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Niosomes as Modern Drug Carrier Systems: Concepts and Advancements

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ABSTRACT

Drug delivery systems are formulations that convey medicine to the target site of action inside the body. A good carrier protects the medicine from being broken down or removed quickly, resulting in higher drug concentration in the target tissues. Because of their biodegradability, biocompatibility, and non-immunogenic character, niosomes, which are formed by the self-association of non-ionic surfactants and cholesterol in an aqueous phase, are prospective drug carriers. In recent years, several study articles have been published in scientific publications describing the capacity of niosomes to function as a carrier for the delivery of different types of drugs. The present study examines niosomal drug delivery systems' manufacturing processes, characterization methodologies, and latest research, as well as offering up-to-date information on novel niosomal drug delivery applications.

Key Words: Niosomes, Vesicular drug delivery system, Components, Applications, Characterizations, Preparation methods

INTRODUCTION [1,2]

Medication administration at a controlled pace and with targeted distribution has received a lot of attention in recent years. The use of nanotechnology in medicine has resulted in the development of multifunctional nanoparticles that can be loaded with a variety of drugs and used as drug carriers. Nanocarriers have properties such as drug protection against degradation and cleavage, controlled release, and, in the case of targeted delivery systems, drug molecule distribution to the target regions. Niosomes, which have a bilayer structure and are produced by self-association of non-ionic surfactants and cholesterol in an aqueous phase, are one of the most promising drug carriers. Niosomes are biocompatible, non-immunogenic, and biodegradable. They have a long shelf life, are very stable, and enable controlled and/or continuous drug administration at the target site. In recent years, there has been a lot of investigation into the possibility of niosomes as a drug carrier. Niosomes are produced by a variety of non-ionic surfactants, allowing a wide range of drugs with differing solubilities to be entrapped. The composition, size, number of lamellae, and surface charge of niosomes may all be modified and tweaked to increase drug delivery performance. The purpose of this research is to present an overview of niosome manufacture and characterization, as

well as a description of their use in drug administration, with an emphasis on more recent studies. The purpose of this research is to provide an overview of the rising interest in niosomes as medication delivery vehicles.

STRUCTURE AND COMPONENTS OF NIOSOMES [3-5]

The major components of niosomes include nonionic surfactants, hydration medium, and lipids such as cholesterol. Hexadecyl diglycerol ether (C16G2), Bola, Brij 30/52/72/76/78, Tween 20/40/60/80/65/85/20, Span 20/40/60/80/65/85, octyl-decyl polyglucoside (OrCG110), BRM-BG surfactant, stearyl alcohol, decyl polyglucoside, myristyl alcohol, cetyl alcohol, palmitic acid, stearic acid, Pluronic L64/105, myristic acid, phosphatidic acid, diacetyl phosphate, dihexadec, lipoamino acid, etc. In aquatic settings, nonionic surfactants self-assemble to create closed bilayer structures (Figure 1). Water and the hydrophobic tails of the amphiphile create an interfacial tension that encourages them to interact. The hydrophilic termini of the non-ionic surfactant point outwards and come into contact with water due to steric and hydrophilic repulsion between the non-ionic surfactant's head groups. Closing bilayers usually requires

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some type of energy input, such as mechanical or thermal. Niosomes are classified into three groups depending on their bilayer structure and size. Multilayer vesicles include SUVs (small unilamellar vesicles) (10–100 nm), LUVs (large unilamellar vesicles) (100–3000 nm), and MLVs (multilamellar vesicles).

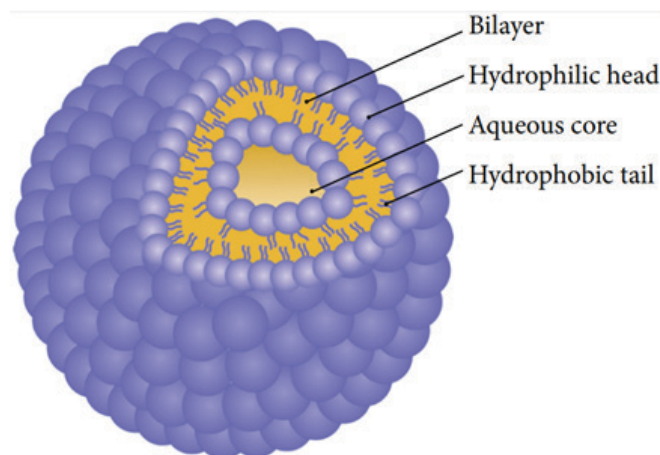


Figure 1: Structure of niosomes.

