ISSN- 2230-7346
Journal of Global Trends in Pharmaceutical Sciences

NIOSOMES IN MODERN DRUG DELIVERY: A MULTIFUNCTIONAL AND VERSATILE NANOCARRIER SYSTEM FOR TARGETED THERAPEUTICS

Patnala Vaishnavi Gayathri*, Mamindla Chandrika, B. Rashmitha, Bikkannagari Harivardhan, Thotla Thanvika Yadav, Algola Vamshi Krishna

Department of Pharmaceutics, Pulla Reddy Institute of Pharmacy, affiliated with Jawaharlal Nehru Technological University, Dundigal, Hyderabad, Telangana, India, 502313.

***Corresponding author E-mail:** vaishnavigayathri21@gmail.com

ARTICLE INFO

Key words:
Niosomes, Nanocarriers, Drug Delivery Systems, Nanoparticles, Nanomedicine, Surface-Active Agents, Drug Carriers, Vesicular Drug Delivery, Non-ionic Surfactants, Site-Specific Delivery, Controlled Release Systems.

Access this article online
Website:
https://www.jgtps.com/
Quick Response Code:

ABSTRACT

Nanotechnology has accelerated the development of drug delivery methods, with niosomes emerging as a promising type of non-ionic surfactant-based vesicular carriers. Niosomes are bilayered vesicles made of synthetic non-ionic surfactants and cholesterol that have high biocompatibility, stability, and a non-immunogenic profile. Their structural plasticity enables the encapsulation of both hydrophilic and lipophilic compounds, allowing for regulated and targeted drug release while minimising systemic toxicity.

This paper summarises the underlying principles that drive niosome formation, including important physicochemical characteristics such as the hydrophilic-lipophilic balance (HLB) and the critical packing parameter (CPP). This study examines how several preparation processes, including thin-film hydration, ether injection, reverse-phase evaporation, microfluidization, and the supercritical CO_2 process, affect vesicle size, lamellarity, and encapsulation efficiency. DLS, SEM, TEM, zeta potential analysis, and in vitro release experiments are used to investigate structural and functional stability.

The article also highlights the therapeutic potential of niosomes in a variety of pharmacological domains, including oncology, virology, and targeted therapy. Notable uses in anticancer therapy, brain targeting, and multidrug administration highlight niosomes' potential to change traditional therapeutic paradigms. Furthermore, their role in diagnostic imaging, vaccine delivery, and cosmetic compositions demonstrates their multidisciplinary utility.

Overall, this study highlights niosomes as a resilient and versatile nanocarrier platform with important implications in precision medicine, as well as a prospective area for next-generation drug delivery techniques.

1.0 INTRODUCTION

In recent years, there has been a lot of interest in drug delivery at a controlled rate and with a focused approach. The use of nanotechnology in medicine has resulted in the development of multifunctional nanoparticles that can be loaded with a variety of medications. Nanocarriers offer a potential method to drug delivery, including drug protection from degradation and cleavage, controlled release, and, in the case of targeted delivery systems, delivery of drug molecules to target areas **(1).** Niosomes are one of the promising drug carriers that have a bilayer structure and are generated by self-association of nonionic surfactants and cholesterol in an aqueous phase. Niosomes are biodegradable, biocompatible, and nonimmunogenic. They have a long shelf life, great stability, and can administer drugs to target sites in a regulated and sustained manner **(2).** In recent years, the efficacy of niosomes as a drug delivery system has been thoroughly investigated **(3-5).** According to reports, a variety of nonionic

surfactant types can create niosomes and allow for the entrapment of numerous drugs with a broad range of solubility **(6-8).** The effectiveness of niosomes for drug delivery can be improved by adjusting and optimising their size, composition, number of lamellae, and surface charge.

This article provides an overview of niosome manufacture and characterisation, as well as its usage in drug delivery, with a focus on recent investigations. This paper explores the increasing interest in niosomes for drug delivery.

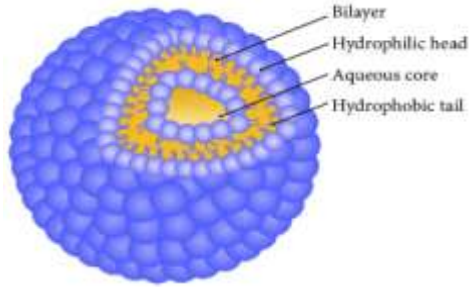

Figure 1. Structure of Niosomes.

2.0 FACTORS LEADING TO NIOSOME FORMATION: The self-assembly of amphiphilic molecules into closed bilayers, as seen in liposomes and niosomes, is not spontaneous, but requires some energy input, such as physical shaking (hand shaking, ultrasound, heat, etc.) **(9,10).** Thermodynamically stable vesicles require specific combinations of surfactants and charge-inducing chemicals. Previous studies indicate that niosomes are more resistant to micellar solubilization than liposomes **(11,12).** However, both types of vesicles arise from identical sources. Amphiphile self-assembly is primarily influenced by thermodynamic and physicochemical parameters, including the hydrophilic-lipophilic balance (HLB) and geometric features of the molecules. However, other factors such as aqueous interlayer, lipid chain length, chain-packing, and membrane asymmetry also play a role in vesicle formation. The energy needed to produce vesicles with amphiphilic molecules comes from three sources: surface energy, mechanical energy from overpressure, and excess chemical potential. When non-ionic surfactant monomers are hydrated, they form vesicles due to the high interfacial tension between water and the hydrophobic groups of the amphiphile.

Figure 2. Factors Influencing Niosomal Formation.

The steric, hydrophilic, and/or ionic repulsion of the head groups assures their interaction with water. Temperature and monomer concentration are critical factors in vesicle formation. Self-assembly overcomes negative entropy (ΔS) and reduced free energy (ΔG) through favourable enthalpy (ΔH) contributions from van der Waals attractions, hydrophobic forces, hydrogen bond formation, and screened electrostatic interactions. As previously stated, vesicle production may be determined by the HLB value; consequently, the advice provided by the HLB number is valuable in evaluating novel classes of chemicals for their potential to form vesicles. An HLB value ranging from 4 to 8 was shown to be compatible with vesicle formation while using sorbitan monostearate surfactants **(13).** Hydrophilic surfactants cannot form free hydrated units (vesicles) due to their high water solubility. Instead, they aggregate and agglomerate to create lamellar structures **(14,15).** Surfactants with an HLB value between 14 and 17 do not often generate niosomes **(16)**, while surfactants with an HLB value around 10 require the presence of cholesterol for vesicle production **(17).** The geometric feature of the single vesicle-forming unit may also play a role in defining the type of aggregation generated in aquatic conditions **(18).** Several years ago, a hydrophobic effect was postulated to explain the behaviour of non-ionic surfactants in water, increasing global system-free energy. The surfactant molecule's nominal geometric properties can

accurately predict the shape of spontaneously produced association colloids. Israelachvili et al. (1976) **(19)** identified the critical packing parameter (CPP, commonly known as Ps) as the following relation:

$CPP = V / a_0 l_c$

Where: V is the tail volume of the molecule,

- a_0 is the surface area per molecule at the hydrocarbon–water interface,
- l_c is the critical, i.e. the greatest, span of a fluid molecular chain in an aggregate.

