IOSR Journal Of Pharmacy
(e)-ISSN: 2250-3013, (p)-ISSN: 2319-4219
Volume 13, Issue 8 Series. I (August 2023), PP. 26-38
www.iosrphr.org

Niosomes a novel nanocarrier: its potential application and emerging trends in therapeutics delivery

[1]Manpreet Singh *, [2]Nirmala, [3] Rohit Kundal, [4]Jhuma Samanta
[1, 2, 3] *University School of Pharmaceutical Sciences, Rayat Bahra University, Mohali, Punjab, India*
[4] *Kingston Imperial Institute of Technology and Sciences Dunga Dehradun Uttarakhand, India*

Prof (Dr.) Jhuma Samanta
Principal
Kingston Imperial Institute of Technology and Sciences Dunga Dehradun Uttarakhand

Ms. Nirmala
Assistant Professor
University School of Pharmaceutical Sciences, Rayat Bahra University, Mohali, Punjab, India
Received 10 August 2023; Accepted 25 August 2023

Abstract:
Numerous publications on reviews and research on niosomes have been published in the last decade. This demonstrates the interest in niosomes among researchers due to their benefits over other vesicular carrier systems. Niosomes demonstrate great potential as drug carriers due to their ability to maintain biocompatibility, biodegrade and induce minimal immune response. The primary constituents of pharmaceutical administration systems is a suitable transporter that shield the medication from swift breakdown and amplifies drug levels in the anticipated tissues. They are produced when nonionic surfactants and cholesterol self-associate in liquid facet(water based). The current review provides information on contemporary niosomal drug delivery system, preparation methodologies, characterization approaches, research, as well as niosomes as drug carriers.
Keywords: Niosomes, novel drug delivery system, Cholesterol, Proniosomes, thin film hydration method, anti-cancer drugs

I. INTRODUCTION

In recent times, the field of drug administration through specific, regulated release has garnered significant interest. The employment of nanotechnology in the medical domain has resulted in the expansion of versatile nanoparticles that act as drug transporters and can accommodate a diverse range of medications. Using nanocarriers to carry drugs is a fantastic idea with several positive benefits, including the drug's protection from cleavage and degradation[1–2]. Niosomes, characterized by a double-layered configuration and formed through the self-aggregation of cholesterol and nonionic surfactants in a water-based environment, emerge as a highly favorable option for transporting medications. Niosomes possess non-immunogenic, biocompatible, and immunologically inert properties.They demonstrae extended storage duration, exhibit exceptional stability, and enable controlled and/or prolonged drug delivery to the intended destination[1,3]. Niosomes are multi-layered vesicular formations composed of nonionic surfactants, similar to liposomes, with the distinction that they do not contain the phospholipids typically found in liposomes. These transport systems guard against the drug molecules being prematurely degraded and rendered ineffective as a result of unintended immunological and pharmacological effects[4–6]. Niosomes are named as such because they are composed of non-ionic surfactants, which also make them non-toxic. Beside non-ionic surfactants, niosomes might also encompass charged compounds, cholesterol, or cholesterol derivatives. Cholesterol gives the structure its rigidity, while the charged molecule makes the preparation stable. Niosomes are a vesicular, new medication transport system that can be leveraged to deliver medications to specific areas of the body over time in a regulated and sustained manner[7–13]. Niosomes have been intensively investigated in recent years because of the possibility that they could transport pharmaceuticals, antigens, hormones, and other bioactive substances. Additionally, niosomes have been used to address the issues of drug instability, fast disintegration, and insolubility[6].

This review's objective is to introduce the basics of niosome formation and characterisation while also outlining how they are used in medication administration.

STRUCTURE OF NIOSOMES

Non-ionic surface-active substances have a bi-layered structure called niosomes. When cholesterol and surfactants are combined properly and the temperature is above the gel-to-fluid transition temperature, all such thermodynamically stable bilayered structures must only form[14-16]. Niosomes do have the capability to encapsulate both hydrophilic and lipophillic drugs. Hydrophillic drugs have the ability to attach to the surface of the double-layer or the inner aqueous compartment of niosomes, facilitating entrapment, while lipophilic medications distribute themselves within the bilayer architecture[8,14].

COMPONENTS OF NIOSOMES:

The primary constituents of niosomes consist of non-ionic surfactants, aqueous solution, and lipids like cholesterol.

1.**Non ionic surfactants:** The non-ionic surfactants self-organize into duplex structures, with the hydrophilic or hydrophilic heads confronting the surrounding hydrous environment, and the hydrophobic head or hydrocarbon chains arranged to minimize contact with the aqueous media[6]. In contrast to anionic and cationic surfactants, nonionic surfactants are largely harmless and do not carry a charge. They are utilized in the creation of niosomes [17]. A diversity of compounds, including amino acids, fatty acids, amides, alkyl esters, and alkyl ether surfactants, can be used to make non-ionic surfactant vesicles.

Alkyl ethers: Derived from the information, structure of the hydrophilic head group, alkyl ether surfactants can be broadly classified into two classes: those whose hydrophilic head groups are made up of repeating glycerol subunits, related isomers, or larger sugar molecules, and those whose hydrophilic head groups are made up of repeating ethylene oxide subunits [9,18-20].

Alkyl esters: In this group of surfactants, sorbitan esters are the surfactant that are most frequently employed to create niosomes. Vesicles formulated using polyoxyethylene sorbitan monolaurate exhibit greater solubility compared to vesicles prepared using alternative surfactant-based methods[21-22].

Alkyl amides: The production of niosomal vesicles has been accomplished using alkyl amide, such as galactosides and glucosides[23].

2.**Cholesterol:** Through its mutual contact with non-ionic surfactants, cholesterol affects the niosomes' physical characteristics and structure[9,24]. Niosome systems are known to undergo a gel to liquid phase transition that is known to be abolished by cholesterol, making niosomes less leaky. Due to its amphipathic nature, cholesterol aligns itself so that its -OH group faces the aquatic facet and its aliphatic chain is parallel to the hydrocarbon chain of the surfactant[25-26]. A steroid derivative called cholesterol is primarily employed in the creation of niosomes. Although its involvement in bilayer formation may be minimal, the importance of cholesterol cannot be ignored in the generation and regulation of niosomes, as well as the modulation of membrane properties. The incorporation of cholesterol influences various aspects of niosome characteristics, including membrane permeability, stiffness, encapsulation efficiency, rehydration capability of lyophilized niosomes, and potential adverse effects[6,27]. Cholesterol enhances the rigidity of vesicles, stabilises niosomes against the effects of Plasma and serum constituents that induce destabilization and hinder vesicle permeability for encapsulated substances are mitigated, thereby preventing leakage[28].

3.**Charged Molecules:** By introducing electrostatically charged moieties to the lipid bilayer of vesicles,charged molecules make the vesicles more stable. In doing so, they reduce vesicle aggregation and boost surface charge density. Stearylamine and stearyl pyridinium chloride are widely recognized positively charged molecules employed in niosomal formulations, and Diacetyl phosphate and phosphatidic acid are widely utilized as the predominant negatively charged compounds for the synthesis of niosomes[1,29]. Due to the possibility that an elevate abundance of charged molecules could hinder the development of niosomal structures, the charged molecule is frequently integrated into niosomal formulations in a quantity of 2.5–5 mol%[29-30]. Moreover, charged molecules can be employed to create charged niosomes that are beneficial for enhancing skin permeability, increasing the effectiveness of drug encapsulation[9,31-32].

