ISSN: 2754-4966

Journal of Nanosciences Research & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Niosomes As an Ideal Drug Delivery System

Vikram B Madane, Nagesh H Aloorkar and Vinod J Mokale*

Department of Pharmaceutics, Gourishankar Education Society's Satara College of Pharmacy, Satara, Maharashtra, India

ABSTRACT

Niosomes are a non-ionic spherical surfactant that is biodegradable, non-toxic, more durable, and cost effective as compare to liposomes. Through niosomes delivery of both hydrophilic and liophilic drug can be achieve very constructively. To achieve targeted drug delivery, drug binds to receptor site and then we can get the therapeutic action without attaching to other sites to prevent the undesirable or side effect of active pharmaceutical ingredient to the systemic circulation, hence niosomes is a very novel drug delivery system by which we can achieve very safe drug delivery at the site of action needed with high efficacy. In this review paper we try to compile all the information related with niosomes like introduction, structure, composition advantages, types, disadvantage, preparation methods, factor affecting, evaluation studies, applications of niosomes, difference between liposomes and niosomes, current available marketed formulation and patents, final conclusion and at last future perspective of niosomes.

***Corresponding author**

Dr. Vinod J Mokale, Department of Pharmaceutics, Gourishankar Education Society's Satara College of Pharmacy, Satara, Maharashtra, India. E-mail: drvjmscop@gmail.com

Received: July 31, 2021; **Accepted:** August 10, 2021; **Published:** August 30, 2021

Keywords: Composition of Niosomes, Types of Niosomes, Method of Preparation, Targeted Drug Delivery, Ideal Drug Delivery, Application, Evaluation etc.

Introduction

When Paul Ehrlich, a physicist, predicted a drug delivery system that would target diseased cells directly in 1909, he kicked off the production of targeted delivery. Since then, a variety of carriers such as serum proteins, immunoglobulins, synthetic polymers, liposomes, microspheres, erythrocytes, and niosomes have been used to transport drugs to the target organ/tissue [1]. Niosomes are a novel drug delivery mechanism that encapsulates the medication in a vesicle. Since the vesicle is made up of a bilayer of non-ionic surface-active agents, it is called a noisome [2].

Structure of Niosome

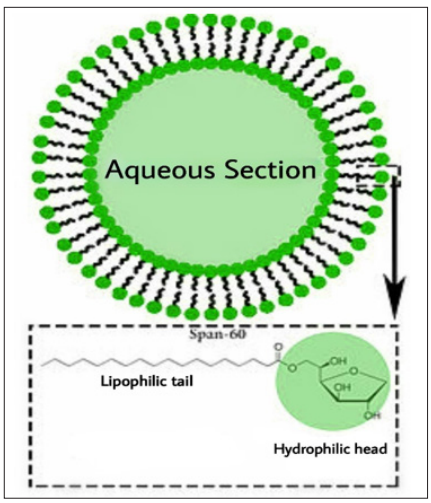


Figure 1: Strcture of niosomes

Composition of Niosomes- In the preparation of niosomes, two components is used:

1. Cholesterol
2. Non-ionic surfactants

A. Cholesterol have steroid like structure that provides stability and proper shape, as well as configuration to the niosome form.

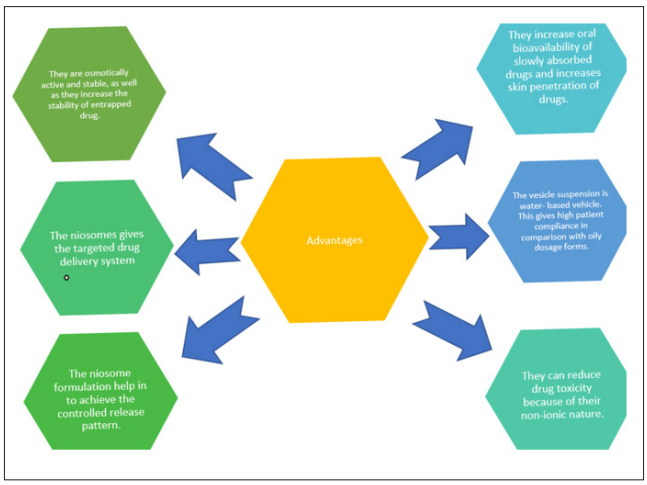
B. For the Manufacturing of niosomes, non-ionic surfactants are commonly used.

Examples: a. Tween 40, Tween 20, Tween 60, Tween 80

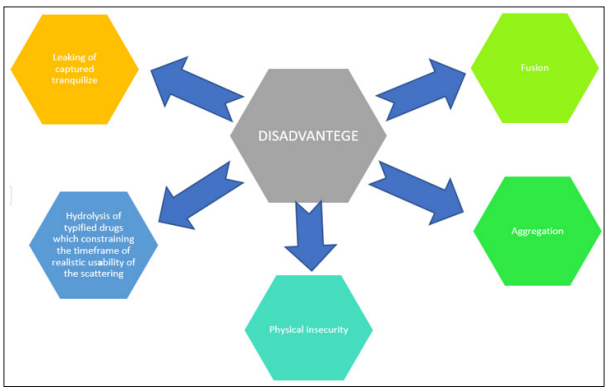
b. Span 80, Span 60, Span 40, Span 20, and Span 85

c. Brij 76, Brij 30, Brij 35, Brij 52, Brij 58, Brij 72[16],

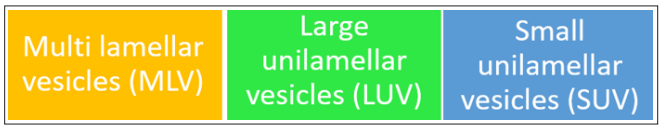
Advantages of Niosome [1-4].



Disadvantages of Niosome [14].



Types of Niosomes



Multilamellar Vesicles (MLV): The aqueous lipid compartment is surrounded by a number of bilayers. The diameter of these vesicles is approximately 0.5-10 µm. The most commonly used niosomes are multilamellar vesicles. It's easy to make and mechanically stable when held for a long time. Lipophilic compounds are well-suited to these vesicles as drug carriers.

Large Unilamellar Vesicles (LUV): This form of niosome has a high ratio of aqueous to lipid compartments, allowing for larger amounts of bioactive materials to be entrapped with minimal membrane lipid use.

