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NIOSOMES AS NANO CARRIER SYSTEM AND A NOVEL APPROACH IN MODERN DRUG DELIVERY SYSTEM

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Abstract

In the last few years, a huge numbers of targeted drug delivery carriers are developing such as niosomes, proniosomes, liposomes, ethosomes, electrosomes and transferosomes, etc. As compared to other nano carriers, niosomes and proniosomes are much good carriers to increase bioavailability and therapeutic efficiency by reducing its adverse effects. Niosomes or Non- ionic surfactant vesicles are microscopic lamellar structures formed on admixture of non-ionic surfactant of the alkyl or dialkylpolyglycerol ether class and cholesterol with subsequent hydration in aqueous media and its similar to liposomes that can be used as carriers for lipophilic and amphiphilic drugs. Niosomes have been widely evaluated for controlled release and targeted delivery for treatment of viral infections, cancer and other microbial disease. This article reviews advantages, disadvantages, comparison with liposomes, its types, mechanisms involved within niosomes and proniosomes to enhance transdermal drug delivery, composition and its different preparation techniques, factors affecting, its physical as well as chemical characterizations and niosomal applications.

Keywords: Nano-carrier, Niosomes, Nano-carrier and modern Drug Delivery System, Hydrogel, Nano-gel, Nonionic Surfactant, HLB Scale.

Introduction

Novel vesicular drug delivery systems have made great progress in the field of nanotechnology. As these systems have a potential to carry a variety of drugs and have been widely used for various purposes, such as drug targeting, controlled release, and permeation enhancement of the drugs [1, 2]. These systems are also valuable in evading various drawbacks associated with conventional dosage forms like low aqueous solubility, poor bioavailability, poor membrane permeability, variable plasma concentration, undesirable effects, poor patient compliance, and finally poor patient efficacy [3, 4, 5]. The phenomenon of targeting drug delivery systems is to deliver the drug in the body in such a manner that it should show its action to the targeted desired site to achieve the therapeutic response where its action should be needed by limiting undesirable interaction to non-targeted tissues [6]. Paul Ehrlich introduced this idea in 1909, and he called this strategy “magic bullets” [7]. Novel approaches like nanotechnology have developed in the field of science, which has introduced various targeted novel vesicular drug carrier systems like liposomes, Niosomes, proniosomes, ethosomes, and electrosomes. Among these, niosomes and proniosomes have distinct advantages over the other vesicles by acting as drug containing reservoirs [8, 9]. Niosomes were first introduced in the future of cosmetic industry. Nonionic surfactants such as span-60 are preferred due to their less irritation power which decreases in order of cationic >anionic> ampholytic> nonionic surfactants which contains polar and non-polar segments are possess high interfacial activity upon hydration bilayer in and

entrap both hydrophilic and lipophilic drugs [10]. A niosome is defined as a nonionic surfactant based liposome. Niosomes are formed mostly by with or without incorporation of cholesterol as an excipient and their lipids as an excipient [11].
Niosomes or non-ionic surfactants vesicles are microscopic lamellar structures formed on the admixture of a non-ionic surfactant, cholesterol and phosphate with subsequent hydration in aqueous media. Handjani-vila et al. introduced the class of noisome [12, 13]. These are amphiphilic, biocompatible, biodegradable, non-toxic materials to encapsulate the medication in vesicles that improve the bioavailability of the drug, therapeutic efficiency, drug penetration through the skin, releases the drug in a sustained and controlled manner, and used to target the desired site by adjusting the composition that helps to reduce the side effects [14]. Another advantage of niosomes is the development of a simple practical method for the routine and large-scale production without the use of pharmaceutically unacceptable solvents [15].

This review provides a brief overview of issues related to niosomes by explaining their chemical composition, structure, advantages, and applications, makes general remarks on niosomes as percutaneous permeation enhancers, and discusses the findings of investigations done over the past 5 years on niosomal drug delivery systems for transdermal applications.