The CPP value determines the shape and size of the equilibrium aggregate, which can range from spherical micelles (CPP ≤ 1/3) to cylindrical micelles (1/3 ≤ CPP ≤ ½), bilayers (1/2 ≤ CPP ≤ 1), or inverse micelles (CPP N 1). A comparison of Polysorbates (Tw) 21 and 20 with the same alkyl chain (dodecanoic acid) but different hydrophilic head groups (Tw21:4 PEG units; Tw20:20 PEG units) confirmed the impact of polar head surface, a0, on the ability to form vesicles **(20).** This also influenced the HLB value (Tw20: 16.7; Tw21: 13.3). Cevc **(21)** found that analysing amphiphile aggregation using standard molecular descriptors (e.g. CPP or HLB number) may not accurately predict bilayer vesicle production due to their static nature. A new predictor for bilayer vesicle production and deformability has been proposed: the effective area per lipid chain (cross-section of a "tail"), which appears to correlate almost exponentially. An Ac value above 0.43 nm2 indicates a micellar structure, while a value slightly lower indicates bilayer vesicle production. Amphiphiles with smaller chain areas (Ac ≪ 0.43 nm2) create multilamellar structures. Assigning absolute values to geometric or chemical properties is inaccurate and misleading. This is due to the sensitivity of molecular and geometric descriptors to boundary conditions, component combinations, and experimental conditions during surfactant vesicle production. To accurately anticipate the ability of amphiphilic molecules to assemble into bilayer vesicles, it's important to regard all provided factors as changeable.

3.0 METHODS OF PREPARATION:

3.1 Thin-Film Hydration Method (TFH): The thin-film hydration method is a straightforward and well-known preparation method. This process involves dissolving surfactants, cholesterol, and charged molecules in an organic solvent in a round-bottomed flask. The organic solvent is evaporated using a rotating vacuum evaporator, resulting in a thin layer on the inside wall of the flask.

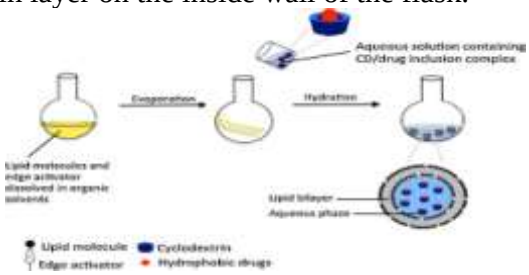

Figure 3. Thin-Film Hydration Method.

To hydrate the dry film, add an aqueous drug solution and shake continuously above the surfactant's transition temperature (Tc) for a given duration **(22,23).** This approach produces multilamellar niosomes.

3.2 Ether Injection Method (EIM)

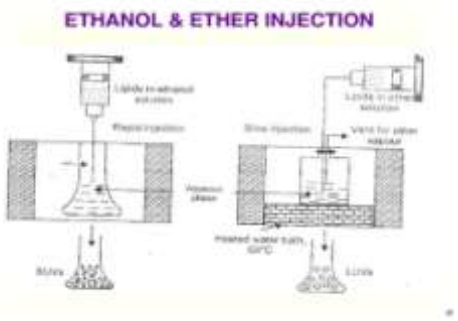

Figure 4. Ether Injection Method.

The ether injection method involves dissolving surfactants and additives in diethyl ether and slowly injecting them through a needle into an aqueous drug solution at a temperature above the organic solvent's boiling point. An organic solvent is evaporated using a rotary evaporator. Vaporisation leads to the production of single-layered vesicles **(24-26).**

3.3 Reverse Phase Evaporation Method (REV): This process involves dissolving niosomal components in ether and chloroform before adding them to an aqueous phase containing the medication. The mixture is sonicated to create an emulsion, and the organic phase is then evaporated. The evaporation of an organic solvent creates large unilamellar vesicles **(27-29).**

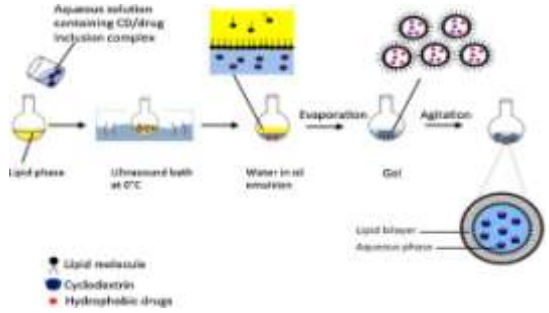

Figure 5. Reverse Phase Evaporation Method.

3.4 Micro fluidization Method

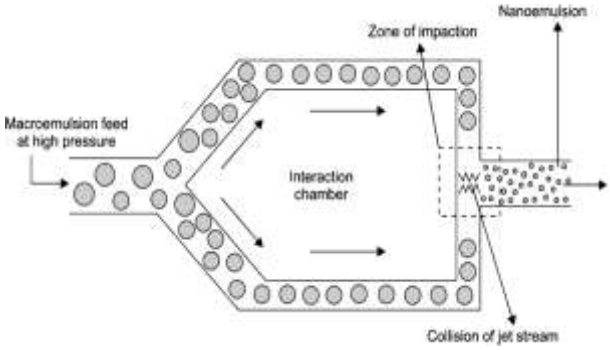

Figure 6. Microfluidization Method.

The microfluidization process is based on the submerged jet principle. In this technology, the drug and surfactant fluidised streams interact at high speeds in precisely specified microchannels within the interaction chamber. The high-speed impingement and energy involved cause the production of niosomes. This approach produces homogenous, tiny, unilamellar vesicles with remarkable reproducibility for niosome formulation **(30,31).**

3.5 Supercritical Carbon Dioxide Fluid ($scCO_2$): Manosroi et al. developed the supercritical reverse phase evaporation approach for niosome production **(32, 33).** The view cell was treated with Tween 61, cholesterol, glucose, PBS, and ethanol before being exposed to CO2. Niosomal dispersions were created by releasing pressure after achieving equilibrium through magnetic stirring **(32).** This technology allows for one-step production and easy scale-up. The proniosome approach involves covering a water-soluble carrier, such as sorbitol or mannitol, with surfactants. The coating procedure creates a dry formulation. Niosomes are generated with the addition of the aqueous phase.