Small Unilamellar Vesicles (SUV): The inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 dependent niosomes electrostatically stabilises these small unilamellar vesicles, which are mostly formulated by separating multilamellar vesicles sonication process.

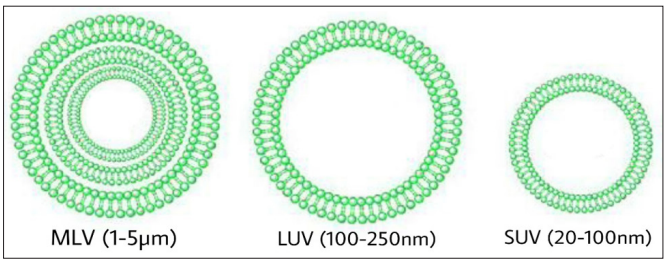
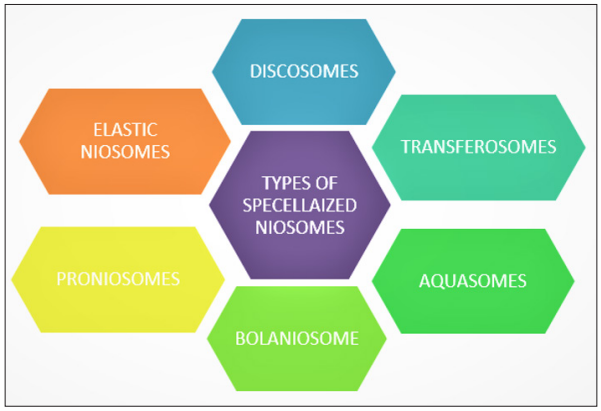


Figure 2: Types of Niosomes

Types of Specialized Niosomes



Proniosomes

Proniosomes are made by covering a water-soluble carrier with a Narrow layer of non-ionic surfactant. The water-soluble carriers used to make proniosomes must be non-toxic, clean, free-flowing, and have to allow for good water solubility for easy hydration. Proniosomes were made with sorbitol, maltodextrin, glucose monohydrate, mannitol, sucrose stearate, lactose monohydrate. Proniosomes come in a dry powder form and have many benefits over traditional niosomes, including greater durability, a lower likelihood of forming aggregates, and less drug leakage. Proniosomes can be made in a variety of ways, including slurry, slow spray coating, and coacervation phase separation. They come in two forms: dry granular proniosomes and liquid crystalline Proniosomes, depending on how they're produced.

Elastic Niosomes

Elastic niosomes are niosomes that are flexible enough to move through pores smaller than their size without losing their structure. Surfactants, cholesterol, water, and ethanol are all components of these vesicles. Because of their ability to move through small pores and thus increase penetration through the skin barrier, they are widely used in topical or transdermal drug delivery. Manosroi and colleagues produced elastic niosomes for transdermal delivery of diclofenac diethylammonium, which had a deformability index 14 times higher than standard niosomes, Another analysis by the same group of researchers discovered that elastic niosomes prepared with sodium cholate improved papain transdermal delivery for scar treatment.

Discomes

Discomes are niosomes that look like big discs. Uchegbu and colleagues previously used mechanical agitation and sonication to prepare discomes from hexadecyl diglycerol ether, cholesterol, and dicetyl phosphate. They discovered that discomes were wide (11–60 µm) and that their size increased after sonication. Discomes are also thermoresponsive; as the temperature rises above 37 °C, their structure becomes less coordinated. Abdelkader et al. looked at discomes for naltrexone ocular delivery in the treatment of diabetic keratopathy.

Bola Niosomes

Bola surfactants are used to make bola niosomes. In the early 1980s, this form of surfactant was discovered in the membrane of archaebacteria.They have two hydrophilic heads with one or two lipophilic linkers connecting them. Bola surfactants pusses the following Property a good assembling capacity, as evidenced by their much lower essential micelle concentration and higher surface tension than traditional surfactants, according to Zakharova (2010); further research revealed their tolerability in vitro and in vivo.

Transfersomes

Transfersomes are deformable vesicular carrier systems that self-assemble into a lipid bilayer in an aqueous environment and close to form a vesicle. To increase permeability, lipid bilayer flexibility and a lipid bilayer softening component is added. it is also called as an edge activator. An edge activator is a non-ionic single-chain surfactant that allows the lipid bilayer to destabilise, enhancing its fluidity and elasticity. Since transfersomes contain both hydrophilic and Lyophillic moieties, they can accept a wide variety of drug molecules. They have the ability to transport both low and high molecular weight drugs.

Aspasomes

Ascorbyl palmitate is a bilayer-forming substance that forms

vesicles with ascorbyl palmitate, cholesterol, and a lipid which Having Negative Charge (dicetyl phosphate).The film hydration method is used to make aspsomes, which is then sonicated. Aspasomes have been investigated for transdermal delivery of active ingredients, and it has been discovered that they can improve transdermal penetration through the skin barrier. Azidothymidine (AZT)-loaded aspasomes were developed by Gopinath and colleagues for topical application. AZT loaded in aspasomes had much higher transdermal permeation than AZT solution or ascorbyl palmitate aqueous dispersion. While no research has been done to establish the mechanism by which aspasomes enhance AZT permeation, it is possible that its lipophilicity causes it to partition into skin lipids, and its amphiphilic character alters the intercellular space, improving permeation.This research also discovered that after transforming ascorbyl palmitate into vesicles, the antioxidant potency of the ascorbyl moiety is preserved, and that aspasomes have significantly higher antioxidant activity than ascorbic acid. Aspasomes have been used in transdermal drug delivery mechanism due to their antioxidant and skin enhancing permeation properties [1,5,39-47].

Method of Preparation of Niosomes
Noisome can be prepared by the following method

Ether Injection Method
In this form, the surfactant is solubilise in diethyl ether to make a solution. This solution is then injected into warm water or an aqueous vehicle containing the drug at 60°C using a 14-gauge needle. The development of single-layered vesicles is caused by the vaporisation of ether. The particle size of the niosomes produced varies depending on the circumstances and may vary from 50 to 1000μm.