Advantages of niosomes as compared to other drug carrier [16-18]

- Since the structure of the noisome offers place to accommodate hydrophilic, lipophilic as well as ampiphilic drug moieties, they can be used for a variety of drugs.
- Niosomes exhibits flexibility in their structural characteristics (composition, fluidity and size) and can be designed according to the desired situation.
- They improve the therapeutic performance of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug.
- Niosomes can act as a depot to release the drug slowly and offer a controlled release.
- They can increase the oral bioavailability of drugs.
- They are osmotically active and stable.
- They increase the stability of the entrapped drug.
- They can enhance the skin penetration of drugs.
- They can be made to reach the site of action by oral, parenteral as well as topical routes.
- The surfactants are biodegradable, biocompatible, and non-immunogenic.
- The niosomal dispersions in an aqueous phase can be emulsified in a non-aqueous phase to control the release rate of the drug and administer normal vesicles in external non-aqueous phase.
- Handling and storage of surfactants do not require any special conditions.
- The vesicle suspension being water based offers greater patient compliance over oily dosage forms.
- Niosome act as a reservoir to release drug in a gradual and controlled manner
- Niosomes are osmotically active and stable. Also, the stability of the drug over long storages time is much higher compared to liposomes.
- They are improving the medication-taking behavior in one of the following ways: the clearance of the drug is delayed, the drug is protected from the biological environment, and the drug effect is restricted to the target site.
- Niosomes have low toxicity and high compatibility with biological systems because the commonly used nonionic surfactants are biocompatible, biodegradable, and non-immunogenic.
- The administration routes of niosomes are diverse (intravenous, oral, etc.).
- The oral bioavailability of drugs with low absorption has been improved by niosomes and increases permeability of the drug into skin.
- A wide variety of drugs (hydrophilic and lipophilic ones) with different solubility can be entrapped in the niosomes.
- Niosomes are effectively use to deliver various drugs to targeted organs.
- Niosomes are flexible and easily modified because of the functional groups on their hydrophilic heads.
- Storage and handling of surfactant does not require special conditions.

Disadvantages of Niosomes [19]

- Aggregation.
- Leaking of Entrapped Drug.
- Physical instability.
- Time consuming.

Table 1: comparison between niosomes and liposomes [20, 21]

Sr no.	NIOSOMES	LIPOSOMES
1	Less Expensive	More Expensive
2	No special methods require for such formulations	Require special methods for storage and handling of the final formulation
3	Non-ionic surfactant is uncharged.	Phospholipids may be neutral and charged
4	Main Components: Surfactants	Main Components: Phospholipids
5	Component availability: High	Component availability: Low
6	Component purity: Good	Component purity: Variable
7	Preparation and storage: No special conditions required	Preparation and storage: Inert atmosphere and low temperature
8	Stability: Very good	Stability: Low
9	Cost: Low	cost: High

Types of Niosomes

Niosomes can be divided into different categories according to their size (small and large) and the number of membrane bilayers (unilamellar and multilamellar) as follows

- Small unilamellar vesicles or SUV (20-50 nm in diameter).
- Large unilamellar vesicles or LUV (50-1000 nm in diameter).
- Multilamellar vesicles or Giant vesicles or MLV (1-20 μm in diameter).

Given that we are interested to produce giant niosomes, therefore we further divide giant vesicles into three groups based on lamellarity

- Giant oligolamellar vesicles or GOLV.
- Giant multishell vesicles or GMSV.
- Giant multilamellar vesicles or GMLV. [22, 23]

Proniosomes

These are the niosomal formulation made up of carrier and surfactants, which are to be hydrated before use.

Carrier + surfactant = Proniosomes,
Proniosomes + Water = Niosomes.

Bola Surfactant Containing Niosome

They are special type of surfactants made up of omegahexadecylbis-(1-aza-18crow-6) : Span80: cholesterol in 2:3:1 ratio [24]

Aspasomes

Aspasomes are the vesicles made up of acorbyl palmitate, cholesterol and highly charged lipid such as diacetyl phosphate. To obtain niosomes, the aspasomes are first hydrated with aqueous solution and then sonicated. These are mainly used in dermal drug delivery to enhance the permeation of drugs [25].

Vesicles in Water and Oil System (V/W/O):

The formation of the v/w/o is done by adding suspension of niosomes into the oily phase at 60°C. It forms a gel like consistency it can entrap the hydrophilic active ingredients. These vesicles are used in controlled drug delivery.

