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Niosomes: The Next Wave in Smart Drug Delivery

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Abstract: *Because of their capacity to improve drug stability, bioavailability, and targeted delivery, niosomes—novel, non-ionic surfactant-based vesicular systems—have drawn a lot of attention in contemporary pharmaceutical research. This review outlines the basic characteristics of niosomes, including their composition, structure, and different preparation techniques like thin- film hydration, ether injection, and reverse-phase evaporation. Various niosome types and delivery strategies are discussed to highlight their adaptability in encapsulating both hydrophilic and lipophilic drugs. Their therapeutic potential in fields like cancer, infectious illnesses, immunotherapy, and transdermal drug delivery is demonstrated by the variety of applications, which range from regulated and sustained release to site- specific delivery. Niosomes continue to be a viable and affordable platform for upcoming medicinal discoveries despite some formulation difficulties. The goal of this review is to present a thorough grasp of their development, design, and therapeutic value.*

Keywords: Niosomes, Drug Delivery System, Non-ionic surfactant vesicles, Encapsulation efficiency, Targeted delivery

I. INTRODUCTION

A renewed interest in niosomes has resulted from recent developments in the realm of medicinal nanotechnology. Niosomes have been the subject of a sizable body of published material. These investigations have demonstrated the significance of niosomes in the pharmaceutical sciences. Bangham et al. (1965) first described niosomes as the phospholipid liquid crystalline.[1] In order to achieve a therapeutic impact in humans or animals at a diseased region while simultaneously lowering the concentration of the treatment in surrounding tissues, pharmaceutical substances are administered at a predetermined rate. This technique is referred to as a drug-delivery system. Drug effectiveness is increased and systemic harmful effects on tissues are decreased by localized drug activity. By improving drug selectivity and the therapeutic index while reducing the effective dose, certain drug- delivery methods reduce the urgency of introducing new medications to the market. The function of niosomes as a drug delivery mechanism is covered in this narrative review, along with specifics about their composition, preparation, characteristics, and uses. together to create a closed bilayer structure that contains solutes in an aqueous solution.[2] The potential of niosomes to act as a carrier for the transport of medications, antigens, hormones, and other bioactive molecules has been thoroughly investigated in recent years. In addition, niosomes have been employed to address the issues of drug instability, insolubility, and fast degradation niosomes are more capable of penetrating than earlier emulsion formulations. Niosomes enhance the effectiveness of treatment of medicinal molecules that are enclosed by shielding the medication from hostile biological settings, leading to their postponed clearance.Because of their ability to transport medications, genetic material, vaccinations, and nutraceuticals, niosomes have been thoroughly studied in the pharmaceutical industry. This is because of their flexibility in changing surface properties, which allows for targeted distribution, regulated discharge, and increased therapeutic efficacy[3]. They are useful in many different sectors, including dermatology, cancer treatment, vaccination administration, and other related professions[29] The purpose of this work is to examine published studies about niosome structure, preparation techniques, and pharmaceutical technology applications. For kinds of peer-reviewed journal articles from different sources, such as the Web of Science, Scopus, and PubMed, among many others[30]

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What Is Niosomes?

A unique medicine delivery method called niosomes involves encasing the medication in a vesicle Niosomes get their name from the fact that the vesicle is made up of a bilayer of non- ionic surface active substances. The niosomes are minuscule in size. The nanometric scale describes their size. Despite having a similar structure to liposomes, they have a number of advantages. Increased research on these structures may lead to new medication delivery techniques since niosomes have recently been demonstrated to significantly improve transdermal drug delivery and can be employed in targeted drug delivery. Cholesterol is mostly incorporated as an excipient to produce niosomes. It is also possible to employ other excipients. Compared to earlier emulsion formulations, niosomes have a greater penetration capacity. Although they have a bilayer and are structurally similar to liposomes, niosomes have many more benefits than liposomes because of the materials employed in their manufacture.[4]Alkyl ethers, alkyl glyceryl ethers, sorbitan fatty acid esters, and polyoxyethylene fatty acid esters are a few types of surfactants. Niosomes become less leaky when cholesterol is added because it keeps the bilayer stiff. Charge inducers, on the other hand, give the vesicles a charge and enlarge them, improving the effectiveness of drug entrapment.[3]

STRUCTURE OF NIOSOMES:

Microscopic lamelar (unilamellar or multilamellar) structures make up the spherical niosomes. Nonionic surfactants, either with or without cholesterol and a charge inducer, create the bilayer. Niosomes are created using a variety of surfactants in different combinations and molar ratios[2] Niosomes become less leaky when cholesterol is added because it keeps the bilayer stiff. Charge inducers, on the other hand, give the vesicles a charge and enlarge them, improving the effectiveness of drug entrapment. Stearylamine and cetyl pyridinium chloride are examples of positive charge inducers, while dicetyl phosphate, dihexadecyl phosphate, and lipoamino acid are examples of negative charge inducers that aid in vesicle stabilization[3] The hydrophilic end of nonionic surfactants in niosomes typically faces outward (toward the aqueous phase), whereas the hydrophobic end faces inside The structure of a niosome encloses solutes in an aqueous solution by forming a closed bilayer structure[2] Energy, such as heat or physical agitation, is needed to create the closed bilayer structure. It was discovered that a number of internal forces, including as van der Waals and repulsive forces between surfactant molecules, were crucial in preserving the vesicular structure. The characteristics of the resulting niosomes will probably change if the vesicle's components (such as type, composition, and concentration), size, surface charge, or volume are altered[5]

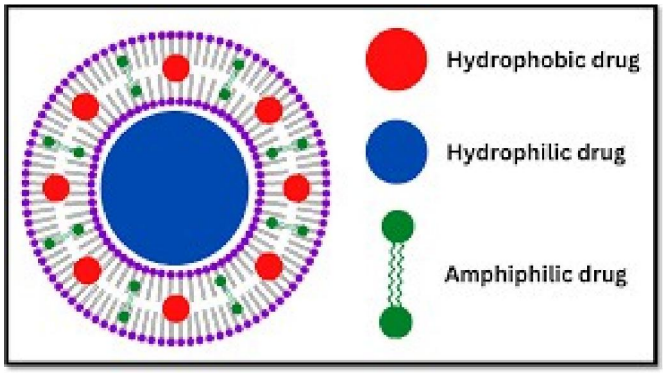

Fig1: Structure Of Niosomes

STUCTURE AND COMPOSITION OF NIOSOME:

The choice of surfactant for niosome preparation is primarily determined by the surfactant's HLB value. Surfactants' capacity to form vesicles is entirely dependent on their hydrophilic- lipophilic balance. The HLB value of the surfactant must be between 4 and 8 in order for niosome vesicles to develop properly and compatibly[6] The niosome is a nonionic surfactant with a circular bilayer structure that needs to be able to produce micelles. Micelles are formed when

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surfactant concentrations exceed the critical micelle concentration (CMC)[3] however non-ionic surfactants can generate circular bilayer structures in place of micelles. Depending on how the niosome is prepared, it may have a unilamellar or multilamellar structure. Drugs of all kinds, including hydrophilic, lipophilic, and amphiphilic ones, can be incorporated into the structure of niosomes[5]

• The niosome is mostly composed of the following elements:

1.Non-ionic surfactant:

Niosomes are surfactant bilayer structures with polar heads facing the aqueous phase and non-polar tails facing one another. Niosome formulation uses a variety of non-ionic surfactants. Some of the non-ionic surfactants listed below were employed in the L'Oréal cosmetic preparation to manufacture niosomes.