Hand Shaking Method
It is also called as a thin film hydration technique In a circular bottom flask, a mixture of cholesterol and surfactant is solubilise in a volatile organic solvent such as diethyl ether or chloroform. A rotary evaporator is used to vaporise the organic solvent at room temperature, leaving a narrow layer of solid mixture on the flask walls. After that, It is possible to rehydrate the dried surfactant film with the aqueous vehicle and gently agitated to produce multilamellar niosomes.

Reverse Phase Evaporation Technique (Rev)
Making a solution of surfactant and cholesterol (1:1) in a mixture of chloroform and ether is the first step in this process. This is then combined with an aqueous phase containing the drug to be loaded, and the two phases are sonicated at 4-5°C.After adding phosphate buffered saline, a clear gel is formed, which is then sonicated (PBS).To remove the organic process, the temperature is raised to 40°C and the pressure is reduced. This produces a viscous niosome suspension that can be diluted with PBS and heated for 10 minutes on a water bath at 60°C to yield niosomes.

Transmembrane pH Gradient Drug Uptake Process
In this step, a surfactant and cholesterol solution is made in chloroform. Similar to the hand shaking process, the solvent is then evaporated under reduced pressure to form a Narrow film on the wall of the round bottom flask. The film is then vortex mixed to hydrate it with citric acid solution. The resulting multilamellar vesicles are then sonicated after going through three freeze-thaw cycles. Aqueous solution containing 10mg/ml of medication is added to the niosomal suspension and vortexes. After adding 1M disodium phosphate to Increase the pH of the sample to 7.0-7.2, the mixture is intense at 140°C for 600 sec. to obtain the niosomes.

The "Bubble" Method
This system, which was recently developed, allows niosomes to be prepared without the use of organic solvents. The bubbling machine is made up of a round bottom flask with three necks that is placed in a water bath to keep the temperature constant. The first and second necks provide a water-cooled reflux and thermometer, while the third neck is used to supply nitrogen. At 158°F, surfactant and cholesterol are distributed in a buffer (pH 7.4). This dispersion is combined with a high shear homogenizer for 15 seconds before being bubbled at 158°F with nitrogen gas to produce niosomes.

Micro Fluidization
Micro fluidization is a new technique for making unilamellar vesicles with a specific size distribution.The submerged jet theory is used in this system, in which two fluidized streams interact at ultra-high velocities in precisely specified micro channels inside the interaction chamber. The impingement of a thin liquid layer along a common front is structured in such a way that the energy supplied to the device stays within the niosome formation area as a result, noisome is shaped with greater uniformity, smaller scale, and better reproducibility.

Multiple Membrane Extrusion Method
By evaporating a mixture of surfactant, cholesterol, and dicetyl phosphate in chloroform, a thin film is formed. The film is hydrous with an aqueous drug polycarbonate membrane solution, and the resulting suspension is extruded from which up to 8 passages can be mounted in sequence. It's a smart way to keep niosome size under control.

Sonication
The sonication of a solution is a popular method of producing vesicles. In this form, a 10 ml glass vial contains an aliquot of drug solution in buffer that is added to the surfactant/cholesterol mixture. To obtain niosomes, the mixture is probe sonicated at 140 °F for 180 sec. using a sonicator with a titanium probe.

Formation of Niosomes From Proniosomes
Another way to make niosomes is to use a surfactant to coat a water-soluble carrier like sorbitol.The coating process produces a dry formulation. A thin film of dry surfactant is applied to each water-soluble particle. "Proniosomes" is the name given to this preparation. The addition of aqueous phase at Temperature Gretter, followed by the mean phase transition temperature and brief agitation, is used to identify theniosomes. Niosomes are made from Proniosomes.

Separation of Unentrapped Drug
Various methods may be used to remove the unentrapped solute from the vesicles, including: -

1)Dialysis: Dialysis tubing is used to dialyze the aqueous niosomal dispersion against phosphate buffer, standard saline, or glucose solution.

2)Gel Filtration: Gel filtration of niosomal dispersion via a Sephadex-G -50 column and elution with phosphate buffered saline or regular saline removes the unentrapped drug.

3)Centrifugation: The supernatant is isolated from the niosomal suspension after centrifugation. To acquire a niosomal suspension free of unentrapped drug, the pellet is flow over and then resuspended [1-39].

Factor Affecting on Preparation of Niosomes

Nature of Surfactants

A surfactant for niosome preparation should have a aquaphilic head and a aquaphobic tail. One or two alkyl or perfluoroalkyl groups, or in some cases a single steroidal group, make up the hydrophobic tail. The hydrophobic tail of ether type surfactants with a single chain alkyl is more toxic than the dialkylether chain. Since ester-linked surfactants are degraded by esterases in vivo to triglycerides and fatty acids, the former is less toxic than the latter.Surfactants with alkyl chains ranging from C12 to C18 are ideal for making niosome.

Structure of Surfactants

The geometry of a surfactant vesicle is influenced by its structure, which is linked to important packing parameters. The geometry of the vesicle to be developed can be predicted using critical packing parameters of surfactants. The following equation can be used to determine critical packing parameters: CPP (Critical Packing Parameters) =v /lc* a0, where v denotes the volume of the hydrophobic group, lc denotes the critical length of the hydrophobic group, and a0 denotes the region of the hydrophilic head group. The type of miceller structure formed can be determined from the critical packing parameter value as shown below. If CPP is less than 12, spherical micelles form, if CPP is less than 12, bilayer micelles form, and if CPP is greater than 1, inverted micelles form.

Membrane Composition

Different additives, as well as surfactants and medications, may be used to make stable niosomes. Niosomes can have a variety of morphologies, and their permeability and stability properties can be changed by adjusting membrane properties with various additives. When a small amount of solulan C24 (cholesteryl poly-24-oxyethylene ether) is added to polyhedral niosomes made from C16G2, the shape of the polyhedral niosomes is not affected, preventing aggregation due to the formation of steric hindrance.

Nature of Encapsulated Drug

The charge and rigidity of the niosome bilayer are influenced by the physico-chemical properties of the encapsulated compound. The drug interacts with surfactant head groups, causing mutual repulsion between surfactant bilayers and thus increasing vesicle size.

Hydration Temperature

The shape and size of the obtrusive is influenced by the temperature of the hydration. It should be above the system's gel to liquid phase transition temperature for optimal results. The assembly of surfactants into vesicles is affected by temperature changes in the niosomal system, as well as vesicle shape transformation.