Deformable Niosomes:

The mixture of non-ionic surfactants, ethanol and water forms the deformable niosomes. These are smaller vesicles and easily pass through the pores of stratum corneum, which leads to increase penetration efficiency. It can be used in topical preparation [26.]

Structure and Components of Niosomes

The two major components utilized for the preparation of niosomes exist: lipid compounds (cholesterol or L-α-soya phosphatidylcholine) and nonionic surfactants. Lipid compounds are utilized to provide unbending nature, appropriate shape, and adaptation to the niosomes [27]. (e part surfactants assume the main part in the

development of niosomes. (e accompanying nonionic surfactants for the most part utilized for the arrangement of niosomes are the spans (spans 60, 40, 20, 85, and 80), tweens (tweens 20, 40, 60, and 80), and Brij (30, 35, 52, 58, 72, and 76) [28–30]. Nonionic surfactant-based vesicles or niosomes are the capable drug carriers which require a bilayer structure that are made mostly by nonionic surfactant and lipid compounds (cholesterol or L-α-soya phosphatidylcholine) incorporated in an aqueous phase [31]

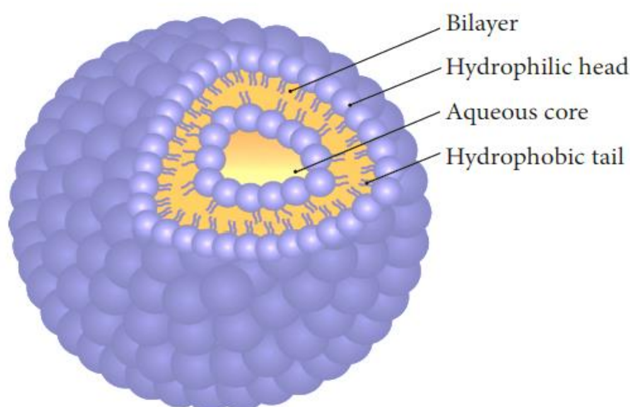

figure 1: structure of niosomes [32]

Non-ionic surfactants:

Surfactant selection must be based on HLB quality. Because Hydrophilic Lipophilic Balance (HLB) is a reliable indicator of any surfactant's ability to establish vesicles, it has been found that the HLB number between 4 and 8 is consistent with vesicle development. Due to increased aqueous solubility, this is also recorded that the hydrophilic surfactant. On hydration, in allowing free hydrated devices to occur aggregates as well as to type a lamellar structure, they may not attain a nation of concentrated technologies.

Alkyl esters

Within this group of surfactants, sorbitan esters are by far the most favoured surfactant who used it to prepare niosomes. Vesicles formed by the monolaurate of polyoxyethylene sorbitan are more soluble than most other vesicles of surfactant. For illustration, polyoxyethylene was used to encapsulate diclofenac sodium (polysorbate 60).

Alkyl amide

Alkyl amide (e.g. galactosides and glucosides) was being used to produce fatty acid and amino acid compounds in the niosomal vesicles (d): Long-chain fatty acids and molecules of amino acids were also used in the production of certain niosomes.

Cholesterol

Steroids are critical elements of the cell membrane and inϑluence the ϑluidity and permeability of both the bilayer through their inclusion in the layer. Cholesterol is a steroid variant which is used primarily for the niosome methodology. It may have no position in bilayer formulation, its signiϑicance in niosome structure and the control of layer properties could not be dismissed. In particular, the introduction of cholesterol affects the compounds of niosomes such as membrane permeability, inϑlexibility, the effectiveness of encapsulation, easiness of rehydration of freeze-dried niosomes and their toxic effects [32].

METHODS OF PREPARATION OF NIOSOMES

Ether injection method [33]

This approach offers the possibility of producing niosomes by progressively introducing a compound of the surfactant submerged in diethyl ether at 60 ◦ C in warm water. This surfactant mixture in ether is injected via a 14-gage needle into an aqueous substance solution. Ether vaporisation contributes to single-layered vesicles being formed. The vesicle's size ranges between 50 to 1000 nm, based on the circumstances utilised.