4.**Hydration Medium:** The hydration medium is an additional crucial ingredient needed in the preparation of niosomes in along with the previously listed components. Phosphate buffer is commonly leveraged as a solvent for hydration. However, the solubility of the encapsulated medicine determines the buffer's pH[3,10,33-34].

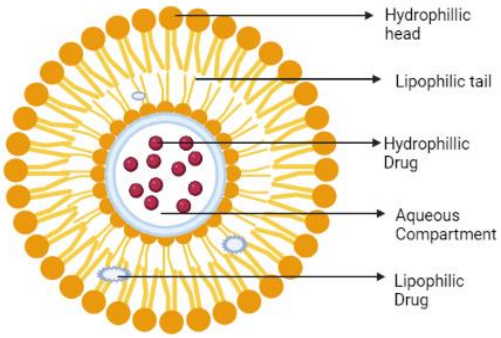

Figure 1: Structure of Niosomes

ADVANTAGES OF NIOSOMES:

Compared to the conventional delivery method, niosomes provide a number of advantages.

1. Niosomes have the capacity to accommodate a diverse array of pharmacological moieties, including hydrophilic, lipophilic, and ampiphilic substances.
2. By adjusting the composition of the vesicle, size of the vesicle, lamellarity of the vesicle, surface charge of the vesicle, tapped volume and concentration of the vesicle, vesicles properties can be altered.
3. A sustained, controlled release of the medication is feasible.
4. Surfactants can be managed and stored without the need for specific conditions.
5. It permits a controlled release of the medication because of the depot formulation.
6. Enhanced oral bioavailability has been achieved for medications with limited solubility.
7. Surfactants are degradable, compatible with living organisms, non-harmful, and non-immune-reactive among many other characteristics.
8. Niosomes have the ability to shield the active moiety from biological circulation.
9. They improve the therapeutic efficacy of drug molecules by prolonging their retention in the bloodstream, providing a protective barrier against the biological milieu, and restricting their impact to target cells.
10. They intensify the resilience of encapsulated drugs and exhibit osmotic activity and stable.
11. In contrast to oily dosage formulations, this offers good patient compliance[35-37].

DISADVANTAGES OF NIOSOMES

1. Despite the numerous advantages of the niosomal delivery method, the drug may be hydrolyzed, which could impact stability when niosomes are suspended in water.
2. Due to drug hydrolysis, entrapped drug leakage, fusion, and aggregation, niosome aqueous solutions have a short shelf life.
3. Extrusion and sonication are labor-intensive processes that really need specialized tools to prepare multilamellar vesicles.
4. Another potential scenario involves drug leaking from the niosome's entrapment area[33,35,38].

TYPES OF NIOSOMES[33]

According to their size, niosomes can c be categorized into three distinct groups:

a. Small unilamellar vesicles (SUV), which have a size range of 10–100 nm.
b. Large unilamellar vesicles (LUV), with a size range of 100–3000 nm.
c. Multilamellar vesicles (MLV) are bilayer structures with more than one layer[1,8,33,39].

Besides the aforementioned ones, several other unique niosomes are also referenced in the literature. Here, we delve into a few significant ones for discussion.

1. **Proniosomes**: Proniosomes are the dehydrated versions of niosomes. Proniosomes need to be hydrated prior to usage. They form an aqueous niosome dispersion after being hydrated. Proniosomes have advantages over niosomes due to their dry form, including aggregation, fusion, less caking, and flexibility of transportation and distribution[6,7,10,33,40-42]. Spray coating, coacervation phase separation, and the slurry

approach can all be used to synthesize Proniosomes[33,43]. Proniosomes have been observed to elevate the oral bioavailability of the medication orlistat, which has a weak water solubility[33,44].

2. **Surfactant Ethosomes**Ethanol is employed in surfactant ethosomes at a relatively elevated concentration. Non-ionic surfactants, along with ethanol or isopropyl alcohol, and water, synergistically combine to form ethosomes. According to reports, surfactant ethosomes penetrate the stratum corneum and have a substantially larger transdermal flux than niosomes[10,33,45]. According to their composition, ethosomes are generally divided into three classes: transethosomes, binary ethosomes, and classical ethosomes[33,46-48].
3. **Bola–surfactant niosomes:** Bola surfactant niosomes are the surfactants derived from omega-hexadecyl-bis-(1-aza-18 crown-6) (bola surfactant): Span-80/cholesterol in a 2: 3: 1 molar ratio[6,33,49].
4. **Aspasomes**: The literature also highlights the presence of water-soluble lamellar vesicles comprising ascorbyl palmitate. To enhance the rigidity of the bilayer, cholesterol is incorporated, while the formulation is stabilized through the inclusion of highly charged lipid diacetylphosphate[33,50]. In order to produce niosomes, this component was first hydrated in an aqueous solvent. Drug transdermal permeability can be increased using aposomes, which can also reduce the problem caused on by oxygen[6,51-52].
5. **Discomes:** The enormous niosomes in the shape of discs are discomes. Discomes are only visible in a specific condition of the non-ionic surfactant phase diagram. Beforehand globular-shaped niosomes are subjected to incubation with varying ratios of Solulan 24 at a temperature of 74 °C in a water bath with continuous agitation for a duration of 1 hour, discomes of 11–60 m size are produced. Discomes are utilised as a vehicle for the drug's prolonged administration to the ocular region. Naltrexone discomes were created utilizing a modified reverse-phase evaporation process for ocular delivery. The formulation was conducted at a temperature of 60 °C, which is below the previously stated temperature requirements and can prove advantageous for heat-vulnerable substances[10,40,33,53-55].
6. **Elastic niosome:** They are synthesized using ethyl alcohol, a non-ionic surface-active agent, along with water.They are able to pass through the stratum's pores having larger-sized corneum than vesicle-sized cornea[10,33,56]. They can be employed to administer pharmaceutical compounds of both low and high molecular weights. Its duration of action is longer than that of conventional niosomes, and their penetration depends on trans-epidermal hydration rather than concentration[33,57-59].
7. **Vesicles in Water and Oil System (v/w/o):** According to research, the emulsification of aqueous niosomes into an oil phase results in the formation of vesicles in water in oil emulsions (v/w/o). This can be achieved by combining a niosome suspension consisting of sorbitol monostearate, cholesterol, and solulan C24 (poly-24-oxyethylene cholesteryl ether) with the oil facet at a temperature of 60 °C. As a result, an emulsion of vesicles in water and oil (v/w/o) is formed, which, upon cooling to room temperature, transitions into a gel of vesicles in water and oil (v/w/o gel)[6,22,60].
8. **PEGylated niosomes:** Niosomes modified with polyethyleneglycol (PEG) possess the ability to evade the mononuclear phagocytic system's (MPS) absorption, which enables the pharmaceutical to be encapsulated, thereby extending its circulation duration[8,61]. Cholesterol, dicetyl phosphate, and span 60 can be employed to manufacture these niosomes. The provision is done using the ether injection technique. They are modified after preparation using polyethylene glycol monosterate-15[33].
9. **Niosomes of Hydroxyl Propyl Methyl Cellulose**: In this type, niosomes were added to a base that had been prepared beforehand and contained 10% glycerin of hydroxy propyl methyl cellulose. This niosomal system was reported to have a greater bioavailability and reduce paw edema caused by carrageenan than the plain formulation of flurbiprofen[6,21,60].

