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A DETAILED REVIEW ON NIOSOMES; RECENT ADVANCEMENTS IN FORMULATIONS, CHARACTERIZATION AND ITS APPLICATIONS

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ABSTRACT

A Niosomes is a non-ionic surfactant based liposomes, found to be mixture of cholesterol and non-ionic surfactants and are proved to be a promising drug carrier and has potential to reduce the side effects of drugs and increased therapeutic effectiveness in various diseases. Niosomes are multilamellar or unilamellar vesicles in which an aqueous solute solution is completely encapsulated by a membrane formed by surfactant macromolecules organised as a bilayer. Their structure is identical to that of a liposome, hence they can be used to represent alternate vesicular systems to liposomes. Niosomes addressed the issues related to drug insolubility, instability, low bioavailability, and rapid deterioration. This overview article represents the structure of niosomes, advantages, disadvantages, methods for niosomes preparations, characterization, and its application of the vesicular system.

Keywords: Niosomes; Drug delivery; Applications; Types; Methods; Vesicular

INTRODUCTION:

Niosomes are a unique drug delivery system that encapsulates drugs in vesicles. Vesicles are niosomes in solution because they consist of a bilayer of non-ionic, land-active sellers. Niosomes are tiny and microscopic in length. Their duration is deceptive on the nanometer scale. Niosomes are structurally similar to liposomes, and itshave few advantages. Niosomes greatly enhance transdermal drug delivery and are widely used for targeted drug delivery, improved structural studies may suggest novel drug delivery methods. Niosomes are non-ionic surfactants based entirely on vesicles obtained from hydration of synthetic non-ionic surfactants, with or without LDL cholesterol LDL or single factor lipids. Liposome are like vesicle systems and can be used in amphiphilic and lipophilic formulations. Niosomes are a promising drug delivery vehicle and are non-ionic. A valuable resource for using a migratory restriction on target cells is much less toxic and improves the recovery index of drugs. Niosomes were described by scientists Vanlerberghe *et al*., Handjanivila *et al*. Afterwards, Van Abbe explained that the choice was made in favor of non-ionic surfactants decreased in the order of anionic > amphoteric > non-ionic **[1, 2]**.

STRUCTURE OF NIOSOMES:

As shown in **Figure 1**, it is a two-layer circular vesicules composed of a non-ionic surfactant and cholesterol. Non-ionic surfactants are placed in this style, with the hydrophobic septum facing inward (facing the lipophilic phase). In contrast, hydrophilic niches face outward (towards the aqueous phase), resulting in the formation of a closed lipid bilayer surrounding the solute in the aqueous phase corresponding to the outer and inner surfaces of the hydrophilic site **[3]**.

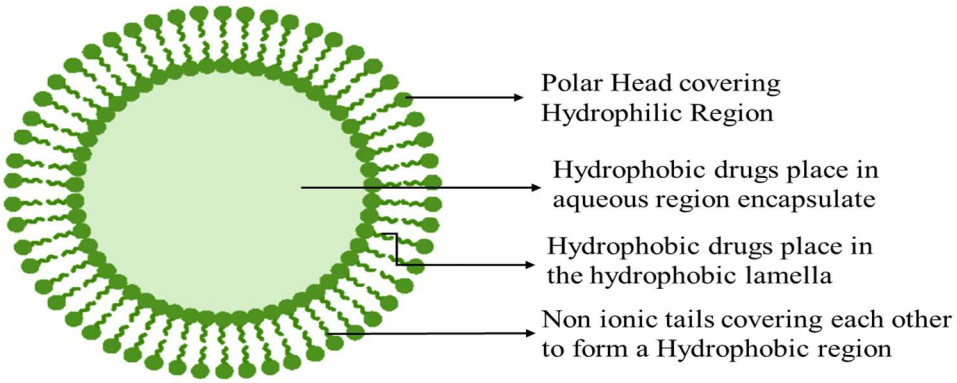


Figure 1: Structure of Niosomes

NIOSOMES AND ITS VARIOUS TYPES

The different types of niosomes are:

i) Multi lamellar vesicles (MLV)

ii) Largeunilamellar vesicles (LUV)

iii) Small unilamellar vesicles (SUV)

multilamellar vesicles (mlv): It consists of several bilayers that individually surround aqueous lipid compartments. The approximate size of this bubble is 0.510 µm in diameter. Multilamellar vesicles are the most widely used niosomes. These cysts are well suited as drug carriers for lipophilic compounds **[4]**.