Alkyl Ether

Some of the non-ionic surfactants listed below were employed in the L'Oréal cosmetic preparation for niosome.

1.) Surfactant-I: The molecular weight of this surfactant is approximately 473 Daltons. Surfactant-I is a monoalkyl glycerol unit with 16 carbons.

2) Surfactant-II: This compound has a molecular weight of 972 This diglycerol

3) Surfactant-III is an ester-linked surfactant with a molecular weight of 393.

Alkyl Ester

Sorbitan esters are surfactants that fall under the alkyl ester surfactant family. Niosome preparation is the main application for the Sorbitan surfactant. Oxyethylene poly Although sorbitan monolaurate is a surfactant that forms niosomal vesicles, these vesicles are less soluble than other types of surfactant vesicles. Diclofenac sodium was encapsulated in a niosomal vesicle using polysorbate-60 (polyoxyethylene). Glyceryl laurate: polyoxyethylene- 10-stearyl ether: cholesterol (27:15:57) This combination is used to create niosomes, which are utilized to distribute cyclosporin-A transdermally. This surfactant is used to create methotrexate niosomes.[3]

2 .Cholestrol:

Cell membranes include cholesterol, a steroid that is crucial for permeability, fluidity, and stiffness. One steroid that is crucial to the niosome production process is cholesterol. A very little amount of cholesterol is added to niosomes because a substantial amount of cholesterol interferes with the permeability or penetration of niosomal vesicles. It improves permeability, stiffness, and encapsulation effectiveness. It also demonstrates the toxicity and ease of rehydration of free dried niosomes[7]

3. Charge molecule:

To prevent niosome aggregation, a charge molecule is introduced to the niosomal formulation. Particle repulsion occurs and aggregation does not occur if the same charge is present in the formulation. Ionic surfactants with both positive and negative charges were added to the niosomal mixture. Diacetyl phosphate, phosphatidic acid, lipoamino acid, and dihexadecyl phosphate are compounds with a negative charge[8].

TYPES OF NIOSOME:

Niosomes are categorized according to the size (LUV, SUV), the number of bilayers present (MLV, SUV), or the preparation technique (REV, DRV). The niosome types mentioned above are as follows:

1. Small Uni-lamellar vesicle (SUV)
2. Multi-lamellar Vesicle (MUV)
3. Large Uni-lamellar Vesicle (LUV)

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1. Small Uni-lamellar vesicle (SUV)

French press extrusion electrostatic stabilization and the sonication method are used to create little unilamellar vesicles from large unilamellar vesicles (LUV). tiny unilamellar vesicle with a size range of roughly 25–50 nm or 0.025–0.05 µm[9]

2. Multi-lamellar Vesicle (MUV):

The method utilized to prepare the niosome determines the creation of SUV, MLV, and LUV. MLV has many bilayers encircling the aqueous lipid compartment independently. MLVs typically have a diameter of 0.5–10 µm[3] MLV niosomes are mostly utilized for medication inclusion. The MLV is more stable over an extended length of time and is very easy to prepare. This vesicle is more suited for medicinal compounds that are lipidic. The thin film hydration process is primarily used to prepare this sort of niosome[4]

3. Large Uni-lamellar Vesicle (LUV).

The LUV is a unilamellar vesicle with a single bilayer membrane and a huge diameter. This vesicle is larger due to its higher aqueous and lipidic content[10] These vesicles are typically made using the reverse phase evaporation and ether injection methods. High encapsulation of water-soluble drugs, consistent drug release rates, and lipid economy are some of the advantages LUV have over MLV Compared to other varieties, this vesicle contains a higher amount of drug entrapment. Large unilamellar vesicles are typically 100 nm in size. 3 These vesicles are typically made using the reverse phase evaporation method and the ether injection method[2]

ADVANTAGES OF NIOSOMES[3]

• To control the drug delivery rate and provide a normal vesicle in external non-aqueous media, niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase.
• The suspension system of the vehicle is water-based. When compared to oily dose forms, this enables higher patient compliance.
• Niosomes can hold medicinal molecules with a variety of solubilities because they have an architecture made up of hydrophilic, amphiphilic, and lipophilic moieties.
• They enhance the stability of the medicine that is trapped and are osmotically active and stable.
• They increase the epidermal penetration of medications and the oral bioavailability of poorly absorbed medications.
• Because the surfactants are non-immunogenic, biocompatible, and biodegradable, is safe to utilize while making niosomes.

DISADVANTAGES OF NIOSOMES[11]

• Instability in the body
• Combination
• encapsulated medication hydrolysis, which reduces the dispersion's shelf life.
• More expensive than traditional formulas
• Greater amounts of surfactants
• Challenges in large-scale manufacturing

Literature Review:

1. Mawazi S.M., Ge Y., Widodo R., (2025):

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2. Yeo P. L., Lim C.L., Chye S. M., Ling A. K., Koh R.Y., (2017):
In order to achieve a therapeutic impact in humans or animals at a diseased region while simultaneously lowering the concentration of the treatment in surrounding tissues, pharmaceutical substances are administered at a predetermined rate. This technique is referred to as a drug-delivery system. Drug effectiveness is increased and systemic harmful effects on tissues are decreased by localized drug activity. By improving drug selectivity and the therapeutic index while reducing the effective dose, certain drug-delivery methods reduce the urgency of introducing new medications to the market. The function of niosomes as a drug delivery mechanism is covered in this narrative review, along with specifics about their composition, preparation, characteristics, and uses. together to create a closed bilayer structure that contains solutes in an aqueous solution
3. Umbarkar M.G., (2021):
The potential of niosomes to act as a carrier for the transport of medications, antigens, hormones, and other bioactive molecules has been thoroughly investigated in recent years. In addition, niosomes have been employed to address the issues of drug instability, insolubility, and fast degradation niosomes are more capable of penetrating than earlier emulsion formulations. Niosomes enhance the effectiveness of treatment of medicinal molecules that are enclosed by shielding the medication from hostile biological settings, leading to their postponed clearance.Because of their ability to transport medications, genetic material, vaccinations, and nutraceuticals, niosomes have been thoroughly studied in the pharmaceutical industry. This is because of their flexibility in changing surface properties, which allows for targeted distribution, regulated discharge, and increased therapeutic efficacy.
4. Mujariya R.Z, Muzumdar A., (2019):
The nanometric scale describes their size. Despite having a similar structure to liposomes, they have a number of advantages. Increased research on these structures may lead to new medication delivery techniques since niosomes have recently been demonstrated to significantly improve transdermal drug delivery and can be employed in targeted drug delivery. Cholesterol is mostly incorporated as an excipient to produce niosomes. It is also possible to employ other excipients. Compared to earlier emulsion formulations, niosomes have a greater penetration capacity. Although they have a bilayer and are structurally similar to liposomes, niosomes have many more benefits than liposomes because of the materials employed in their manufacture.
5. Shakya V, Bansal B. K., (2014):
Energy, such as heat or physical agitation, is needed to create the closed bilayer structure. It was discovered that a number of internal forces, including as van der Waals and repulsive forces between surfactant molecules, were crucial in preserving the vesicular structure. The characteristics of the resulting niosomes will probably change if the vesicle's components (such as type, composition, and concentration), size, surface charge, or volume are altered.

METHOD OF PREPARATION :

In order to prepare niosomes, a lipid and surfactant mixture is first hydrated at high temperatures. This is followed by optional niosome size reduction to create a colloidal suspension[12] The breakdown of surfactant in diethyl ether is the initial step in the synthesis of niosomes via ether injection. A 14-gauge needle is then used to inject the solution into a drug aqueous solution that is kept at 60°C. The vaporization of ether then results in the formation of single layer vesicles with sizes ranging from 50 to 1000 nm[2] The hand-shaking method, also called the thin-film hydration technique, involves dissolving cholesterol and surfactant in a volatile organic solvent before transferring the mixture to a rotary evaporator. A thin layer of the solid mixture is deposited on the flask wall following evaporation. The medicine of interest is then added to an aqueous phase to hydrate the dried layer. This procedure can be done with mild stirring at room temperature. Another method for creating niosomes is to sonicate a mixture of surfactant, cholesterol, and aqueous phase containing the medication for three minutes at 60°C. This process typically yields vesicles that are uniformly tiny in size[13] Since then, many techniques for niosome preparation have been developed. Using the multiple membrane extrusion approach, a thin film is created by evaporating a mixture of surfactant, cholesterol, and dicetyl phosphate in chloro form. After hydrating the film with an aqueous drug solution, the resulting suspension is

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extruded through polycarbonate membranes that are arranged in series for a maximum of eight passes.In addition to ether and chloroform, the reverse-phase evaporation method uses a mixture of surfactant and cholesterol in a 1:1 ratio. The mixture is sonicated at 4–5°C after an aqueous phase containing the target medication is introduced. A tiny amount of phosphate- buffered saline is added to the mixture, and sonication is then continued. Phosphate-buffered saline is used to dilute the residual suspension after the organic solvent is extracted at 40°C under low pressure. The mixture is heated to 60°C for 10 minutes to produce the final niosome product[14]

1. Thin film hydration method:

Thin-film hydration, sometimes referred to as the hand shaking method or a lipid thin-film hydration method, is one of the traditional techniques for creating niosomes. Lipids and surfactants are typically dissolved in an appropriate organic solvent in varying ratios. After the solvent had evaporated, a thin film was produced using a rotary evaporator operating at lower pressure[15] An aqueous solution should thereafter be used to disperse the resulting film. The lipids swell and peel off the circular-bottomed flask wall after being hydrated for a while at a temperature marginally over the phase transition temperature of the surfactants used, with sporadic light shaking (hydration time[17] The type and solubility of the medicine determine the addition of the active ingredient. The medicine should be added to the mixture of lipids and surfactants if it is hydrophobic.

The medication is combined with a hydration combination when it is hydrophilic. Large unilamellar vesicles (LUVs) are created by non-shaking, whereas multilamellar vesicles (MLVs) are created by hand shaking[16] Both hydrophilic and lipophilic medications can be encapsulated using this method. Lipophilic medicines incorporate into the lipid bilayer, whereas hydrophilic medications are better contained in the aqueous phase. It creates multilamellar vesicles with a high encapsulation efficiency, although the distribution is uneven and the particle sizes are bigger[17]

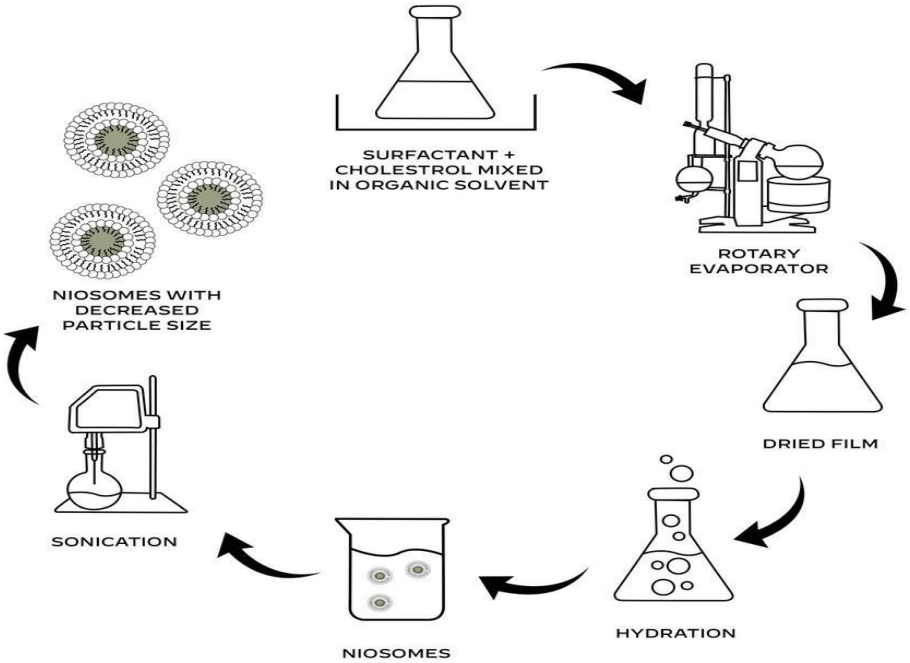

Fig 2:Thin Film Hydration Method For The Preparation Of Niosomes.

