PRONIOSOMES: AS A CARRIER FOR TRANSDERMAL DRUG DELIVERY SYSTEM

Avinash Mangave , Sardar Shelake , Nilesh Chougule, Avadhut Talwar , Aditya Kesarkar, Radhika Subhedar

Ashokrao Mane Institute Of Pharmacy, Ambap. Tal-Hatkanangale, Dist-Kolhapur 416 112.

Abstract: Of course! Nanotechnology is a field of science that deals with extremely small objects. It is making significant advances in domains such as medicine and healthcare. One interesting thing it is doing is assisting in the development of novel methods for delivering medications and improving medical equipment.

Consider microscopic particles capable of transporting medicine to the precise location where it is required in your body. These particles are so minute that they cannot be seen without specialized instruments. Regular versions of these particles can occasionally cluster together, shatter, or spill medication. But now there's a brilliant enhancement known as proniosomes.

Proniosomes are essentially dried copies of these small drug carriers. They are easy to store and manage. You simply put a little water to them, and they transform into the ordinary small Medicine carriers that perform very effectively. They are like quick medicinal carriers! These proniosomes are more stable, which means they do not clump or leak as much as conventional ones. The most significant factors to consider are how they seem, how big they are, how equally sized they are, and how they distribute the medication. Scientists are investigating all of these factors to determine if proniosomes outperform ordinary ones. This sort of science improves pharmaceutical distribution and therapy!