Surfactants

Entrapment efficiency of non-ionic surfactants is affected by chain length and hydrophilic head, for example, stearyl chain C18 non-ionic surfactant vesicles have higher entrapment efficiency than lauryl chain C12 non-ionic surfactant vesicles. For water soluble drugs, the tween series surfactants with a long alkyl chain and a large hydrophilic moiety in a 1:1 ratio with cholesterol have the highest entrapment performance. Entrapment efficiency is affected by the HLB value of surfactants; for example, HLB values of 14 to 17 are not ideal for niosomes, but HLB values of 8.6 have the highest entrapment efficiency, and entrapment efficiency decreases as HLB value decreases from 8.6 to 1.730.

Cholesterol Contents

The addition of cholesterol to the niosome's bilayer composition causes membrane stabilisation and reduces membrane leakiness. As a result, adding cholesterol to a bilayer improves entrapment effectiveness. The addition of cholesterol reduces the permeability of the vesicle bilayer to 5, 6-carboxy fluorescein (CF) by a factor of ten.

Effect of Drug Concentration

The drug entrapment efficiency of the niosome decreases as the drug concentration exceeds 50 mg.

Zeta Potential

The hydrophilicity of the surfactant increases the zeta potential value of the span formulation. This is due to the fact that the surface free energy of the span surfactant increases as the HLB value rises.

Effect of Osmotic Pressure

If addition of hypotonic solution into niosomal suspension may leads to the shrink of niosome and decrease diameter of niosome. Addition of hypertonic solution may lead to the swelling of niosome and fast release of the content take place.

Effect of Hydration Time

The hydration time selected should be optimum. If it is not optimum it may lead to the leakage of the niosome take place [2,13,48-56].

Evaluation of Niosomes or Characterization of Niosomes

Determination of Production Yield

Determination of production yield is done for determination of efficiency by using following formula: - Determination of production yield = Practical yield / Theoretical yield × 100

Actual Drug Content and Entrapment Efficiency

Actual drug content and efficiency done by Niosomes centrifugation, then free drug taking place in centrifugation technique, separated drug then use for spectroscopy technique for its confirmation

Infrared Spectroscopy

To check the functional group of drug, infrared spectroscopy is using to check any interaction between drug and additives through spectrogram.

Differential Scanning Colorimetry

Thermal analysis of pure drug, span 60, cholesterol and drug loaded niosomes carry out with a differential scanning calorimeter. Thermogram gives us idea about drug excipients.

Scanning Electron Microscopy

scanning electron microscopy gives us all the surface morphology information and also to find the physical morphology of individual particle by the scanning electron microscopy.

Transmission Electron Microscopy

Transmission electron microscopy done for to checking internal morphology, characteristics of niosomes. Transmission microscopy gives idea about the internal characteristics of our formulations.

Zeta Potential

The charges on the vesicular surface will be measured using the zeta potential apparatus at 25 °C using a combination of laser Doppler velocimetry and phase analysis light scattering. With

bidistilled water, GLM niosomes dispersions can dilute tenfold. At room temperature, the samples will be transferred to a quartz cuvette and weighed. All measurements will be done in triplicate, with the mean values and standard deviations recorded.

Particles Size Analysis
Total average particles size analysis will be carried out by using the particles size analyzers to know the actual average particle size of our formulation.

The In Vitro Permeation
Transdermal niosomal drug release pattern can be check by using different animal skins such as male albino rat, shed snake skin, Albino porcine ear, and male guinea pig in order to detect the absorption of drug. The in-vitro skin permeation studies were also carried out using Franz diffusion cell. The temperature of receptor phase was maintained at 37 ± 1 C throughout the experiment. At programmed time intervals, samples from the receptor compartment were taken to find the amount of drug permeated through the above declared various animal skins. Samples withdrawn were analysed Samples withdrawn were analysed spectrophotometrically.

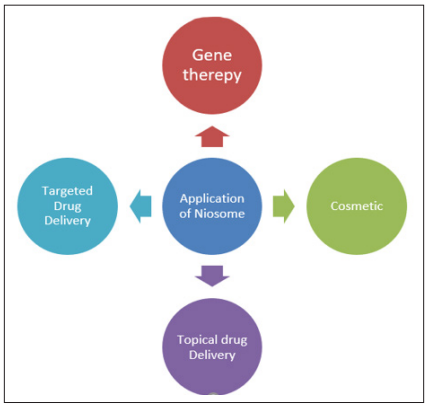
Stability Study
All niosomal formulations were exposed to stability studies by keeping at 4°C, 25°C and 37°C in thermostatic oven for the period of three months. After one month, drug content of all the formulations were analysed by using suitable method. In-vitro release studies of selected formulations can also be carried out to find the drug release pattern.

Osmotic Shrinkage
The osmotic shrinkage of vesicles can be monitored by measuring the reduction in vesicle diameter that occurs when a hypertonic salt solution is added to niosomal suspension. In comparison to vesicles containing cholesterol, niosomes prepared from pure surfactant are osmotically more sensitive, confirming the lipid's membrane stabilising activity.

Number of Lamellae
NMR spectroscopy, small angle X-ray spectroscopy and electron microscopy has been utilized for determination of number of lamellae.

Membrane Rigidity
The membrane rigidity of certain niosomal formulations has been determined using the mobility of a fluorescence probe as a function of temperature [6-10,15].

Niosomes As an Ideal Drug Delivery System or Application of Niosome Drug Delivery System [57-69].



Niosome As A Carrier for Haemoglobin
Niosomal suspension has a visible spectrum that is super imposable to that of free haemoglobin, allowing it to be used as a haemoglobin carrier. Vesicles are permeable to oxygen, and the dissociation curve of encapsulated haemoglobin can be altered similarly to that of non-encapsulated haemoglobin.

Ophthalmic Drug Delivery
Due to tear formation, corneal epithelium impermeability, non-productive absorption, and transient residence time, it is difficult to achieve excellent bioavailability of drugs in ocular dosage forms such as ophthalmic solution, suspension, and ointment. However, niosomal vesicular systems have been suggested to improve drug bioavailability. Multiple dosing with sodium stibogluconate loaded niosomes was found to be more effective against parasites in the liver, spleen, and bone marrow than a simple sodium stibogluconate solution, according to Carter et al.

