



Niosomes - A Novel Drug Delivery System

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ABSTRACT :

Microscopic nonionic vesicles known as Niosomes are formed through hydration of synthetic non ionic surfactants with or without cholesterol. They are like liposomes & they can be transport amphiphilic & lipophilic. Although they have similar bilayer structure like liposomes, niosomes are more stable due to the materials employed in their preparation which gives them many additional benefits over liposomes. This review paper concentrate on idea of niosome, its structure, advantages & disadvantages, components, types, method of preparation, Characterization & application. There are many uses for niosome technology, including the treatment of some diseases like leishmaniasis.

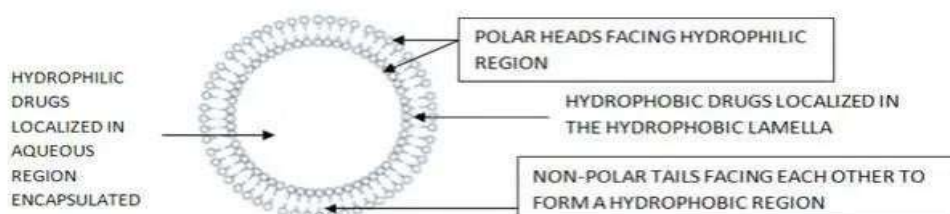
INTRODUCTION

Niosomes are bitsy nonionic surfactant vesicles attained from the hydration of synthetic nonionic surfactants with or without cholesterol. (1) They're analogous to liposomes. Both act as active carriers of both amphiphilic & lipophilic medicines. Niosomal bilayer is made up of non ionic surfactant & liposomal bilayer is made up of phospholipids. Tone assembly of non ionic surfactant form niosomes in waterless media as globular, unilamellar, Bilayered, multilamellar system & polyhedral structure depending on system used to prepare and the Inverse structure in case of non waterless detergent. The surfactant's exposure in the niosome is similar that its hydrophilic ends face outward and its hydrophobic ends face each other, forming a bilayer of surfactant. The stabilization of niosomal vesicles generated by non-ionic surfactant is achieved by adding cholesterol together with a bitsy quantum of anionic surfactant, similar as dicetyl phosphate. (2) Since phospholipids are more readily hydrolyzed due to the ester link and have lower chemical stability than surfactants, niosomes are allowed to be superior to liposomes in terms of both cost and functionality. Niosomes are a promising form of drug delivery. (3) Niosomal expression can be administered in a number of ways, including as intramuscular, intravenous, peroral and transdermal. (4,5,6,7).

DEFINATION

A non-ionic liposome grounded on surfactants is called a niosome. The main process used to produce niosomes is the objectification of cholesterol as an excipient. You can use different excipients as well. Niosomes are more suitable to access than earlier conflation phrasings. Although they partake a bilayer structure with liposomes, niosomes are more stable due to the accoutrements employed in their medication, which gives them numerous fresh benefits over liposomes [39,40]. Niosomes range in size from bitsy to nanometric. The range of flyspeck sizes is 10nm – 1000nm.

STRUCTURE OF NIOSOMES:⁴⁹



ADVANTAGES:

1. The vesicle suspense being water- grounded vehicle offers high case compliance when compared to unctuous Lozenge forms.

2. medicine moles of wide range of solubilities can be accommodated in the niosomes handed by the structure conforming of hydrophilic, lipophilic and amphiphilic halves.
3. They're suitable to release the drug gradationally and under control.
4. Surfactant running and storehouse do n't bear any particular terrain, similar as a cold room or an inert atmosphere.
5. They've the capability to serve as a depot expression, enabling regulated drug release
6. They can stop the drug from being metabolized by enzymes
7. In addition to being active and osmotically stable, they also increase the stability of the medicine that's entangled.
8. They may ameliorate the way that specifics access the skin.
9. The delayed junking of drug from rotation can enhance the remedial efficacy of the medicine moles.
10. They're suitable to keep natural rotation from affecting the active half.
11. Since waterless phase niosomal dissipation can be emulsified in the nonaqueous phase and typical vesicles can be supplied in an externalnon-aqueous phase, they can limit the pace of medicine delivery. [28,29]

DISADVANTAGES:

1. Due to medicine encapsulation hydrolysis, emulsion, aggregation, and leakage, the waterless dormancies of niosomes have a limited shelf life.
2. The fashion of creating multilamellar vesicles through extrusion and sonication takes a lot of time and specific outfit. [31]

COMPONENTS OF NIOSOMES

The primary element types set up in niosomes are as follows :

1. **Non ionic surfactant:** The hydrophobic head or hydrocarbon parts align in a way that minimizes commerce with the waterless media, whereas the polar or hydrophobic heads align facing the waterless bulk(media) in bilayer structures formed by thenon-ionic surfactants. Every bilayer generates vesicles, or crowds over itself as a nonstop membrane, to achieve thermodynamic stability, precluding the hydrocarbon/ water contact from being eexposed.[8] The following orders ofnon-ionic surfactants are primarily employed in the niosome conformation process:

a. **Alkyl Ethers** : L'Oreal listed a manysurfactants [8] for the conflation of niosomes that carry substances or specifics as

i) With an normal of three glycerol units, surfactant(molecular weight(MW 473)) is a C16 monoalkyl glycerol ether.

ii) Diglycerol ether with an normal of seven glycerol units is surfactant- II(MW 972).

iii) Ester linked surfactant III(MW 393) is a surfactant. Niosome expression also uses alkyl glycosides and alkyl ethers with polyhydroxyl head groups in addition to alkyl glycerol.[8,9,10]

b) **Alkyl Esters** : Among this group of surfactants, sorbitan esters are the most frequently employed for niosome product.[11,12] Vesicles prepared by the polyoxyethylene sorbitan monolaurate are fairly answerable than other surfactant vesicle.[10] For illustration, diclofenac sodium has been reprised using polyoxyethylene (polysorbate 60).[13] Cyclosporine- A has been transdermally delivered using a polyoxyethylene-10-stearyl ether, glyceryl laurate, and cholesterol(27 15 57) admixture.[8,14].

c) **Alkyl Amides** : Niosomal vesicles have been made using alkyl amides, similar as galactosides and glucosides.[15].

d) **Adipose Acid and Amino Acid composites:** In certain niosome manufacturing processes, long- chain adipose acids and amino acid halves have also been employed. [16]

2. Cholesterol: Steroids are significant membrane ingredients that impact the fluidity and permeability of the bilayer. One of the main steroid derivations employed in the creation of niosomes is cholesterol. Indeed if it might not indicate a part in the conformation Of bilayer, its significance in niosome conformation and controlling subcaste parcels can not be disregarded. The features of niosomes similar as membrane permeability, severity, encapsulation effectiveness, ease of rehydration of snap- dried niosomes, and toxin are generally impacted by the objectification of cholesterol. It stops the vesicle from adding up due to the addition of moles to the system to stabilize it against the creation of clusters via electrostatic or repulsive steric forces factors that beget the gel to change into a liquid niosome systems' phase. This means that the niosome lessens its natural leakiness.[17]

3. Charged Molecule :To boost niosome stability and avoid coalescence, some charged moles are introduced to the niosomes. This process is known as electrostatic aversion. Phosphatidic acid and diacetyl phosphate(DCP) are the negatively charged moles that are employed. By the same commemorative, stearylamine(STR) and Stearyl pyridinium chloride is a familiar and salutary ions that are charged and employed in niosomal medications. The primary

purpose of charged moles is to stop the aggregation of Niosomes.[18,19] It's only respectable to have charged moles at 2.5 – 5 spook attention since advanced attention can help the product of niosomes.[18,20]

TYPES OF NIOSOMES :

- 1) **Bola Surfactant Containing Niosomes** : Bola surfactant including niosomes is a type of surfactant conforming of omega - hexadecyl-bis-(1-aza-18 crown - 6) span- 80/ cholesterol in a 231 molar rate. (21,22)
- 2) **Proniosomes**: Proniosomes are a type of niosomal expression that need to be doused before to use. They contain a carrier and a surfactant. Waterless niosome dissipation is formed as a result of hydration. Proniosomes reduce the issue of niosomal expression – related aggregation, leakage, and fusing.(23)