Non-ionic Surfactants

Non-ionic surfactants are those that have no charged groups in their hydrophilic heads. They are more stable, biocompatible, and less dangerous than anionic, amphoteric, or cationic counterparts. As a consequence, they are preferred for the generation of stable niosomes *in vitro* and *in vivo*. Non-ionic surfactants are amphiphilic molecules having two separate hydrophilic (water-soluble) and hydrophobic (water-insoluble) regions (organic-soluble). Alkyl ethers, alkyl esters, alkyl amides, and fatty acids are the most common non-ionic surfactant classes used in niosome production. The hydrophilic-lipophilic balance (HLB) and critical packing parameter (CPP) values are vital in the choosing of surfactant molecules for niosome synthesis.

Hydrophilic-Lipophilic Balance

The Hydrophilic-Lipophilic Balance (HLB) is a dimensionless indicator of the solubility of a surfactant molecule. The HLB value represents the balance between the hydrophilic and lipophilic components of the non-ionic surfactant. The HLB range for non-ionic surfactants is 0 to 20. The lower the HLB, the more lipophilic the surfactant is, and the higher the HLB, the more hydrophilic the surfactant is. Surfactants with an HLB of 4 to 8 may be used to produce vesicles. Hydrophilic surfactants with an HLB value of 14 to 17 are not suitable for producing a bilayer membrane due to their high water solubility. When the right quantity of cholesterol is added, Polysorbate 80 (HLB value = 15) and Tween 20 (HLB value = 16.7) do form niosomes. Tween 20 forms permanent niosomes in the presence of equimolar cholesterol concentrations. The hydrophobic region of the amphiphile

next to the head group interacts with the 3-OH group of cholesterol in an equimolar ratio, which might explain cholesterol's influence on Tween 20 niosomal membrane formation and hydration behaviour. The drug entrapment effectiveness of niosomes is affected by the surfactant's HLB value. Using the lipid film hydration approach, researchers were able to incorporate nimesulide into niosomes by changing the HLB. When the surfactant's HLB value reduces from 8.6 to 1.7, entrapment efficiency decreases.

Critical Packing Parameter (CPP)

During niosomal preparation, the critical packing parameter controls the form of the vesicle. The CPP of a surfactant may be used to anticipate the shape of nanostructures formed by self-assembly of amphiphilic molecules. The symmetry of the surfactant determines the critical packing parameter, which may be computed using the equation below:

$$CPP = \frac{v}{lc \times a_0}$$

where v is the volume of the hydrophobic group, lc is the critical length of the hydrophobic group, and a_0 is the area of the hydrophilic head group. Small hydrophobic tail spherical micelles may develop if $CPP \leq 1/3$, which corresponds to a bulky head group, for example. Non-spherical micelles may form if $1/3 \leq CPP \leq 1/2$, while bilayer vesicles may form if $1/2 \leq CPP \leq 1$. Inverted micelles form when a surfactant has a large hydrophobic tail and a tiny voluminous tail ($CPP \geq 1$). In amphiphilic fluids, CPP may be used to see, rationalize, and predict self-assembled structures and their morphological changes.

Cholesterol

Cholesterol establishes hydrogen bonds with the hydrophilic head of a surfactant in the bilayer structure of niosomes. The amount of cholesterol in niosomes affects their structure and physical features such as entrapment efficiency, long-term stability, payload release, and biostability. Cholesterol enhances vesicle rigidity and protects niosomes from the destabilizing effects of plasma and serum components, as well as decreasing vesicle permeability for encapsulated compounds, limiting leakage. Drug entrapment efficiency is critical in niosomal formulations, and it may be altered by adjusting the cholesterol content. Studies have shown that increasing cholesterol content improves the stability of enoxacin-loaded niosomes, resulting in enhanced entrapment efficiency. Researchers looked into the effect of cholesterol on flurbiprofen entrapment and found that cholesterol had very little effect on flurbiprofen entrapment in Span 20 and Span 80 niosomes. However, when 10% cholesterol was added to niosomes produced from Span 40 and Span 60, flurbiprofen entrapment efficiency improved significantly, followed by a

decrease when the cholesterol content was raised further. The amount of cholesterol added and how much is added should be modified depending on the physical-chemical characteristics of surfactants and loaded medications, according to the results.