3.6 Proniosome:

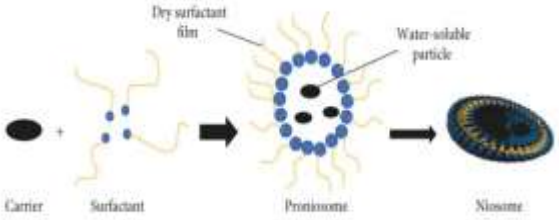

Figure 7. Proniosome

This approach reduces physical stability issues including aggregation, leakage, and fusing, while also providing convenience for dosage, distribution, transportation, and storage, with better results than traditional niosomes **(34).**

3.7 Transmembrane pH Gradient: This process involves dissolving surfactant and cholesterol in chloroform, which is then evaporated to create a thin lipid layer on the wall of a round flask. To create niosomes, the film is hydrated with a citric acid (pH = 4) solution through vortex mixing and then freeze-thawed. To prepare the niosomal suspension, add an aqueous drug solution followed by phosphate buffer to maintain a pH range of 7.0-7.2 **(35).** This approach indicates that the inside of niosomes has a lower pH than the outside medium. The unionised substance enters the niosome after passing through its membrane. The medication ionises in an acidic solution and cannot pass through the niosomal bilayer **(36).**

3.8 Heating Method: Mozafari et al. **(37, 38)** developed a patented method in which surfactants and cholesterol are separately hydrated in buffer and heated to 120°C with stirring to dissolve cholesterol. The temperature is then reduced, and surfactants and other additives are added to the buffer while stirring continues. Niosomes form at this stage and are kept at 4-5°C under nitrogen **(39).**

3.9 The "Bubble" Method: This method involves adding surfactants, additives, and buffer to a three-necked glass flask. Niosome components are disseminated at 70°C and combined using a homogeniser. After that, place the flask in a water bath and bubble nitrogen gas at 70°C. Nitrogen gas passes through a sample of homogenized surfactants, forming enormous unilamellar vesicles **(40).**

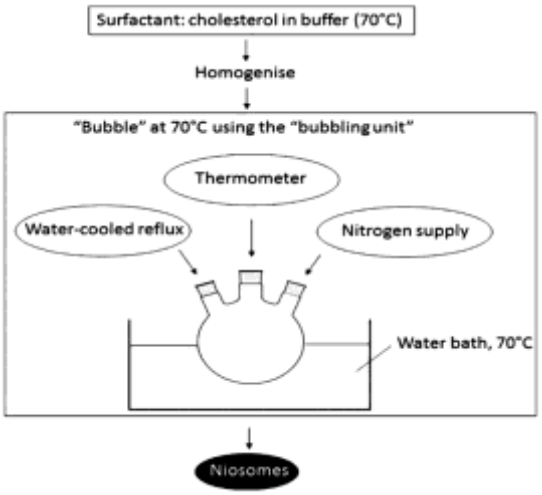

Fig 8: Bubble Method

4.0 CHARACTERIZATION OF NIOSOMES: Characterising niosomes is vital for clinical applications. Characterisation parameters directly affect niosome stability and function in vivo. Several criteria, including shape, size, polydispersity index (PI), number of lamellae, zeta potential, encapsulation efficiency, and stability, must be examined.

4.1 Size and Morphology: The most commonly used methods for determining niosome size and morphology include dynamic light scattering (DLS) **(41),** scanning electron microscopy (SEM) **(42),** transmission electron microscopy (TEM) **(43),** freeze fracture replication-electron microscopy (FF-TEM) **(33),** and cryotransmission electron microscopy (cryo-TEM) **(33).** DLS gives cumulative information on particle size and solution homogeneity. A single sharp peak in the DLS profile indicates a single population of scatterers. The PI is beneficial in this regard. Less than 0.3 indicates a homogeneous population in colloidal systems **(41).** Microscopic methods are commonly employed to examine the morphology of niosomes.

4.2 Zeta Potential: Niosomes' surface zeta potential can be measured using zetasizer and DLS devices. Niosome behavior is significantly influenced by their surface charge. In general, charged niosomes are more stable against aggregation than uncharged vesicles. Bayindir and Yuksel studied the physicochemical features of paclitaxel-loaded niosomes, including their zeta potential. Negative zeta potential ranges of -41.7 to -58.4 mV were shown to be sufficient for electrostatic stabilization of niosomes **(44).**

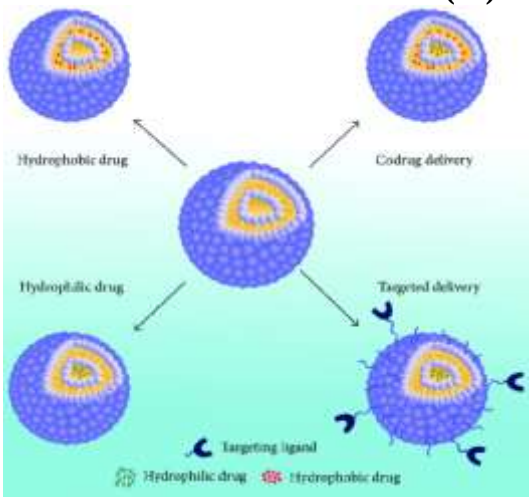

Figure 9. Niosomes in Drug Delivery.

4.3 Bilayer Characterisation: Niosomes' bilayer properties impact drug entrapment efficiency. AFM, NMR, and SAXS can determine the number of lamellae in multilamellar vesicles **(45).** Niosomal formulations' membrane stiffness can be assessed using fluorescence probe mobility as a function of temperature (source: **(46)**). DPH (1,6-diphenyl-1,3,5-hexatriene) is a commonly used fluorescent probe added to niosomal dispersion. DPH is typically found in the hydrophobic area of bilayer membranes. Fluorescence polarization determines the microviscosity of a niosomal membrane. significant fluorescence polarization indicates a membrane with significant microviscosity **(47).** The latter approach, combined with in-situ energy-dispersive X-ray diffraction (EDXD), can quantify bilayer thickness **(48).**

4.4 Entrapment Efficiency: Entrapment efficiency (EE%) is the percentage of the drug that is captured by the niosomes. Centrifugation **(49),** dialysis **(50),** or gel chromatography **(51)** can all be used to extract unencapsulated free medication from niosomal solutions. Following this stage, the medication can be liberated from niosomes by destroying the vesicles. Niosomes can be killed by adding 0.1% Triton X-100 or methanol to their solution. A spectrophotometer **(52)** or high-performance liquid chromatography (HPLC) can measure drug concentrations, both loaded and free **(53).**

4.5 Stability: To assess niosome stability, the mean vesicle size, size distribution, and entrapment efficiency can be measured after several months of storage at various temperatures. During storage, niosomes are sampled at regular intervals and the percentage of drug retention is evaluated using UV spectroscopy or HPLC techniques **(52,54).**

4.6 *In Vitro* Release: Dialysis tubing is commonly used to evaluate in-vitro release. The dialysis bag is cleansed and immersed in distilled water. After 30 minutes, the drug-loaded niosomal suspension is transferred to this bag. The vesicle bag is placed in a buffer solution and shaken at either 25∘ or 37∘C. At regular intervals, samples were withdrawn from the release medium and replaced with new buffer. Samples are tested for drug content using an appropriate assay method **(55).**

5.0 NIOSOMES AS DRUG CARRIERS

Niosomes are a promising carrier for delivering various pharmacological and diagnostic substances. Several papers have explored the synthesis, characterization, and usage of niosomes as drug carriers. Their nonionic nature makes them very biocompatible and low in toxicity. Niosomes' unusual structure enables excellent drug delivery systems that can load both hydrophilic and lipophilic medicines. Niosomes entrap hydrophilic and lipophilic medicines in their aqueous core and membrane bilayers, respectively.