2. Reverse Phase Evaporation:

Reverse-phase evaporation was used in two different ways to create niosomes; Papahadjopoulos and Miller carried out the method's first experimental implementation in 1967[18] Surfactants and cholesterol are combined in different molar ratios and dissolved in enough organic solvent in a round-bottomed flask to create the organic phase. The water-soluble

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components are dissolved to create the aqueous phase, which is then combined with the organic phase to create the emulsion in a different round-bottomed flask. The niosomes are then created by employing a rotary evaporator to evaporate the organic solvent at 60 °C under low pressure after it has been violently agitated or sonicated[30] Guinedi et al. (2005) detailed the second technique (Figure 4) for niosome preparation via reverse phase inversion. In a round-bottomed flask, surfactant and cholesterol are mixed in various molar ratios and dissolved in an adequate volume of an organic solvent mixture, such as methanol and chloroform. After that, a rotary evaporator is used to evaporate the organic solvent. A thin, dry layer of the particles develops on the rotary evaporator's inner wall. A mixture comprising a specific amount of the active ingredient (the medicine) is added to the generated film after it has been redissolved in an appropriate volume of ether. The mixture is then dissolved in an appropriate organic solvent, such as acetone combined with phosphate- buffered saline (pH 7.4). The combination is sonicated for a few minutes in a bath sonicator, then manually spun before being sonicated again for a few more minutes. The resultant dispersion is rapidly broken up by rotational evaporation. After adding 10 mL of phosphate- buffered Pharmaceutics 2025, 17, x FOR PEER REVIEW saline (pH 7.4), the rotary evaporation process is continued for a further 15 minutes to ensure that any leftover diethyl ether is eliminated[3]

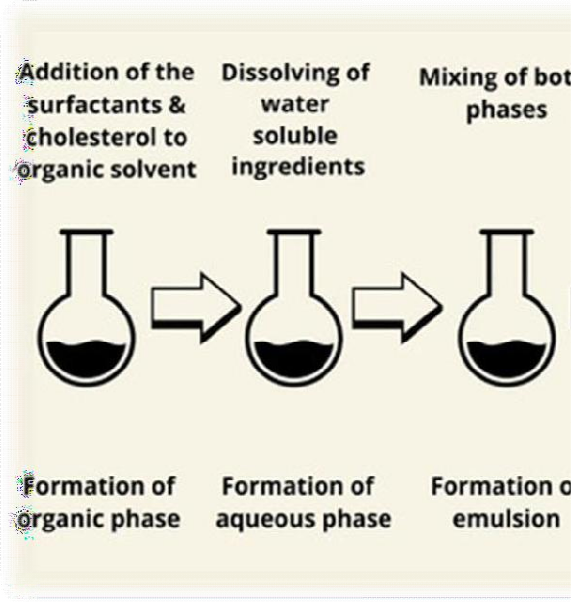

Fig 3:First Method Of Reverse Phase Evaporation.

3. Microfluidics Method:

The microfluidics approach was initially proposed in 1947, and microfluidic channels were first used in the 1990s. In the 1990s, microfluidic technology was also adopted[3] Microfluidics devices can be used to produce niosomes. In addition to central channels, it has side channels. An interaction chamber filled with ice is reached by pumping the organic and aqueous phases via separate channels under pressure at a predetermined flow rate. Typically, a glass vial is used to gather the niosomes from the mixing channels[19] Through carefully regulated flow rates of aqueous and organic phases in microchannels, microfluidics allows for the controlled creation of small and homogeneous niosomes. This method is ideal for producing cholesterol-free formulations and vesicles with minimal size dispersity, both of which are crucial for focusing on active drug delivery. Particle size and stability are directly impacted by the f lowrate ratio. The encapsulation of biomolecules like mRNA and siRNA has shown tremendous potential in recent advancements, making the approach extremely important to gene therapy[20]

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4. The Bubble Method

A round-bottomed flask with three neck positions in a water bath is used in the abubbling process to create the niosomes. Each flask neck has a thermometer, nitrogen supply, and water-cool reflux. Niosomes are created by dispersing cholesterol and surfactants in buffer (pH 7.4) at 70 °C, mixing them for 15 seconds with a high shear homogenizer, and then "bubbling" them with nitrogen gas. Additionally, it can create vesicles by bubbling nitrogen gas through an aqueous solution of cholesterol and surfactants. This is a one-step, solvent- free approach that reduces environmental problems. Vesicle formation and encapsulation efficiency are directly impacted by the size of the bubble and pressure, and the methods used in the encapsulation of volatile chemicals are compromised[21]

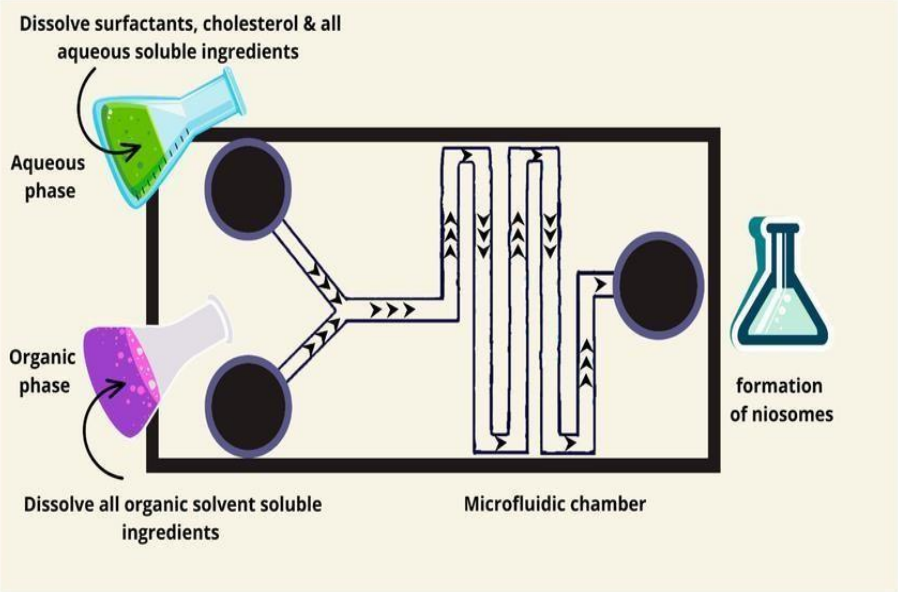

Fig 4 :The Microfluidic Method For The Preparation Of Niosomes

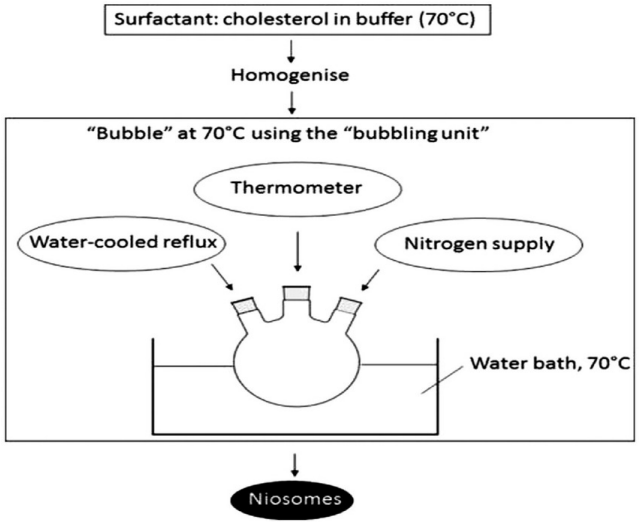

Fig5. The Bubble Method For The Preparation Of Niosomes.