Charged Molecule

The addition of charged groups to the vesicle bilayer by charged molecules improves the vesicle's stability. By raising the surface charge density of vesicles, they prevent them from aggregating. Negatively charged compounds like dicetyl phosphate and phosphatidic acid, as well as positively charged molecules like stearylamine and stearyl pyridinium chloride, are often used in niosomal preparations. In most cases, the charged molecule is introduced to the niosomal formulation at a concentration of 2.5–5 mol%. Increasing the quantity of charged molecules, on the other hand, may hinder the formation of niosomes.

METHODS OF PREPARATION [6-8]

Thin-Film Hydration Method

A well-known and simple method of preparation is thin-film hydration. This approach involves dissolving surfactants, cholesterol, and other additions such as charged molecules in an organic solvent in a round-bottomed flask. A revolving vacuum evaporator is then used to evaporate the organic solvent, leaving a thin coating on the flask's inner wall. The dry film is hydrated above the surfactant's transition temperature (T_c) for a preset duration with continuous shaking after the aqueous drug solution is introduced. Multilamellar niosomes are created using this method.

Ether Injection Method

The surfactants with additives are dissolved in diethyl ether and slowly injected via a needle into an aqueous drug solution kept at a steady temperature above the organic solvent's boiling point in the ether injection method. The organic solvent is evaporated using a rotary evaporator. During the vaporisation process, single-layered vesicles are created.

Reverse Phase Evaporation Method

In this procedure, niosomal components are dissolved in a mixture of ether and chloroform before being added to an aqueous phase containing the drug. After the mixture has been sonicated to generate an emulsion, the organic phase is evaporated. Large unilamellar vesicles form during the evaporation of the organic solvent.

Microfluidization Method

The microfluidization approach employs the submerged jet idea. In this technology, the drug and surfactant fluidized

streams interact at ultrahigh velocities in precisely defined microchannels within the interaction chamber. The high-speed collision and the energy involved cause niosomes to develop. This approach gives superior homogeneity, smaller size, unilamellar vesicles, and high reproducibility in the creation of niosomes.

Supercritical Carbon Dioxide Fluid

The technique of niosome synthesis using supercritical reverse-phase evaporation was described. Tween 61, cholesterol, glucose, PBS, and ethanol were introduced into the view cell, followed by CO₂. After magnetic churning until equilibrium was attained, the pressure was released, and niosomal dispersions were formed. Simple scale-up and one-step production are possible with this method.

Proniosome

In the proniosome approach, a water-soluble carrier, such as sorbitol or mannitol, is coated with surfactant. As a result of the coating procedure, a dry formulation is generated. Proniosomes is the name of this preparation, and it must be hydrated before use. The production of niosomes is caused by the presence of the aqueous phase. This approach, as compared to standard niosomes, lowers physical stability difficulties including aggregation, leakage, and fusing while also making dosage, distribution, transportation, and storage easier.

Transmembrane pH Gradient

In this process, surfactant and cholesterol are dissolved in chloroform and evaporated to produce a thin lipid layer on the flask's wall. The film is hydrated with a citric acid solution (pH = 4) and then freeze-thawed for niosome synthesis using vortex mixing. The aqueous solution of the medication is mixed with the niosomal suspension, then phosphate buffer is added to maintain the pH between 7.0 and 7.2. According to this method, the niosome's core has a lower pH than the surrounding medium. After passing through the niosome membrane, the extra unionized medicine enters the niosome. The drug ionizes in an acidic environment and is unable to pass through the niosomal bilayer.

Heating Method

Surfactants and cholesterol are hydrated separately in a separate buffer, then heated to 120°C with stirring to dissolve cholesterol. While stirring continues, the temperature is lowered, and surfactants and other chemicals are introduced to the buffer in which the cholesterol is dissolved. This procedure produces niosomes, which are then allowed to cool to room temperature before being kept in a nitrogen atmosphere at 4–5°C until required.