II. METHOD OF PREPARATION

1. **Formation of Niosome by the Proniosomes Techniques**
   Proniosomes, also known as dry niosomes, are non-ionic surfactant vesicles in dry form that, when hydrated, quickly transform into niosomes. As a result of their excellent stability, they are now frequently used in the formulation of niosomes[63,64-66]. Proniosomes can be easily hydrated into niosomes before use and are made up of a water-soluble carrier covered in non-ionic surfactants . This process has various benefits, including superior physical and chemical stability for long-term storage, ease of transportation, and simplicity in scaling up[67-68]. This is the most effective approach to reduce the amount of water in niosomes to improve their stability, and it might offer a solution for long-term storage.
2. **Thin Film Hydration Method**
   One of the most popular techniques for creating liposomes is thin film hydration, or TFH. Niosomes could be created using this method as well. It is a straightforward procedure that requires putting the membrane-forming components in a flask with an organic solvent. A dry thin-film layer develops inside the flask following the vacuum evaporation of the organic solvent. The drug is employed to hydrate the dry film after being dissolved in an aqueous solution, such as water or a buffer. Niosomes are formed by incubating it in a

water bath at a temperature above the surfactant's transition point. Multilamellar vesicles (MLV) niosomes are produced using the TFH technique[69-71].

3. **Microfluidization**
   A novel technique for creating niosomes called micro fluidization uses the jet principle by combining two different fluids, such water and alcohol, in micro channels. By optimising the variables, such as the mixing conditions, surfactants, and other components, niosomes can be produced with the desired particle sizes and size distribution[72]. Micro fluidization techniques have been widely used in the formulation of niosomes in recent years due to its benefits, which include the production of niosomes with smaller diameters, improved repeatability, and ease of formulation. And this approach is thought to be a promising one for the commercialization of niosomes[63].
4. **Sonication**
   The traditional method for making niosomes is sonication. Operating this approach is simple. To obtain the appropriate niosomes, the drug solution (in buffer) must simply be introduced to the correct mixture of non-ionic surfactant at an optimised ratio and then sonicated at a specified frequency, temperature, and time. This is also an effective method for managing the niosome's particle sizes[73]. However, probe sonication uses a lot of energy, which could result in a fast rise in temperature and the degradation of titanium[14].
5. **Reverse Phase Evaporation Method**
   The non-ionic surfactant and other supplementary substances are dissolved in an organic solvent as part of the reverse phase evaporation technique. To create an emulsion through sonication, the loaded drugs are initially dissolved in an aqueous solution, such as water or PBS, and introduced into the organic phase. To generate niosomes, the organic solvent is vaporized utilizing a rotary vacuum evaporator at temperatures ranging from 40 to 60 °C. Niosomes produced using the reverse phase evaporation approach exhibited nanoparticles of uniform size and unilamellar or oligolamellar structures, as compared to those prepared using the thin film hydration method[74-76].
6. **Ether Injection Method**
   In this method, a surfactant solution dissolved in diethyl ether is gradually added to warm water maintained at a temperature of 60°C. The surfactant blend dissolved in ether is subsequently introduced into a watery solution of the desired substance using a 14-gauge needle. Vaporisation of ether results in the formation of single-layered vesicles[77-78].
7. **Multiple membrane extrusion method:**
   Evaporation is employed to generate a thin film from a combination of dicetyl phosphate. chloroform, cholesterol, and surfactant. A series of aqueous drug polycarbonate membranes have been arranged consecutively for up to 8 passages are employed to saturate the film. The solution and the resulting colloidal suspension are extruded through these membranes. With this approach, niosome size can be effectively controlled[79].
8. **The Bubble Method**
   The "Bubble" methodology, a recently developed technique, allows for the fabrication of niosomes in the absence of necessity of non-aqueous solvents. The bubbling apparatus comprises a round-bottomed flask with three openings, which is immersed in aqueous medium to regulate the temperature. The initial and subsequent of the three openings are employed to position a water-cooled thermometer and reflux, while the third opening is utilized for the introduction of nitrogen gas. By utilizing a high-shear homogenizer, Cholesterol and surfactant are blended and dispersed in a buffer solution (pH 7.4) at a temperature of 70 °C for a duration of 15 seconds. Immediately, the mixture is subjected to bubbling with nitrogen gas at a temperature of 70 °C to generate niosomes[80].

III. SPECIALIZED NIOSOMES[81]

1. **pH-Responsive Niosomes:** Because of their acidic properties (pH ranging from 5.5 to 7.0) in contrast to the usual pH of 7.4 found in healthy extracellular tissues, pH-sensitive niosomes exhibit promise as carriers of medications and are extensively studied for their aptitude in delivering drugs specifically to cancerous and inflammatory tissues[82]. Non-ionic surfactants and cholesterol are the primary building blocks of these niosomes; pH sensitivity is obtained by adding substances like peptides[83], derivatized surfactants[84].
   Pereira et al. designed pH-sensitive niosomes using the pH (low) insertion peptide (pHLIP) to target cancerous cells. As opposed to some of the peptide-based pH-sensitive niosomes, pHLIP direct cytoplasmic delivery does not trap therapeutics and the conveyance mechanism within endosomes and lysosomes. Improved therapeutic index may result from the application of pHLIP in the formulation of nano drug delivery systems by overcoming the specificity of cancer cells that exhibit limited or no increased permeability and retention[85].

Ayat Allam et.al formulated pH sensitive in situ forming gel to extend precorneal retention of drugs. In comparison to free drug placed into the in situ gel or into the niosomes, niosomes loaded into the pH sensitive in situ gelling system were able to control drug release more effectively. It seems that the in situ gel's increased viscosity and mucoadhesive abilities, along with the sustained drug release from the niosomes over an extended period, could increase ocular residency, increase bioavailability, and reduce the need for repeated drug instillations[86].

2. **Magnetic Niosomes:** For the treatment and diagnostics of cancer, niosomes may be used to combine medication delivery and magnetic targeting. The main concept behind employing magnetic materials is to enable the application of extracorporeal magnets to target drug-loaded magneto-niosomes to particular organs or tissues[87-88].

   Barani et al. studied the potential for cytoplasmic and nuclear gene delivery using magnetic niosomes. The study, that was the first of its kind, according to the researchers, demonstrated that ergosterol niosomes exhibit greater bilayer stability of lipid membranes than cholesterol because of the many hydrogen bonds that ergosterol forms with surfactants. For the delivery of big molecules, this was crucial[89].

   Ag Seleci.et.al developed Transferrin-Decorated Niosomes with Integrated InP/ZnS Quantum Dots(QDs) and Magnetic Iron Oxide Nanoparticles(MIONs) for the imaging of glioma. In vitro studies showed that QDs/MIONs/Tf produces an obvious negative-contrast enhancement effect on glioma cells by magnetic resonance imaging (MRI) and also improved fluorescence intensity under fluorescence microscopy[90].

3. **Immune Niosomes:** Niosomes have been combined with antibodies to generate immuno-niosomes, and cyanuric chloride derivatized Tween® 61 was used to attach monoclonal IgG antibodies to vesicle surfaces. Hood E.et.al delivered anti-inflammatory drugs to fixed cells known to express CD44 using the anti-CD44 antibody IM7 linked via a cyanuric chloride. As compared to controls, the synthetic niosomes displayed selectivity and specificity. These results imply that the resulting immuno-niosomes may offer an efficient means of delivering targeted drugs[91].