***Keywords*:**

Introduction –

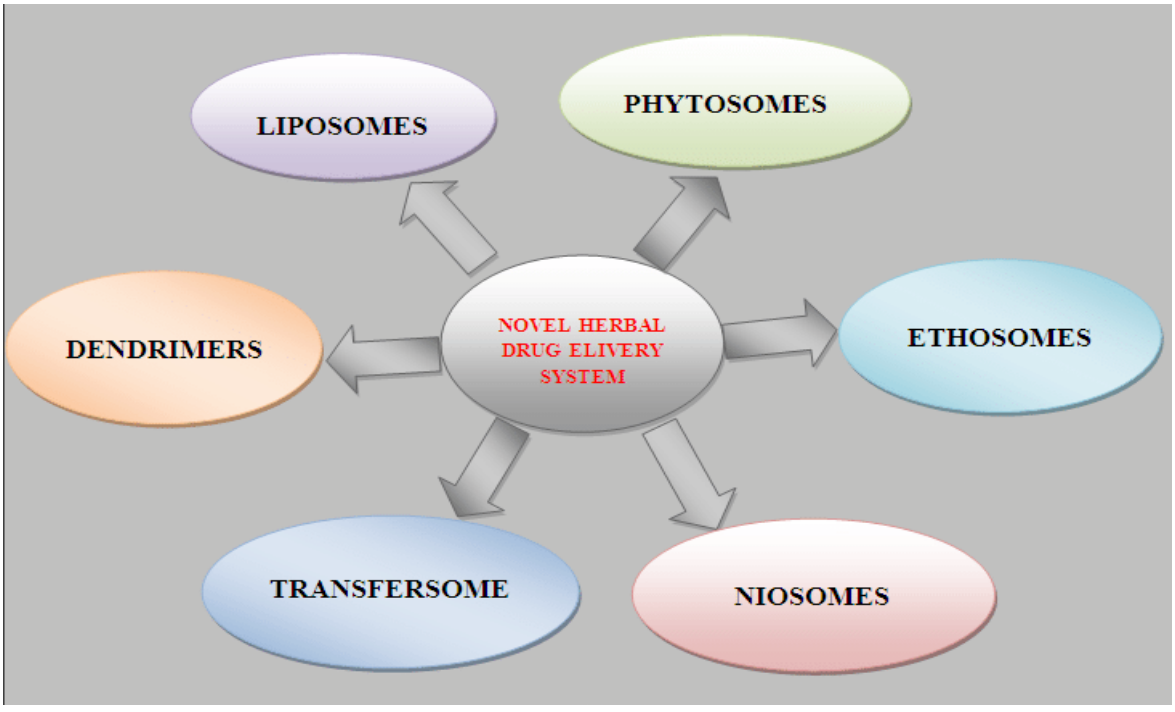


Fig: Recent advancements in herbal medicine delivery systems

niosomes

In 1909, Paul Ehrlich had an idea for a medication delivery method that would directly target diseased cells. Since then, a range of carriers—such as immunoglobulins, serum proteins, synthetic polymers, liposomes, microspheres, erythrocytes, and niosomes—have been employed to carry medications to the intended organ or tissue.[1] Both hydrophilic and hydrophobic medicines can be incorporated into niosomes thanks to a novel drug delivery technique that captures hydrophilic pharmaceuticals in the core cavity and hydrophobic drugs in the non-polar region inside the bilayer. Because niosomes are ampiphillic, the term comes from the fact that the medicine is encased in a vesicle made of a nonionic surfactant. The niosomes are miniscule and quite small.[2] The first niosome structures These goods were created and copyrighted by L'Oreal in 1975. in the presence of charge-inducing agents from thermodynamically stable vesicles and appropriately blended surfactants. Since niosomes lessen the issues with liposomes, they are mainly being researched as a liposome substitute [3]. The chemical instability of liposomes is mitigated by niosomes. Liposomes' vulnerability to oxidative degradation and fluctuating phospholipid purity levels make them chemically unstable. Chemical stability, biodegradability, biocompatibility, low toxicity, low production costs, and simplicity of handling and storage are the main objectives of creating niosomal systems [4,5]. There are several ways to give niosomes, including topical, parenteral, and oral. A variety of pharmaceuticals, both synthetic and herbal, are transported by niosomes.

hormones, antigens, and other bioactive compounds [6, 7, 8]. Some of the key features of niosomes are covered on this page, along with a summary of their production processes and current applications in the distribution and encapsulation of bioactive substances.

salient features of niosomes -

The osmotic stability and solute-entrapment capabilities of niosomes are important features.

• The architecture of niosomes, which is mostly made up of hydrophobic and hydrophilic components, gives medication atoms a broad spectrum of dissolvability.

• Niosomes' bilayers, which facilitate the encapsulated drug's arrival, allow for the controlled release of medication.

As the body's drug storage, niosomes release the medication in a controlled way through their bilayer, allowing the encapsulated drug to be released over an extended period of time. Targeted drug delivery, which entails delivering the medication straight to the body part where the therapeutic effect is intended, is another application for niosomes. As a result, less medication is required to get the desired result.

Microscopic lamellar structures with sizes ranging from 10 to 1000 nanometers are known as niosomes.1) The heads of niosomes are hydrophilic, whereas the tails are hydrophobic. To achieve maximum interaction with the solvent, the hydrophilic heads of the molecules are oriented toward the aqueous solvent, while the hydrophobic tails are oriented away from the solvent [2,9,10].

Advantages –

1. There may be several advantages to using vesicular (lipid and non-ionic surfactant vesicle) systems in cosmetics and medicine.

2. By restricting the drug's effects on target cells, protecting it from the biological environment, and postponing its removal from the circulation, they improve the therapeutic efficacy of drug molecules.

3. To adjust delivery, niosomal dispersion in an aqueous phase can be emulsified in a non-aqueous phase.

4. Calculate the dosage and provide regular vesicles in the non-aqueous phase outside.

5. They enhance the stability of the entrapped drug and are osmotically stable and active.

6. There are no specific handling or storage requirements for surfactants.

7. They boost drug penetration via the skin and enhance the oral bioavailability of poorly absorbed medications.

8. They can be administered topically, parenterally, or orally to get to the site of action.

9. They may take up medicinal compounds with a broad range of solubility because of their architecture, which consists of hydrophilic, amphiphilic, and lipophilic components.