Carrier + Surfactant = Proniosomes

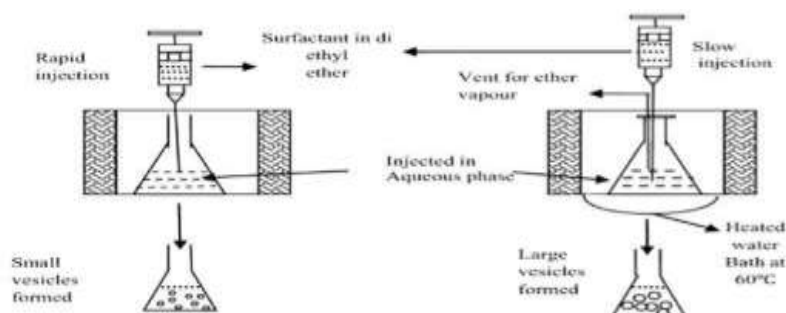
Poniosomes + Water = Niosomes

- 3) **Aspasomes** :Aspasomes are vesicles that are formed when cholesterol, acorbyl palmitate, and the largely charged lipid diacetyl phosphate are combined. Apeomes are sonicated to prize the niosomes after being originally doused with water or an waterless result. Medicines can have their transdermal penetration increased by aspasmomes. Those with a spade also been employed, due to its natural antioxidant parcels, to reduce complaint brought on by reactive oxygen species.(24)
- 4) **Niosomes in Carbopol Gel** : Cholesterol, spans, and medicines were used to construct niosomes. The performing niosomes were also added to a 1 w/ w carbopol- 934 gel base that also included 10 w/ w propylene glycol and 30 w/ w glycerol. Exercising skin from mortal corses , in vitro prolixity exploration on niosomal gel, general drug gel, and marketable gel were conducted inside a prolixity cell. It was noted that the Diffusion measure and mean inflow value were five to seven times reduced for niosomal gel in discrepancy to standard drug gels. Also, carrageenan- convinced repression of paw edema(i.e. When comparing the niosome expression to normal gel, the result was 66.68 519) advanced.(25,26)
- 5) **Vesicles in Water and Oil System(v/ w/ o)**: It has been reported that the emulsification of an waterless niosomes into an oil painting phase form vesicle in water in oil painting conflation(v/ w/ o). Niosome suspense made of sorbitol monostearate, cholesterol, and solulan C24(poly-24-oxyethylene cholesterol ether) can be added to the oil painting phase at 60 °C to prepare this. This leads to the vesicle generation in an oil painting/ water/ oil painting(v/ w/ o) conflation which reaches room temperature and condenses to form vesicles in unctuous water gel(v/ w/ o gel). The performing v/ w/ o gel may entrap proteins and proteinous specifics, as well as guard it from enzymatic declination following controlled release and oral ingestion.Both w/ o gel and v/ w/ o gel's immunogenic rates have been shown to have an immunoadjuvant tendency. In this system, emulsifying the waterless niosomes(v/ w) into the unctuous stage.(25,26)
- 6) **Niosomes of Hydroxyl Propyl Methyl Cellulose** : In this type, niosomes were added to a base that had been made with 10 glycerin of hydroxypropyl methyl cellulose. Paw edema- convinced bioavailability and reduced was discovered to be lesser by carrageenan using this niosomal system than the standard flurbiprofen expression. [25,27]

METHODS OF PREPARATION :

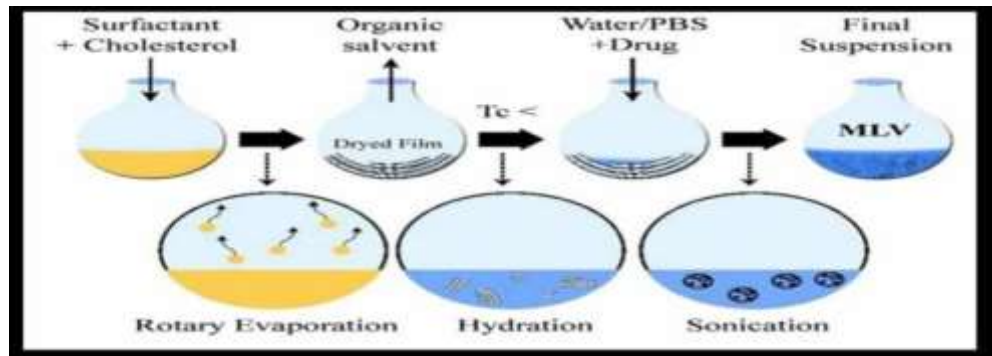
The medication fashion affects the vesicles' membrane permeability, ruse effectiveness of the waterless phase, size, size distribution, and number of bilayers:

- 1) **Ether injection system**⁵⁰: Using this approach, surfactant that has been dissolved in diethyl ether is added to warm water that's kept at 60 degrees Celsius. The ether result containing surfactant is fitted into a waterless result of the material using a 14-hand needle. The conformation of single-layered needles is caused by ether 13 vaporization. Depending on the situation, the vesicle's periphery can be anywhere between 50 and 1000 nm.[41]

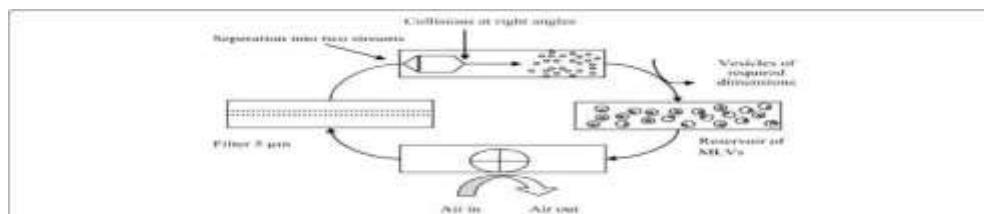


- 2) **Thin film hydration system with hand shaking**⁵¹: Similar to diethyl ether, chloroform, or menthol, surfactant and cholesterol are dissolved in an unpredictable organic detergent. A small subcaste of solid admixture remains on the beaker wall after the organic detergent is faded using

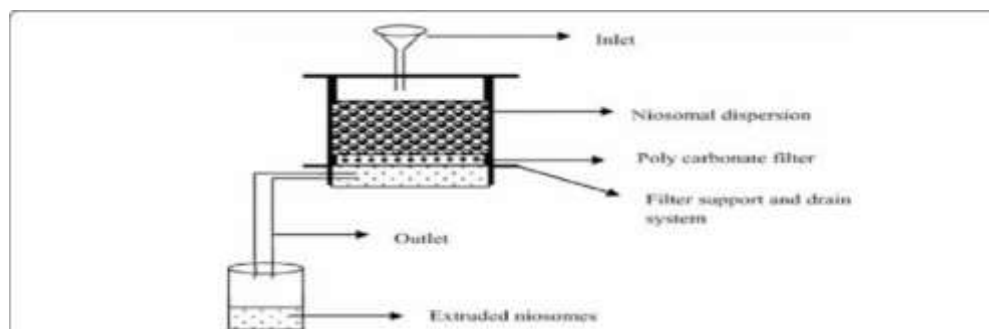
a rotating flash evaporator at room temperature (20°C). After that, the dried surfactant film is gently agitated and rehydrated with a waterless drug result at the temperature of the surfactants employed for the designated quantum of time (the “time of hydration”). This process forms multilamellar niosomes [42]. The rotary beaker evaporator is used to induce thermosensitive niosomes by sinking organic detergent at 60°C, leaving a thin coating on the wall. The medicine-containing waterless result is also gradually added, shaken at normal temperature, and eventually sonicated.



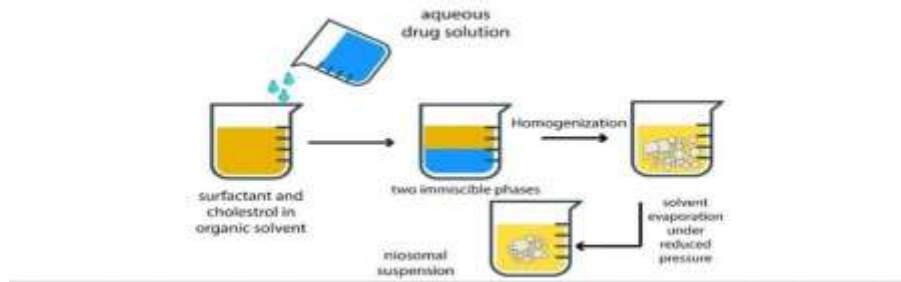
- 3) **Tiny fluidization**⁵²: A procedure called “micro fluidization” produces unilamellar niosomes with a predetermined size distribution that are uniform and very repeatable. This system operates on the submerged spurt conception, which describes how two fluidized aqueducts interact in the commerce chamber’s microchannels at extremely high rapidity. The common front and thin liquid distance shocks are deposited so that the energy supplied stays constant in the region where niosomes develop. Niosomal vesicles with bettered repetition, size reduction, and uniformity are formed as a result [43]