large unilamellar vesicles (luv): This type of niosome has a high ratio of an aqueous solution to lipid component membrane .lipids can be used very economically to capture large amounts of bioactive substances **[3, 5]**.

small unilamellar vesicles (suv): These small unilamellar vesicles are mainly obtained from multilamellar vesicles by sonication, and electrostatic stabilization by French press extrusion incorporates diethyl phosphate into Span 60 niosomes loaded with 5(6) carboxyfluorescein (CF).

CHARACTERISATION OF NIOSOMES:

double layer stiffness and uniformity: The biodistribution and biodegradation of niosomes are affected by the paralysis of the bilayer. If homogeneous, it can be found both in the structure of niosomes and between dispersed niosomes and can be identified everywhere. p NMR, differential scanning calorimetry (DSC), and Fourier transform infrared spectroscopy (FTIR).

size and shape: Various strategies are used to determine the inner diameter, such as soft laser scattering, except that they are determined by electron microscopy, molecular chromatography, photon correlation microscopy, and light microscopy **[6]**.

stability study: The niosome composition was stored for 3 months in temperature-controlled ovens at 4 °C, 25 °C, and 37 °C to represent the situation for equilibrium studies. After one month, drug content substances in all formulations are identified using capture efficiency parameters **[7]**.

In-vitro Release

In-vitro launch use of 3 types

A. Dialysis Tubing

B. Reverse dialysis

C. Franz diffusion cell

a. Dialysis tubing: Related Analysis Pouch | Qualitative analysis} Wash with distilled water. The organized cyst suspension is pipetted directly into a bag made of a dialysis tube, and the bag is sealed **[8]**. Then find a bubble sac in 200 ccs of buffer in a 250 ml beaker with constant shaking at 25 °C. At various time intervals, buffers are the most

efficient analytical method for drug content analysis **[9]**.

b. Reverse dialysis: An immense shape of small dialysis containing 1ml of dissolution medium is positioned in proniosomes. The proniosomes are then displaced into the dissolution medium. The direct dilution of the proniosomes is viable with this technique, and the quick launch cannot be quantified the usage of this technique **[10]**.

c. Franz diffusion cell: In vitro diffusion studies can be achieved using the Franz diffusion movable element. Proniosomes are located inside the donor chamber of Franz's diffusion movable element equipped with a cellophane membrane **[2]**. The proniosomes are then dialyzed against an appropriate dissolution medium at room temperature. Samples are removed from the environment for a reasonable period and tested for drug content. The use of proper techniques

Scanning electron microscopy: Niosomes were placed under a scanning electron microscope (SEM) (JSM 6100 JEOL, Tokyo, Japan). They were attached directly to the SEM sample using double-sided tape and covered with an nm gold film under a reduced pressure of 0.001 mm Hg. Photos were taken at the appropriate magnification **[8]**.

Vesicle charge: The rate of vesicle disruption may play an essential role in the behavior of niosomes in vivo and invitro. Charged niosomes are more resistant to aggregation and fusion than unchanged vesicles **[11, 12]**. To evaluate the potential of the Earth, microelectrophoresis can be used to measure the zeta potential of characteristic niosomes. A possible approach use an pH-sensitive fluorophore. More recently, dynamic light scattering has been used to demonstrate the zeta potential of niosomes.

Niosomal drug loading and encapsulation efficiency: To determine drug loading and encapsulation efficiency, ultracentrifuge the aqueous suspension of niosomes, remove the supernatant, and wash the pellet twice with distilled water to remove the adsorbed drug **[13]**.

FORMULATION OF NIOSOMES:

Preparation methods

Passive trapping techniques

This includes maximal strategies used for niosomal training, during which drugs are incorporated throughout their formation **[14, 15]**.