10. The vesicle formulation has changeable and variable characteristics. Vesicle characteristics can be affected by changes in vesicle composition, size, lamellarity, tapping volume, surface charge, and concentration. [11]

Comparison of liposomes and niosomes

Despite their near-identical nature, liposomes and niosomes can both be employed in a targeted and controlled sedative delivery system. Both improve bioavailability while reducing body leeway, and their characteristics rely on the bilayer's structure and planning techniques. The following are the main differences between liposomes and niosomes: [11,12] Many anti-neoplastic medications have been encapsulated in this carrier vesicle, which has decreased adverse drug reactions while maintaining or even increasing anti-tumor efficacy. [13] The broad-spectrum anti-tumor action of the anthracycline antibiotic doxorubicin is accompanied by an irreversible cardiotoxic effect that is dosage dependant.[14,15] Niosomes transport this drug to the In addition to having slower rates of sarcoma development, mice with S-180 tumors lived longer. Mice with S-180 tumors that received an intravenous infusion of methotrexate encapsulated in niosomes showed 100% tumor reduction, increased plasma levels, and delayed clearance. It may effectively regulate drug release rates, which is very helpful in the treatment of aggressive brain tumors.[16] The nature of the immune response brought on by antigens has been studied using niosomes.[17] Hemoglobin can be transported via niosomes.[18, 19] The hemoglobin dissociation curve may be altered in the same manner as for non-encapsulated hemoglobin, and vesicles are oxygen permeable. The delayed absorption of the medication via the skin is the primary drawback of transdermal delivery.[20] sex hormones like estradiol and some anti-inflammatory medications like piroxicam and flurbiprofen. Transdermal delivery of niosomes containing levonorgestrel is a common practice to increase the therapeutic efficacy of these medications. Additionally, when administered orally, parenterally, or topically, this vesicular system enhances drug concentration at the site of action. Drugs with a low therapeutic index and water solubility can be treated with niosomes' sustained release action. Because niosomes are tiny and have minimal penetration into connective tissue and epithelium, they can be used to administer drugs in a way that achieves localized drug activity while keeping the medication at the injection site. Medication that acts locally is more effective and has fewer negative systemic effects. For instance, mononuclear cells absorb antimonials contained in niosomes, increasing their efficacy by drug localization, which lowers dose and toxicity.[13]

VARIOUS TYPES OF NIOSOME

Based on the size of their vesicles, niosomes are divided into three categories. Unilamellar vesicles come in three different varieties: large (LUV) (0.10 μm), multilamellar (MLV) (0.05 μm), and small (SUV) (0.025-0.05 μm).