Respiratory Drug Delivery
Researchers have been considering drug delivery through the respiratory system in recent years because it allows drugs to be targeted directly to the lung for both local and systemic care. Because of the high permeability and wide surface area of the alveolar zone, the pulmonary route is very interesting. Despite the advantages of pulmonary administration, there are some drawbacks, such as low inhalation system effectiveness, lower drug mass per puff, and poor drug formulation stability. Niosomes may be used to alleviate these issues, allowing for more efficient drug delivery to the respiratory tract. Until now, researchers have recommended various niosome formulations for drug delivery through the pulmonary route (Jatav et al., 2011; Moazeni et al., 2010). Proniosomes of the antiasthma steroid beclometasone dipropionate were created to produce niosomes that could be aerosolized using either an air-jet or a vibrating-mesh nebulizer (Elhissi et al., 2013).

Niosomal Drug Delivery for Cancer Therapy
New drug delivery systems are being developed to improve drug bioavailability while also reducing drug degradation and harmful side effects. Niosomes have been found to be a promising messenger. The majority of anticancer drugs have significant side effects. Niosomes can reduce drug side effects by causing improvements in metabolism (longer circulation and half-life). If built properly, niosomes containing anti-cancer drugs should be able to accumulate well within tumours. Paclitaxel (PCT) is an anticancer drug that has been successfully entrapped in a number of niosome formulations.

Niosmoal Drug Delivery for Gene Therapy
The success of gene therapy is highly dependent on the characteristics of the vector. Despite the fact that niosomes have been around for almost three decades, only a few studies have looked into their potential as gene delivery vectors. Niosomes have been used as a cutaneous gene delivery mechanism to treat a wide range of skin diseases (Geusens et al., 2011). To function as a vector, niosomes must be charged in their bilayer structure (Huang et al., 2011; Manosroi et al., 2008c). Basiri et al. designed negatively charged niosomes for gene delivery. For DNA (PUC18 supercoiled plasmid) complexation, niosomes were used in this analysis.

Niosomes As an Oral Drug Delivery System
For the oral drug administration, drugs deal with problems, such as acids and digestive enzymes in the stomach and small intestine, poor absorption, and inconstant bioavailability of drug. As a

result, drugs were administered using a new drug delivery system, such as niosomes, to increase bioavailability. Azmin et al. (1985) announced the first oral administration of niosome in a study involving the noisome containing methotrexate.

Niosome Having Role in Diagnostic Imagining

The niosomes carry iobitridol, a diagnostic agent used in X-ray imaging. These niosomes were made with, D-alpha tocopheryl polyethylene glycol 1000 succinate, polyoxyethylene glycol 4000 stearate sorbitan monostearate, and dicetylphosphate cholesterol, (Muller et al., 2000).Luciani and colleagues tested an MR imaging contrast agent for tumour detection based on a combination of polyethyleneglycol (PEG) and glucose conjugates to the surface of niosomes for the targeting of overexpressed glucose receptors. This niosomal method substantially enhanced tumour targeting of an encapsulated paramagnetic agent in a human carcinoma as measured by MR imaging (Luciani et al., 2004).

Niosomes Having Role in Antibody-Based Treatment

Immune niosomes are vesicles with antibodies attached to their surfaces that function as a potent adjuvant with high immunological selectivity, low toxicity, and long-term stability. Brewer and Alexander (1992) found that niosomes containing Leishmania major (ALM) have a mild impact in preventing cutaneous Leishmaniasis in BALB/c mice.).

Niosome Having Role in The Transdermal Drug Delivery System Drug delivery through the skin choose to keep drugs from having a first-pass effect on metabolism Ramkanth, S. a., et al. Invented the transdermal drug delivery mechanism for atenolol [6,11,12].

Difference Between Niosomes and Liposomes

Table 1: Difference Between Liposome and Niosomes

Formulation	Noisome	Liposomes
Components	Surfactant	Phospholipids
Components availability	High	Low
Component purity	Good	Variable
Preparation and storage	No specific condition required	Inert atmosphere, low temperature
Stability	Very Good	Low
Cost	Low	High

Route of Application of Niosomal Drug Delivery System

Table 2: Route of Niosomal Drug Delivery System

Route of administration	Example of drugs
Nasal Route	Sumatriptan
Transdermal Route	Piroxicam, Nimesulide, Estradiol
Intravenous Route	Doxorubicin, Insulin, Rifampicin
Ocular Route	Cyclopentol

Marketed Formulations of Niosomes

Table 3: Marketed formulation of Niosomes

SR.	Brand	Name of the product
1.	Lancôme-Foundation and complexation	Flash Retouch Brush on Concealer
2.	Britney Spears-Curious	Curious coffret: Edp Spray 100ml +Dualended Parfum & pink lipgoss + Body souffle 100 ml
3.	Loris Azzaro - Chrome	Chrome Eau De Toilette Spray 200 ml
4.	Orlane – Lipcolor and Lipstick	Lip Gloss

Patent Citation

Table 4: Patent of Niosomal Formulation [16-26]

Publication number.	Priority date.	Publication date.	Assignee.	Title.
US4873088A	06-09-1983	10-10-1989	Liposome Technology, Inc.	Liposome drug delivery method and composition.
US4891208A	10-04-1985	02-01-1990	The Liposome Company, Inc.	Steroidal liposomes.
US5741515A	20-10-1994	21-04-1998	Bayer Aktiengesellschaft	Ketoprofen liposomes
US6403056B1	21-03-1997	11-06-2002	Imarx Therapeutics, Inc.	Method for delivering bioactive agents using cochleates
US6428811B1	11-03-1998	06-08-2002	Wm. Marsh Rice University	Temperature-sensitive polymer/ nanoshell composites for photothermally modulated drug delivery
US20020143385A1	13-03-2000	03-10-2002	Jun Yang	Stent having cover with drug delivery capability

Expert Opinion on Niosome As Drug Delivery

Niosomes have a lot of potential for drug delivery, and their use in the near future may be very beneficial for a variety of pharmacological therapies and other applications. Given the above-mentioned characteristics of niosomes as drug carriers, they can be considered a viable alternative to liposomes.