1. Sonication:

Mixture of drug solution in the buffer, surfactant and cholesterol

⬇

sonicated with a titanium probe sonicator at 60°C for 3 minutes to yield niosomes

2. Ether injection method:

Niosomes by slowly introduce in a solution of surfactant dissolve in diethyl ether into warm water maintain at 60 C

⬇

Mixture in ether is injected through 14-gauge needle into an aqueous solution of material.

⬇

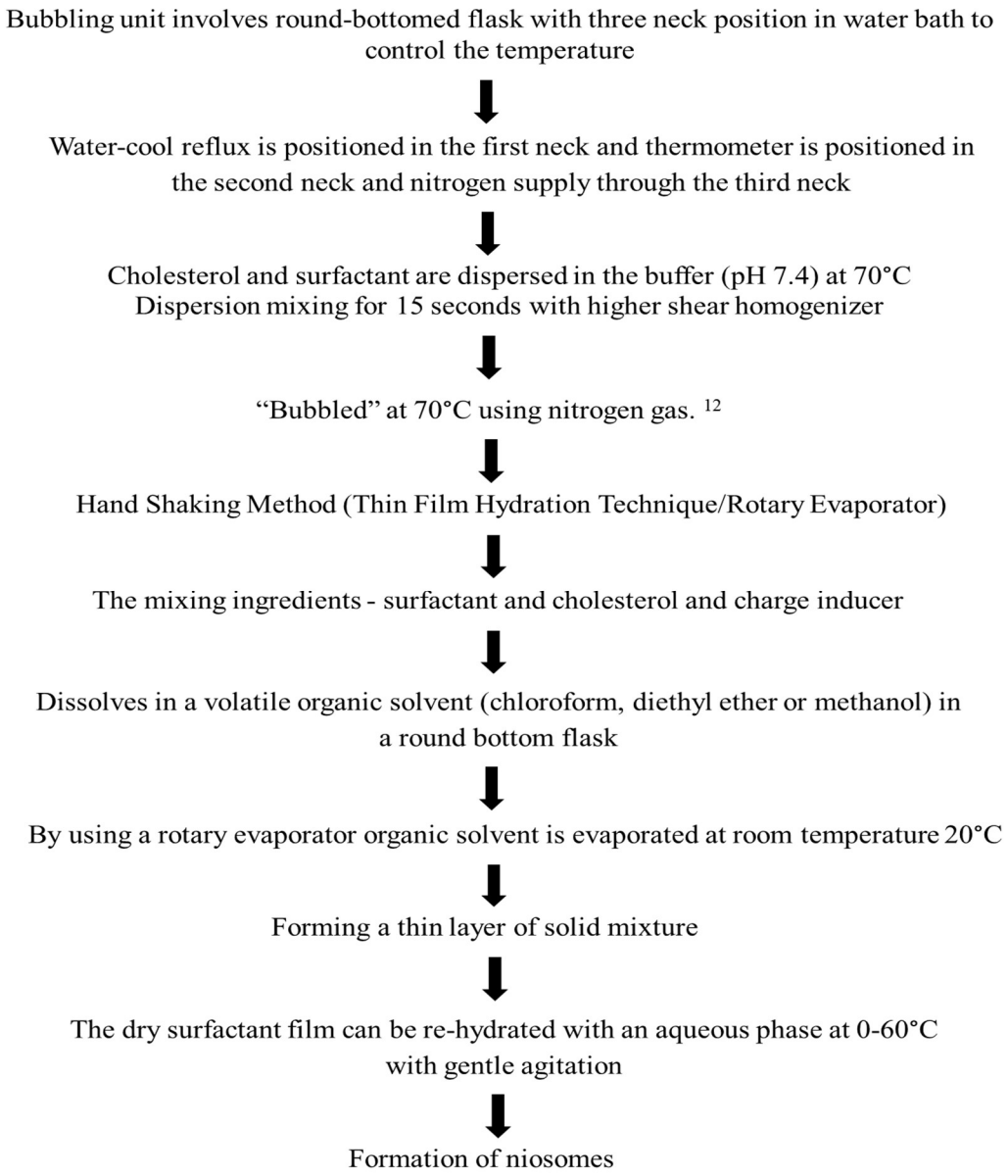
Vaporization of ether leads to the formation of the single layer vesicles