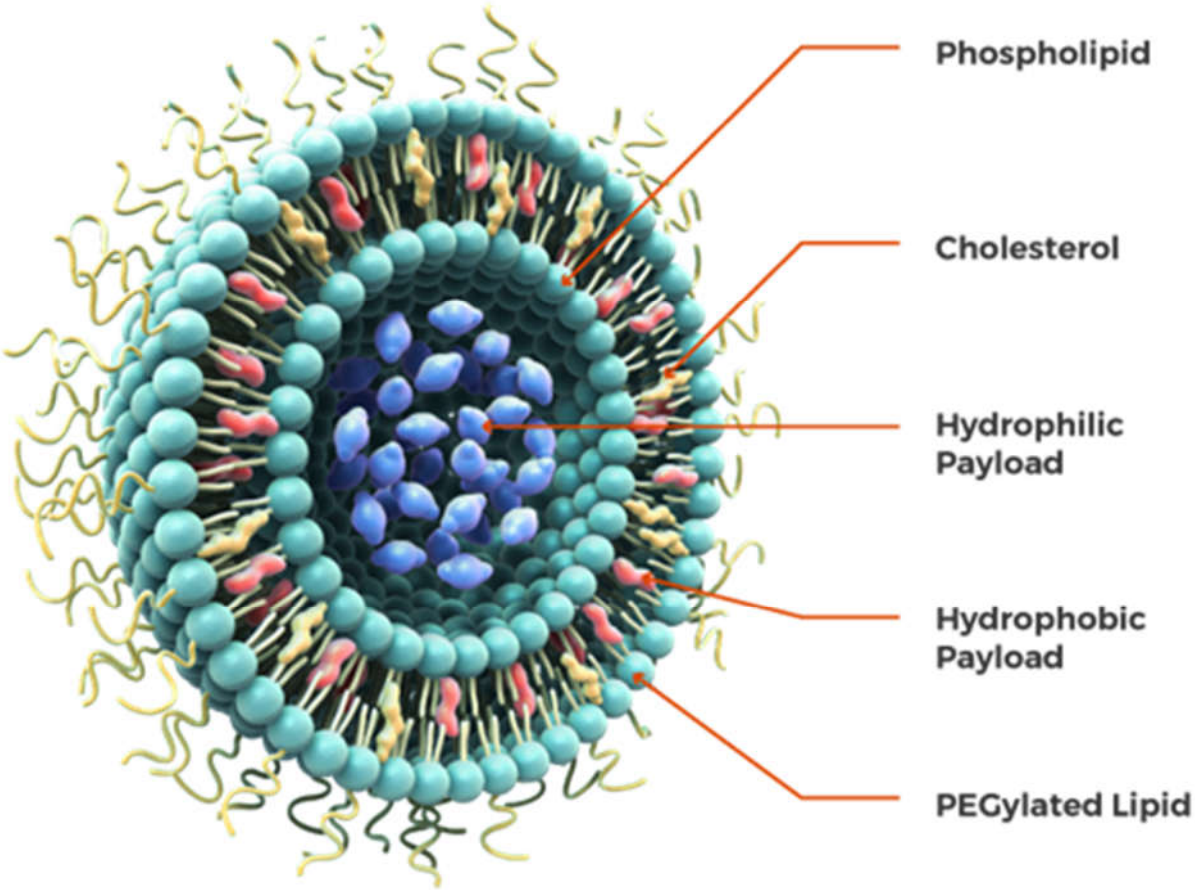
Methods of Preparation

The number of double layers, the permeability of the vesicle membrane, the entrapment efficiency of the aqueous phase, and the size and distribution of the vesicles all influence how niosomes are formed.

The drug-containing aqueous phase is mixed with a mixture of cholesterol and surfactant in a scintillation vial.[21]

Vesicular forms:

Liposomes are vesicular, colloidal particles having concentric bilayers of phospholipids. It contains an aqueous core that encapsulates the hydrophilic drug; lipophilic drugs can be entrapped because of the phospholipid bilayer [22].



Proniosomes

Proniosomes are a dry mixture of surfactant-coated water-soluble carrier particles. Shortly before use, they are rehydrated by stirring in a boiling aqueous solution for a few minutes to create niosomal dispersion. Proniosomes maintain their physical stability during transit and storage. Drug encapsulation in proniosomes' vesicular structure boosts the drug's penetration into target tissue, decreases toxicity, and extends its duration in the systemic circulation.[23]

Action of Proniosomes

After hydration, proniosomes change into niosomes and carry out their role. When hydrated, proneosomes change into niosomes. Aqueous solvents can be added to cause hydration. Both hydrophilic and lipophilic materials can be encapsulated by proneosomes [Table 1].[24] The different materials used and how they affect the generation of proniosomes are displayed in Table 1.

Materials	Specification	Action
Span and tween	Surfactants	Maintains HLB level
Cholesterol and lecithin	Membrane stabilizers	Cholesterol: Influences the stability and permeability of vesicles Lecithin: Penetration enhancer
Maltodextrin, lactose, sorbitol, mannitol	Carriers	Holds the drug
Methanol, chloroform, ethyl alcohol	Organic solvents	Influence on vesicle size and permeability of drug

HLB: Hydrophilic lipophilic balance

Types of Proniosomes

Proniosomes are divided into two groups according to the kind of carrier and production technique.

Granular, dry proniosomes

1. Sorbitol-derived pioniosomes

2. Maltodextrin-derived proniosomes

By using sorbitol as a carrier and coating it with a non-ionic surfactant, sorbitol-based proniosomes are a dry formulation that may be used as a noisome in a matter of minutes by adding hot water and stirring. The fast slurry method is used to make maltodextrin-based proneosomes.