4. **Thermoresponsive Niosomes:** Additional kind of stimuli-responsive niosomes being researched for cancer cell-specific drug delivery are thermoresponsive niosomes. These systems work by accumulating in solid tumours as a result of the EPR phenomenon and release drugs when the target tissue is given little hypothermic stimulus by local application of heat. The non-ionic surfactant membrane undergoes a phase transition (Tc) when heat is applied, causing the bilayer to become unstable and the drug to be released[92].

   The creation of thermoresponsive niosomes using a thermo-sensitive polymeric surfactant was initially reported by Tavano.et.al[93]. Utilising film hydration, niosomes were created with or without cholesterol using Pluronic® L64 and L64ox, a derivative of L64. In the formation process, multilamellar niosomal vesicles had strong stability (>4 weeks), good EE (85%), and a nano-size range (335-600 nm).

   Kerdmenee k.et.al[94] explored the advancement and assessment of a heat-sensitive azithromycin-filled niosome gel (AZG) to seek an optimal composition for periodontitis therapy. The formulated AZG relying on P407–HA connections and AZM-filled niosomes exhibited satisfactory characteristics, including effortless application and prolonged drug liberation, along with heightened drug penetration. Furthermore, it enhanced the availability of AZM in periodontal tissue. The devised compositions demonstrated efficacy in eradicating harmful bacteria.

5. **Stealth niosomes**: Stealth or long-circulating niosomes have been produced to avoid being quickly eliminated from blood circulation by the mononuclear phagocytic system (MPS), which prevents them from reaching the target site.PEGylation of nanoparticles to produce stealth qualities has been widely documented in recent years. PEG chains shield the nanoparticles from MPS by forming a hydrophilic layer on their surface that deters the interactions between serum proteins that lead to opsonization[95-96].

   Haroun and colleagues documented the utilization of Brij® 52, Span® 60, and Poloxamer 184 surfactants in the formulation of stealth niosomes.The results of the research suggested that PEGylation of these niosomes could be used to create targeted drugs delivery systems. The study found that Span® 60-PEGylated niosomes exhibited superior performance in terms of serum protein interactions, leading to reduced interactions in buffer and serum-based in vitro release assessments, as well as demonstrating enhanced in vivo anti-tumor efficacy[97].

   Pengnam .et al. documented the utilization of PEGylated niosomes to surmount these hurdles. They employed PEGylated plier-like cationic niosomes comprising Span® 20 and cholesterol for gene transportation..The resulting cationic nioplexes displayed a positive zeta potential that decreased as more PEG was applied. In contrast to the regular cationic niosomes, the 2% PEG-containing niosomes had a considerable increase in transfection efficiency (118%)[98].

6. **Radio niosomes:** Radiopharmaceuticals have been administered utilizing radio niosomes. Niosomes loaded with radiopharmaceuticals exhibit promising applications in numerous cancer types. Radiolabeled niosomes are crucial for the diagnostic visualization of organs such as the liver and spleen.As an illustration, imaging potential has been demonstrated for 99mTc-labeled diethylenetriamine pentaacetate (DTPA)[99].

De Silva and colleagues effectively showcased how to develop archetypal 99mTc conjugated niosomes using a straightforward, quick approach. Their research indicated that the generated radio-niosomes can potentially be administered in vivo, leading to significant tumor-to-muscle uptake[100].

NIOSOMES AS DRUG CARRIERS

1. **Protein and Peptide drugs**: Insulin and bacitracin are two examples of proteins and peptides that may serve as significant pharmaceutical agents for the therapy of medical conditions. However, their poor bioavailability,instability during storage and after administration, as well as various adverse reactions during application, restrict their clinical implementation. Niosomes may help solve these issues by acting as effective vehicles for the delivery of variety of protein and peptide therapeutics. They also function well when used in the development and administration of vaccines. According to reports, niosome have been investigated for use in parenteral and vaginal insulin delivery and demonstrated a strong ability to prevent insulin from deteriorating[63].Ning M .et.al prepare and research the niosome vaginal delivery system's potential for systemic insulin administration(composed of Span40 and Span60) and the comparative pharmacological bioaccesibility and the relative bioaccesibility of insulin vesicles through vaginal administration were evaluated, as well as the subcutaneous infusion of an insulin solution. The findings indicates insulin-Span 60, Span 40 niosomes had an enhancing effect on vaginal delivery of insulin[101].

2. Cosmeceutical Drugs:

2.1. **Delivering of anti scarring ingredients:** In comparison to conventional nanomaterials, the efficacy of a topical gel comprised of elastic niosome particles loaded with papain has been assessed. Increased papain penetration, less scarring, and enhanced transdermal absorption were found when elastic manufactured niosome particles were compared to conventional nanomaterials. Gallic acid's chemical stability and cutaneous penetration were improved by elastic-fabricated niosome particles, indicating that they may potentially make excellent carriers for skin-anti-aging substances.

2.2. **Delivering of anti-aging effects ingredients:** Manosroi et al. examined the advantages of lipid vesicles manufactured from bran from rice grains in combating ageing. The unentrapped rice bran particles and entrapped rice bran niosomes were compared in this study. The formulations enhanced the characteristics of the skin, including dryness, excessive pigmentation, thickness and roughness, and skin suppleness. They also prevented the ageing of the skin by stopping the breakdown of skin collagen. Niosomes made of rice bran offer synergic benefits for postponing skin aging in cosmetic product utilization, claims the study[102].

3. **Anti-cancer drugs:** Chemotherapy is typically the cancer treatment of choice today. Many anticancer medications' therapeutic efficiency is constrained by their low tumour tissue penetration and their detrimental negative consequences on normal cells. Numerous initiatives have been developed to address these issues, such as the application of niosomes as a cutting-edge medication delivery mechanism.

3.1. **Lung cancer:** Mohammad Saimi.et.al. developed Gemcitabine and cisplatin loaded aerosolized niosomes for the treatment of lung cancer.NGC prepared by the straightforward heating technique and optimized using a D-optimal mixture design.Cytotoxicity of developed niosomes was investigated over Normal lung(MRC5) and lung cancer(A549) cell lines. When compared to the control (Gem + Cis alone), the findings indicated that the optimised NGC demonstrated reduced cytotoxic effects on MRC5 and A549 cells, as evidenced by the decrease in IC50 values from highly harmful or toxic (IC50 1.56 g/mL) to slightly toxic (IC50 280.00 g/mL) and moderately toxic (IC50 = 46.00 g/mL) after 72 hours of treatment[103].

3.2. **Ovarian cancer:** Xu YQ.et.al formulated curcumin loaded niosomes and studied its cytotoxic effects on ovarian cancer. Niosomes were formulated using Span 80, Tween 80, and Poloxamer 188. Cur($C_{21}H_{20}O_6$) is a naturally occurring yellow chemical that is generally found in Curcuma longa and is present in many other types of herbs. Anticancer, anti-inflammatory, antioxidant, antibacterial, anti-rheumatic, and hepatoprotective effects are only a few of the therapeutic benefits of curcumin. This technique allowed for the controlled release of curcumin, enhancing its therapeutic value. To assess the in vitro drug release of curcumin-niosomes, dynamic dialysis was used. In comparison to freely dispersed curcumin, curcumin-niosomes showed the toxicity to cells and rate of cell apoptosis in conflict with A2780 ovarian cancer cells were augmented, leading to an enhanced anticancer effect.These findings show that a promising method for delivering curcumin for ovarian cancer treatment is the curcumin-niosome system[104].