- 4) **Multiple membrane extrusion system**⁵³: This approach can be used to manufacture vesicles of the asked size. Up to eight channels of polycarbonate membranes can be arranged in sequence to negotiate this. Evaporation is used to produce a thin coating of the admixture of dicetyl phosphate, cholesterol, and surfactant. After that, the film is rehydrated using the medicine-containing waterless result (44). Using C16G12, the final result is extruded through a polycarbonate membrane (0.1 μm nucleophore).



- 5) **Rear phase evaporation fashion**⁵⁴: The admixture of ether and chloroform dissolves cholesterol and surfactant in a 1:1 ratio. To this, waterless drug result is added. The two stages undergo sonication at 4-5°C. The transparent gel is given a small addition of phosphate softened saline (PBS) and given another sonication. The organic phase is gone at 40°C and lower pressure. The process of creating niosomes involves adding PBS to the thick niosomal product and heating it for ten minutes at 60 degrees Celsius in a water bath. [45].



CHARACTERIZATIONS OF NIOSOMES:

- 1) **Vesicle periphery:** Niosomes range in size from 20 nm to 50 μm and have a globular shape. colorless styles similar as light microscopy, coulter counter, photon correlation microscopy, and indurate fracture electron microscopy are employed to ascertain the size and dissipation of the vesicles. infinitesimal force microscopy, cytology, and surveying electron microscopy The niosomes' form and face parcels are caught on via transmission electron microscopy.(32)
- 2) **Vesicle charge:** A significant factor impacting the stability and geste of niosomes is the vesicle face charge. It's discovered that charged niosomes show further stability against emulsion and aggregation than uncharged niosomes. Niosome face eventuality can be calculated using the zeta implicit attained via dynamic light scattering or micro electrophoresis 29. PH as a backup plan, sensitive fluorophores mightbe employed.(33)
- 3) **Bilayer conformation:** Using light polarization microscopy, bilayer vesicle product can be linked by the creation of an-x-cross caused by the assembly of non-ionic surfactants.(34)
- 4) **Number of plates :** Small angle X-ray scattering, electron microscopy, and NMR spectroscopy are used to determine the number of plates in vesicles.(35)
- 5) **Membrane unity and stiffness :** The way in which niosomes are distributed and degraded is told by the stiffness of the membrane. The mobility of the luminescence inquiry as a function of temperature can be used to calculate the bilayer stiffness of the vesicles. Differential surveying calorimetry(DSC), Fourier transfigure- infrared spectroscopy(P- NMR), and Fourier transfigure- infrared both luminescence resonance energy transfer(stew) and spectroscopy(FT- IR).(36)
- 6) **Transmission Electron Microscopy(TEM:** Niosome size, shape, and lamellarity can all be caught on via TEM. To put it compactly, 1 phosphotungstic acid is combined with a set suspense(in sufficient quantum).

Following full drying, a drop of the performing was applied to a carbon- carpeted grid, allowing the excess to drain out. The grid was also examined and photos were taken under an applicable exaggeration under a TEM(Philips TEM).(45,46)

- 7) **indurate Fractured Microscopy :** It was shown that the size and form of niosomes were told by the type of medicine used, the type of surfactant, and the medicine ruse. Vesicles are frequently indurate- fused and also observed under a snap- fractured electron microscope in order to determine their size. At low pressure(10~2 Pa), liquid propane is generally employed for the cryo- obsession of the vesicular suspense(glycol may be used as a cryoprotectant). A destined angle is used to fracture the cryofixed vesicles. After that, the face is shadowed at a 45 $^{\circ}$ angle using carbon or platinum vapor. This system's operation of carbon coating strengthens the created duplicate. After drawing, the replica is viewed and delved with a TEM.(47)