Proniosomes that are liquid crystalline

This kind of proniosome acts as a reservoir for the delivery of drugs transdermally. A plastic sheet and aluminum foil are used to make the transdermal patch. On a circular plastic sheet, pronesomal gel is evenly distributed before being coated with nylon mesh.[25]

Preparation of Proniosomes

The main component of proniosomes is a non-ionic surfactant called cholesterol orlecithin. Some of the methods for making proniosomes that have been described are as follows:

1. The method of shaking hands.

2. The Slurry Method.

3. The method of slow spray coating.Method of shaking hands

Vesicle-forming chemicals like cholesterol and surfactants combined with ether, methanol, or chloroform are contained in a round-bottom flask. In the rotary evaporator, the organic solvent evaporates at room temperature (20°C), leaving the sides of the round-bottomed flask with a thin layer of solid mixture. With little stirring, the dried surfactant film may be rehydrated with the aqueous phase at temperatures between 0 and 60 degrees Celsius. Typically, this process produces multi-lamellarniosomes.[26]

Slurry method

A 2:1 chloroform:methanol solution was used to create a 250 µmol stock solution of surfactant and membrane stabilizer. A 100 mL round-bottom flask holding the carrier material was filled with a predefined volume of stock solution and drug dissolved in a chloroform:methanol (2:1) solution. To create a slurry, add extra organic solvent solution if the surfactant dosage is low. The flask was attached to a rotary flash evaporator, which produced a dry, free-flowing product by

evaporating the solvent at 60–70 rpm, 45 ± 2°C, and 600 mmHg pressure. Overnight at room temperature, these materials were vacuum-dried in a desiccator. "Proniosomes" is the name of this dry preparation, which was utilized for preparations.more research on the properties of powder. Until additional evaluation, these finished products—proniosomes—were kept at refrigerator temperature in a hermetically sealed container.[26]

Proniosomal gel (Coacervation - Phase separation method):

A medication including cholesterol, lecithin, and surfactants was mixed with 100% ethanol in a wide mouth glass tube. For five minutes, the glass tube was covered and heated to 65±3°C in a water bath. Tiny amounts of phosphate buffer (pH 7.4) were added, and the mixture was heated on the water bath for approximately two minutes until a clear solution was seen. Until the dispersion gelled, the mixture was let to cool at room temperature. A proniosomal gel is the name given to the resulting gel.[27]

Interaction-

Between skin and proniosomes: It is crucial to take into account the potential interactions between skin and the vesicles produced in proniosome/niosome formulations as the proniosome formulation comes into direct contact with the skin upon application. As mentioned before, vesicles are composed exclusively of non-ionic surfactants, which are the building blocks of proniosomes or proniosome-derived niosomes. Therefore, it is wise to look at how non-ionic surfactants interact with the skin. Non-ionic surfactants are amphipathic substances that have a hydrophilic component (usually variable-length ethylene oxide chains) and a hydrophobic component (alkylated phenol derivatives, fatty acids, long chain linear alcohols, etc.). To increase stability, solubility, and penetration, nonionic surfactants are widely used in pharmaceuticals. There is substantial proof that the degree The physicochemical characteristics of the surfactant molecules that comprise niosomes or proniosomes primarily dictate the interaction between vesicles and skin. Many bioactive substances, including as proteins, amino acids, peptides, and membrane phospholipids, are found in skin. Low molecular mass molecules can leak through vesicles and phospholipid membranes due to surfactants' increased permeability. While phospholipid turnover and biosynthesis rates were increased two to four times, the interaction between biological membranes and non-ionic surfactants was tested for phospholipid composition and rate of biosynthesis of major phospholipid components, and the results showed no significant change in phospholipid composition [28].

Comparison of proniosomes with niosomes-

• Proniosomes are dry formulations of surfactant-coated carrier vesicles that may be hydrated to create niosomes just before use, whereas niosomes are small lamellar vesicles produced in aqueous circumstances from a mixture of non-ionic surfactants and cholesterol.

Proniosomes are a dry formulation that cannot be hydrolyzed, although niosomes may be dissolved by hydrolysis. Niosomes were made with the wrong solvents.

• The lipid or surfactant coating is not fully hydrated during the hydration process for niosomal compositions [29].

Characterisation of Proniosome:

Additional evaluation studies are conducted for the produced proniosomes to ascertain the

• Angle of repose measurement
• SEM analysis
• Optical microscopy
• Vesicle size measurement
• Drug content
• Entrapment efficiency
• In-vivo release experiments
• Stability studies

Measurement of angle of repose

The angle of repose of dried proniosomes was measured by funnel method and cylinder method.