Sonication Method [34]

A standard technique of vesicle development is by solution sonication as described in Cable. In this technique, a substance solution aliquot in the buffer is introduced in a 10-ml glass vial to the surfactant / choleste mixture. The solution is sonicised for 3 minutes at 600C, using just a sonicator with a titanium sample to generate niosomes.

The "Bubble" Method [35]

Bubbling unit involves round-bottomed flask with three neck position in water bath to control the temperature

↓

Water-cool reflux is positioned in the first neck and thermometer is positioned in the second neck and nitrogen supply through the third neck

↓

Cholesterol and surfactant are dispersed in the buffer (pH 7.4) at 70°C Dispersion mixing for 15 seconds with high shear homogenizer

↓

"Bubbled" at 70°C using nitrogen gas.

Trans Membrane pH Gradient Drug Uptake Process [36]

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 17.

Ethanol Injection Method [37]

An ethanol solution of surfactant is injected rapidly through a fine needle

↓

Into excess of saline or other aqueous medium

↓

Vaporization of ethanol Formation of vesicles.

5. Hand Shaking Method (Thin Film Hydration Technique/Rotary Evaporator) [38]

The mixing ingredients - surfactant and cholesterol and charge inducer

↓

Dissolves in a volatile organic solvent (chloroform, diethyl ether or methanol) in a round bottom flask

↓

By using a rotary evaporator organic solvent is evaporated at room temperature 20°C

↓

Forming a thin layer of solid mixture

↓

The dry surfactant film can be re-hydrated with an aqueous phase at 0-60°C with gentle agitation

↓

Formation of niosomes.

Heating Method [38, 39]

This method is in one-step, scalable and non-toxic and also based on the patent procedure. A suitable aqueous medium such as buffer distilled water, etc. in which mixtures of non-ionic surfactants, cholesterol and/or charge inducing molecules are added in the presence of the polyol like as glycerol. The mixture is heated with (at low shear forces) until the vesicles were form.

Micro fluidization [39, 40]

Micro fluidization is a recent technique used to prepare unilamellar vesicles of defined size distribution. This method is based on submerged jet principle in which two fluidized streams interact at ultra-high velocities, in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. The result is a greater uniformity, smaller size and better reproducibility of niosomes formed.

Reverse Phase Evaporation Technique (REV) [41]

Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicate at 4-5°C. The clear gel formed is further sonicate after the addition of a small amount of phosphate buffered saline (PBS). The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield niosomes. Raja Naresh et al [13] have reported the preparation of Diclofenac Sodium niosomes using Tween 85 by this method.]

FACTORS INFLUENCING NIOSOMAL FORMULATION [42-47]