In- vitro medicine release : The following ways can be used to characterize niosome medicine release in vitro.(48)

Dialysis

Reverse dialysis

Franz proximity cell

1. **Dialysis :** It's the most straightforward fashion for figuring out the niosomal- loaded medicine's invitro release kinetics. One uses dialysis tubing. The hermetically sealed dialysis sack is filled with niosomal suspense. Dialysis is carried out by immersing the bag in 200 milliliters of buffer result and stirring it constantly at morever 25 or 27 degrees Celsius. Periodically, samples are taken out, and an applicable fashion is used to dissect the medicine content.
2. **Rear dialysis:** One milliliter of dissolving liquid is filled with niosomes and placed into several bitsy dialysis tubes. Next, the niosomes are removed from the result that dissolves.

3. **Franz proximity cell:** In a Franz proximity cell, niosomes are dialyzed at room temperature against applicable dissolving fluids via a cellophane membrane. The samples are uprooted on a regular base, and their analysis determines the medicine content. Stew is being employed these days to track the release of material enclosed in niosomes.

APPLICATIONS OF NIOSOMES : [37,38]

Niosome technology has a wide range of applications and is useful in the treatment of certain illnesses.

The applications of niosomes that are either established or being studied are as follows.

1. The purpose of it is drug targeting.
2. It is applied to cancer patients as an anti-neoplastic treatment.
3. It is used as Leishmaniasis i.e. Dermal and Mucocutaneous infections e.g. Sodium stibogluconate.
4. It serves as a vehicle for peptide drug delivery.
5. Niosomes as Hemoglobin Carriers.
6. It's applied to immunological response research.
7. Drug delivery for the eyes uses it.

CONCLUSION

There has been a significant breakthrough in the creation of innovative drug delivery systems in the last several decades. Niosome technology is still in its infancy as a potential drug delivery method. Niosomes have demonstrated a significant impact on the targeted organ and tissue. Niosomes are more effective as diagnostic agents, nasal, transdermal, ocular, and vaccine delivery systems, as well as agents that target tumors. For niosomal products to be sold commercially, a great deal of research must be done.

Reference

- 1) Malhotra M, Jain NK. Niosomes as Drug Carriers. *Indian Drugs*. 1994; 31(3): 81-86
- 2) Buckton G, Harwood. *Interfacial Phenomena in Drug Delivery and Targeting*. Academic Publishers, Switzerland. 1995; 154-155.
- 3) Handjani-Vila RM, Ribier A, Rondot B, Vanlerberghe G. Dispersions of lamellar phases of non-ionic Lipids in cosmetic products. *Int.J. Cosmetic Sci*. 1979; 1: 303-314.
- 4) Arunothayanam P, Turton JA, Uchegbu IF, Florence AT. Preparation and In Vitro/In Vivo Evaluation of Luteinizing Hormone Releasing Hormone (LHRH)-Loaded Polyhedral and Spherical/Tubular Niosomes. *J Pharm Sci*. 1999; 88: 34-38.
- 5) Uchegbu IF, Double JA, Turton JA, Florence AT. Distribution, metabolism and tumoricidal activity of Doxorubicin administered in sorbitan monostearate (Span 60) niosomes in the mouse. *Pharm Res*. 1995; 12:1019.
- 6) Rentel C O, Bouwstra J A, Naisbett B, Junginger H E, Niosomes as a novel peroral vaccine delivery System. *Int J Pharm*. 1999; 186:161-167
- 7) Purnima Negi, Farhan J Ahmad, Dabeer Ahmad, Gaurav K Jain, Gyanendra Singh. Development of a Novel formulation for transdermal delivery of an anti-depressant drug. *Int J Phar Sci and Res*. 2011; 2(7): 1766-177.
- 8) Vyas S. P., Khar R. K., "Targeted and Control Drug Delivery," 1st ed. Chap. 6, CBS Publishers and Distributors, New Delhi, 2002, pp.249-276.
- 9) Kiwada H., Niimura H., Fujisaki Y., Yamada S., Kato Y., *Chem.Pharm. Bull.*, 33, 753-759 (1985).
- 10) Kiwada H., Niimura H., Kato Y., *Chem. Pharm. Bull.*, 33, 2475-2482 (1985).
- 11) Reddy D. N., Udupa N., *Drug Dev. Ind. Pharm.*, 19, 843-852 (1993).
- 12) Yoshioka T., Stermberg B., Florence A. T., *Int. J. Pharm.*, 105, 1-6 (1994).
- 13) Raja Naresh R. A., Chandrashekhar G., Pillai G. K., Udupa N., *Indian J. Pharmacol.*, 26, 46-48 (1994).
- 14) Niemiec S. M., Hu Z., Ramachandran C., Wallach D. F. H., Weiner N, *STP Pharma Sci.*, 4, 145-149 (1994).
- 15) Sahin N. O., "Nanomaterials and Nanosystems for Biomedical Applications," Chap. 4, ed. by Mozafari M. R., Springer, The Netherlands, 2007, pp. 67-81.
- 16) Gebicki J. M., Hicks M., *Chem. Phys. Lipids*, 16, 142-160 (1976).