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5. Sonication Method:

A common technique for repairing eniosomes is the sonication method. It is an easy, inexpensive approach that doesn't require the use of organic solvents. In short, surfactant and cholesterol are mixed with the medicine and the aqueous phase. The mixture was sonicated in a titanium probesonicator at 60°C for a few minutes. Theniosomes are typically collected by freeze-drying or filtration using filter sheets. The main benefit of this approach is that it doesn't require any kind of organic solvent, and the resulting iiosomes are extremely small. According to the preceding remark, this approach is not a good fit for medications that are insoluble in water. This technique could result in tiny multilamellar vesicles[22]

A titanium probe with a diameter of 1 mm was used in a probe sonicator (series UP200Ht, Hielscher, Germany) to sonicate the niosome suspensions. For fifteen minutes, the sample (3 mL) was sonicated at a power of 150 W. The beaker was submerged in an ice bath to prevent the sample from becoming overheated. Sonication of the solution is a common technique for producing the vesicles. This procedure involves adding an aliquot of the drug solution in buffer to a 10-ml glass vial containing the surfactant/choleste mixture. To produce niosomes, the mixture is probe sonicated for three minutes at 60°C using a titanium probe in a sonicator[23]

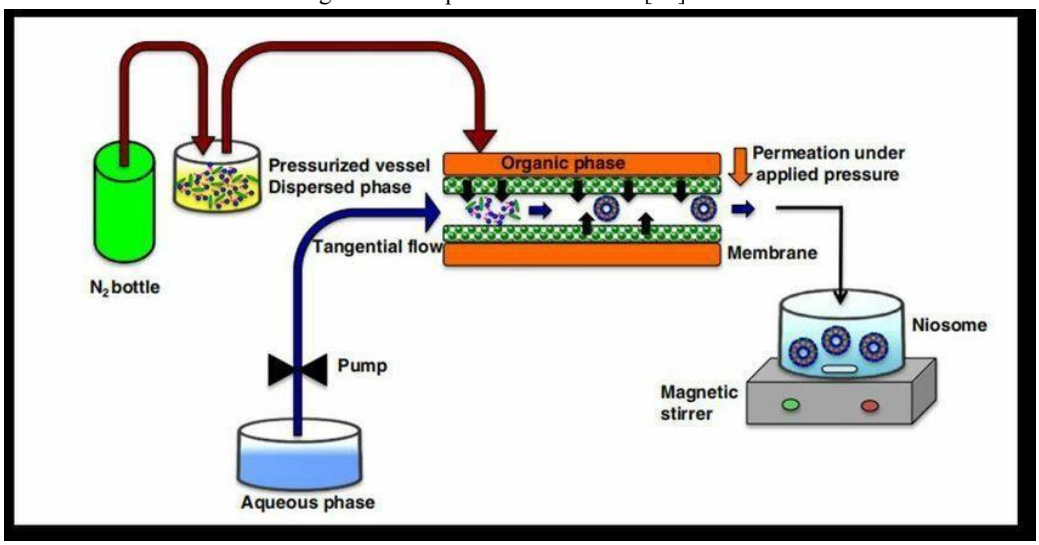

Fig 6: The Sonication Method For The Preparation Of Niosomes

Characterization studies:

Niosome characteristics include size, dispersion, zeta potential, shape, EE, and in vitro release behavior. These are investigated to ascertain the niosomes' quality in formulation development and their potential use in upcoming clinical trials. These factors directly affect in vivo performance and stability[34]

1. Particle Size and Size Distribution:

• controls circulatory dynamics, cellular uptake, and biodistribution.

• Measured with:

DLS, or dynamic light scattering

Tracking Analysis of Nanoparticles (NTA)

Uniform vesicles are indicated by a low polydispersity index (PDI

2. Zeta Potential:

• determines niosome surface charge and forecasts colloidal stability.

• Electrophoretic light scattering (ELS) was used to measure it.

• Stable dispersions are usually indicated by values greater than ±30 mV.

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3. Morphology:
• verifies the lamellarity, surface properties, and form of the vesicle.
• Methods:
Spherical shape and bilayer thickness are shown via Transmission Electron Microscopy (TEM).
Surface morphology using scanning electron microscopy (SEM).
3D morphology using Atomic Force Microscopy (AFM).
4. Encapsulation Efficiency (EE%):
• determines how much medication is trapped in niosomes.
• Ascertained by:
• To separate free drug, use centrifugation or dialysis.
• quantification by HPLC or UV-Vis spectrophotometry.
• EE% is computed as follows:
• EE%=Total drug(Total drug−Free drug)×100
5. Vesicle Lamellarity:
• indicates if niosomes are multilamellar (MLV) or unilamellar (ULV). assessed using:
• TEM
• Nuclear Magnetic Resonance (NMR) at 31P
6. In-Vitro Drug Release:
• establishes the mechanism and kinetics of release.
• investigated with:
• Dialysis bag techniqueFranz diffusion cell data fitted to zero-ord
• Korsmeyer-Peppas, and Higuchi models.
7. Stability Studies:
• nalyze medication retention and long-term integrity.
• Parameters under observation:
• Modification in size
• Zeta potential
• Physical characteristics
• Drug spills
• carried out under accelerated conditions and at 4 °C and 25 °C.
8. Thermal Behavior:
• Differential Scanning Calorimetry (DSC) was used to measure.
• detects drug-excipient interactions and phase transitions.
9. Surface pH:
• guarantees the compatibility of the formulation, particularly for topical or ocular administration.
• measured with a pH meter.
10. Viscosity (for niosomal gels):
• rucial for topical and transdermal applications.
• measured with a Brookfield viscometer.[35]

Niosomes: The Next Wave in Smart Drug Delivery

Marketed Products of Selected Drugs:

Drug Encapsulated	Therapeutic Use	Route Studied
Acyclovir	Anti-viral	Topical, Oral
Doxorubicin	Anti-cancer	Intravenous
Diclofenac Sodium	Anti-inflammatory	Transdermal