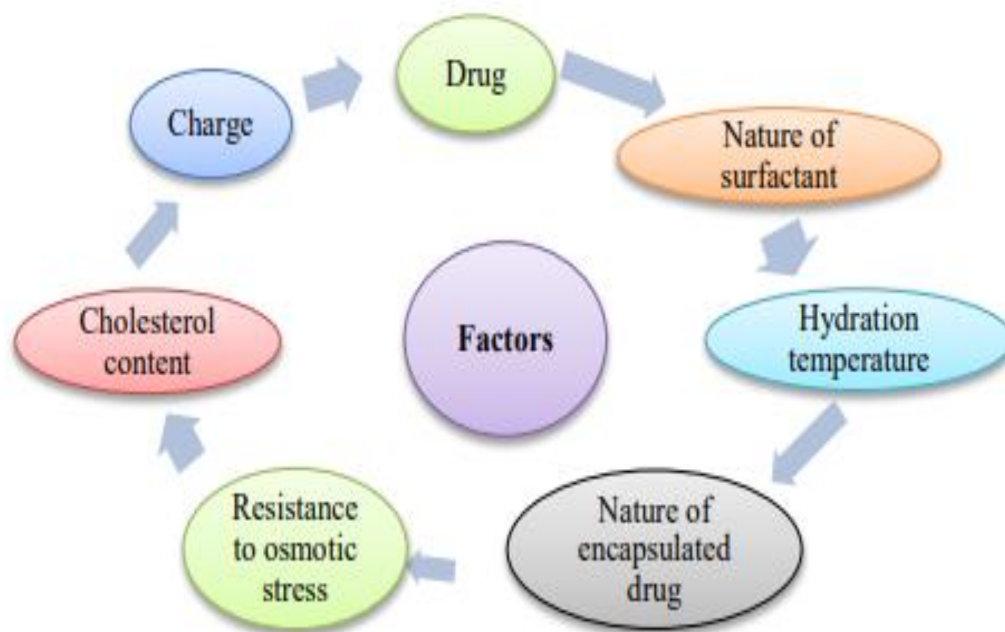

figure 2: factors influencing niosomal formulation

Nature of Surfactant: Increase in the HLB value of surfactants leads to the increase in the mean size of niosomes due to the decrease in surface free energy with an increase in the surfactant hydrophobicity. The bilayers of the niosomes can exist either as a liquid state or in a gel state. It depends upon the temperature, type of surfactant and cholesterol. Alkyl chains are well ordered in the gel state, whereas disordered in the liquid state. Entrapment efficiency is affected by the gel, liquid phase transition temperature (TC) of the surfactant. Eg: span 60 with higher TC exhibits better entrapment. The HLB value of surfactants ranging between 14 and 17 are not suitable for niosomal preparations. Decrease in the HLB value of surfactants from 8.6 to 1.7 decreases the entrapment efficiency and highest entrapment efficiency is found with the HLB value of 8.6.

Nature of Encapsulated Drug: The charge and the rigidity of the niosomal bilayer are greatly influenced by physical chemical properties of the encapsulated drug. Entrapment of drug occurs by interacting with the surfactant head groups leading to the increasing charge and creates mutual repulsion of the surfactant bilayer and thus increases the vesicle size. The HLB of drug influences the degree of entrapment.

Hydration Temperature: The size and shape of the niosome are affected by the temperature of hydration. Hydration temperature should be above the gel, liquid phase transition temperature. Change in temperature affects the assembly of surfactants into vesicles and vesicle shape modification. Hydration time and volume of hydration medium also accounts for the modification. Improper selection of the hydration temperature, time and hydration medium volume produces fragile niosomes / drug leakage problems may arise.

Cholesterol Content: Incorporation of cholesterol increases the entrapment efficiency and hydro-dynamic diameter of niosomes. Cholesterol acts in two ways

a. Increases the chain order of liquid state bilayers.
b. Decreases the chain order of gel state bilayers.

An increase in the cholesterol concentration causes an increase in the rigidity of the bilayers and decrease in the release rate of encapsulated material.

Charge: Presences of charge leads to an increase in inter lamellar distance between successive bilayers in multi lamellar vesicle structure and greater overall entrapped volume.

Resistance to Osmotic Stress: Addition of hypertonic solution causes reduction in vesicle diameter. In hypotonic solution, inhibition of eluting fluid from vesicles results in the slow release initially followed by the faster release due to the mechanical loosening of vesicle structure under osmotic stress.

Characterization test of Niosomes

Determination of vesicle size

A small aliquot of freshly prepared niosome dispersion sample was used to characterize the particle size and size distribution, by light scattering based on laser diffraction technique (Horiba's LA-300 Laser Diffraction Particle Size Distribution Analyzer). [48]. Also the vesicle size and shape for each formulation was determined by optical microscope (Motic Image, Germany) each formulation was spread uniformly on glass slide and observed under optical microscope under 1gm of 45X optical lens for vesicular shape[49].

The particle size (nm) and polydispersity index (PDI) of the niosomes were measured by cumulant analysis with DLS using the Zetasizer Nano ZS [50].

Morphology of niosomes

Scanning electron microscopy was used to examine the morphology of niosomes. The formulation was coated with gold in the nano-structure coating DSR1 and observed in SEM (HITACHI S-4160) at a magnification of 15,000 and an acceleration voltage equal to 20.0 kV [51].