3.3. **Breast cancer:** Folate targetted curcumin formulated niosomes for targeted delivery in the treatment of breast cancer by Honarvari B.et.al. Three different nonionic surfactants (Span 20, 60, and 80) were utilized to generate diverse niosomes loaded with Curcumin (Nio-Cur) in order to improve Cur's ability to treat cancer. Then, to prevent breast cancer, synthetic Nio-Cur was embellished with folic acid(FA) and polyethylene glycol (PEG). Curcumin (Cur) (1,7-bis (4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a bioactive substance originally extracted from Curcuma longa's root and rhizome. It has a yellow colour and a variety of uses. Cur suppresses epithelial-mesenchymal transition (EMT) and possesses the capability to trigger programmed cell death in cancer cells, which lowers cancer dissemination. Due to Cur's low bioavailability, its potential health advantages are only partially absorbed by the intestine after

oral consumption, with the remainder being excreted. Cur's bioavailability is reduced by its quick liver and plasma metabolism. When the absorption of PEG-FA@Nio-Cur and Nio-Cur was evaluated in MCF7 and 4T1 cells, the findings indicated that PEG-FA-modified niosomes exhibited the perponderant level of endocytosis. PEG-FA@Nio-Cur represents potential method for the conveyance of Curcumin in the treatment of breast cancer, according to in vitro research[105].

4. **Anti-Inflammatory Drugs:** NSAIDs are the anti-inflamtory agents that are frequently used to lower a high temperature, reduce inflammation, and relieve pain.Among the often utilized non-steroidal anti-inflammatory medicines (NSAIDs) to alleviate pain disorders is ibuprofen. NSAIDs have a challenging time crossing biological membranes for a number of reasons. To get over these limitations, Marzoli f.et.al[106] investigate the outcomes of a novel pH-sensitive formulation of niosomes encapsulating Polysorbate 20 derivatized by Glycine and loaded with ibuprofen (NioIbu) in an assortment of mouse animal pain models. When NioIbu was given two hours before the test, it had no effect on reducing ciception, while the free form of Ibuprofen had no such effect. NioIbu caused a persistent decrease exaggerated pain sensitivity in mice when used in a representative of inflammatory pain where hyperalgesia had been created by zymosan. NioIbu decreased both neuropathy-induced allodynia and hyperalgesia in a model of neuropathic pain caused by prolonged sciatic nerve constriction.
5. **Antibiotics:** Amikacin is an aminoglycoside antibiotic used to treat bacterial infections that are drug-resistant. Because of concurrent drug-resistant bacteria and SARS-CoV-2 hospitalised patients, the proliferation of bacterial infections has become a serious worry for the medical system. The possibility of biofilm generation makes Klebsiella strains, one of the foremost frequent bacteria in the evolution of drug resistance, a serious hazard. To get over this, Rahmati M.et.al. synthesized Amikacin loaded niosomes nanoparticles to ameliorate the amikacin activity in conflict with antibiotic resistant Klebsiella pneumoniae strains.Thin film hydration method was adopt using span 60 and tween60. Rahmati and workers investigated that Niosomes with optimised amikacin structures offer robustness and regulate drug release for antibacterial activity. The altered allocation of amikacin in the host cells' organelles demonstrated non-toxicity to the HFF cells and simultaneously improved Klebsiella pneumonia's absorption of medications. Drug-resistant Klebsiella pneumonia had a considerable reduction in the expression of genes related to biofilms as a result of noisome-amikacin's penetration into the bacterial cells. As a result, these nanostructures can improve treatment for persistent infections brought on by the drug-resistant Klebsiella bacteria[107]. Another study to increase efficacy of antibiotics, Allam A.et.al formulated vancomycin loaded niosomes integrated within pH sensitive in situ forming gel for the treatment of ocular infection. This formulation was synthesized to alleviate ocular irritataion and elonagate effect of Vancomycin. The developed formulations proved encouraging in-vivo biocompatibility and antibacterial efficacy, indicating their viability use as an ophthalmic preparation to treat ocular infections brought on by resistant bacterial strains while reducing drug sensitivity and boosting patient obedience[108].

IV. CONCLUSION

To create efficient medication delivery systems, niosomes are new nanoscale drug carriers. They bestow an incredible prospect for encapsulating hydrophilic, lipophilic, or both types of drugs. Numerous studies have been conducted utilizing diverse divisions of niosomal preparation to facilitate the delivery of anticancer, anti-inflammatory, anti-infective, and other therapeutic agents.The relevant research demonstrated that niosomes offer targeted delivery to specific tissue types, reduce dosage requirements, and enhance the stability of encapsulated drugs. Employing distinctive formulations, loading methods, and modification techniques for specific administration routes can enhance the structural characteristics and properties of niosomes. Therefore, niosomes emerge as potential therapeutic agents with potential for commercial availability.

REFERENCES

[1]. Ag Seleci D, Seleci M, Walter JG, Stahl F, Scheper T. Niosomes as nanoparticular drug carriers: fundamentals and recent applications. Journal of nanomaterials. 2016 Oct;2016.

[2]. Seleci M, Seleci DA, Joncyzk R, Stahl F, Blume C, Scheper T. Smart multifunctional nanoparticles in nanomedicine. BioNanoMaterials. 2016 May 1;17(1-2):33-41.

[3]. Mahale NB, Thakkar PD, Mali RG, Walunj DR, Chaudhari SR. Niosomes: novel sustained release nonionic stable vesicular systems—an overview. Advances in colloid and interface science. 2012 Nov 15;183:46-54.

[4]. Cosco D, Paolino D, Muzzalupo R, Celia C, Citraro R, Caponio D, Picci N, Fresta M. Novel PEG-coated niosomes based on bola-surfactant as drug carriers for 5-fluorouracil. Biomedical microdevices. 2009 Oct;11:1115-25.