Bubble Method

Surfactants, additives, and the buffer are all packed into a

three-necked glass flask in this procedure. With the aid of a homogenizer, the components of niosomes are dispersed and blended at 70°C. After that, the flask is put in a water bath and nitrogen gas is bubbled at 70°C. When nitrogen gas is passed over a sample of homogenised surfactants, large unilamellar vesicles develop.

CHARACTERIZATION OF NIOSOMES [9-11]

Characterization of niosomes is crucial for therapeutic applications. Characterization criteria have a direct effect on the stability of niosomes, and they also have a significant impact on their in vivo performance. As a consequence, properties such as form, size, polydispersity index (PI), number of lamellae, zeta potential, encapsulation efficiency, and stability must be evaluated.

Size and Morphology

Dynamic light scattering (DLS), scanning electron microscopy (SEM), transmission electron microscopy (TEM), frozen fracture replication electron microscopy (FF-TEM), and cryotransmission electron microscopy are the most used methods for measuring niosome sizes and shape (cryo-TEM). At the same time, DLS provides essential information on the solution's homogeneity as well as cumulative particle size information. The existence of a single scatterer population is indicated by a single sharp peak in the DLS profile. The PI is advantageous in this sense. A value of less than 0.3 indicates a homogenous population in colloidal systems. Microscopic approaches are often used to characterize the morphology of niosomes.

Zeta Potential

The surface zeta potential of niosomes may be measured using the zetasizer and DLS devices. A niosome's surface charge has a big influence on how it behaves. In general, charged niosomes are less prone to aggregation than uncharged vesicles. Researchers created paclitaxel-loaded niosomes and investigated their physicochemical properties, including as zeta potential. Niosome electrostatic stabilisation was shown to be sufficient at negative zeta potential values ranging from -41.7 mV to -58.4 mV.

Bilayer Characterization

The bilayer characteristics of niosomes have an impact on drug entrapment efficacy. AFM, NMR, and small-angle X-ray scattering (SAXS) may all be used to count the number of lamellae in multilamellar vesicles. The membrane stiffness of niosomal formulations may be determined by measuring the mobility of a fluorescent probe as a function of temperature. DPH (1,6 diphenyl-1,3,5-hexatriene), which is added to niosomal dispersion, is the most often used fluorescent probe. DPH is frequently present in the hydrophobic

portion of a bilayer membrane. The microviscosity of the niosomal membrane is determined by fluorescence polarisation. A high membrane microviscosity is shown by strong fluorescence polarisation. Furthermore, the bilayer thickness may be estimated using the latter approach in combination with in situ energy-dispersive X-ray diffraction (EDXD).

Entrapment Efficiency

Entrapment efficiency is the proportion of the applied drug that is caught by the niosomes (EE percent). To separate un-encapsulated free medicine from the niosomal solution, centrifugation, dialysis, or gel chromatography may be utilised. The loaded medicine may be liberated from niosomes by disintegrating vesicles following this procedure. Niosomal suspensions with 0.1 percent Triton X-100 or methanol may be killed. To determine the loaded and free drug concentrations, a spectrophotometer or high-performance liquid chromatography may be utilized (HPLC).

Stability

The stability of niosomes may be determined by observing the mean vesicle size, size distribution, and entrapment efficiency over a long period of time at different temperatures. Throughout storage, niosomes are collected at regular intervals, and the percentage of medicine maintained in the niosomes is evaluated using UV spectroscopy or HPLC procedures.

In vitro Release

The use of dialysis tubing to evaluate in vitro release is a popular method. After cleaning, a dialysis bag is submerged in distilled water. After 30 minutes, the drug-loaded niosomal suspension is placed in this bag. The bag containing the vesicles is immersed in buffer solution and agitated continually at 25°C or 37°C. At predefined intervals, samples were removed from the outer buffer (release medium) and replaced with the equal quantity of fresh buffer. The drug content of the samples is determined using an appropriate test method.