- 17) Sahin N. O., "Nanomaterials and Nanosystems for Biomedical Applications," Chap. 4, ed. By Mozafari M. R., Springer, The Netherlands, 2007, pp. 67—81.
- 18) Cosco D., Paolino D., Muzzalupo R., Celia C., Citraro R., Caponio D. Picci N., Fresta M., *Biomed. Microdevices*, 11, 1115—1125 (2009).
- 19) [19] Uchegbu I. F., Vyas S. P., *Int. J. Pharm.*, 172, 33—70 (1998)
- 20) Hu C., Rhodes D. G., *Int. J. Pharm.*, 185, 23—35 (1999)
- 21) Junyaprasert V. B., Teeranachaiideekul V. Supaperm T., *AAPS PharmSciTech*, 9, 851—859 (2008).
- 22) <http://pharmaxchange.info/articles/niosomes/niosomes.html>
- 23) Rhodes D. G., Chengjiu H., *Int. J. Pharm.*, 185, 23—35 (1999).
- 24) Gopinath D., Ravi D., Rao B.R., Apte S.S., Renuka D., Rambhau D, *Int. J. Pharm.*, 271, 95—113 (2004).
- 25) Biswal S., Murthy P. N., Sahu J., Sahoo P., Amir F., *International Journal of Pharmaceutical Sciences and Nanotechnology*, 1, 1—8 (2008)
- 26) Yoshioka T., Stermberg B., Florence A. T., *Int. J. Pharm.*, 105, 1—6 (1994).
- 27) Reddy D. N., Udupa N., *Drug Dev. Ind. Pharm.*, 19, 843—852 (1993).
- 28) Biju SS, Telegaonar S, Mishra PR, Khar RK. Vesicular system: an overview. *Ind J Pharm Sci.* 2006; 68: 141-153.
- 29) Vyas SP, Khar RK. *Controlled drug delivery system: concept and advances.* New Delhi: CBS Publishers And Distributors; 2002
- 30) Verma S, Singh SK, Navneet S, Mathur P, Valecha V. Nanoparticle vesicular systems: a versatile tool For drug delivery. *J Chem Pharm Res.* 2010; 2(2): 496-509.
- 31) Kumar Abhinav, Pal Jagendar Lal, Jaiswal Amit, Singh Vishwanabhan. Review of niosomes as novel drug delivery system. *Int Res J Pharm.* 2011; 2(5): 61-65.
- 32) Prabagar Balakrishnan, Srinivasan Shanmugam, Won Seok Lee, Won Mo Lee, Jong Oh Kim, Dong Hoon Oh, Dae-Duk Kim, Jung Sun Kimc, Bong Kyu Yoo, Han-Gon Choi, Jong SooWoo, Chul Soon Yong. Formulation and in vitro assessment of minoxidil niosomes for enhanced skin delivery. *Int J Pharm.* 2009; 377: 1–8
- 33) Manosroi A. Characterization of Vesicles Prepared with Various Nonionic Surfactants mixed with Cholesterol. *Colloids surf. Biointerfaces.* 2003; 30: 129-138.
- 34) Kreuter J. *Colloidal Drug Delivery System of Niosome*, Dekker series, Dekker publication.66:73.
- 35) Muzzalupo R, Trombino S, Iemma F, Puoci F, Mesa CL, Picci N. Preparation and characterization of Bolaform surfactant vesicles. *Colloids Surf B. Biointerfaces.* 2005; 46(2): 78–83.
- 36) Chandraprakash KS, Udupa N., Umadevi P., Pillai GK., *Formulation And Evaluation of Methotrexate Niosomes.* *Ind J Pharm.Sci.* 1992, 54(5): 197.
- 37) Mark chasin, *Biodegradable polymers as drug delivery systems.* 2008, 2618338.
- 38) Khandare JN., Madhavi G., Tamhankar BM., *Niosomes Novel Drug Delivery System.* *The Eastern Pharmacist.* 1994, 37: 61864.
- 39) Baillie AJ., Florence AT., Hume LR., Muirhead GT., Rogerson A., *The preparation and properties of niosomes non8ionic surfactant vesicles.* *J. Pharm. Pharmacol.* 1985, 37: 8638 868.
- 40) Srinivas S, Anand kumar Y, Hemanth A, Anitha M. Preparation and evaluation of niosomes containing Aceclofenac. *Dig J Nano Mat and Biostr.* 2010; 3(2):199-203
- 41) Vijay S Jatav, Santosh K Singh, Pankaj Khatri, Ashish K Sharma, Rambir Singh. Formulation and invitro evaluation of Rifampicin-Loaded Niosomes. *J. Chem. Pharm. Res.* 2011; 3(2):199-203.
- 42) Khandare JN, Madhavi G and Tamhankar BM. Niosomes novel drug delivery systems. *The Eastern Pharmacist.* 1994; 37: 61-64
- 43) Suggy S, Murari CR, Ahmad. Niosomes- A review. *Biopharm.* 2004,24-37.
- 44) Cosco D., Paolino D., Muzzalupo R., Celia C., Citraro R., Caponio D.Picci N., Fresta M., *Biomed. Microdevices*, 11, 1115—1125 (2009)
- 45) Kiwada H., Niimura H., Kato Y., *Chem. Pharm. Bull.*, 33, 2475—2482 (1985).
- 46) Vyas S. P., Khar R. K., "Targeted and Control Drug Delivery," 1st ed., Chap. 6, CBS Publishers and Distributors, New Delhi, 2002, pp.249—276.