[5]. Paolino D, Muzzalupo R, Ricciardi A, Celia C, Picci N, Fresta M. In vitro and in vivo evaluation of Bola-surfactant containing niosomes for transdermal delivery. Biomedical microdevices. 2007 Aug;9:421-33.
[6]. Rajera R, Nagpal K, Singh SK, Mishra DN. Niosomes: a controlled and novel drug delivery system. Biological and Pharmaceutical Bulletin. 2011 Jul 1;34(7):945-53.
[7]. Marianecci C, Di Marzio L, Rinaldi F, Celia C, Paolino D, Alhaique F, Esposito S, Carafa M. Niosomes from 80s to present: the state of the art. Advances in colloid and interface science. 2014 Mar 1;205:187-206.
[8]. Moghassemi S, Hadjizadeh A. Nano-niosomes as nanoscale drug delivery systems: an illustrated review. Journal of controlled release. 2014 Jul 10;185:22-36.
[9]. Rinaldi MC, Alhaique FC, Niosomes FE. from 80s to present: the state of the art. Adv. Colloid Interface Sci. 2014;205:187-206.
[10]. Kumar GP, Rajeshwarrao P. Nonionic surfactant vesicular systems for effective drug delivery—an overview. Acta pharmaceutica sinica B. 2011 Dec 1;1(4):208-19.
[11]. Kazi KM, Mandal AS, Biswas N, Guha A, Chatterjee S, Behera M, Kuotsu K. Niosome: a future of targeted drug delivery systems. Journal of advanced pharmaceutical technology & research. 2010 Oct;1(4):374.
[12]. Kaur D, Kumar S. Niosomes: present scenario and future aspects. Journal of drug delivery and therapeutics. 2018 Sep 6;8(5):35-43.
[13]. Biswas GR, Majee SB. Niosomes in ocular drug delivery. Eur. J. Pharm. Med. Res. 2017;4(7):813-9.
[14]. Abdelkader H, Alani AW, Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug delivery. 2014 Mar 1;21(2):87-100.
[15]. Azmin MN, Florence AT, Handjani- Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The effect of non- ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate in mice. Journal of pharmacy and pharmacology. 1985,Apr;37(4):237-42.
[16]. Sahin NO. Niosomes as nanocarrier systems. Nanomaterials and nanosystems for biomedical applications. 2007:67-81.
[17]. Handjani-Vila RM, Ribier A, Rondot B, Vanlerberghie G. Dispersions of lamellar phases of non-ionic lipids in cosmetic products. International journal of cosmetic Science. 1979 Oct 1;1(5):303-14.
[18]. Morigaki K, Walde P. Fatty acid vesicles. Current Opinion in Colloid & Interface Science. 2007 Apr 1;12(2):75-80.
[19]. Namani T, Ishikawa T, Morigaki K, Walde P. Vesicles from docosahexaenoic acid. Colloids and Surfaces B: Biointerfaces. 2007 Jan 15;54(1):118-23.
[20]. Harvey RD, Heenan RK, Barlow DJ, Lawrence MJ. The effect of electrolyte on the morphology of vesicles composed of the dialkyl polyoxyethylene ether surfactant 2C18E12. Chemistry and physics of lipids. 2005 Jan 1;133(1):27-36.
[21]. Reddy DN, Udupa N. Formulation and evaluation of oral and transdermal preparations of flurbiprofen and piroxicam incorporated with different carriers. Drug development and industrial pharmacy. 1993 Jan 1;19(7):843-52.
[22]. Yoshioka T, Sternberg B, Florence AT. 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. 1994 Apr 25;105(1):1-6.
[23]. Guedj C, Pucci B, Zarif L, Coulomb C, Riess JG, Pavia AA. Vesicles and other supramolecular systems from biocompatible synthetic glycolipids with hydrocarbon and/or fluorocarbon chains. Chemistry and physics of lipids. 1994 Aug 8;72(2):153-73.
[24]. Bandyopadhyay P. Fatty alcohols or fatty acids as niosomal hybrid carrier: effect on vesicle size, encapsulation efficiency and in vitro dye release. Colloids and Surfaces B: Biointerfaces. 2007 Jul 1;58(1):68-71.
[25]. Azeem A, Anwer MK, Talegaonkar S. Niosomes in sustained and targeted drug delivery: some recent advances. Journal of drug targeting. 2009 Nov 1;17(9):671-89
[26]. Vyas SP, Khar RK. Controlled drug delivery concepts and advances. vallabh prakashan. 2002;1:411-7.
[27]. Mozafari MR, editor. Nanomaterials and nanosystems for biomedical applications. Springer Science & Business Media; 2007 Sep 19.
[28]. Liu T, Guo R, Hua W, Qiu J. Structure behaviors of hemoglobin in PEG 6000/Tween 80/Span 80/H2O niosome system. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2007 Feb 1;293(1-3):255-61.
[29]. Junyaprasert VB, Teeranachaideekul V, Supaperm T. Effect of charged and non-ionic membrane additives on physicochemical properties and stability of niosomes. AAPS pharmscitech. 2008 Sep;9:851-9.

[30]. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. International journal of pharmaceutics. 1999 Aug 5;185(1):23-35.
[31]. Pardakhty A, Shakibaie M, Daneshvar H, Khamesipour A, Mohammadi-Khorsand T, Forootanfar H. Preparation and evaluation of niosomes containing autoclaved Leishmania major: a preliminary study. Journal of microencapsulation. 2012 May 1;29(3):219-24.
[32]. Oh YK, Kim MY, Shin JY, Kim TW, Yun MO, Yang SJ, Choi SS, Jung WW, Kim JA, Choi HG. Skin permeation of retinol in Tween 20- based deformable liposomes: in- vitro evaluation in human skin and keratinocyte models. Journal of pharmacy and pharmacology. 2006 Feb;58(2):161-6.
[33]. Bhardwaj P, Tripathi P, Gupta R, Pandey S. Niosomes: A review on niosomal research in the last decade. Journal of Drug Delivery Science and Technology. 2020 Apr 1;56:101581.
[34]. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. International journal of pharmaceutics. 1998 Oct 15;172(1-2):33-70.
[35]. Vadlamudi HC, Sevukarajan M. Niosomal drug delivery system-a review. Indo American Journal of Pharmaceutical Research. 2012;2(9).
[36]. Muzzalupo R, Tavano L. Niosomal drug delivery for transdermal targeting: recent advances. Res. Rep. Transdermal Drug Deliv. 2015 Jul 29;4:23-33.
[37]. Yadav JD, Kulkarni PR, Vaidya KA, Shelke GT. Niosomes: a review. Journal of Pharmacy Research. 2011 Mar;4(3):632-6.
[38]. Sutar SN, Gavhane YN. NOVEL DRUG DELIVERY SYSTEM-NIOSOMES.
[39]. Kaur IP, Garg A, Singla AK, Aggarwal D. Vesicular systems in ocular drug delivery: an overview. International journal of pharmaceutics. 2004 Jan 9;269(1):1-4.
[40]. Gharbavi M, Amani J, Kheiri-Manjili H, Danafar H, Sharafi A. Niosome: a promising nanocarrier for natural drug delivery through blood-brain barrier. Advances in Pharmacological and Pharmaceutical Sciences. 2018 Dec 11;2018.
[41]. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. International journal of pharmaceutics. 1999 Aug 5;185(1):23-35.
[42]. Jadon PS, Gajbhiye V, Rajesh SJ, Kavita R, Narayanan G. A Controlled and Novel Drug Delivery System. AAPS Pharm. Sci. Tech. 2009;10:1187-92.
[43]. Yasam VR, Jakki SL, Natarajan J, Kuppusamy G. A review on novel vesicular drug delivery: proniosomes. Drug delivery. 2014 Jun 1;21(4):243-9.
[44]. Samyuktha R, Vedha HB. Niosomal formulation of Orlistat: Formulation and in-vitro evaluation. Int J drug dev res. 2011;3:300-11.
[45]. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes—novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of controlled release. 2000 Apr 3;65(3):403-18.
[46]. Zhou Y, Wei Y, Liu H, Zhang G, Wu XA. Preparation and in vitro evaluation of ethosomal total alkaloids of Sophora alopecuroides loaded by a transmembrane pH-gradient method. Aaps Pharmscitech. 2010 Sep;11:1350-8.
[47]. Song CK, Balakrishnan P, Shim CK, Chung SJ, Chong S, Kim DD. A novel vesicular carrier, transethosome, for enhanced skin delivery of voriconazole: characterization and in vitro/in vivo evaluation. Colloids and surfaces B: biointerfaces. 2012 Apr 1;92:299-304.
[48]. Abdulbaqi IM, Darwis Y, Khan NA, Abou Assi R, Khan AA. Ethosomal nanocarriers: the impact of constituents and formulation techniques on ethosomal properties, in vivo studies, and clinical trials. International journal of nanomedicine. 2016;11:2279.
[49]. Junyaprasert VB, Teeranachaideekul V, Supaperm T. Effect of charged and non-ionic membrane additives on physicochemical properties and stability of niosomes. AAPS pharmscitech. 2008 Sep;9:851-9.
[50]. 한상화. Structure of Ascorbyl Palmitate Bilayers (Aspasomes) from Molecular Dynamics Simulation. Bulletin of the Korean Chemical Society. 2018;39(7):887-90.
[51]. Khoee S, Yaghoobian M. Niosomes: A novel approach in modern drug delivery systems. InNanostructures for drug delivery 2017 Jan 1 (pp. 207-237). Elsevier.
[52]. Bhaskaran S, Lakshmi PK. Comparative evaluation of niosome formulations prepared by different techniques. Acta Pharmaceutica Sciencia. 2009;51(1).
[53]. Uchegbu IF, Bouwstra JA, Florence AT. Large disk-shaped structures (discomes) in nonionic surfactant vesicle to micelle transitions. The Journal of Physical Chemistry. 1992 Dec;96(25):10548-53.
[54]. Abdelkader H, Alani AW, Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly, fabrication, characterization, drug delivery applications and limitations. Drug delivery. 2014 Mar 1;21(2):87-100.