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Ibuprofen	Anti-inflammatory	Transdermal, Oral
Norfloxacin	Anti-bacterial	Oral
Tacrolimus	Immunosuppressant	Ocular

APPLICATION:

a) It is employed in the delivery of ocular medications.
b) Drug targeting is one of its uses.
c) It is possible to use niosomal targeting systems as diagnostic tools.
d) The nature of the immunological response elicited by antigens has been studied using niosomes.
e) Niosome-based transdermal drug delivery systems.
f) It is applied as a targeted and specific anti-neoplastic treatment for cancer.
g) Immune response research uses it.
h) For example, sodium stibogluconate is used to treat leishmaniasis (dermal and mucocutaneous diseases).
i) Similar to hemoglobin, niosomes can be utilized as carriers.
j) It serves as a peptide medication delivery system.
k) Niosomes can exhibit localized drug action.
l) Moreover, it is employed in gene delivery.
m) They are used to distribute and encapsulate herbal chemicals, which are well-liked in the cosmetics industry due to their anti-aging and antioxidant qualities.
n) They improve the bioavailability and stability of medications that are encapsulated[24]

DELIVERY STATERGIES:

Niosomes have been administered by a variety of methods, and it is evident that the method is crucial when creating a vesicular formulation.

1. Oral Route:

Since the oral method is typically favored, research has focused on delivering niosomes orally. In an in vivo investigation using rabbits, a niosome formulation of acyclovir that offers a Higuchi pattern of drug release was found to improve sustained drug release. In comparison to a tablet dosage form, the oral bioavailability and MRT of acyclovir were more than twice as high in this study. When compared to a tablet dose form, the oral bioavailability and MRT of acyclovir were more than doubled in this study. Similarly, prolonged release by zero order followed by first order kinetics was seen in a Span 60 niosome formulation of fluconazole with an encapsulation effectiveness >91%.An in vitro–in vivo correlation research of griseofulvin-loaded niosomes revealed that niosomes were an effective means of improving the bioavailability and long-term oral administration of griseofulvin. Niosomes are a potential delivery mechanism for prolonged drug release, according to all of these investigations. Mannosylated nonionic surfactant-based vesicles have been created for oral immunization in order to effectively transfer plasmid DNA encoding the hepatitis B virus's small subunit proteins[25]

2. Transdermal Route:

Transdermal drug administration from niosomes has been investigated in several disease models in recent years, and current efforts are concentrated on process optimization, novel compositions, and final formulations[26] However, due to the many benefits provided by topical and transdermal delivery methods, including increased patient compliance, a greater surface area for absorption, and the avoidance of first-pass hepatic metabolism, there is also growing interest in the applications of these nanocarriers[44] Niosomes improve transdermal medication distribution through a variety of methods since their effectiveness cannot be fully explained by a single channel. Depending on the local moisture circumstances, niosomes may enter the stratum corneum intact or undergo structural metamorphosis into smaller vesicles within the skin. Several teams of researchers have created niosomes that contain nonsteroidal anti-

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inflammatory medicines (NSAIDs). After being taken orally, these medications may irritate the local mucosa and undergo first-pass metabolism in the liver, which results in partial inactivation. A novel tenoxicam transdermal formulation with enhanced safety and significant therapeutic efficacy[23]

3. Intraveneous Route:

Niosomes interact with plasma proteins and may become opsonized when administered intravenously. Because the reticuloendothelial system (RES) is essential to their removal, surface modification with polyethylene glycol (PEG) can prolong circulation. Encapsulated medications can be delivered gradually through diffusion or membrane destabilization at the target tissue thanks to the bilayer structure. To provide site-specific delivery, targeting ligands like antibodies, peptides, or folic acid can be coupled to niosomes. Anticancer, antifungal, and anti-inflammatory drugs have been studied in niosomal formulations administered intravenously. For instance, compared to free medications, niosomal doxorubicin and paclitaxel have demonstrated improved tumor targeting and less cardiotoxicity. Intravenous administration of amphotericin B niosomes has shown less nephrotoxicity. Moreover, IV niosomes may be used to transfer genes and vaccines[27]

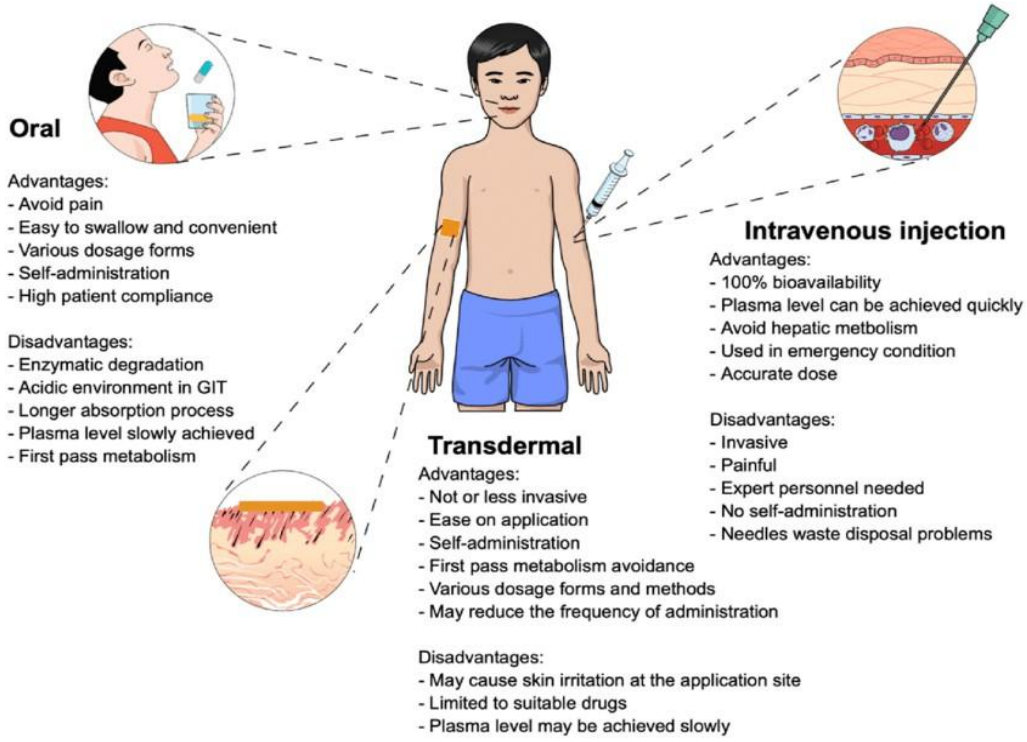

Fig7: Niosome Based A Smart Nano Carrier For Effective And Advance Delivery System.