⬇

Diameter of the vesicle range from 50 to 1000 nm depends upon the conditions use

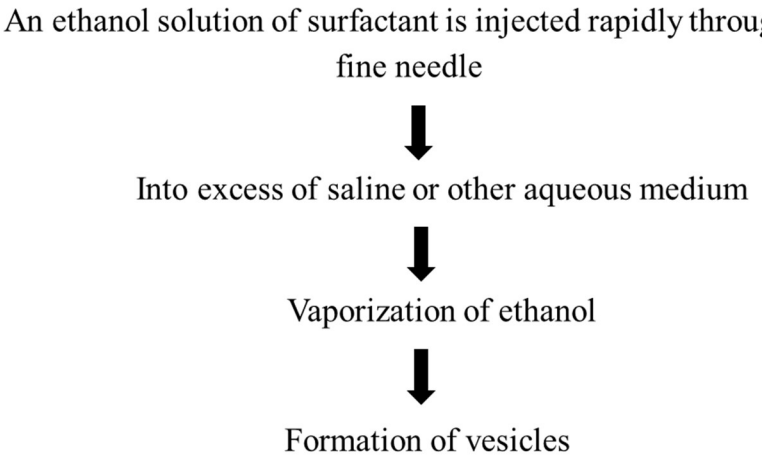
3. Reverse phase evaporation technique: Dissolve cholesterol and wetting agent (1:1 ratio) in a mixture of natural solvents (ether and chloroform). When a binary compound drug selection is added, a water-in-oil emulsion is formed; The stage is sonicated at 45ºC. The emulsion is dried on a rotary evaporator at 40 °C to form a solid gel from a giant bubble. Transfer a small amount of phosphate-buffered saline (PBS) to the clear gel and sonicated. Remove the natural incision at 40ºC and reduce the pressure. The viscous suspension of niosomes is further diluted with phosphate-buffered saline and then heated in a water bath at 60ºC for 10 minutes to form niosomes **[16]**.

4. The "bubble" method



5. Multiple membrane extrusion method: A mixture of surfactant, LDL cholesterol, and dicetyl phosphate on a chloroform bureau film using a rotary evaporator. The film is hydrated with an aqueous polycarbonate membrane. The solution and resulting slurry are squeezed through a polycarbonate membrane and collected in a collector for up to 8 passes. This is an excellent approach for controlling the length of niosomes [**18]**.

6. Ethanol injection method



7. Micro fluidization: In this approach, the principle involves submerged jet rules in which fluidized streams interact with each other at highly excessive velocities within microchannels and interaction chamber. At the side of the peculiar place, the striking of a thin liquid layer is organized, which includes the fact that the electrical source remains the same within the niosome formation region, the formation of niosome bubbles of greater homogeneity, shorter length, and higher reproducibility **[4]**.

a. Active trapping techniques: It consists in loading the drug after the formation of the niosome. After the niosomes are organized, the drug is loaded to maintain a pH gradient or ion gradient, promoting drug absorption by the niosome. The various advantages of the niosome form are 100% absorption, excess drug lipid ratio, no leakage, high potency, and suitability for unstable drugs.

b. Drug uptake in a trans membrane pH gradient: It consists in loading the drug after the formation of the niosome. After the niosomes are organized, the drug is loaded to maintain a pH gradient or ion gradient, promoting drug absorption by the niosome. The various advantages of the niosome form are 100% absorption, excess drug lipid ratio, no leakage, high potency, and suitability for unstable drugs **[19]**.

In remote loading process surfactants and cholesterol are dissolved in organic solvent (chloroform)

⬇

Solvent evaporates under reduced pressure to get a thin film on the wall of the round bottom flask Film hydrates with 300 mM citric acid (pH4.0) by vortex mixing.