Entrapment Efficiency

After preparing niosomal dispersion, unentrapped drug is separated by dialysis, centrifugation, [52] or gel filtration[53] and the drug remained entrapped in niosomes is determined by complete vesicle disruption using 50% n-propanol or 0.1% Triton X-100 and analysing the resultant solution by appropriate assay method for the drug. Where,

Entrapment efficiency (EF) = (Amount entrapped / total amount) × 100 [54]

Entrapment efficacies of hydrophilic and lipophilic compounds depend on the preparation method. Baillie et al. concluded that niosomes prepared by ether injection method resulted in entrapment efficacies of carboxy fluorescein that were significantly higher than those of vesicles prepared by hand shaking. Both baillie et al and hunter at al used glycerol surfactants and reported tha the entrapment efficacy decreased as the amount of cholestrol added in the nonionic surfactant vesicle increased [55].

In-Vitro Release

A method of in-vitro release rate study includes the use of dialysis tubing. A dialysis sac is washed and soaked in distilled water. The vesicle suspension is pipetted into a bag made up of the tubing and sealed. The bag containing the vesicles is placed in 200 ml of buffer solution in a 250 ml beaker with constant shaking at 25°C or 37°C. At various time intervals, the buffer is analyzed for the drug content by an appropriate assay method [52].

Bilayer formation

Assembly of non-ionic surfactants to form a bilayer vesicle is characterised by an X-cross formation under light polarisation microscopy.

Membrane rigidity

Membrane rigidity can be measured by means of mobility of fluorescence probe as a function of temperature [56].

Number of lamellae

This is determined by using nuclear magnetic resonance (NMR) spectroscopy, small angle X-ray scattering and electron microscopy [46].

Stability studies

Stability studies for the formulated niosomal dispersion are carried out by storing at 4°±2°C, 25°±2°C and 40°±2°C in for the period of three months . Drug content and invitro release studies has been carried out on the selected formulations after one month and periodically thereafter for three months [57].

Zeta potential

The significance of zeta potential is that its value can be related to the stability of colloidal dispersions. The zeta potential indicates the degree of repulsion between adjacent, similarly charged particles in dispersion. The zeta potential for the niosomal dispersion was determined using Malvern instruments [58].

Therapeutic and Medical Applications of Niosomes

Niosomal drug delivery has been studied using various methods of administration including intramuscular, intravenous, peroral, and transdermal. In addition, as drug delivery vesicles, niosomes have been shown to enhance absorption of some drugs across cell membranes, to localize in targeted organs and tissues, and to elude the reticuloendothelial system.

Sustained Release and Localized Drug Action of niosomes

Sustained release action of niosomes can be applied to drugs with low therapeutic index and low water solubility since those could be maintained in the circulation via niosomal encapsulation. The evolution of niosome drug delivery technology has shown promise in cancer chemotherapy and anti-leishmanial therapy [58].

Targeting of bioactive agent

To reticulo-endothelial system (RES)

The cells of RES preferentially take up the vesicles. The uptake of niosomes by the cells is also by circulating serum factors known as opsonins, which mark them for clearance. Such localized drug accumulation has, however, been exploited in treatment of animal tumors known to metastasize to the liver and spleen and in parasitic infestation of liver [59].

Ophthalmic drug delivery

A single study reports on the biological evaluation of a niosomal drug delivery system for ophthalmic delivery. Cyclopentolate was encapsulated within niosomes prepared from polysorbate 20 and cholesterol and found to penetrate the cornea in a pH dependant manner within these niosomes. Permeation of cyclopentolate increased at pH 5.5 but decreased at pH 7.4. Contrary to these findings, in vivo there was increased mydriatic response with the niosomal formulation irrespective of the pH of the formulation It is concluded that the increased absorption of cyclopentolate may be due to the altered permeability characteristics of the conjunctival and sclera membranes. Additionally discomes have been proposed as ophthalmic drug delivery agents [60].

To organs other than RES.

Immunoglobulins seem to bind quite readily to the lipid surface, thus offering a convenient means for targeting of drug carrier [61]. It has been suggested that carrier system can be directed to specific sites in the body by use of antibodies. Many cells possess the intrinsic ability to recognize and bind particular carbohydrate determinants and this can be exploited to direct carriers system to particular cells [62].

Niosomes as carriers for Hemoglobin.