NIOSOMES AS DRUG CARRIERS [12-15]

Niosomes have been found to be efficient transporters of a wide range of pharmacological and diagnostic compounds. A number of studies have discussed the creation, characterization, and use of niosomes as drug carriers. Because of their non-ionic nature, they have a high biocompatibility and low toxicity. Niosomes may be utilised to develop innovative drug delivery systems that can load both hydrophilic and lipophilic drugs due to their unique structure. Hydrophilic and lipophilic drugs are imprisoned in the watery core and membrane bilayer of the niosome, respectively (Figure 2).

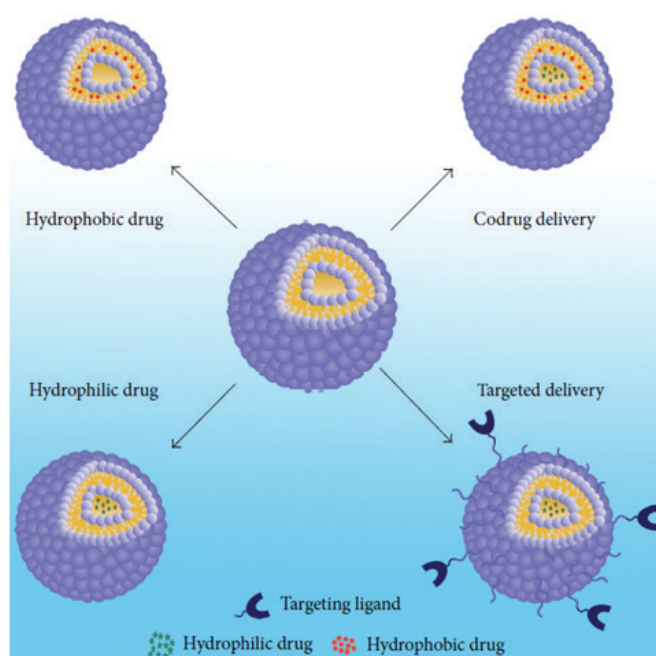


Figure 2: Applications of niosomes in modern drug delivery.

Anti-cancer Drug Delivery

The most prevalent cancer treatment is chemotherapy. The therapeutic efficacy of many anti-cancer drugs is limited by their failure to enter tumor tissue and their substantial side effects on healthy cells. To overcome these constraints, other ways have been tried, including the use of niosomes as a novel drug delivery route:

Melanoma

Artemisone is an anti-malarial and anti-cancer 10-amino-artemisinin derivative. Artemisone was encapsulated in niosomes using a thin-film hydration method. The formulations showed highly specific cytotoxicity against melanoma cells while causing negligible harm in healthy skin cells. 5-fluorouracil (5-FU) was encapsulated in a novel bola-niosomal system made up of, -hexadecyl-bis-(1-aza-18-crown-6) (bola-surfactant), Span 80, and cholesterol to treat different types of skin malignancies. Human stratum corneum and epidermal membranes were used to investigate the percutaneous penetration of 5-FU-loaded bola-niosomes. When compared to a free drug aqueous solution, bola-niosomes boosted drug penetration by 8 and 4 times, respectively. The use of cisplatin is limited because of its severe toxicity. The anti-metastatic effectiveness of niosomal cisplatin was investigated in an experimental metastatic type of B16F10 melanoma using Span 60 and cholesterol. Their results show that cisplatin encapsulated in niosomes has significant anti-metastatic activity and decreased toxicity when compared to free cisplatin.

Breast Cancer

Experiments were carried out on breast cancer cell lines using

5-FU-loaded polyethylene glycol-coated and -uncoated bola-niosomes (MCF7 and T47D). Both bola-niosome formulations had a higher cytotoxic effect than the free medicine. In vivo investigations on MCF-7 xenograft tumour SCID mouse models demonstrated that the PEGylated niosomal 5-FU exhibited more effective anti-cancer action at a dosage ten times lower (8 mg/kg) than the free medicine (80 mg/kg) after 30 days of treatment. Cantharidin-entrapped niosomes were created using the injection procedure. Their capacity to boost the drug's anti-cancer effects while decreasing its toxicity was evaluated on the human breast cancer cell line MCF-7. In addition, the efficacy of in vivo therapy in S180 tumor-bearing mice was investigated. The anti-cancer activity of mice given 1.0 mg/kg niosomal cantharidin was 52.76 percent, which was significantly higher than the anti-cancer activity of animals given the same dose of free cantharidin (1.0 mg/kg, 31.05 percent). Tamoxifen citrate niosomes were recently created for localised cancer therapy utilising a film hydration approach, as shown by in vitro breast cancer cytotoxicity and in vivo solid anti-tumor efficiency. The enhanced niosomal formulation of tamoxifen showed significantly greater cellular absorption (2.8-fold) and considerably stronger cytotoxic effect in the MCF-7 breast cancer cell line. In vivo research showed that niosomal tamoxifen reduced tumors volume more than free tamoxifen.