[55]. Abdelkader H, Wu Z, Al-Kassas R, Alany RG. Niosomes and discomes for ocular delivery of naltrexone hydrochloride: morphological, rheological, spreading properties and photo-protective effects. International journal of pharmaceutics. 2012 Aug 20;433(1-2):142-8.
[56]. Cevc G. Transfersomes, liposomes and other lipid suspensions on the skin: permeation enhancement, vesicle penetration, and transdermal drug delivery. Critical reviews™ in therapeutic drug carrier systems. 1996;13(3-4).
[57]. Negi LM, Garg AK, Chauhan M. Ultradeformable vesicles: concept and execution. Pharma Times. 2009;41(9):11-4.
[58]. Manosroi A, Jantrawut P, Khositsuntiwong N, Manosroi W, Manosroi J. Novel elastic nanovesicles for cosmeceutical and pharmaceutical applications. Chiang Mai J Sci. 2009 May 1;36(2):168-78.
[59]. van den Bergh BA, Vroom J, Gerritsen H, Junginger HE, Bouwstra JA. Interactions of elastic and rigid vesicles with human skin in vitro: electron microscopy and two-photon excitation microscopy. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1999 Nov 9;1461(1):155-73.
[60]. Biswal S, Murthy PN, Sahu J, Sahoo P, Amir F. Vesicles of non-ionic surfactants (niosomes) and drug delivery potential. International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN). 2008 May 31;1(1):1-8.
[61]. Laouini A, Jaafar-Maalej C, Sfar S, Charcosset C, Fessi H. Liposome preparation using a hollow fiber membrane contactor—application to spironolactone encapsulation. International journal of pharmaceutics. 2011 Aug 30;415(1-2):53-61.
[62]. Lin T, Fang Q, Peng D, Huang X, Zhu T, Luo Q, Zhou K, Chen W. PEGylated non-ionic surfactant vesicles as drug delivery systems for Gambogenic acid. Drug delivery. 2013 Sep 1;20(7):277-84.
[63]. Ge X, Wei M, He S, Yuan WE. Advances of non-ionic surfactant vesicles (niosomes) and their application in drug delivery. Pharmaceutics. 2019 Jan 29;11(2):55.
[64]. Khatoon M, Shah KU, Din FU, Shah SU, Rehman AU, Dilawar N, Khan AN. Proniosomes derived niosomes: recent advancements in drug delivery and targeting. Drug delivery. 2017 Nov 1;24(2):56-69.
[65]. Khalil RM, Abdelbary GA, Basha M, Awad GE, El-Hashemy HA. Design and evaluation of proniosomes as a carrier for ocular delivery of lomefloxacin HCl. Journal of liposome research. 2017 Apr 3;27(2):118-29.
[66]. Muzzalupo R, Pérez L, Pinazo A, Tavano L. Pharmaceutical versatility of cationic niosomes derived from amino acid-based surfactants: Skin penetration behavior and controlled drug release. International journal of pharmaceutics. 2017 Aug 30;529(1-2):245-52.
[67]. Yuksel N, Bayindir ZS, Aksakal E, Ozcelikay AT. In situ niosome forming maltodextrin proniosomes of candesartan cilexetil: in vitro and in vivo evaluations. International journal of biological macromolecules. 2016 Jan 1;82:453-63.
[68]. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. International journal of pharmaceutics. 1999 Aug 5;185(1):23-35.
[69]. Tavano L, Muzzalupo R, Mauro L, Pellegrino M, Andò S, Picci N. Transferrin-conjugated pluronic niosomes as a new drug delivery system for anticancer therapy. Langmuir. 2013 Oct 15;29(41):12638-46.
[70]. Pardakhty A, Varshosaz J, Rouholamini A. In vitro study of polyoxyethylene alkyl ether niosomes for delivery of insulin. International journal of pharmaceutics. 2007 Jan 10;328(2):130-41.
[71]. Kamble B, Talreja S, Gupta A, Patil D, Pathak D, Moothedath I, Duraiswamy B. Development and biological evaluation of Gymnema sylvestre extract-loaded nonionic surfactant-based niosomes. Nanomedicine. 2013 Aug;8(8):1295-305.
[72]. Lo CT, Jahn A, Locascio LE, Vreeland WN. Controlled self-assembly of monodisperse niosomes by microfluidic hydrodynamic focusing. Langmuir. 2010 Jun 1;26(11):8559-66.
[73]. Pando D, Gutiérrez G, Coca J, Pazos C. Preparation and characterization of niosomes containing resveratrol. Journal of Food Engineering. 2013 Jul 1;117(2):227-34.
[74]. Zarei M, Norouzian D, Honarvar B, Mohammadi M, Shamabadi HE, Akbarzadeh A. Paclitaxel loaded niosome nanoparticle formulation prepared via reverse phase evaporation method: an in vitro evaluation. Pakistan journal of biological sciences: PJBS. 2013 Mar 15;16(6):295-8.
[75]. Jain S, Vyas SP. Mannosylated niosomes as adjuvant-carrier system for oral mucosal immunization. Journal of liposome research. 2006 Jan 1;16(4):331-45.
[76]. Shegokar R, Al Shaal L, Mitri K. Present status of nanoparticle research for treatment of tuberculosis. Journal of Pharmacy & Pharmaceutical Sciences. 2011 Apr 8;14(1):100-16.
[77]. Sharma A, Kumar L, Kumar P, Prasad N, Rastogi V. Niosomes: a promising approach in drug delivery systems. Journal of Drug Delivery and Therapeutics. 2019 Jul 15;9(4):635-42.
[78]. Satturwar PM, Fulzele SV, SN V, Kh JN. Formulation and evaluation of ketoconazole niosomes. Indian journal of pharmaceutical sciences. 2002;64(2):155.