Funnel method

Following the funnel's fastening, the proniosomal powder was added until the output hole was 10 cm above the surface. The powder formed a cone on the surface as it poured down from the funnel. The cone's height and base diameter were then measured in order to establish the angle of repose.

Cylinder method

A cylinder was filled with proniosome powder and secured such that the cylinder's outflow opening was 10 cm above the ground. The powder formed a cone on the surface of the cylinder as it flowed down. By taking measurements of the cone's height and base diameter, the angle of repose was further determined.[30]

The angle of repose is calculated using the equation □ = Tan-1 □ (h/r).**SEM**

One crucial factor is the size of the proneosome particles. SEM was used to analyze the size distribution and surface appearance of proniosomes. The proniosomal powder was spread on aluminum stubs that had been covered with double-sided tape. A scanning electron microscope (XL 30 ESEM with EDAX, Philips, the Netherlands) was used to hold the aluminum stub in its vacuum chamber. A gaseous secondary electron detector (working pressure of 0.8 Torr, acceleration voltage of 30.00 KV) XL 30 (Philips, Netherlands) was used to evaluate the morphological properties of the samples.[31]

Optical microscopy

A microscope (Medilux-207RII, Kyowa-G etner, Ambala, India) was used to analyze niosomes that had been placed on glass slides. After sufficient dilution, the microscope provides a magnification of ×1200 for morphological analysis. Using a digital single lens reflex (SLR) camera, the photomicrograph of the preparation was captured from the microscope.[31]

Measurement of vesicle size

The same liquid that was utilized to make the vesicle dispersions was used to dilute them roughly 100 times. A particle size analyzer was used to measure the vesicles' dimensions. The apparatus includes a small volume sample holding cell and a multi-element detector, with a 632.8 nm He-Ne laser beam focused with a minimum power of 5Mw using a Fourier lens (R-5). Before determining the vesicle size, the samples were stirred.[32]

Drug content

100 mg of proneosomes were gathered in a standard volumetric flask. For fifteen minutes, they were shook after being lysed with fifty milliliters of methanol. 100 cc of methanol was added to the solution to dilute it. Then, using saline phosphate buffer at a certain pH, 10 ml of this solution was diluted to 100 ml. The calibration curve was used to calculate the drug concentration after aliquots were taken out and absorbance was measured at a certain wavelength.[33]

Entrapment effi ciency

Centrifugation and thorough dialysis were used to extract the unentrapped drug from the niosomal solution. An osmotic cellulose membrane was securely attached to one side of a dialysis tube containing the theniosomal fluid. A magnetic stirrer was used to whirl the dialysis tube while it was suspended in 100 milliliters of saline buffer at a certain pH. An osmotic cellulose membrane was used to separate the unentrapped drug and niosomal suspension into the solution. Following six hours of intense dialysis, optical density readings were taken, and the UV spectrophotometric method was used to assess the amount of medication entrapped. The formula was used to estimate entrapment efficiency.[34]

The quantity of drug captured increased by 100 Total drug amount equals entrapment efficiency.

In vivo release studies

Numerous techniques, such as the Franz diffusion cell, Keshary-Chien diffusion cell, cellophane dialyzing membrane, United States Pharmacopeia (USP) dissolving equipment Type-1, and spectrapor molecular porous membrane tubing, were used to evaluate the drug release from the proniosomal formulations. Desorption from the vesicle surface, drug diffusion from the bilayered membrane, or a combination of the two can be the method by which drugs are released from niosomal vesicles generated from proniosomes.[35]

Stability studies

For one to three months, the generated proniosomes were kept at room temperature (25° ± 0.5°C), refrigeration (2°-8°C), and high temperature (45° ± 0.5°C) in order to perform stability tests. Regular measurements were made on the average vesicle diameter changes and drug content. Stability tests for dry proniosome powders meant for reconstitution should be carried out at 40°C/75% relative humidity in compliance with worldwide climatic zones and conditions, as recommended by the worldwide Conference on Harmonization (ICH) (WHO, 1996). Countries in zones I and II require a temperature of 25°C/60% RH for long-term stability studies, whereas countries in zones III and IV require a temperature of 30°C/65% RH. St appearance, color, assay, pH, particle matter, preservative content, pyrogenicity, and sterility are all things that should be checked in a product.[35]

Advantages of Proniosomes

1. Proniosome phospholipids and non-ionic surfactants can function as penetration enhancers to facilitate drug diffusion.