Ovarian Cancer

Doxorubicin-containing niosomes were developed. A human ovarian cancer cell line and its doxorubicin-resistant subline were studied using doxorubicin in hexadecyl diglycerol ether (C16G2) and Span 60 niosomes. According to the research, the IC50 against the resistant cell line was somewhat lower when the medication was encapsulated in Span 60 niosomes compared to the free drug in solution.

Lung Cancer

Using monoalkyl triglycerol ether to encapsulate adriamycin into the niosome, the activity of niosomal adriamycin was compared to free adriamycin solution on human lung tumour cells cultured in monolayer and spheroid culture, as well as tumour xenografted nude mice. Adriamycin (15 days) and niosomal adriamycin (11 days) took much longer than control to double tumour volume (5.8 days). Administering adriamycin in niosomal form might potentially boost the therapeutic ratio even further. Another study produced pentoxifylline-loaded niosomes using the lipid film hydration method. In an experimental metastatic B16F10 mouse, intravenous treatment with niosomal pentoxifylline (6 mg/kg and 10 mg/kg) resulted in a substantial decrease in lung nodules, suggesting accumulation of pentoxifylline in a distant target. The number of tumour islands in the lungs was reduced after light microscopic examination of histologic sections.

Targeted Delivery

Through utilising a ligand attached to the surface of niosomes that may be actively taken up, for example, by receptor-mediated endocytosis, active targeting for tumour treatment may increase the efficiency and particularly the specificity of cellular targeting of niosomal drug delivery systems. To offer cell-specific targeting, niosome surfaces may be coupled with small molecules and/or macromolecular targeting ligands. The most often utilised compounds that bind selectively to an overexpressed target on the cell surface include proteins and peptides, polysaccharides, aptamers, antibodies, and antibody fragments. A glucose derivative was used as a targeting ligand in a brain-targeted niosomal formulation developed by researchers. They developed niosomal doxorubicin, which has the following components: N-palmitoylglucosamine is an N-palmitoylglucosamine solulan. Preliminary in vivo studies in rats showed that intravenous administration of a single dose of the developed targeted-niosomal formulation reduced heart accumulation of the drug and kept it in the blood circulation longer, as well as achieved well detectable doxorubicin brain concentrations, compared to the commercial formulation. A tumor-targeted niosomal delivery system was also created by the researchers. Niosomes were created using a mixture of Pluronic L64 surfactant and cholesterol, with doxorubicin encapsulated within. After synthesis, EDC (N-[3-(dimethylamino) propyl]-N-ethylcarbodiimide hydrochloride) chemistry was used to link transferrin to the surface of niosomes. In MCF-7 and MDA-MB-231 tumor cell lines, doxorubicin-loaded niosomes were shown to have anti-cancer action, with a significant reduction in viability evident in a dose and time-dependent manner.

Co-drug Delivery

In recent years, nanoparticles have emerged as a possible class of carriers for the administration of many drugs in combination therapy. Combination therapies boost therapeutic efficacy and minimise dosage while maintaining or enhancing efficacy and reducing drug resistance. Anti-cancer drugs can cause serious side effects. Studies found that adopting a multidrug delivery system increased anti-cancer activity for carcinoma cells when compared to free drug treatment, but it lowered cytotoxicity against endothelial cells and cardiomyocytes. They developed a simultaneous anti-cancer medication and nitric oxide transport system in which nitric oxide and epirubicin were covalently conjugated to each PEG terminal. Nitric oxide is an anti-cancer medication sensitizer and a protective reagent against anthracycline-induced cardiomyopathy. To strengthen the anti-cancer efficacy and cardiocyte-protecting capacities of the co-delivery technique, they used branched PEG instead of linear PEG as the polymer backbone. Multidrug resistance (MDR) of malignant neoplasm refers to the ability of cancer cells to withstand treat-