Lancome was the first company to introduce a topic formulation to the market in 1987.These devices have cosmeceutical benefits. The development of niosomal nanotechnology is still in its early stages, and more research is needed to determine its significance in the pharmaceutical industry. Niosomes are a relatively new method, with just a few papers in the literature.

Just 4896 research papers on niosomes in drug delivery have been published since their introduction, according to Scopus, compared to 95705 for liposomes. Pharmaceutical researchers have used the flexibility and adaptability of easily adjusted and functionalized non-ionic surfactants to create new targeting instruments or with intrinsic stimuli-responsive properties in the majority of these studies.

The researchers intend to investigate their activity as anticancer carriers or for gene therapy applications. These studies, as well as our experience in the pharmaceutical industry, demonstrate the value of ingenuity and innovation in tailoring niosomes for specific therapeutic purposes. As a result, the multifunctionality of niosome drug delivery is beneficial to the development of personalised medicine.

So, given their significant disadvantages, why not fully substitute phospholipids in vesicular bilayers? The potential of niosomes has long been recognised in dermatological therapy; in fact, clinical trials for the treatment of acne, psoriasis, leishmaniasis, warts, and mucosal ulcers are currently underway. However, it would be ideal if the same enthusiasm was directed to other applications, such as diagnostics, therapeutics, and theragnostic devices.

That is why it is critical to focus new research on the development of novel and advanced surfactants capable of forming niosomal formulations that are suitable for preclinical testing before moving on to clinical trials.

Despite their resemblance to niosomes, liposomes, have unique properties that should be considered in order to increase the availability of more efficacious and less costly pharmaceutical formulations. The true potential of these vesicular systems should be fully considered, and it will be necessary to devote more financial resources to their research soon [70-72].

Conclusion

Niosomes have been proposed as a replacement for liposomes. In contrast to liposomes, they have some advantages, such as improved chemical stability, increased purity, and a lower cost. The drugs, metabolism, plasma clearance kinetics, tissue distribution and cellular interaction are all affected by non-ionic surfactant vesicles.

Hence by going through all the advancements of niosomes over all other formulations or drug delivery systems, niosomes showing their safety and efficacy as an ideal drug delivery system to achieve better patient compliance.

Future Prospects

Niosomes are a type of drug delivery molecule that is capable of delivering drugs safely having specific site targeting property. There is a lot of potential in niosomes for encapsulating toxic anti-cancer drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory drugs, anti-viral drugs, and other drugs and using them as drug carriers to improve bioavailability and targeting properties while reducing toxicity and side effects. Ionic drug carriers are harmful and unsuitable, whereas niosomal drug carriers are less so. The handling and storage of niosomes do not necessitate any special conditions.

Hence there is a vast scope for the researcher to research niosomes in their particular area of research for the betterment of society.

Decleration of Interest

The authors announce that the work presented in this article has not been inflected by existing competing financial interests or personal ties.

References

1. Madhav N VS, Saini A (2011) Niosomes: a novel drug delivery system. International journal of research in pharmacy and chemistry 1: 498-511.
2. Makeshwar KB, Wasankar SR (2013) Niosome: a novel drug delivery system. Asian J. Pharm. Res 3: 16-20.
3. Mujoriya R, Bodla RB, Dhamande K, Singh D, Patle L (2011) Niosomal drug delivery system: The magic bullet. J Appl Pharm Sci 1: 20-23.
4. Gyati Shilakari Asthana, Parveen Kumar Sharma, Abhay Asthana (2016) In Vitro and In Vivo Evaluation of Niosomal Formulation for Controlled Delivery of Clarithromycin, Hindawi Publishing Corporation Scientifica 2016Article ID 6492953, 1-10.
5. Chen S, Hanning S, Falconer J, Locke M, Wen, J (2019) Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications. European Journal of Pharmaceutics and Biopharmaceutics 144:18-39.
6. Ramkanth S, Chetty CM, Sudhakar Y, Thiruvengadarajan VS, Anitha P et al. (2018) Development, characterization & invivo evaluation of proniosomal based transdermal delivery system of Atenolol. Future Journal of Pharmaceutical Sciences 4: 80-87.
7. Muzzalupo R, Tavano L, Cassano R, Trombino S, Ferrarelli T, et al. (2011) A new approach for the evaluation of niosomes as effective transdermal drug delivery systems. European Journal of Pharmaceutics and Biopharmaceutics 79: 28-35.
8. Rajesh Z Mujoriya, Kishor Dhamande, Dr Ramesh Babu Bodla (2011) Niosomal Drug Delivery System – A Review, International Journal of Applied Pharmaceutics 3: 7-10.
9. Mujoriya RZ, Bodla R (2011) Niosomes–challenge in preparation for pharmaceutical scientist. Int J App Pharm 3: 11-15
10. Rajera R, Nagpal K, Singh SK, Mishra DN (2011) Niosomes: a controlled and novel drug delivery system. Biological and Pharmaceutical Bulletin 34: 945-953.
11. Khoee S, Yaghoobian M (2017) Niosomes: A novel approach in modern drug delivery systems. In Nanostructures for drug delivery. Elsevier p207-237.
12. K Venkata, ramanareddy, Sravani K, Vaishnavi STP, Srilatha U et al. (2014) Factors Affecting in Formation of Niosomes, Indo American Journal of Pharmaceutical Research 4: 2087-2092.
13. Vinod Mokale, Komal Patil, Tousif Khatik, Y Sutar et al. (2014) Glyburide nanosuspension: Influence of processing and formulation parameter on solubility and in vitro dissolution behaviour, Asian Journal of Pharmaceutics 7: 111-117.
14. Mohsen AM, abousamra MM, elshebiney SA (2017) Enhanced oral bioavailability and sustained delivery of glimepiride via niosomal encapsulation: in-vitro characterization and in-vivo evaluation. Drug development and industrial pharmacy 43: 1254-1264.
15. Kaur Dhanvir, Kumar Sandeep (2018) Niosomes: Present Scenario and Future Aspects. Journal of Drug Delivery & Therapeutics 8: 35-43.
16. Gopalakrishnan S, Chenthilnathan A (2012) Niosomes—a novel drug delivery device. Research Journal of Pharmaceutical, Biological and Chemical Sciences 3: 1090-1098.
17. Yeo PL, Lim CL, Chye SM, Ling APK, Koh RY (2018) Niosomes: a review of their structure, properties, methods of preparation, and medical applications. Asian Biomedicine 11: 301-314.
18. Singh S (2013) Niosomes: A role in targeted drug delivery system. International Journal of Pharmaceutical Sciences and Research 4: 550.
19. Sharma BS, Bhogale V, Adepu A R, Patil ST, Sangha S K (2015) Proniosomes: A Novel Provesicular Drug Delivery