2. Other advantages of proneosomes include simplicity of dispersion, storage, transportation, and dosage.

3. They stay clear of the problems like physical stability, aggregation, fusion, and leakage that come with either noisome or aqueous dispersion.

4. Proniosomes also avoid the problems that liposomes face, such oxidation or hydrolysis, as well as fusion, aggregation, or sedimentation when being stored.

5. Proniosomes may speed up the repair of the epidermal barrier in addition to showing promise as a means of administering medicine.[36]

Conclusion:

The aforementioned paper states that experts and scholars generally agree with the idea of incorporating medicine into niosomes to improve drug targeting to the proper tissue destination. Niosomes generated from proniosomes have potential as a drug delivery system. Niosomes are similar to liposomes in that they may contain a range of medications inside their multienvironmental structure. Proniosomes are now regarded to be a superior choice for a drug delivery system. There are several uses for niosome-based niosomes that target oral, topical, parental, and opthalmic vaccines for drug delivery. To fully fulfill the promise of the novel medication delivery technique, more research is required.

References

1. Shakya V. Niosomes: A Novel Trend in Drug Delivery. Ijrdp. 2014; 3: 1036- 1041

2. Makeshwar K, Wasankar S. Niosomes: a novel drug delivery system. Asian J. Pharm. Res. 2013; 3: 16-20.
3. Punithavalli G, Vignesh M. Formulation of Niosomal Suspension with enhanced oral bioavailability of Diclofenac sodium. Journal of Global Trends in Pharmaceutical Sciences. 2012; 3: 656-671.

4. Katare R, Gupta P, Mahor S, Rawat A, Khatri K, Katare Y, Panda A, Vyas S. Development of polysaccharide-capped niosomes for oral immunization of tetanus toxoid. Journal Drug Del. Sci. Tech. 2006; 16: 167-172

5. Shahiwala A, Misra A. Studies in topical application of niosomally entrapped nimesulide. Journal of Pharm. Pharmaceut. Sci. 2002; 5: 220-225.

6. Bagheri A, Chu B, Yaakob H. Niosomal Drug Delivery Systems: Formulation, Preparation and Applications. World Applied Sciences Journal. 2014; 32: 1671-1685.

7. Sudheer P, Kaushik K. Review on Niosomes- A Novel Approach For Drug Targeting, Journal of Pharmaceutical Research. 2015; 1-14.

8. Sunilkumar M. Niosomes As novel drug delivery system. International Research Journal of Pharmaceutical and Applied Science. 2015; 5: 1-7.

9. Sankhyan A, Pawar P. Recent Trends in Niosome as Vesicular Drug Delivery System. Journal of Applied Pharmaceutical Science. 2012; 2: 20-32.

10. Gurjar P. Niosome: A Promising Pharmaceutical Drug Delivery. Int. J. Pharm Anal. 2014; 2: 425-431.

11. Madhav N, Saini A. Niosomes: A novel drug delivery system. International journal of research in pharmacy and chemistry. 2011; 1: 498-511.

12. Gandhi A, Sen S, Paul A. Current Trends in Niosomes As vesicular drug delivery system. Asian Journal of Pharmacy and Life Science. 2012; 2: 339- 353

13. Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (Niosome and Liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. *J Pharm Pharmacol.* 1988;40:161–5.