Current applications of niosomes:

Niosome-based transdermal, injectable, and ocular drug delivery systems have also been studied. The sluggish penetration of conventional transdermal methods is overcome by newsome administration via the transdermal channel. Combining medications like diclofenac, flurbiprofen, and nimesulide in niosomal formulations increases their bioavailability and therapeutic efficacy. A niosomal formulation of chitosan-encapsulated timolol maleate was demonstrated to be more successful in lowering intraocular pressure for ocular medication administration than commercially available formulations with less cardiovascular side effects. Because of its very desirable qualities, Newsome's formulation is used for numerous other therapeutic purposes[24]

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Cancer treatment:

Many anticancer medications can be administered using niosomal preparations with minimal adverse effects. In addition to having poor therapeutic efficacy, a high frequency of side effects, and damage to healthy cells, conventional chemotherapy is unable to specifically target the malignant cells. Colloidal niosomal compositions show promise as both passive and active medication delivery methods to malignant areas. limited bioavailability and stability, a high risk of adverse effects, and insufficient drug access due to limited blood-brain barrier penetration can all be addressed by administering anticancer medications using niosomal formulations [28]Non-targeted delivery, short-term drug profiles, and antitumor effects of medications are just a few of the difficulties associated with cancer treatment. In order to support the efficacy and efficiency of cancer cell-targeted medicines, cancer treatment approaches are evolving. Because it is sensitive to signals from physiological systems that might be affected by the environment and disruptions brought on by pathological abnormalities, stimulus-sensitive targeting is crucial for the development of future neosomal drug technologies. Additionally, distribution in multifunctional niosomes has demonstrated significant promise for cancer therapy techniques using two or mormedications is a combination therapy that enhances synergistic benefits[13]

Herbs that show anticancer activity of niosomes:

Traditional medicine is a major component of many global health care systems. Both industrialized and developing nations are growing more aware of this plant's therapeutic and economic advantages. Herbs are plant substances with flavor, fragrance, and/or therapeutic qualities. Plant items used to safeguard or enhance health are referred to as herbal remedies or herbal medicine. An estimated 25% of the Indian pharmacopoeia today consists of herbal medications. Traditional medicinal herbs are substances derived from naturally occurring plants that are used in regional or local healing customs to treat illnesses without the use of chemicals. While Ayurveda and traditional Chinese medicine are widely used worldwide, traditional Tibetan medicine is still largely restricted to its own country. Clinical experiments are being conducted on herbs coated with compounds that have chemopreventive qualities. It has been demonstrated that niosomes can be used in sophisticated drug delivery methods, including intravenous, transdermal, vascular, and pulmonary delivery.

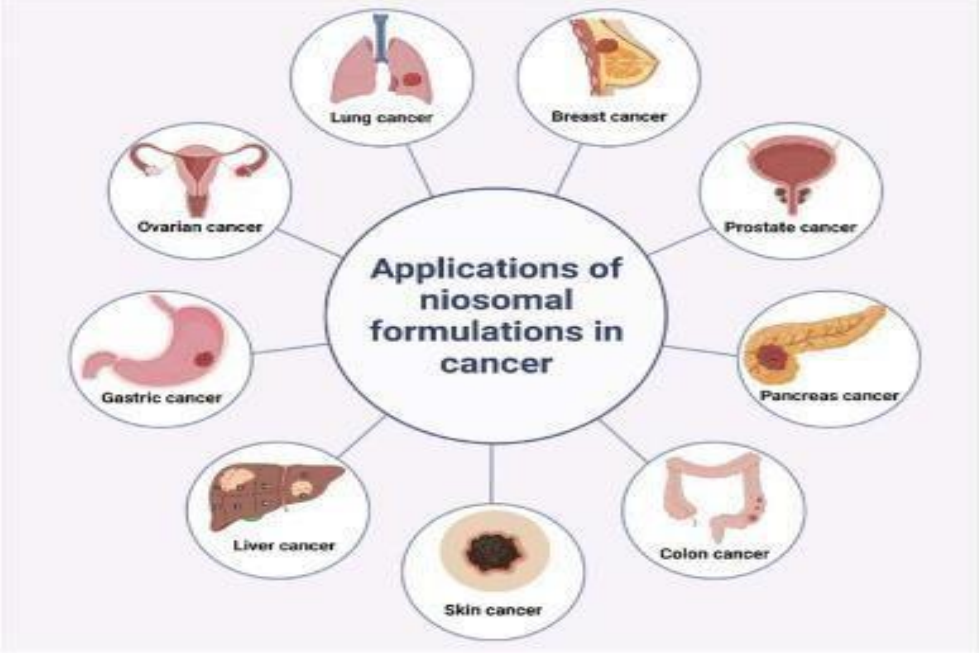

Fig 8: Application Of Niosomal Formulation In Cancer

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Gene delivery:

Using non-viral carriers to enhance the cellular absorption properties of nucleic acids, gene therapy has proven to be an efficient method for treating genetic human illnesses The vector's characteristics have a big influence on how well gene therapy works. Despite the fact that niosomes have been around for nearly thirty years, very little study has been done to examine their potential as gene delivery vectors. In contrast to liposomes Because non-ionic surfactants are present, niosomes offer greater chemical stability and storage capacity. These non-ionic surfactants also lower niosome toxicity and production costs. These characteristics promote studies on the applicability of niosomes for gene delivery. Protamine improved nucleus targeting and enabled transfection of a small percentage of photoreceptor cells after sub-retinal injection while preserving transfection efficiency. Additionally, it was found that encasing genes encoding hepatitis B surface antigens (HBsAgs) in niosomes triggered an immune response that produced endogenous cytokines and blood antibodies similar to those produced by topical liposomes or intramuscularly injected HBsAgs. As a non-viral vector, niosomes have demonstrated favorable characteristics for gene transfer, such as minimal toxicity, high stability, and ease of manufacture. Niosomes' stability, safety, and effective transport of DNA, siRNA, and mRNA make them a viable non-viral gene delivery method. Their targeting, transfection effectiveness, and clinical suitability for gene therapy in conditions like cancer, genetic abnormalities, and viral infections are all being improved by ongoing study. Gene therapy involves delivering genetic material (DNA, RNA, siRNA, mRNA, plasmids) into cells to correct or modify gene expression[2o]

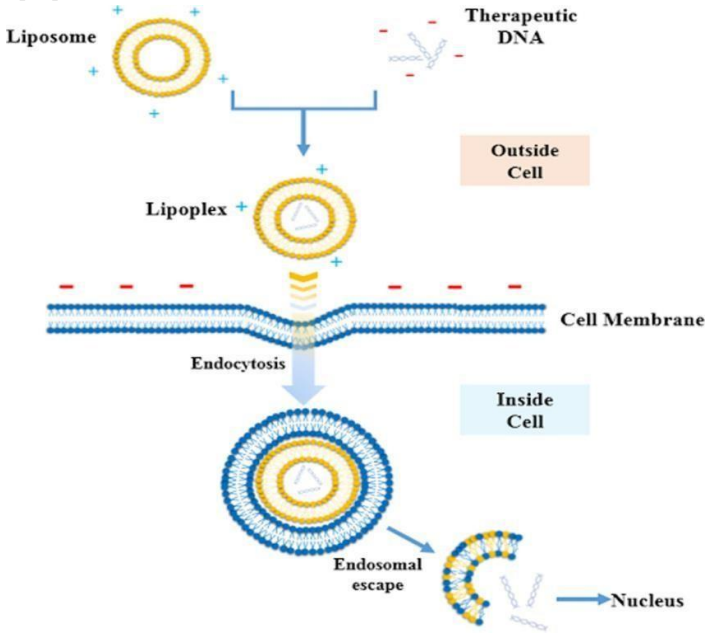

Fig 9:Gene Delivery In Niosome Or Liposome.