ment with structurally and functionally diverse anti-cancer medications. Increased drug efflux is predominantly caused by ATP-driven extrusion pump proteins of the ATP-binding cassette (ABC) superfamily, such as P-glycoprotein (P-gp) encoded by MDR1, multidrug resistance (MDR) proteins (MRPs/ABCC), and breast cancer resistance protein (BCRP/ABCG2). These drug efflux pumps drastically lower the intracellular concentrations of some medical medications. P-gp antagonists, such as Verapamil, Elacridar, Tariquidar, and Cyclosporine A, decrease drug efflux and restore chemosensitivity in MDR cancer cells. Paclitaxel was co-encapsulated with cyclosporine A in active-targeted polymeric lipid-core micelles. When P-gp was suppressed by cyclosporine A, paclitaxel cytotoxicity increased. In MDCKII-MDR1 cells, micellars having this dual cargo produced much higher cytotoxicity than micellars containing just paclitaxel. Niosomes are a possible nanocarrier in multidrug delivery applications. The utilisation of niosomes to encapsulate both hydrophobic curcumin and hydrophilic doxorubicin for cancer therapeutic delivery was recently disclosed. When compared to free pharmaceuticals, dual-drug-loaded niosomes showed greater cytotoxicity on HeLa cells, according to the findings. Gallic acid, ascorbic acid, curcumin, and quercetin were encapsulated into niosomes as single agents or in combination in another study, and the effect of co-encapsulation on the carriers' physicochemical properties, anti-oxidant properties, and ability to release the encapsulated materials were assessed. Lidocaine and ibuprofen were also employed to create, define, and administer multidrug niosomes. When both drugs are supplied dermally at the same time in the same pharmaceutical formulation, the results lead to the potential use of niosomes as carriers for the treatment of many skin conditions, including acute and chronic inflammations in the presence of pain.

Antibiotics

Niosomal carriers may also be used to deliver antibiotics and anti-inflammatory medicines. These carriers have been extensively used to promote medicine retention in the skin and improve poor skin penetration. Rifampicin was developed as a broad-spectrum antibiotic encapsulated in a niosomal delivery method. They put the system to the test in vitro, and the findings showed that a rifampicin niosomal formulation could offer consistent and long-lasting drug release. To improve anti-biotic efficiency and reduce dose, researchers employed the film hydration process to make ciprofloxacin-loaded niosomes with various non-ionic surfactants and cholesterol concentrations. The antibacterial activity of niosomes was examined, as well as drug release through bilayers. Cholesterol concentration and surfactant phase transition temperature were shown to have an impact on niosome performance. Furthermore, all formulations had stronger antibacterial activity than free ciprofloxacin. Vesicular systems, niosomes, and liposomes are often used in ocular-controlled

administration. Researchers looked at whether niosomes may be employed as a carrier for ocular-controlled gentamicin delivery. In different molar ratios, different surfactants (Tween 60/80 or Brij 35) were mixed with cholesterol and the negative charge inducer dicetyl phosphate. The ability of these vesicles to entrap the desired drug was investigated, and it was discovered that cholesterol content, surfactant type, and the presence of a charge inducer all had an impact on gentamicin entrapment efficiency and release rate. The Tween 60, cholesterol, and dicetyl phosphate-based gentamicin-loaded niosomes that extended in vitro drug release the best were those constructed of Tween 60, cholesterol, and dicetyl phosphate.

Anti-Inflammatory Drugs

A number of research institutions have developed NSAID-loaded niosomes. Mucosal inflammation is one of the possible negative effects of these drugs. Topically applied NSAID-loaded niosomes may improve drug penetration considerably. To see whether niosomes might be used to deliver anti-inflammatory drugs, researchers made ammonium glycyrrhizinate (AG) loaded niosomes with various surfactants and cholesterol concentrations. Researchers looked at drug

entrapment efficiency, anisotropy, cytotoxicity, and skin tolerability, among other things, for characterisation. The AG-loaded niosomes were shown to have no toxicity and were able to improve anti-inflammatory activity in animals with good skin tolerance. Furthermore, the anti-inflammatory effectiveness of the niosome-delivered medicine was improved in people with chemically induced cutaneous erythema.