14. Cummings J, Stuart JF, Calman KC. Determination of adriamycin, adriamycinol and their 7-deoxyaglycones in human serum by high-performance liquid chromatography. *J Chromatogr.* 1984;311:125–

15. Suzuki K, Sokan K. The Application of Liposomes to Cosmetics. *Cosmetic and Toiletries.* 1990;105:65–78

16. Alcantar N, Dearborn K, VanAuker M, Toomey R, Hood E. Niosome-hydrogel drug delivery. *US 2008/0050445A1.* 2008

17. 17. Brewer JM, Alexander J. The adjuvant activity of non-ionic surfactant vesicles (niosomes) on the BALB/c humoral response to bovine serum albumin. *Immunology.* 1992;75:570–5.

18. Moser P, Marchand-Arvier M, Labrude P, Handjani -Vila RM, Vignerson C. Hemoglobin niosomes. I. Preparation, functional and physico-chemical properties, and stability. *Pharma Acta Helv.* 1989;64:192–202

19. Moser P, Arvier MM, Labrude P, Vignerson C. Niosomes of hemoglobine. II. *Vitro* interactions with plasma proteins and phagocytes. *Pharm Acta Helv.* 1990;65:82–92

20. Jayaraman SC, Ramachandran C, Weiner N. Topical delivery of erythromycin from various formulations: An *in vivo* hairless mouse study. *J Pharm Sci.* 1996;85:1082–4.

21. Baillie AJ, Coombs GH, Dolan TF, Laurie J. Non-ionic surfactant vesicles, niosomes, as delivery system for the anti-leishmanial drug, sodium stibogluconate. *J Pharm Pharmacol.* 1986;38:502–5.

22. Charcosset C, Pham TT, Jaafar-Maalej C, Fessi H. Liposome and niosome preparation using a membrane contactor for scale-up. ColloidsSurf B 2012; 94: 15–21.

23. 6. Akhilesh D, Prabhu P, Faishal G. Comparative study of carriers used in proniosomes. *Int J Pharm Chem Sci.* 2012;4:307–14

24. Mishra A, Kapoor A, Bhargava S. Proniosoml gel as a carrier for improved transdermal drug delivery. *Asian J Pharm Life Sci.* 2011;1:370–9.

25. Kakr R, Rao R, Goswami A, Nanda S, Saroha K. Proniosomes: An emerging vesicular system in drug delivery and cosmetics. *Der Pharmacia Lettre.* 2010;2:227–39.

26. Walve JR, Rane BR, Gujrathi NA. Proniosomes: A surrogate carrier for improved transdermal drug delivery system. *Int J Res Ayurveda Pharm.* 2011;2:743–50.

27. K Srikanth, M Nappinnai, VRM Gupta. Proniosomes: A Novel Drug Carrier System. Research J. Pharm. and Tech.3 (3): July-Sept. 2010; Page 709-711

28. Honeywell-Nguyen PL, Bouwstra JA. Vesicles as a tool for transdermal and dermal delivery. Drug Discov Today. 2005; 2:67-74.

29. Reddy SM et al., A Review On Proniosomes: Formulation, Characterization and Applications. American Journal of Pharmacy & Health Research 2020.6

30. Mishra A, Kapoor A, Bhargava S. Proniosoml gel as a carrier for improved transdermal drug delivery. Asian J Pharm Life Sci 2011;1:370-9.

31. Kakkar R, Rao R, Kumar DN. Formulation and characterisation of valsartan proniosomes. Maejo Int J Sci Technol 2011;5:146-58.

32. Pavala Rani N, Suryaprakashand TN, Senthamarai R. Formulation and evaluation of rifampicin and gatifl oxacinniosomes on logarithmicphase cultures of mycobacterium tuberculosis. Int J Pharm Biol Sci 2010;1:379-86.

33. Keservani RK, Sharma AK, Ayaz MD. Novel drug delivery system for the vesicular delivery of drug by the niosomes. Int J Res Control Release 2011;1:1-8.

34. Kapil S, Rao R, Saini V. Preparation and evaluation of lornoxicamniosomal gel. Int Res J Pharm 2012;3:378-83

35. Kumar GP, Rao PR. Nonionic surfactant vesicular systems for effective drug delivery – An overview. Acta Pharm Sinica B. 2011;1:208-19.

36. Arunothayanun P, Bernard MS, Craig DQ, Uchegbu IF, Florence AT. The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. Int J Pharm 2000;201:7-14.