5.1 Anticancer Drug Delivery: Chemotherapy is currently the main treatment for cancer. Many anticancer medicines have limited efficiency due to inadequate tumor tissue penetration and substantial negative effects on healthy cells. To address these limitations, niosomes have been proposed as a potential medication delivery mechanism.

5.1.1 Melanoma: Artemisone is a 10-amino-artemisinin derivative with antimalarial and anticancer action. Dwivedi et al. encapsulated artemisone in niosomes using the thin-film hydration process. The formulations demonstrated extremely specific cytotoxicity toward melanoma cells while having low toxicity toward normal skin cells **(56).** 5-Fluorouracil (5-FU), commonly used in skin cancer treatment, was encapsulated in a novel bola-niosomal system composed of α, ω-hexadecyl-bis-(1-aza-18-crown-6) (bola-surfactant), Span 80, and cholesterol. The percutaneous penetration of 5-FU-loaded bola-niosomes was studied utilizing human stratum corneum and epidermis membranes. Bola-niosomes increased drug penetration by 8- and 4-fold compared to free drug aqueous solutions **(57).** Cisplatin's toxicity limits its use. Gude et al. produced niosomal cisplatin from Span 60 and cholesterol, and tested its antimetastatic effectiveness in an experimental metastatic form of B16F10 melanoma. Niosome-encapsulated cisplatin had higher antimetastatic activity and lower toxicity than free cisplatin, according to their findings **(58).**

5.1.2 Breast Cancer: Cosco et al. evaluated 5-FU-loaded polyethylene glycol (PEG)-coated and uncoated bola-niosomes on breast cancer cell lines MCF-7 and T47D. Both bola-niosome formulations increased cytotoxicity compared to the free medication. In vivo tests on MCF-7 xenograft tumor SCID mice revealed that PEGylated niosomal 5-FU, at a concentration ten times lower (8 mg/kg), outperformed the free solution of the medication (80 mg/kg) after 30 days of treatment **(59).** Niosomes encapsulated with cantharidin were created through injection. The effectiveness of these compounds in lowering drug toxicity and improving anticancer activity was tested on the MCF-7 human breast cancer cell line. Additionally, treatment efficacy was assessed in S180 tumor-bearing animals. Mice treated with 1.0 mg/kg niosomal cantharidin had considerably higher antitumor activity (52.76%) compared to those treated with free cantharidin (1.0 mg/kg, 31.05%) **(60).** Tamoxifen citrate niosomes were created using a film hydration approach for localized cancer therapy, demonstrating in vitro breast cancer cytotoxicity and in vivo solid antitumor effectiveness. The improved niosomal formulation of tamoxifen increased cellular absorption (2.8-fold) and cytotoxic efficacy against MCF-7 breast cancer cells. In vivo studies found that niosomal tamoxifen reduced tumor volume more effectively than free tamoxifen **(61).**

5.1.3 Ovarian Cancer: Uchegbu et al. developed doxorubicin-loaded niosomes. Doxorubicin activity in hexadecyl diglycerol ether (C16G2) and Span 60 niosomes was tested against a human ovarian cancer cell line and its doxorubicin-resistant subline. The study found that encapsulating the drug in Span 60 niosomes resulted in a somewhat lower IC50 against the resistant cell line compared to the free drug in solution **(62).**

5.1.4 Lung Cancer: Kerr et al. used a monoalkyl triglycerol ether to encapsulate adriamycin into the noisome, and the activity of niosomal adriamycin was compared to free adriamycin solution on human lung carcinoma cells cultivated in monolayer and spheroid culture, as well as tumor xenografted nude mice. The growth delay (the time it takes for the tumor volume to double) was substantially longer for adriamycin (15 days) and niosomal adriamycin (11 days) than for the control (5.8 days). It is possible that administering adriamycin in niosomal form would improve its therapeutic ratio **(63).** Another study utilized the lipid film hydration approach to create niosomes filled with pentoxifylline. In an experimental metastatic B16F10 model, administering niosomal pentoxifylline (6 mg/kg and 10 mg/kg) significantly reduced lung nodules, indicating pentoxifylline accumulation in a distant target. Light microscopic examination of histologic sections revealed fewer tumor islands in the lungs **(64).**

5.2 Targeted Delivery: Active targeting for tumor therapy can improve the efficiency and specificity of niosomal drug delivery systems. This involves attaching a ligand to the surface of niosomes and actively taking it up through receptor-mediated endocytosis. Niosome surfaces can be coupled with tiny or macromolecular targeting ligands for cell-specific targeting **(65).** Proteins, peptides, polysaccharides, aptamers, antibodies, and antibody fragments are routinely employed molecules to bind to overexpressed targets on cell surfaces **(66-68).** Bragagni et al. created a brain-targeted niosomal formulation employing a glucose derivative as the ligand. Niosomal doxorubicin was created by combining span, cholesterol, solulan, and N-palmitoylglucosamine. Preliminary in vivo studies in rats found that administering a single dose of the targeted-niosomal formulation intravenously reduced drug heart accumulation and increased blood circulation, resulting in detectable doxorubicin brain concentrations **(69).** Tavano et al. developed an effective tumor-targeting niosomal delivery method. Niosomes were formed by combining Pluronic L64 surfactant and cholesterol, and doxorubicin was entrapped within them. EDC (N-[3-(dimethylamino)propyl]-N-ethylcarbodiimide hydrochloride) was used to conjugate transferrin to the surface of niosomes. Doxorubicin-loaded niosomes demonstrated anticancer action against MCF-7 and MDA-MB-231 tumor cell lines, resulting in significant reductions in viability over time and dose **(50).** Table 2 summarizes recent investigations on targeted medication delivery by niosomes.

5.3 Codrug Delivery: In recent years, nanoparticles have become a promising class of carriers in the delivery of multiple drugs for combination therapy **(70).** Combinational therapies improve therapeutic efficacy and reduce dosage while achieving equal or greater levels of efficacy and reducing drug resistance **(71).** Anticancer drugs frequently have serious side effects. Pasut et al. developed a multidrug delivery system that increased anticancer activity for carcinoma cells while decreasing cytotoxicity against endothelial cells and cardiomyocytes compared to free drug treatment. In their system, they developed a simultaneous anticancer drug epirubicin and nitric oxide conjugated to each terminal of PEG. Nitric oxide works as both a protective reagent against anthracycline-induced cardiomyopathy and a sensitizer for anticancer drug treatment. They employed branched PEG as the polymer backbone instead of a linear one to maximize anticancer activity and cardiocyte protection in the codelivery system **(72).** Multidrug resistance (MDR) of malignant neoplasms refers to cancer cells' ability to survive therapy with a wide range of anticancer medications. Increased drug efflux is primarily mediated by ATP-driven extrusion pump proteins from the ATP-binding cassette (ABC) superfamily, such as P-glycoprotein (P-gp) encoded by MDR-1, multidrug resistance