[79]. Namdeo A, Jain NK. Niosomal delivery of 5-fluorouracil. Journal of microencapsulation. 1999 Jan 1;16(6):731-40.
[80]. Blazek–Welsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharmaceutical research. 2001 May;18:656-61.
[81]. Witika BA, Bassey KE, Demana PH, Siwe-Noundou X, Poka MS. Current advances in specialised niosomal drug delivery: Manufacture, characterization and drug delivery applications. International Journal of Molecular Sciences. 2022 Aug 26;23(17):9668.
[82]. Edlow DW, Sheldon WH. The pH of inflammatory exudates. Proceedings of the Society for Experimental Biology and Medicine. 1971 Sep;137(4):1328-32.
[83]. Das SS, Bharadwaj P, Bilal M, Barani M, Rahdar A, Taboada P, Bungau S, Kyzas GZ. Stimuli-responsive polymeric nanocarriers for drug delivery, imaging, and theragnosis. Polymers. 2020 Jun 22;12(6):1397..
[84]. Marzoli F, Marianecci C, Rinaldi F, Passeri D, Rossi M, Minosi P, Carafa M, Pieretti S. Long-lasting, antinociceptive effects of pH-sensitive niosomes loaded with ibuprofen in acute and chronic models of pain. Pharmaceutics. 2019 Feb 1;11(2):62.
[85]. Pereira MC, Pianella M, Wei D, Moshnikova A, Marianecci C, Carafa M, Andreev OA, Reshetnyak YK. pH-sensitive pHLIP® coated niosomes. Molecular membrane biology. 2016 Jul 3;33(3-5):51-63.
[86]. Allam A, Elsabahy M, El Badry M, Eleraky NE. Betaxolol- loaded niosomes integrated within pH- sensitive in situ forming gel for management of glaucoma. International journal of pharmaceutics. 2021 Apr 1;598:120380.
[87]. Widder K, Flouret G, Senyei A. Magnetic microspheres: synthesis of a novel parenteral drug carrier. Journal of pharmaceutical sciences. 1979 Jan 1;68(1):79-82.
[88]. Kong M, Park H, Feng C, Hou L, Cheng X, Chen X. Construction of hyaluronic acid noisome as functional transdermal nanocarrier for tumor therapy. Carbohydrate polymers. 2013 Apr 15;94(1):634-41.
[89]. Barani M, Nematollahi MH, Zaboli M, Mirzaei M, Torkzadeh-Mahani M, Pardakhty A, Karam GA. In silico and in vitro study of magnetic niosomes for gene delivery: The effect of ergosterol and cholesterol. Materials Science and Engineering: C. 2019 Jan 1;94:234-46.
[90]. Ag Seleci D, Maurer V, Barlas FB, Porsiel JC, Temel B, Ceylan E, Timur S, Stahl F, Scheper T, Garnweitner G. Transferrin-decorated niosomes with integrated InP/ZnS quantum dots and magnetic iron oxide nanoparticles: dual targeting and imaging of glioma. International journal of molecular sciences. 2021 Apr 27;22(9):4556.
[91]. Hood E, Gonzalez M, Plaas A, Strom J, VanAuker M. Immuno-targeting of nonionic surfactant vesicles to inflammation. International journal of pharmaceutics. 2007 Jul 18;339(1-2):222-30.
[92]. Mazzotta E, Tavano L, Muzzalupo R. Thermo-sensitive vesicles in controlled drug delivery for chemotherapy. Pharmaceutics. 2018 Sep 5;10(3):150.
[93]. Tavano L, Rossi CO, Picci N, Muzzalupo R. Spontaneous temperature-sensitive Pluronic® based niosomes: Triggered drug release using mild hyperthermia. International journal of pharmaceutics. 2016 Sep 25;511(2):703-8.
[94]. Kerdmanee K, Phaechamud T, Limsitthichaikoon S. Thermoresponsive azithromycin-loaded niosome gel based on poloxamer 407 and hyaluronic interactions for periodontitis treatment. Pharmaceutics. 2022 Sep 24;14(10):2032.
[95]. Dreher MR, Raucher D, Balu N, Colvin OM, Ludeman SM, Chilkoti A. Evaluation of an elastin-like polypeptide–doxorubicin conjugate for cancer therapy. Journal of controlled release. 2003 Aug 28;91(1-2):31-43.
[96]. Shehata T, Kimura T, Higaki K, Ogawara KI. In-vivo disposition characteristics of PEG niosome and its interaction with serum proteins. International journal of pharmaceutics. 2016 Oct 15;512(1):322-8.
[97]. Haroun, M., Elsewedy, H.S., Shehata, T.M., Tratrat, C., Al Dhubiab, B.E., Venugopala, K.N., Almostafa, M.M., Kochkar, H. and Elnahas, H.M., 2022. Significant of injectable brucine PEGylated niosomes in treatment of MDA cancer cells. Journal of Drug Delivery Science and Technology, 71, p.103322.
[98]. Pengnam, S., Patrojanasophon, P., Rojanarata, T., Ngawhirunpat, T., Yingyongnarongkul, B.E., Radchatawedchakoon, W. and Opanasopit, P., 2019. A novel plier-like gemini cationic niosome for nucleic acid delivery. Journal of Drug Delivery Science and Technology, 52, pp.325-333.
[99]. Korkmaz M, Özer AY, Hincal AA. DTPA niosomes in diagnostic imaging. InSynthetic surfactant vesicles 2000 Feb 23 (pp. 263-278). CRC Press.
[100]. De Silva L, Fu JY, Htar TT, Wan Kamal WH, Kasbollah A, Muniyandy S, Chuah LH. Biodistribution study of niosomes in tumor-implanted BALB/C mice using scintigraphic imaging. Frontiers in Pharmacology. 2022 Jan 7;12:778396.

[101]. Ning M, Guo Y, Pan H, Yu H, Gu Z. Niosomes with sorbitan monoester as a carrier for vaginal delivery of insulin: studies in rats. Drug delivery. 2005 Jan 1;12(6):399-407.
[102]. Mawazi SM, Ann TJ, Widodo RT. Application of Niosomes in Cosmetics: A Systematic Review. Cosmetics. 2022 Nov 25;9(6):127.
[103]. Mohamad Saimi NI, Salim N, Ahmad N, Abdulmalek E, Abdul Rahman MB. Aerosolized niosome formulation containing gemcitabine and cisplatin for lung cancer treatment: Optimization, characterization and in vitro evaluation. Pharmaceutics. 2021 Jan 5;13(1):59.
[104]. Xu YQ, Chen WR, Tsosie JK, Xie X, Li P, Wan JB, He CW, Chen MW. Niosome encapsulation of curcumin: characterization and cytotoxic effect on ovarian cancer cells. Journal of nanomaterials. 2016 Jan 1;2016.
[105]. Honarvari B, Karimifard S, Akhtari N, Mehrarya M, Moghaddam ZS, Ansari MJ, Jalil AT, Matencio A, Trotta F, Yeganeh FE, Farasati Far B. Folate-targeted curcumin-loaded niosomes for site-specific delivery in breast cancer treatment: In silico and In vitro study. Molecules. 2022 Jul 20;27(14):4634.
[106]. Marzoli F, Marianecci C, Rinaldi F, Passeri D, Rossi M, Minosi P, Carafa M, Pieretti S. Long-lasting, antinociceptive effects of pH-sensitive niosomes loaded with ibuprofen in acute and chronic models of pain. Pharmaceutics. 2019 Feb 1;11(2):62.
[107]. Rahmati M, Babapoor E, Dezfulian M. Amikacin-loaded niosome nanoparticles improve amikacin activity against antibiotic-resistant Klebsiella pneumoniae strains. World Journal of Microbiology and Biotechnology. 2022 Dec;38(12):230.
[108]. Allam A, El-Mokhtar MA, Elsabahy M. Vancomycin-loaded niosomes integrated within pH-sensitive in-situ forming gel for treatment of ocular infections while minimizing drug irritation. Journal of Pharmacy and Pharmacology. 2019 Aug;71(8):1209-21.