⬇

Multilamellar vesicles are frozen and thawed 3 times and later sonication

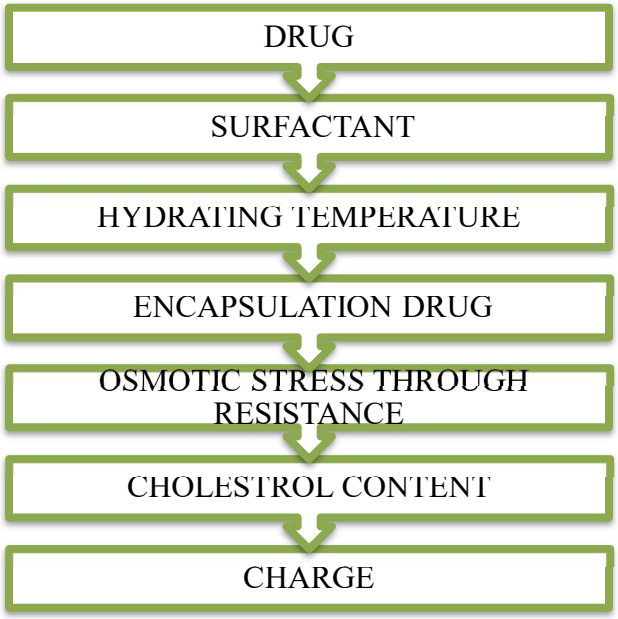
⬇

For niosomal suspension, aqueous solution containing 10 mg/ml of drug is added and vortex Sample pH is raises to 7.0-7.2 with 1M disodium phosphate

⬇

The mixture is later heated at 60°C for 10 minutes to yield niosomes

FACTORS INFLUENCE OF NIOSOMES:



Drug: Entrapment of drugs in niosomes will grow vesicle size, most possibly with the resource of the usage of elevating the rate and mutual repulsion of the surfactant bilayers or with the aid of using the touch of the surfactant bilayers. Surfactant head companies as a solute, **[17]** However, certain drugs aren't safe. They were entangled in PEG chains of varying lengths. Suppose vesicles coated with polyoxyethylene glycol (PEG). The tendency to get more significant decreases. The extent to which the drug's

hydrophilic lipophilic balance affects entrapment.

Surfactant: Intra-HLB surfactant growth results in the in-length increase of niosomes due to a loose power discount along with hydrophobic growth within the surfactant **[20]**. The bilayer of niosomes can be found in liquid or gel-like states. , temperature, type of surfactant, and cholesterol. In the gel state the alkyl chains are well ordered, but in the liquid form, they are disordered. (TS).

Hydrating temperature: Hydration temperature affects the size and shape of niosomes. The temperature of the hydration reaction should be better than the transition temperature of the gel-liquid section. The assembling of surfactants into vesicles and the modulation of vesicle shape are both affected by temperature changes **[22]**. The adjustment is also accounted by the hydration period and the volume of the hydration medium. Fragile niosomes and drug leakage difficulties can occur if the hydration temperature, duration, and hydration medium volume are not chosen correctly.

Encapsulation drug: The physical chemical properties of the encapsulated medication have a significant impact on the niosomal bilayer's charge and stiffness. Drug capture occurs when the surfactant head groups communicate, generating a rise in demand and mutual repulsion of the surfactant bilayer, resulting in increased vesicle size **[20]**. The level of trapping is determined by the drug's HLB—rate and mutual repulsion of the surfactant bilayer, ensuing in improved vesicle size. The stage of trapping is decided through the drug`s HLB.

Osmotic stress through resistance: The addition of a hypertensive response reduces the diameter of the vesicles. Due to the mechanical weakening of the bubble shape under the influence of osmotic pressure, vesicle eluting fluid inhibition occurs at some stage in the slow launch, observed faster launch at first **[22]**.

Cholestrol content: Cholesterol increases the capture efficiency of niosomes and increases the hydrodynamic diameter of niosomes. Cholesterol Possibility Increase the order of the bilayer chains within the liquid state and decrease the demand of the chains within the bilayer gel state. The stiffness of the bilayers improves with an upward thrust in ldl cholesterol concentration, and the charge of the encapsulated content material decreases.