(MDR) proteins (MRPs/ABCC), and breast cancer resistance protein (BCRP/ABCG2). These medication efflux pumps significantly reduce the intracellular concentrations of several therapeutic drugs **(73).** Chemosensitizers including Verapamil, Elacridar, Tariquidar, and Cyclosporine A inhibit P-gp, reducing drug efflux and restoring chemosensitivity in MDR cancer cells. Paclitaxel and cyclosporine A were encapsulated in polymeric lipid-core micelles for targeted delivery. Cyclosporine A inhibited P-gp, which increased paclitaxel's cytotoxicity. Micelles loaded with this dual cargo showed considerably more cytotoxicity in MDCKII-MDR1 cells than those treated with paclitaxel alone **(74).** Niosomes show promise as nanocarriers for multidrug delivery **(75).** Sharma et al. described encapsulating both hydrophobic curcumin and hydrophilic doxorubicin in niosomes for cancer multidrug delivery **(76).** Dual-drug loaded niosomes exhibited greater cytotoxicity on HeLa cells compared to free drugs. In another study, gallic acid, ascorbic acid, curcumin, and quercetin were encapsulated into niosomes as single agents or in combination. The effect of drug coencapsulation on carrier physicochemical properties, antioxidant properties, and ability to release encapsulated materials was evaluated **(77).** Mari-anecci et al. created, characterized, and applied multidrug nanosomes containing lidocaine and ibuprofen. Niosomes can be used as carriers for treating skin illnesses, including acute and chronic inflammations and discomfort, in a single medicinal formulation **(78).**

5.4 Antiviral Drugs: Niosomes have also shown the ability to deliver a variety of antiviral medicines. Ruckmani and Sankar produced zidovudine, the first anti-HIV drug licensed for clinical use, encapsulated it in niosomes, and investigated its entrapment efficiency and release sustainability. The niosomes were created by mixing Tween, Span, and cholesterol. Niosomes made of Tween 80 captured high amounts of zidovudine, and the addition of dicetyl phosphate increased drug release for a longer time **(79).** The drug leakage from Tween 80 formulations held at ambient temperature was substantial compared to niosomes stored at 4°C for 90 days. Furthermore, the results of a pharmacokinetic investigation in rabbits revealed that Tween 80 formulations containing dicetyl phosphate were eliminated from the blood within five hours **(80).**

6.0 APPLICATIONS OF NIOSOMES

Niosomal technology has numerous applications and can treat a range of ailments.

1) Niosomes as Drug Carriers – Niosomes can transport iobitridol, a diagnostic chemical used in X-ray imaging.

2) Targeting of Bioactive Agents

a) To Reticulo-Endothelial System (RES) – The RES cells preferentially take up vesicles. Opsonins, which are circulating serum factors, help cells ingest niosomes and mark them for clearance. Localized drug accumulation has been used to treat animal cancers that spread to the liver and spleen, as well as parasite infections of the liver.

b) To Organs, Other than RES – Antibodies can guide the carrier system to specific locations within the body. Immunoglobulins can bind to lipid surfaces, making them a useful tool for targeting drug carriers. Cells have the ability to detect and bind specific carbohydrate determinants, which can be used as a direct carrier system between cells.

3) Anti-neoplastic Treatment – Most antineoplastic medications have substantial negative effects. Niosomes can change drug metabolism, extending circulation and reducing negative effects. Niosomes suppress tumor proliferation and increase plasma levels by slowing removal.

4) Leishmaniasis – Leishmaniasis is caused by a parasite from the Leishmania genus that infects liver and spleen cells. The use of niosomes in studies has demonstrated the ability to provide higher doses of a medicine without causing side effects, leading to increased treatment efficacy.

5) Delivery of Peptide Drugs – Niosomes are being studied for their ability to effectively shield peptides from gastrointestinal degradation. An in-vitro investigation found that oral delivery of a vasopressin entrap derivative in niosomes improves the stability of the peptide.

6) Use in Studying Immune Response – Niosomes are utilized to research the nature of immune responses elicited by antigens due to their immune system selection, low toxicity, and increased stability. Non-ionic surfactant vesicles are effective adjuvants for parenteral delivery of various antigens and peptides.

7) Cosmetics – L'Oreal pioneered the use of non-ionic surfactant vesicles in cosmetics. In the 1970s and 1980s, L'Oréal developed and patented niosomes. Lancôme introduced their first product, 'Niosome', in 1987. Niosomes have advantages in cosmetic and skin care applications, such as improving drug stability, bioavailability, and skin penetration.

8) Other Applications

a) Sustained Release – Niosomes can provide sustained release for medications with poor therapeutic index and water solubility, allowing them to remain in circulation through encapsulation

b) Localised Drug Action – Niosomal drug delivery focuses on localised action due to its small size and poor penetration of the epithelium and connective tissue.

c) Niosome Formulation As A Brain Targeted Delivery System For The Vasoactive Intestinal Peptide (VIP) – Mice get an intravenous injection of radiolabeled (I125) VIP-loaded glucose-bearing niosomes. Encapsulating VIP in glucose-bearing niosomes results in greater brain uptake compared to the control.

d) Niosomes As Carriers For Hemoglobin – Niosomes are capable of transporting hemoglobin. Niosomal suspension has a similar visual spectrum to free hemoglobin. Vesicles are oxygen-permeable and the hemoglobin dissociation curve can be adjusted similarly to non-encapsulated hemoglobin **(81-90).**

CONCLUSION

Niosomes are at the crossroads of innovation and therapeutic application, marking a significant advancement in nanocarrier-based drug delivery systems. Their unique bilayer structure, which includes non-ionic surfactants and cholesterol, provides a high level of stability, encapsulation efficiency, and targeted administration capabilities, all of which improve the pharmacokinetic and pharmacodynamic profiles of a wide range of medicines. This paper explains the numerous factors that underpin niosomal formation, from thermodynamic parameters to geometric considerations, and discusses scalable preparation strategies designed to produce uniform vesicular features. Niosomes are particularly suitable for site-specific and sustained drug release applications due to their ability to mix hydrophilic and lipophilic medicines in a single delivery vehicle, as well as their customizable surface characteristics and modifiable size distribution. Critically, niosomes outperform conventional oncological drug delivery systems, notably in terms of overcoming multidrug resistance and increasing the efficacy of chemotherapeutics. Targeted delivery strategies based on ligand-conjugated vesicles improve their precision in site-specific therapy, whilst co-delivery systems broaden the scope of combination regimens with synergistic effects. Their capacity to deliver delicate macromolecules like peptides and proteins, as well as their efficacy in antiviral and dermatological applications, demonstrate their versatility. Furthermore, the incorporation of niosomal systems into cosmetic and diagnostic platforms demonstrates their utility beyond traditional therapies. As creative research and technological refinement solve issues such as vesicle aggregation, stability, and large-scale production, niosomes have the potential to redefine drug delivery standards. In summary, niosomes provide a transformational, adaptive, and therapeutically relevant nanocarrier technology that will help advance the future of personalized and targeted medicine.