- 47) Muller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. *Adv Drug Deliv.* 2002; 54: 131-155.
- 48) Formulation and evaluation of Metformin Hydrochloride-loaded Curcumin–Lycopene Niosomes - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Structure-of-niosome-2_fig1_337603473 [accessed 24 Sept 2024].
- 49) Recent advances of non-ionic surfactant-based nano-vesicles (niosomes and proniosomes): a brief review of these in enhancing transdermal delivery of drug – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Schematic-diagram-of-the-preparation-of-niosomes-via-ether-injectionmethod-2_fig6_347257772 [accessed 9 Oct 2024]
- 50) A Review on Niosomal Drug Delivery System - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Hand-Shaking-Method-Thin-Film-Hydration-Technique-Rotary-Evaporator_fig2_381195727 [accessed 9 Oct 2024]
- 51) Recent advances of non-ionic surfactant-based nano-vesicles (niosomes and proniosomes): a brief review of these in enhancing transdermal delivery of drug - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Schematic-diagram-of-the-preparation-of-niosomes-via-multiplemembrane-extrusion-method_fig10_347257772 [accessed 9 Oct 2024]
- 52) Recent advances of non-ionic surfactant-based nano-vesicles (niosomes and proniosomes): a brief review of these in enhancing transdermal delivery of drug – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Schematic-diagram-of-the-preparation-of-niosomes-via-multiplemembrane-extrusion-method_fig10_347257772 [accessed 9 Oct 2024]
- 53) Niosomes: A Novel Targeted Drug Delivery System – Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Illustrative-depiction-of-the-preparation-of-niosomes-with-the-reversephase-evaporation_fig2_357186343 [accessed 9 Oct 2024]