Anti-viral Drugs

Antiviral drugs have also been shown to be delivered via niosomes. The researchers encased niosomes in zidovudine, the first anti-HIV medicine approved for clinical use, and studied their entrapment efficiency as well as their release sustainability. The niosomes were made by combining Tween, Span, and cholesterol amounts. Zidovudine was collected in substantial amounts by niosomes produced from Tween 80, and the addition of dicetyl phosphate extended drug release. When niosomes were stored at 4°C for 90 days, medication leakage from Tween 80 formulations left at room temperature was considerable. Tween 80 formulations containing dicetyl phosphate were similarly removed from the blood in rabbits after five hours, according to the findings of a pharmacokinetic investigation.

Table 1. Recent studies on niosomes drug delivery systems.

Drug	Composition	Experimental model
Candesartan cilexetil	Span 60, cholesterol, dicetyl phosphate, maltodextrin	In vitro dissolution test for proniosomal tablets, in vivo evaluation of proniosomal tablets, and pharmacokinetic analysis
Cefixime	C-Glycoside derivative surfactant, cholesterol	In vitro release study, biocompatibility, and bioavailability studies using experimental animals
Dexamethasone	Span 60, cholesterol	Characterization of niosomes, in vitro release studies, and stability test
Doxorubicin	Span 60, cholesterol, dicetyl phosphate, N-lauryl glucosamine	Optimization studies for the formulation, skin irritancy, and histopathological investigation of rat skin
Famotidine	Span 60, cholesterol	Kinetic analysis of drug-release profiles and ex vivo permeability study
Moxifloxacin	Tween 60, cholesterol	In vitro release studies and antimicrobial activity
Naproxen	Tween 80, Tween 20, cholesterol	In vitro drug release study and preformulation study
Nevirapine	Tyloxapol, cholesterol	Diffusion kinetics of drug, microviscosity studies, and in vitro release study
Paclitaxel	Span 40, cholesterol, dicetyl phosphate	Formulation studies, Pharmacokinetic, and tissue distribution studies

RECENT STUDIES [16-18]

During the past three decades, niosomes have been successfully used as drug carriers to solve various critical biopharmaceutical challenges including as insolubility, adverse effects, and poor chemical stability of medicinal compounds.

STRENGTHS AND LIMITATIONS [19,20]

One of the most notable benefits of niosomes over liposomes is chemical stability. Niosomes are more resistant to chemical degradation or oxidation than liposomes and have longer storage duration. Biodegradable, biocompatible, and non-immunogenic surfactants are used in the creation of niosomes. There are no guidelines for surfactant handling and storage. Furthermore, the composition, size, lamellarity, stability, and surface charge of niosomes may be affected by the kind of manufacturing procedure, surfactant, cholesterol content, surface charge additions, and suspension concentration. Niosomes, on the other hand, have problems with physical stability. During storage, niosomes in dispersion are vulnerable to aggregation, fusion, drug leakage, and hydrolysis of encapsulated medications. Furthermore, sterilizing niosomes is a time-consuming process. Heat sterilization and membrane filtration are not suitable for niosomes. As a consequence, further research in these areas is required in order to generate commercially viable niosomal preparations.

CONCLUSION

Niosomes are a novel kind of nano-drug carrier that might be exploited to develop more effective medication delivery systems. They're a great approach to load both hydrophilic and lipophilic medications at the same time. Various types of niosomes have been used in the delivery of anti-cancer, anti-inflammatory, and anti-infective medications, among other things, in many studies. According to the study, niosomes improve the stability of the entrapped medicine, reduce the dose, and enable targeted delivery to a specific kind of tissue. Novel niosome preparations, loading, and modification strategies for particular administration routes may help to enhance structural characteristics and qualities. As a consequence, niosomes seem to be promising therapeutic tools in commercially available treatments.

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CONFLICT OF INTEREST

The authors declare no Conflict of Interest regarding the publication of the article.

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