REFERENCES:

1. Seleci, D. Ag Seleci, R. Joncyzk, F. Stahl, C. Blume, and T. Scheper, "Smart multifunctional nanoparticles in nanomedicine," BioNanoMaterials, vol. 17, no. 1-2, pp. 33–41, 201
2. N. B. Mahale, P. D. Thakkar, R. G. Mali, D. R. Walunj, and S. R. Chaudhari, "Niosomes: novel sustained release nonionic stable vesicular

systems—an overview," Advances in Colloid and Interface Science, vol. 183, pp. 46–54, 2012.
3. L. Tavano, L. Gentile, C. Oliviero Rossi, and R. Muzzalupo, "Novel gel-niosomes formulations as multicomponent systems for transdermal drug delivery," Colloids and Surfaces B: Biointerfaces, vol. 110, pp. 281–288, 2013.
4. K. B. Bini, D. Akhilesh, P. Prabhakara, and K. Jv, "Development and characterization of non-ionic surfactant vesicles (niosomes) for oral delivery of lornoxicam," International Journal of Drug Development and Research, vol. 4, no. 3, pp. 147–154, 2012.
5. Q. Li, Z. Li, W. Zeng et al., "Proniosome-derived niosomes for Tacrolimus topical ocular delivery: in vitro cornea permeation, Ocular irritation, and in vivo anti-allograft rejection," European Journal of Pharmaceutical Sciences, vol. 62, pp. 115–123, 2014.
6. Z. S. Bayindir, A. Bes¸ikci, and N. Yuksel, "Paclitaxel-loaded ¨Niosomes for intravenous administration: pharmacokinetics and tissue distribution in rats," Turkish Journal of Medical Sciences, vol. 45, no. 6, pp. 1403–1412, 2015.
7. Marianecci, F. Rinaldi, M. Mastriota et al., "Anti-inflammatory activity of novel ammonium glycyrrhizinate/niosomes Delivery system: human and murine models," Journal of Controlled Release, vol. 164, no. 1, pp. 17–25, 2012.
8. S. K. Mehta and N. Jindal, "Tyloxapol niosomes as prospective drug delivery module for antiretroviral drug nevirapine," AAPS PharmSciTech, vol. 16, no. 1, pp. 67–75, 2014.
9. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. J Pharm Pharmacol1985;37:863.
10. Mozafari MR, Reed CJ, Rostron C. Pharmazie 2007;62:205.
11. Lesieur S, Madelmont CT, Patenostre M, Moreau JM, Handjani-Vila RM, Ollivon M.Chem Phys Lipids 1990; 56:109.
12. Vanlerberghe G, Morancais JL. STP Pharm Sci 1996;1:5.
13. Uchegbu IF, Florence AT. Adv Colloid Interface Sci 1995; 58:1.
14. Jousma H, Joosten JGH, Gooris GS, Junginger HE. Colloid Polym Sci 1989; 267:353.
15. Jousma H, Joosten JGH, Junginger HE. Colloid Polym Sci 1988; 266:640.
16. Shahiwala A, Misra A. J Pharm Pharm Sci 2002;5:220.
17. Tavano L, Alfano P, Muzzalupo R, de Cindio B. Colloids Surf B Biointerfaces 2011;87:333.
18. Israelachvili JN. In Intermolecular and surface forces. 2nd ed. Academic Press; 1992.
19. Israelachvili JN, Mitchell DJ, Ninham BW. J Chem Soc Faraday Trans 1976; 2:1525.
20. Dai WG, Dong LC, Li S, Pollock-Dove C, Chen J, Mansky P, et al. Int J Pharm 2007; 336:1.
21. Cevc G. J Control Release 2012; 160:135.
22. Bhaskaran and P. K. Lakshmi, "Comparative evaluation of Niosome formulations prepared by different techniques," Acta Pharmaceutica Scien.cia, vol. 51, no. 1, pp. 27–32, 2009.
23. A J. Baillie, A. T. Florence, L. R. Hume, G. T. Muirhead, and A. Rogerson, "The preparation and properties of niosomes non-ionic surfactant vesicles," The Journal of Pharmacy and Pharmacology, vol. 37, no. 12, pp. 863–868, 1985.
24. Marwa, S. Omaima, E. L. G. Hanaa, and A.-S. Mohammed, "Preparation and in-vitro evaluation of diclofenac sodium niosomal formulations," International Journal of Pharmaceutical Sciences and Research, vol. 4, no. 5, pp. 1757–1765, 2013.
25. A. Rogerson, J. Cummings, N. Willmott, and A. T. Florence, "The distribution of doxorubicin in mice following administration in niosomes,"

Journal of Pharmacy and Pharmacology, vol. 40, no. 5, pp. 337–342, 1988.
26. S. Srinivas, Y. A. Kumar, A. Hemanth, and M. Anitha, "Preparation and evaluation of niosomes containing aceclofenac," Digest Journal of Nanomaterials and Biostructures, vol. 5, no. 1, pp. 249– 254, 2010.
27. Moghassemi, E. Parnian, A. Hakamivala et al., "Uptake and Transport of insulin across intestinal membrane model using Trimethyl chitosan coated insulin niosomes," Materials Science and Engineering C, vol. 46, pp. 333–340, 2015.
28. Budhiraja and G. Dhingra, "Development and characterization of a novel antiacne niosomal gel of rosmarinic acid," Drug Delivery, vol. 22, no. 6, pp. 723–730, 2015.
29. Kiwada, H. Niimura, Y. Fujisaki, S. Yamada, and Y. Kato, "Application of synthetic alkyl glycoside vesicles as drug carriers. I. Preparation and physical properties," Chemical and Pharmaceutical Bulletin, vol. 33, no. 2, pp. 753–759, 1985.
30. Zidan, Z. Rahman, and M. A. Khan, "Product and Process understanding of a novel pediatric anti-HIV tenofovir Niosomes with a high-pressure homogenizer," European Journal Of Pharmaceutical Sciences, vol. 44, no. 1-2, pp. 93–102, 2011.
31. Verma, S. K. Singh, N. Syan, P. Mathur, and V. Valecha, "Nanoparticle vesicular systems: a versatile tool for drug delivery," Journal of Chemical and Pharmaceutical Research, vol. 2, No. 2, pp. 496–509, 2010.
32. Manosroi, R. Chutoprapat, M. Abe, and J. Manosroi, "Characteristics of niosomes prepared by supercritical carbon dioxide (scCO2) fluid," International Journal of Pharmaceutics, vol. 352, No. 1-2, pp. 248–255, 2008.
33. Manosroi, W. Ruksiriwanich, M. Abe, H. Sakai, W. Manosroi, and J. Manosroi, "Biological activities of the rice bran extract and physical characteristics of its entrapment in niosomes by Supercritical carbon dioxide fluid," The Journal of Supercritical Fluids, vol. 54, no. 2, pp. 137–144, 2010
34. V. R. Yasam, S. L. Jakki, J. Natarajan, and G. Kuppusamy, "A Review on novel vesicular drug delivery: proniosomes," Drug Delivery, vol. 21, no. 4, pp. 243–249, 2014
35. L. D. Mayer, M. B. Bally, and P. R. Cullis, "Uptake of adriamycin into large unilamellar vesicles in response to a pH gradient," Biochimica et Biophysica Acta (BBA)—Biomembranes, vol. 857, No. 1, pp. 123–126, 1986.
36. **A**. K. Verma and J. C. Bindal, "A vital role of niosomes on Controlled and novel drug delivery," Indian Journal of Novel Drug Delivery, vol. 3, pp. 238–246, 2011.
37. M. R. Mozafari, "A new technique for the preparation of non-toxic liposomes and nanoliposomes: the heating method," in Nanoliposomes: From Fundamentals to Recent Developments, pp.91–98, Trafford Publishing, Oxford, UK, 2005.
38. M. R. Mozafari, C. J. Reed, and C. Rostron, "Cytotoxicity evaluation of anionic nanoliposomes and nanolipoplexes prepared by the heating method without employing volatile solvents and Detergents," Die Pharmazie, vol. 62, no. 3, pp. 205–209, 2007.
39. S. Moghassemi and A. Hadjizadeh, "Nano-niosomes as Nanoscale drug delivery systems: an illustrated review," Journal of Controlled Release, vol. 185, no. 1, pp. 22–36, 2014.
40. H. Talsma, "A novel technique for the one-step preparation of liposomes and nonionic surfactant vesicles without the use of organic solvents. Liposome formation in a continuous Gas stream: the 'bubble' method," Journal of Pharmaceutical Sciences, vol. 83, no. 3, pp. 276–280, 1994.