Ocular Disease:

The human eye is a sensory organ that is shielded from its environment by a number of barriers and protection systems. This particular structure makes it extremely difficult to treat ocular illnesses and administer medications to various eye compartments. The most common method of ocular therapy for the anterior portion of the eye, which includes the conjunctiva, cornea, sclera, and anterior uvea, is topical eye drops. However, there are certain restrictions on this drug administration method. The sorption time for medications utilizing eye drops is roughly two to three minutes. As a result, administered drops are rapidly removed from the eye's surface. The most frequent causes of blindness and visual impairment are posterior segment ocular diseases such as diabetic macular edema, age-related macular degeneration,

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proliferative vitreo retinopathy, glaucoma, and CMV infection. Genetic disorders may sometimes occasionally be the cause of retinal degeneration and the ensuing blindness. By offering specific carriers, nanotechnology benefits ophthalmology by prolonging therapeutic efficacy, facilitating intracellular administration, and offering new methods of transfer and release. Natarajan et al. reported the successful production of nanocarriers loaded with specific medications to reduce intraocular pressure in the eye, presenting this structure as a key sustained-release nanodrug candidate for glaucoma therapy[31].

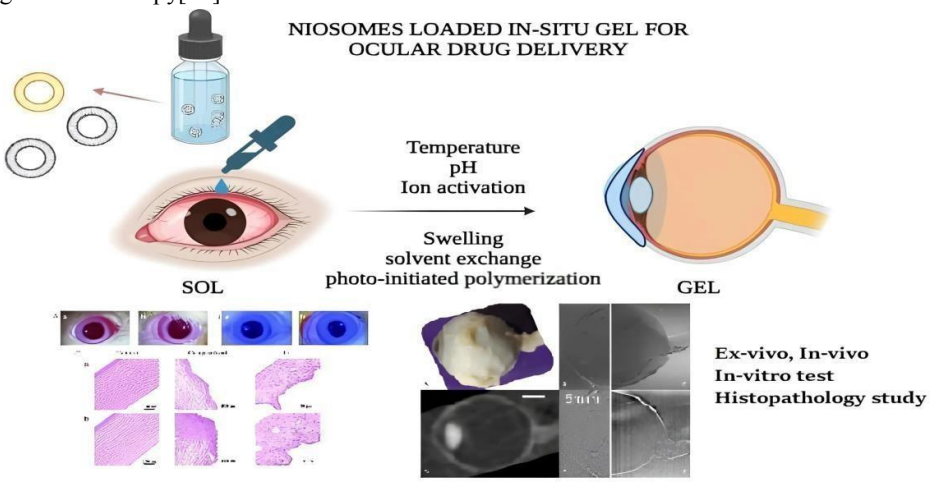

Fig10:Niosome For Ocular Drug Delivry

Anti-Diabetic Activity:

The formulation did not significantly alter behavior when taken orally at doses of 1000 to 5000 mg/kg. or toxicity in the rats, demonstrating that the formulation is safe under the conditions that can be observed (OECD revised draft 420). fter 14 days of lycopene nano- niosome formulation administration (100 and 200 mg/kg) the blood glucose level of animals with diabetes as opposed to the diabetic control group. The blood glucose level significantly dropped on the seventh ($p<0.01$) and fourteenth ($p<0.001$) days of the diabetes induction, demonstrating the lycopene niosome's anti-diabetic efficacy formulation[32]

FUTURE PROSPECT:

One proposed medication delivery molecule is niosomes. Toxic anti-cancer, anti-infective, anti-AIDS, anti-inflammatory, anti-viral, and other medications can all be encapsulated in niosomes and used as promising drug carriers to improve the drugs' bioavailability and targeting qualities while also lowering their toxicity and side effects. Niosomal drug carriers are safer than ionic drug carriers, which are comparatively toxic and inappropriate. There are no particular requirements for handling and storing niosomes[28] Although niosomes have shown promise as a nanocarrier system, its ultimate potential is still a long way off. With continual developments in nanotechnology, material science, and pharmaceutical engineering, the future of niosomal research is predicted to expand dramatically. They can be created to improve therapeutic activity, minimize adverse effects, and administer drugs in a targeted and regulated manner. Treatment precision is anticipated to be enhanced by sophisticated stimuli-responsive niosomes that release medications in response to pH, temperature, enzymes, or light. Additionally, niosomes exhibit promise as efficient carriers and immune boosters in gene transfer, mRNA/siRNA transport, and vaccine production. Their use in brain-targeted delivery, cancer treatment, and personalized medicine is expanding quickly. Future developments will concentrate on the creation of multifunctional hybrid niosomes for theranostic (therapy + diagnosis) applications, enhanced stability, and scalable production. Niosomes are anticipated to develop into clinically dependable and

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extensively used medication delivery methods thanks to developments in nanotechnology and AI-based formulation optimization[33].

II. CONCLUSION

Niosomes have proven to be a potent and versatile nanocarrier technology that can enhance the therapeutic efficacy of several medications. Because of their well-defined structure, adaptable content, and variety of manufacturing methods, vesicle features may be precisely controlled, making them appropriate for a wide range of medicinal applications. When paired with cutting-edge delivery techniques, niosomes' capacity to encapsulate both hydrophilic and lipophilic compounds provides substantial benefits for attaining targeted, prolonged, and effective medication release. Their potential to revolutionize present therapeutic procedures is further demonstrated by their successful application in vaccine delivery, cancer therapy, infectious illness management, and transdermal systems. Even though there are still issues with long-term stability, regulatory acceptability, and large-scale production, these constraints should be resolved by continued developments in formulation science and nanotechnology. All things considered, niosomes offer a promising platform for upcoming advancements in drug delivery, with great potential to improve clinical results and broaden therapeutic options.

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