Niosomes can be used as a carrier for hemoglobin. Niosomal suspension shows a visible spectrum superimposable onto that of free hemoglobin. Vesicles are permeable to oxygen and hemoglobin dissociation curve can be modified similarly to non-encapsulated hemoglobin [63].

Diagnostic imaging with Niosomes

Niosomes are considered as a carrier of iobitridol, a diagnostic agent for X-ray imaging. The noisome prepared using the film hydration method followed by sonication. Method allows the increasing encapsulation and the stability of vesicles were carried out [64].

Anti-inflammatory agents

Diclofenac sodium noisome reportedly prepared from polysorbate 60, cholesterol and DCP (22:73:5) & 3 μ m in size were found to reduce the inflammation in rats with carrageen induced paw edema on intraperitoneal administration to a greater extent than the free drug. This increase in activity is a direct result of an observed increase in the area under the plasma time curve [65].

Following are the molecules which work has been done

Sr.No.	Drug	Reference
1	Ketoconazole	Shirsand S, Kanani K, Keerthy D, Nagendrakumar D, Para M. Formulation and evaluation of Ketoconazole niosomal gel drug delivery system. *Int J Pharm Investig*. 2012;2(4):201. doi:10.4103/2230-973x.107002
2	Etodolac	Shilakari Asthana G, Asthana A, Singh D, Sharma PK. Etodolac Containing Topical Niosomal Gel: Formulation Development and Evaluation. *J Drug Deliv*. 2016;2016:1-8. doi:10.1155/2016/9324567
3	Benzoyl peroxide	Vyas J, Vyas P, Raval D, Paghdar P. Development of Topical Niosomal Gel of Benzoyl Peroxide. *ISRN Nanotechnol*. 2011;2011(1996):1-6. doi:10.5402/2011/503158
4	Benzoyl peroxide and tretinoin	Gupta A, Singh S, Kotla NG, Webster TJ. Formulation and evaluation of a topical niosomal gel containing a combination of benzoyl peroxide and tretinoin for antiacne activity. *Int J Nanomedicine*. 2014;10:171-182. doi:10.2147/IJN.S70449
5	Gamma oryzanol	Shah HS, Gotecha A, Jetha D, et al. Gamma oryzanol niosomal gel for skin cancer: formulation and optimization using quality by design (QbD) approach. *AAPS Open*. 2021;7(1). doi:10.1186/s41120-021-00041-2
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7	Fernesol	Barot T, Rawtani D, Kulkarni P. Development, characterization and in vitro–in vivo evaluation of Farnesol loaded niosomal gel for applications in oral candidiasis treatment. *Heliyon*. 2021;7(9):e07968. doi:10.1016/j.heliyon.2021.e07968
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9	Aceclofenac	Fathalla D. In-vitro and In-vivo valuation of Niosomal Gel Containing Aceclofenac for Sustained Drug Delivery. *Int J Pharm Sci Res*. 2014;1(1):1-11. doi:10.15344/23941502/2014/105

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11	Diclofenac	Alalor CA, Jokor PE. Evaluation of diclofenac niosomal gel formulated with *Grewia* gum for topical delivery. *J Pharm Bioresour*. 2020;17(1):13-18. doi:10.4314/jpb.v17i1.3
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13	Brimonidine	Patil A, Tagalpallewar A, Rasve G, Bendre A, Khapekar P. Formulation and Evaluation of Thermo-Sensitive In Situ Gel of Brimonidine Tartrate. *Int J Life Sci Pharma Res*. 2012;5(7):3597-3601.
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15	Loratadine	Vyshnavi V, Indira S, Prathima S. Formulation and Evaluation of Nasal Niosomal in situ Gels of Loratadine. *Int J Pharm Sci Drug Res*.2015;7(1):13-21.
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Conclusion:

Niosomal drug delivery system represent the alternative vesicular systems with respect to liposomes also having many advantages over liposomes like cost, stability etc. and characterize a promising drug delivery technology and much research has to be inspired in this to juice out all the potential in this novel drug delivery system. Most of the researchers and academicians refers niosomal drug delivery system because of its advantages over other drug delivery systems.

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