41. L. Tavano, R. Aiello, G. Ioele, N. Picci, and R. Muzzalupo, "Niosomes from glucuronic acid-based surfactant as new carriers for cancer therapy: preparation, characterization and biological properties," Colloids and Surfaces B: Biointerfaces, vol. 118, pp.7–13, 2014.
42. A. Priprem, K. Janpim, S. Nualkaew, and P. Mahakunakorn, "Topical niosome gel of Zingiber cassumunar Roxb. Extract for anti-inflammatory activity enhanced skin permeation and stability of compound D," AAPS PharmSciTech, vol. 17, no. 3, pp. 631–639, 2016.
43. W. Hua and T. Liu, "Preparation and properties of highly stable innocuous niosome in Span 80/PEG 400/H2O system," Colloids and Surfaces A: Physicochemical and Engineering Aspects, vol. 302, no. 1, pp. 377–382, 2007.
44. Z. S. Bayindir and N. Yuksel, "Characterisation of niosomes prepared with various nonionic surfactants for paclitaxel oral delivery," Journal of Pharmaceutical Sciences, vol. 99, no. 4, pp.2049–2060, 2010.
45. T. Liu, R. Guo, W. Hua, and J. Qiu, "Structure behaviours of Hemoglobin in PEG 6000/Tween 80/Span 80/H2O niosome system," Colloids and Surfaces A: Physicochemical and Engineering Aspects, vol. 293, no. 1–3, pp. 255–261, 2007.
46. L. Di Marzio, C. Marianecci, M. Petrone, F. Rinaldi, and M. Carafa, "Novel pH-sensitive non-ionic surfactant vesicles: Comparison between Tween 21 and Tween 20," Colloids and Surfaces B: Biointerfaces, vol. 82, no. 1, pp. 18–24, 2011.
47. Manosroi, P. Wongtrakul, J. Manosroi et al., "Characterisation of vesicles prepared with various non-ionic surfactants mixed with cholesterol," Colloids and Surfaces B: Biointerfaces, Vol. 30, no. 1-2, pp. 129–138, 2003.
48. D. Pozzi, R. Caminiti, C. Marianecci et al., "Effect of cholesterol on the formation and hydration behaviour of solid-supported Niosomal membranes," Langmuir, vol. 26, no. 4, pp. 2268–2273, 2010.
49. D. Pando, G. Gutierrez, J. Coca, and C. Pazos, "Preparation and Characterisation of niosomes containing resveratrol," Journal of Food Engineering, vol. 117, no. 2, pp. 227–234, 2013.
50. L. Tavano, R. Muzzalupo, L. Mauro, M. Pellegrino, S. Ando, and N. Picci, "Transferrin-conjugated Pluronic niosomes as a new Drug delivery system for anticancer therapy," Langmuir, vol. 29, No. 41, pp. 12638–12646, 2013.
51. M. Tabbakhian, S. Daneshamouz, N. Tavakoli, and M. R. Jaafari, "Influence of liposomes and niosomes on the in vitro permeation and skin retention of finasteride," Iranian Journal of Pharmaceutical Sciences, vol. 1, no. 3, pp. 119–130, 2005.
52. S. K. Mehta and N. Jindal, "Formulation of Tyloxapol niosomes for encapsulation, stabilization and dissolution of anti-tubercular drugs," Colloids and Surfaces B: Biointerfaces, vol. 101, pp. 434–441, 2013.
53. A. Y. Waddad, S. Abbad, F. Yu et al., "Formulation, characterization and pharmacokinetics of Morin hydrate niosomes prepared from various non-ionic surfactants," International Journal of Pharmaceutics, vol. 456, no. 2, pp. 446–458, 2013.
54. Y. Hao, F. Zhao, N. Li, Y. Yang, and K. Li, "Studies on a high encapsulation of colchicine by a niosome system," International Journal of Pharmaceutics, vol. 244, no. 1-2, pp. 73–80, 2002.
55. D. Akhilesh, K. B. Bini, and J. V. Kamath, "Review on span-60 based non-ionic surfactant vesicles (niosomes) as novel drug delivery," International Journal of Research in Pharmaceutical and Biomedical Sciences, vol. 3, pp. 6–12, 2012.
56. Dwivedi, A. Mazumder, L. du Plessis, J. L. du Preez, R. K. Haynes, and J. du