System. International Journal for Pharmaceutical Research Scholars 4: 2.
20. Gadhiya P, Shukla S, Modi D, Bharadia, P (2012) A Review-Niosomes in Targeted Drug Delivery. International Journal for Pharmaceutical Research Scholars 2: 61.
21. Patel SM, Rathod DR, Patel KN, Patel BA, Patel P A (2012) Niosome As an Effective Drug Delivery: A Review. International Journal for Pharmaceutical Research Scholars (IJPRS) 1: 2.
22. Verma NK, Roshan A (2014) Niosomes and its application: A Review. IJRPLS, 2: 182-184.
23. Gupta R, Kumar S, Gupta N, Kumar A (2014) The New Advavancement Nanotechnology: Proniosomes As A Promising and Potential Drug Carrier. International Journal of Research and Development in Pharmacy & Life Sciences 3: 1258-1265.
24. Gupta R, Kumar S, Gupta N, Kumar A (2014) The New Advavancement Nanotechnology: Proniosomes As A Promising and Potential Drug Carrier. International Journal of Research and Development in Pharmacy & Life Sciences 3: 1258-1265.
25. Kaur D, Kumar S (2018) Niosomes: present scenario and future aspects. Journal of drug delivery and therapeutics 8(5): 35-43.
26. Pawar SD, Pawar RG, Kodag PP, Waghmare AS (2012) Niosome: an unique drug delivery system. International journal of biology, pharmacy and allied sciences 3: 406-16
27. Baillie AJ, Coombs GH, Dolan TF, Laurie J (1986) Non-ionic surfactant vesicles, niosomes, as a delivery system for the anti-leishmanial drug, sodium stibogluconate. Journal of pharmacy and pharmacology 38: 502-505.
28. Khandare JN, Madhavi G, Tamhankar BM (1994) Niosomes-Novel Drug Delivery System. Eastern Pharmacist 37: 61-61.
29. Naresh RR, Pillai GK, Udupa N, Chandrashekar G (1994) Anti-inflammatory activity of niosome encapsulated diclofenac sodium in arthritic rats. Indian Journal of Pharmacology 26: 46-48.
30. Rogerson ACJWNFAT, Cummings J, Willmott N, Florence AT (1988) The distribution of doxorubicin in mice following administration in niosomes. Journal of pharmacy and pharmacology 40: 337-342.
31. Baillie AJ, Coombs GH, Dolan TF, Laurie J (1986) Non-ionic surfactant vesicles, niosomes, as a delivery system for the anti-leishmanial drug, sodium stibogluconate. Journal of pharmacy and pharmacology 38: 502-505.
32. Mayer LD, Bally MB, Hope MJ, Cullis PR (1985) Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. Biochimica et Biophysica Acta (BBA)-Biomembranes 816: 294-302.
33. Arunachalam A, Jeganath S, Yamini K, Tharangini K (2012) Niosomes: a novel drug delivery system. International journal of novel trends in pharmaceutical sciences 2: 25-31.
34. Blazek–Welsh AI, Rhodes DG (2001) SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharmaceutical research 18: 656-661.
35. Chauhan S, Luorence MJ (1989) The preparation of polyoxyethylene containing non-ionic surfactant vesicles. J. Pharm. Pharmacol 41(6).
36. Yoshioka T, Sternberg B, Florence AT (1994) Preparation and properties of vesicles (niosomes) of sorbitan monoesters (Span 20, 40, 60 and 80) and a sorbitan triester (Span 85). International journal of pharmaceutics 105: 1-6.
37. Devi SG, Udupa N (2000) Niosomal sumatriptan succinate for nasal administration. Indian Journal of Pharmaceutical Sciences 62: 479-481.
38. Hu C, Rhodes DG (1999) Proniosomes: a novel drug carrier preparation. International journal of pharmaceutics 185: 23-35.
39. Ibrahim MM, Shehata TM (2012) The enhancement of transdermal permeability of water-soluble drug by niosome-emulgel combination. Journal of drug delivery science and technology 22:353-359.
40. Manosroi A, Jantrawut P, Manosroi J (2008) Anti-inflammatory activity of gel containing novel elastic niosomes entrapped with diclofenac diethylammonium. International journal of pharmaceutics 360: 156-163.
41. Manosroi A, Chankhampan C, Manosroi W, Manosroi J (2013) Transdermal absorption enhancement of papain loaded in elastic niosomes incorporated in gel for scar treatment. European Journal of Pharmaceutical Sciences 48: 474-483.
42. Abdelkader H, Ismail S, Kamal A, Alany RG (2011) Design and evaluation of controlled-release niosomes and discomes for naltrexone hydrochloride ocular delivery. Journal of pharmaceutical sciences 100: 1833-1846.
43. Abdelkader H, Wu Z, Al-Kassas R, Alany RG (2012) Niosomes and discomes for ocular delivery of naltrexone hydrochloride: morphological, rheological, spreading properties and photo-protective effects. International journal of pharmaceutics 433: 142-148.
44. Paolino D, Cosco D, Muzzalupo R, Trapasso E, Picci N, et al. (2008) Innovative bola-surfactant niosomes as topical delivery systems of 5-fluorouracil for the treatment of skin cancer. International journal of Pharmaceutics 353: 233-242.
45. Vinod Mokale, Bharti Khatumaria, Umakant Verma, Navin Shimpi, Jitnedra Naik Satyendra Mishra (2014) Formulation and Development of Nanoparticles for Quick and Complete Release of Hydrochlorothiazide by Nanonization Technique, Micro and Nanosystems. Colloids and Surfaces B: Biointerfaces 6: 109-117
46. Gopinath D, Ravi D, Rao BR, Apte SS, Renuka D, et al. (2004) Ascorbyl palmitate vesicles (Aspasomes): formation, characterization and applications. International journal of pharmaceutics 271:95-113.
47. Bhaskaran S, Panigrahi L (2002) Formulation and evaluation of niosomes using different non-ionic surfactants. Indian journal of pharmaceutical sciences 64:63.
48. Arunothayanun P, Bernard MS, Craig DQM, Uchegbu I F, Florence A T (2000) The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. International journal of pharmaceutics, 201: 7-14.
49. Uchegbu IF, Vyas SP (1998) Non-ionic surfactant-based vesicles (niosomes) in drug delivery. International journal of pharmaceutics 172: 33-70.
50. Uchegbu IF, Florence AT (1995) Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Advances in colloid and interface science 58: 1-55.
51. Manosroi A, Wongtrakul P, Manosroi J, Sakai H, Sugawara F, et al. (2003) Characterization of vesicles prepared with various non-ionic surfactants mixed with cholesterol. Colloids and Surfaces B: Biointerfaces 30: 129-138.
52. Balasubramaniam A, Anil Kumar V, Sadasivan Pillai K (2002) Formulation and in vivo evaluation of niosome-encapsulated daunorubicin hydrochloride. Drug development and industrial pharmacy 28: 1181-1193.
53. Shahiwala A, Misra A (2002) Studies in topical application of niosomally entrapped nimesulide. Journal of pharmacy and pharmaceutical sciences 5: 220-225.
54. Rogerson A, Cummings J, Florence AT (1987) Adriamycin-loaded niosomes: drug entrapment, stability and release.

