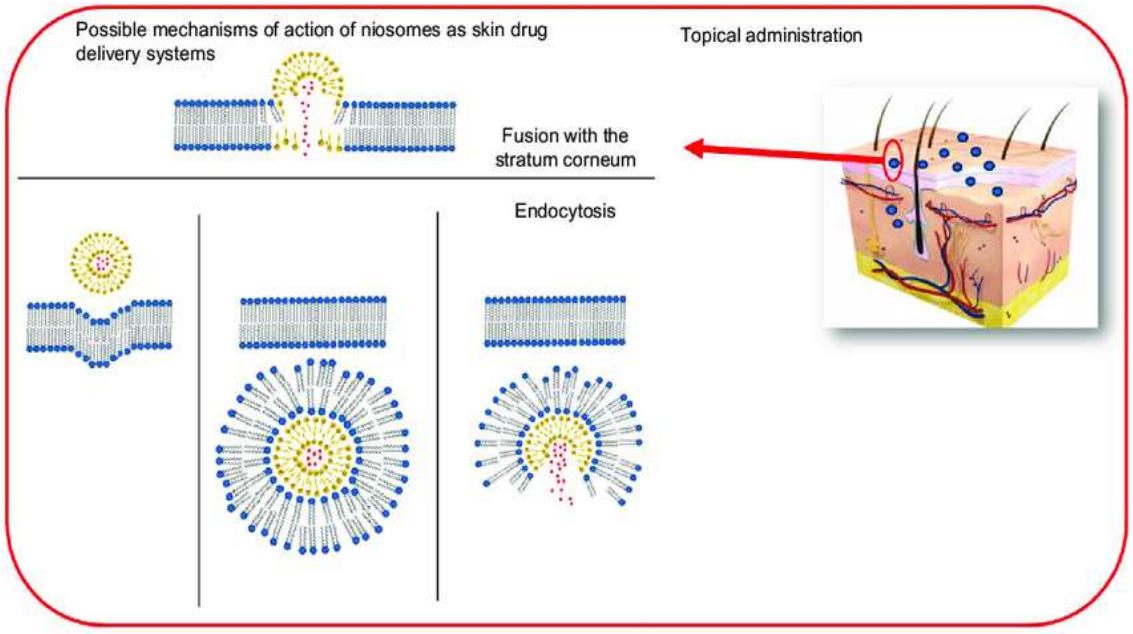

[27]**figure3: mechanism of penetration of proniosomes into the skin**

VARIOUS METHOD OF PREPARATION FOR PRONIOSOMES

a) Spray coating method

Proniosomes were produced by slurry method using maltodextrin as a carrier. The time required to produce proniosomes by this is independent of the ratio of surfactant solution to carrier material. In slurry method, the entire volume of surfactant solution is added to maltodextrin powder in a rotary evaporator and vacuum is applied until the powder appears to be dry and free flowing.27Drug containing proniosomes-derived niosomes can be prepared in manner analogous to that used for the conventional niosomes, by adding drug to the surfactant mixture prior to spraying the solution onto the carrier (sorbitol, maltodextrin) or by addition of drug to the aqueous solution used to dissolve hydrate the proniosomes.[28]

b) Slurry method

Proniosomes are a type of carrier system used to protect active ingredients and surfactants from hydrolysis. They can be prepared by adding a carrier and a surfactant solvent into a round-bottomed flask, which is then attached to a rotary flash evaporator. A vacuum is applied to form a dry and free-flowing powder. The obtained formulation should be stored in a tightly closed container. The time required for proniosomes production is not dependent on the ratio of the surfactant solution and appears to be stable. This method has the advantage of producing a uniform coating on the carrier, which helps protect the active ingredients and surfactants.[29]

c) Coacervation phase separation method

For the preparation of most proniosomal gels, a precise number of drugs, surfactants, and cholesterol is placed in a clean, wide-mouthed glass vial. Then, the solvent is added and warmed in a water bath at 60-70°C until the surfactant and cholesterol is fully dissolved. To prevent the evaporation of the solvent, the open end of the vial should be covered with a lid. Followed by the addition of an aqueous phase in the vial, the mixture was warmed in the water bath to get a dispersion. [4]

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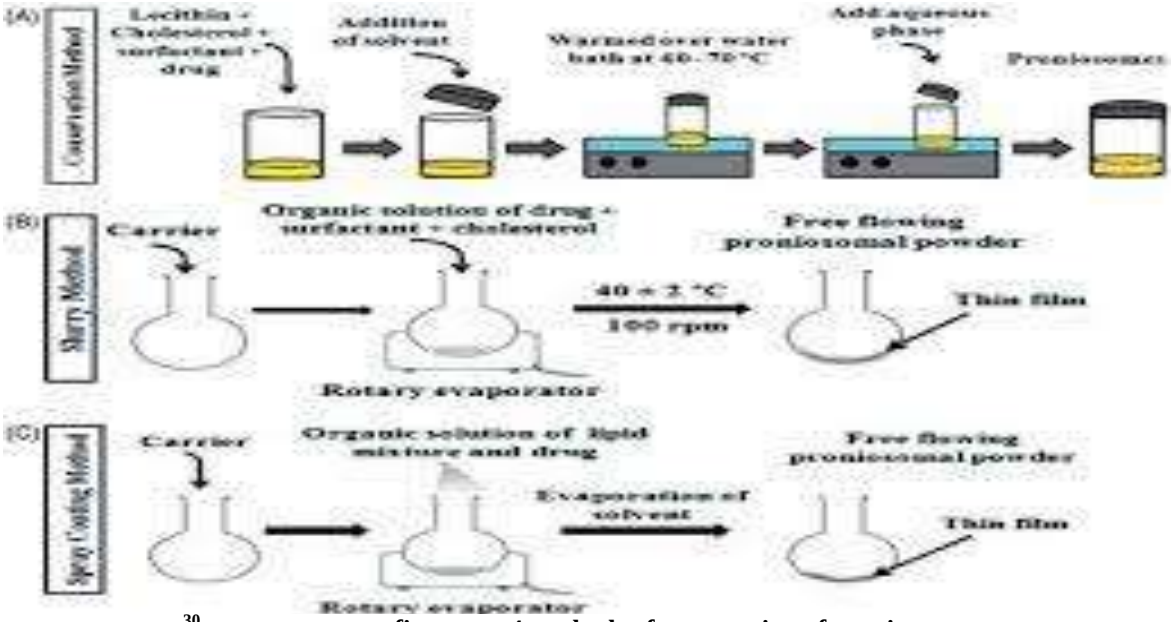

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figure no. 4 methods of preparation of proniosomes

II. CONCLUSION

This review concluded that proniosomal drug delivery have lots of advantages like having low particle size, and improved dosage of the medication with better solubility and stability can be administered via dry proniosomal powder. They have a bilayer shape similar to liposomes but have chemical variations in monomer units that make Proniosomes stable. and it also included what is proniosome and method of preparation of proniosome, structure,and mechanism of action of proniosomes which shows that proniosomes are easy to prepare and easy to penetrate into the skin.

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