Plessis, "In vitro anti-cancer effects of Artemisone nano-vesicular formulations on melanoma cells," Nanomedicine: Nanotechnology, Biology, and Medicine, vol. 11, No. 8, pp. 2041–2050, 2015.
57. Paolino, D. Cosco, R. Muzzalupo, E. Trapasso, N. Picci, And M. Fresta, "Innovative bola-surfactant niosomes as topical delivery systems of 5-fluorouracil for the treatment of skin cancer," International Journal of Pharmaceutics, vol. 353, no. 1-2, pp. 233–242, 2008.
58. R. P. Gude, M. G. Jadhav, S. G. A. Rao, and A. G. Jagtap, "Effects of niosomal cisplatin and combination of the same with Theophylline and with activated macrophages in murine B16F10 Melanoma model," Cancer Biotherapy and Radiopharmaceuticals, vol. 17, no. 2, pp. 183–192, 2002.
59. D. Cosco, D. Paolino, R. Muzzalupo et al., "Novel PEG-coated Niosomes based on bola-surfactant as drug carriers for 5-Fluorouracil," Biomedical Microdevices, vol. 11, no. 5, pp. 1115–1125, 2009.
60. Han, S. Wang, R. Liang et al., "Non-ionic surfactant vesicles simultaneously enhance antitumor activity and reduce the toxicity of cantharidin," International Journal of Nanomedicine, Vol. 8, pp. 2187–2196, 2013.
61. Shaker, M. A. Shaker, and M. S. Hanafy, "Cellular uptake, Cytotoxicity and in-vivo evaluation of Tamoxifen citrate loaded Niosomes," International Journal of Pharmaceutics, vol. 493, no. 1-2, pp. 285–294, 2015
62. I. F. Uchegbu, J. A. Double, L. R. Kelland, J. A. Turton, and A. T. Florence, "The activity of doxorubicin niosomes against an ovarian cancer cell line and three in vivo mouse tumour models," Journal of Drug Targeting, vol. 3, no. 5, pp. 399–409, 1996.
63. D. J. Kerr, A. Rogerson, G. J. Morrison, A. T. Florence, and S. B. Kaye, "Antitumour activity and pharmacokinetics of Niosome encapsulated adriamycin in monolayer, spheroid and Xenograft," British Journal of Cancer, vol. 58, no. 4, pp. 432–436, 1988.
64. S. Y. Gaikwad, A. G. Jagtap, A. D. Ingle, S. G. A. Ra, and R. P. Gude, "Antimetastatic efficacy of niosomal pentoxifylline and its combination with activated macrophages in murine B16F10 Melanoma model," Cancer Biotherapy & Radiopharmaceuticals, Vol. 15, no. 6, pp. 605–615, 2000.
65. M. Kong, H. Park, C. Feng, L. Hou, X. Cheng, and X. Chen, "Construction of hyaluronic acid noisome as functional transdermal nanocarrier for tumor therapy," Carbohydrate Polymers, Vol. 94, no. 1, pp. 634–641, 2013.
66. Narang and R. Mahato, Targeted Delivery of Small and Macromolecular Drugs, CRC Press, 2010.
67. Ag, R. Bongartz, L. E. Dogan et al., "Biofunctional quantum dots as fluorescence probe for cell-specific targeting," Colloids and Surfaces B: Biointerfaces, vol. 114, pp. 96–103, 2014.
68. M. Seleci, D. A. Seleci, M. Ciftci et al., "Nanostructured Amphiphilic star-hyperbranched block copolymers for drug delivery," Langmuir, vol. 31, no. 15, pp. 4542–4551, 2015.
69. Bragagni, N. Mennini, C. Ghelardini, and P. Mura, "Development and characterization of niosomal formulations of doxorubicin aimed at brain targeting," Journal of Pharmacy and Pharmaceutical Sciences, vol. 15, no. 1, pp. 184–196, 2012.
70. S. Gadde, "Multi-drug delivery nanocarriers for combination therapy," MedChemComm, vol. 6, no. 11, pp. 1916–1929, 2015
71. B. Al-Lazikani, U. Banerji, and P. Workman, "Combinatorial Drug therapy for cancer in the post-genomic era," Nature Biotechnology, vol. 30, no. 7, pp. 679–692, 2012.
72. G. Pasut, F. Greco, A. Mero et al., "Polymer-drug conjugates for

combination anticancer therapy: investigating the mechanism of action," Journal of Medicinal Chemistry, vol. 52, no. 20, pp. 6499–6502, 2009.
73. Y. D. Livney and Y. G. Assaraf, "Rationally designed nanovehicles to overcome cancer chemoresistance," Advanced Drug Delivery Reviews, vol. 65, no. 13-14, pp. 1716–1730, 2013.
74. Sarisozen, I. Vural, T. Levchenko, A. A. Hincal, and V. P. Torchilin, "PEG-PE-based micelles co-loaded with paclitaxel and cyclosporine A or loaded with paclitaxel and targeted by Anticancer antibody overcome drug resistance in cancer cells," Drug Delivery, vol. 19, no. 4, pp. 169–176, 2012.
75. M. Thakkar and S. Brijesh, "Opportunities and challenges for Niosomes as drug delivery systems," Current Drug Delivery, vol. 13, pp. 1–15, 2016.
76. V. Sharma, S. Anandhakumar, and M. Sasidharan, "Self- Degrading niosomes for encapsulation of hydrophilic and Hydrophobic drugs: an efficient carrier for cancer multi-drug delivery," Materials Science and Engineering: C, vol. 56, pp. 393– 400, 2015.
77. L. Tavano, R. Muzzalupo, N. Picci, and B. De Cindio, "Co-Encapsulation of antioxidants into niosomal carriers: gastrointestinal release studies for nutraceutical applications," Colloids and Surfaces B: Biointerfaces, vol. 114, pp. 82–88, 2014.
78. C. Marianecci, F. Rinaldi, L. D. Marzio, A. Ciogli, S. Esposito, and M. Carafa, "Polysorbate 20 vesicles as multi-drug carriers: In vitro preliminary evaluations," Letters in Drug Design and Discovery, vol. 10, no. 3, pp. 212–218, 2013
79. K. Ruckmani and V. Sankar, "Formulation and optimization of Zidovudine niosomes," AAPS PharmSciTech, vol. 11, no. 3, pp. 1119–1127, 2010.
80. K. Ruckmani, V. Sankar, and M. Sivakumar, "Tissue distribution, pharmacokinetics and stability studies of zidovudine delivered by niosomes and proniosomes," Journal of Biomedical Nanotechnology, vol. 6, no. 1, pp. 43–51, 2010.
81. Gopalakrishnan S, Chenthilnathan A, Niosomes – A Novel Drug Delivery Device, Research Journal of Pharmaceutical, Biological and Chemical, 2012; 3(3):1090.
82. Pei Ling Yeo, Chooi Ling Lim, Soi Moi Chye, Anna Pick Kiong Ling, Rhun Yian Koh, Niosomes: A Review of Their Structure, Properties, Methods of Preparation, And Medical Applications, Asian Biomed (Res Rev News) 2017; 11(4):301–14
83. Singh S, Niosomes: A Role in Targeted Drug Delivery System, IJPSR, 2013; 4(2):550-557.
84. Sharma BS, Bhogale V, Adepu AR, Patil ST, Sangha SK, Proniosomes: A Novel Provesicular Drug Delivery System, International Journal for Pharmaceutical Research Scholars, 2015; 4(2).
85. Gadhiya P, Shukla S, Modi D, Bharadia P, Niosomes in Targeted Drug Delivery – A Review, International Journal for Pharmaceutical Research Scholars, 2012; 1(2).
86. Patel SM, Rathod DR, Patel KN, Patel BA, Patel PA, Niosome as an Effective Drug Delivery: A Review, International Journal for Pharmaceutical Research Scholars (IJPRS), 2012; 1(2).
87. Verma NK, Roshan A, Niosomes and Its Application-A Review, IJRPLS, 2014; 2(1):182-184.
88. Gupta R, Kumar S, Gupta N, Anurag Kumar, The New Advancement Nanotechnology: Proniosomes as A Promising and Potential Drug Carrier, International Journal of Research and Development In Pharmacy and Life Sciences, October – November 2014; 3(6):1258-1265.

89. Khindri, Role of Niosomes and Proniosomes for Enhancing Bioavailability of Drugs, Journal of Drug Delivery AND Therapeutics. 2015; 5(1):28-33
90. Kalra NG. Jeyabalan, Singh G, Choudhary S, Non-Ionic Surfactant Vesicles and Their Therapeutic Potentials, JIPBS, 2016; 3(2):193-201.