Charge: When a rate is present, the inter lamellar distance among successive bilayers in a multilamellar vesicle shape increase, ensuring in a more significant standard entrapped volume **[21]**.

ADVANTAGES OF NIOSOMES:

Niosomal drug delivery is a drug delivery method for controlled and targeted drug delivery and is a significant blessing for providers of these vesicular drugs.

Niosome dispersion in the aqueous portion can be emulsified in the non-aqueous amount to control the drug delivery rate and introduce existing air bubbles into the non-aqueous amount in the field.

The vesicle suspension is completely waterborne. This provides for an excessive breakdown of the substrate when evaluating oily formulations.

They not only have osmotic energy and stability but also increase the stability of the entrapped drug.

No special conditions are required for operation and storage with surfactants.

Improve oral bioavailability of poorly absorbed tablets and improve porosity and permeability of tablets.

Similar to oral, parenteral, and topical routes, web pages of movements can be used.

Surfactants are biodegradable, biocompatible, and non-immunogenic. Improve the average overall efficiency of drug molecule recovery by exploiting delayed clearance from the bloodstream, protecting the drug from its natural environment, and limiting its effect on target cells **[5]**.

Niosome dispersion in the aqueous part can be emulsified in the non-aqueous part to control the drug delivery rate and introduce existing air bubbles into the non-aqueous position in the open air. Niosomes are an infrastructure that collectively contains hydrophilic, amphiphilic, and lipophilic moieties and can accommodate highly soluble drug molecules as a result **[23]**.

Vesicules technique trends are variable and controllable. Changes in vesicle composition, size, stratification, tap volume, basal velocity, and percentage can drive vesicle trends. Moreover, vesicles can act as depots, releasing drugs in a controlled manner **[25]**.

Improves the average overall efficiency of drug molecule recovery by using delayed clearance from the bloodstream, protecting the drug from its natural environment, and limiting its effect on target cells **[24]**.

DISADVANTAGE OF NIOSOMES:

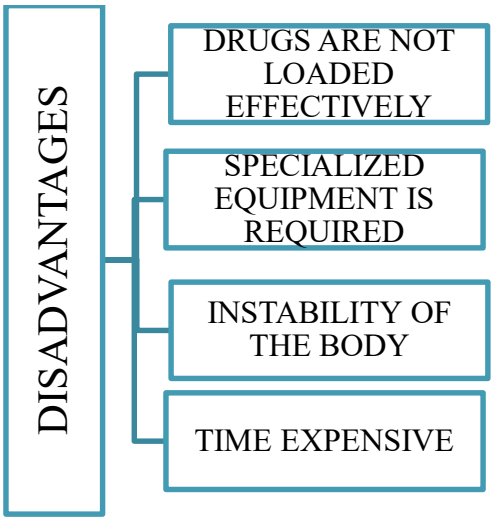


Figure 2: Disadvantages of Niosomes

Table 1: Effects on drug properties and stability

THE DRUG'S NATURE	EXPLOSION FROM THE VESICLES	CONSTANCY
Macromolecules	Decrease	Increase
Amphiphilic drug	Decrease	_
Hydrophobic drug	Increase	Decrease
Hydrophobic drug	Decrease	Increase

APPLICATION OF NIOSOMES:

Targeting of bio active agents:

a) To reticuloendothelial machine (res): The RES cells preferentially devour the vesicles. It may be used to deal with animal cancers that have to unfold to the liver and spleen, in addition to parasitic infestations of the liver **[26]**.

b) To organs aside from res: It has been use of antibodies to attain a selected region within the body. Immunoglobulin is a beneficial device for finding drug services.

Treatment of leishmaniasis: Leishmaniasis is a parasitic infection that affects the cells and liver. The antimony investigation on mice found that increasing sodium stibogluconate efficacy of niosomal formulation improved sodium stibogluconate efficacy, and The impact of doses on consecutive days turned into additive. In experimental leishmaniasis, niosomes also are powerful as drug-loaded liposomes **[27, 30]**.