Journal of microencapsulation 4: 321-328.
55. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, et al. (2010) Niosome: a future of targeted drug delivery systems. Journal of advanced pharmaceutical technology & research 1: 374.
56. Saraswathi TS, Mothilal M, Jaganathan MK (2019) Niosomes as an emerging formulation tool for drug delivery-a review. Int J App Pharm 11: 7-15.
57. Ge X, Wei M, He S, Yuan W E (2019) Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery. Pharmaceutics 11: 55.
58. Mazzotta E, Rossi CO, Muzzalupo R (2019) Different BRIJ97 colloid systems as potential enhancers of acyclovir skin permeation and depot. Colloids and Surfaces B: Biointerfaces 173: 623-631.
59. De A, Venkatesh N, Senthil M, Sanapalli BKR, Shanmugham R, et al. (2018) Smart niosomes of temozolomide for enhancement of brain targeting. Nanobiomedicine 5: 1849543518805355.
60. Imran M, Shah MR, Ullah F, Ullah S, Elhissi AM, et al. (2016) Sugar-based novel niosomal nanocarrier system for enhanced oral bioavailability of levofloxacin. Drug Delivery, 23: 3653-3664.
61. Pereira MC, Pianella M, Wei D, Moshnikova A, Marianecci C, Carafa M, Reshetnyak, Y. K. (2016). Ph-sensitive phlip® coated niosomes. Molecular membrane biology, 33(3-5), 51-63.
62. Masotti A, Vicennati P, Alisi A, Marianecci C, Rinaldi F, et al. (2010) Novel Tween® 20 derivatives enable the formation of efficient ph-sensitive drug delivery vehicles for human hepatoblastoma. Bioorganic & medicinal chemistry letters, 20: 3021-3025.
63. Pengnam S, Patrojanasophon P, Rojanarata T, Ngawhirunpat T, Yingyongnarongkul B E, Radchatawedchakoon W, Opanasopit P (2019) A novel plier-like gemini cationic niosome for nucleic acid delivery. Journal of Drug Delivery Science and Technology 52: 325-333.
64. Yang C, Gao S, Song P, Dagnæs-Hansen F, Jakobsen M, et al. (2018) Theranostic niosomes for efficient sirna/microrna delivery and activatable near-infrared fluorescent tracking of stem cells. ACS applied materials & interfaces 10: 19494-19503. Pinazo A, Pons R, Perez L (2011) Amino acids as raw material for biocompatible surfactants. Ind Eng Chem Res. 50: 4805-4817.
65. Tavano L, Mazzotta E, Muzzalupo R (2018) Innovative topical formulations from diclofenac sodium used as surfadrug: The birth of Diclosomes. Colloids and Surfaces B: Biointerfaces 164: 177-184.
66. Muzzalupo R, Tavano L, La Mesa C (2013) Alkyl glucopyranoside-based niosomes containing methotrexate for pharmaceutical applications: Evaluation of physico-chemical and biological properties. International journal of pharmaceutics 458: 224-229.
67. Tavano L, Muzzalupo R (2016) Multi-functional vesicles for cancer therapy: the ultimate magic bullet. Colloids and Surfaces B: Biointerfaces, 147: 161-171.
68. Vulgaris A (2017) A survey to compare the efficacy of niosomal erythromycin alone versus combination of erythromycin and zinc acetate in the treatment of Acne vulgaris. Journal of Kerman University of Medical Sciences, 24: 420-430.
69. Lakshmi PK, Bhaskaran S (2011) Phase II study of topical niosomal urea gel-an adjuvant in the treatment of psoriasis. Int J Pharm Sci Rev Res 7: 1-7.
70. Farajzadeh S, Ahmadi R, Mohammadi S, Pardakhty A, Khalili M, et al. (2018) Evaluation of the efficacy of intralesional Glucantime plus niosomal zinc sulphate in comparison with intralesional Glucantime plus cryotherapy in the treatment of acute cutaneous leishmaniasis, a randomized clinical trial. Journal of Parasitic Diseases 42: 616-620.
71. Farajzadeh S, Pardakhti A, Mohammadi S, Fadaei F, Khalili M, et al. (2018) A randomized clinical trial of using niosomal zinc sulfate plus cryotherapy in comparison with placebo along with cryotherapy in treatment of common wart. Journal of Kerman University of Medical Sciences 25: 1-8.
72. Arafa MG, Ghalwash D, El-Kersh DM, Elmazar MM (2018) Propolis-based niosomes as oromuco-adhesive films: A randomized clinical trial of a therapeutic drug delivery platform for the treatment of oral recurrent aphthous ulcers. Scientific reports 8: 1-14.