Tumor targeting: A large concentration of an anti-cancer drug is necessary at the tumor location for successful cancer treatment. This reduces the drug's concentration in other tissues. Compartments of the body, hence reducing their adverse effects. Reactions. Several research organizations have looked

into niosomes Niosomes improved anti-cancer drug supply, Cytarabine hydrochloride drug has generated in lymphatics. They were using a method of lipid hydration that did not include dicetyl phosphate to obtain smaller vesicles. The vesicles got ranging in size from 600 to 1000nm. The Span 60 formulation had the slowest release rate among the surfactants tested (Span 60, Span 80, Tween 20, Tween 80). The release was split into two phases: an initial burst that lasted 2–6 hours, followed by a continuous release that lasted at least 16 hours **[30]**.

For the treatment of aids: The human immunodeficiency virus (HIV) causes AIDS, characterized by a severely weakened immune system.

Zidovudine (AZT) is an anti-HIV drug that is used to treat AIDS. It can be used on its own or in combination with anti-viral medications. In one investigation, the noise created by adding Tween 80 revealed many AZT drugs entrapped. The addition of diacetyl phosphate boosted the drug release for a more extended period (88.72 percent over 12 hours). The molecular ratios of non-ionic surfactants with a constant ratio of cholesterol and the entrapment efficiency were measured during the formation of niosomes **[28, 29]**.

Niosome as a carrier for hemoglobin: Hemoglobin is transported via niosomes. The hemoglobin can be changed similarly to non-capsulated hemoglobin because vesicles are readily permeable to oxygen. The visible spectrum of niosomal suspension can be superimposed on that of free hemoglobin **[27, 30]**.

Antibiotics: The ophthalmic distribution of a water soluble local antibiotic is carried out using non-ionic surfactant vesicles (niosomes). The effects of gentamicin sulphate were studied, and the findings revealed that niosomes are the most promising ocular transporters for gentamicin sulphate topical application **[28, 29]**.

Proteins and peptides: Niosomes can be employed to carry peptides and proteins in a long-acting oral form **[30]**.

Distribution through the skin: Niosomes had been investigated as a transdermal medicinal drug transport technology, in addition to its capacity to enhance drug absorption and decrease pores and skin infection thru the intact stratum corneum. Franz diffusion cells investigated the Penetration of Ketorolac (a potent NSAID) into rabbit skin excised from various gel compositions containing proniosomes **[2, 27]**. The generated proniosomes increased

drug penetration and significantly reduced residence time. E

FUTURE PROSPECTS:

The niosome is a medicine delivery device that has a lot of promise. Niosome can be usd to encapsulate hazardous medications such as anti-cancer, anti-viral, and anti-AIDS treatments, increasing their bioavailability and targeting abilities. Niosomes do not need to be stored or handled in any particular way **[31-34]**.

SALIENT FEAUTRES ASPECTS OF NIOSOMES:

Niosomes are extremely osmotic, which means they can entangle solutes and boost the potency of entangled medicines.

Niosomes are biocompatible, non-immunogenic, and biodegradable non-ionic surfactants.

Niosomes have a unique structure that includes spreadable and hydrophobic substances that contain insignificant elements, thus accommodating a wide range of solubility in medicinal compounds

Niosomes allows for easy addition of unstable and sensitive substances.

Niosomes are generally structurally flexible, making them suitable for situations where the design is popular.

The product's availability on a particular web page is better than just protecting the product in its natural environment.

Oral solubility and bioavailability of poorly soluble capsules are superior to niosomes and improve pores and skin permeability of topically applicable drugs **[7, 18]**.

CONCLUSION:

Neosomal drug delivery system is one of the examples of great evolution in drug delivery technologies. Niosomes have great drug delivery potential for targeted delivery of anti-cancer, antiinfective agents. Non-ionic surfactant vesicles alter the plasma clearance kinetics, tissue distribution, metabolism and cellular interaction of the drug. Many studies have been demonstrated that niosomes improve the stability of entrapped drug, reduce the dose and enable targeted delivery to a specific site. These advantages over the liposomes make it a better targeting agent. Ophthalmic, topical, parenteral and various other routes are used for targeting the drug to the site of action for better efficacy.

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