

A review on Proniosomes: Innovative Vesicular Drug Delivery System

Author – Miss Bhagat Tejal Sanjay

Guide – Prof.Jadhav Rushikesh

Principal name – Dr.Megha Salve

Institute name –Shivajirao Pawar College of Pharmacy, Pachegaon

Submitted: 15-11-2023

Accepted: 25-11-2023

ABSTRACT

Proniosomes are a dry formulation of water-soluble carrier particles coated with a surfactant. They are rehydrated immediately before use after a few minutes of stirring in a warm aqueous medium to produce a dispersion of niosomes. Proniosomes are physically stable during storage and transport. The active ingredient enclosed in the vesicular structure of the proniosomes extends their residence time in the bloodstream, increases penetration into the target tissue and reduces toxicity. New Vesicular systems such as proniosomes, which are part of advanced nanotechnologies that minimize problems of vesicular systems such as aggregation, fusion and drug leakage, as well as other problems related to transport, distribution, storage and dosing. Classic vesicular systems such as niosomes and liposomes are distinguished by their nature and are associated with stability. The aim of this work is the introduction and further development of proniosomes as a transport system for various pharmaceutical applications.

Keywords: Proniosomes , Formulation, liposomes, Niosomes , surfactant, Characterization , Nanotechnology .

I. INTRODUCTION

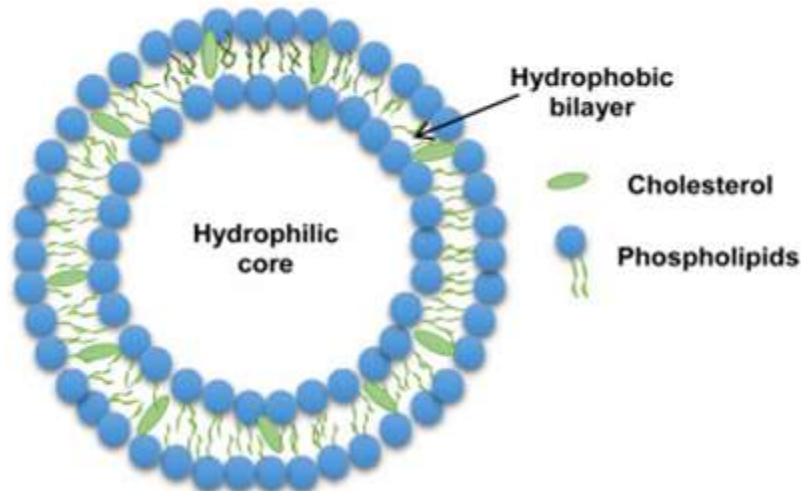
Since the early 1980s, proniosomes have attracted great research interest for their use as targeting agents and drug carriers because they offer various advantages while avoiding the disadvantages associated with conventional

pharmaceutical formulations. Niosomes are water-soluble carrier particles that are dried by briefly stirring in a warm aqueous medium to form a dispersion of niosomes. This dehydrated product is called proniosomes. The resulting niosomes are highly related to conventional niosomes and exhibit greater uniformity in size . The proniosomal approach reduces the problems associated with a dry, liquid product that is more stable during storage and sterilization. Proniosomes represent a versatile delivery system due to their ease of distribution, measurement, transfer, and storage.

Vesicular drug delivery is one of the approaches that encapsulate the drug, such as liposomes, niosomes, transferosomes, pharmacosomes, and ribbons such as proniosomes and proliposomes. The advantage of liposomes and niosomes over other conventional dosage forms lies in their particulate nature, which serves as a reservoir for the active ingredient. You can also make several changes to adjust the pattern and release of the medicine.

Vesicular forms LIPOSOMES

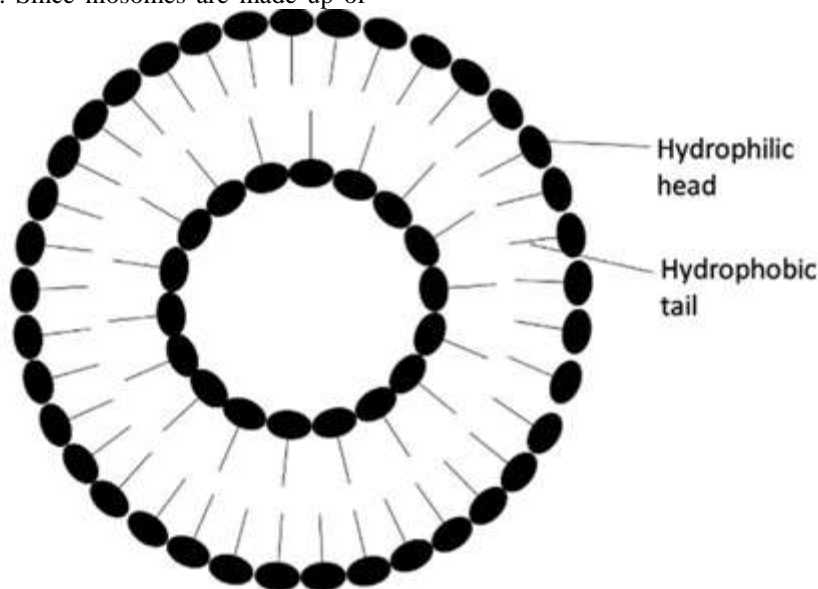
Liposomes are artificially produced vesicles consisting of a lipid bilayer. They can be used as a means of transporting nutrients and medicines. Liposomes can be made by disrupting biological membranes. They consist of natural phospholipids and can also contain mixed lipid chains with surfactant properties.



NIOSOMES

Niosomes are vesicular, novel drug delivery system, which can be used for the sustained, controlled as well as targeted delivery of drugs. Niosomes can be unilamellar, oligolamellar or multilamellar. Since niosomes are made up of

non-ionic surfactants these are named niosomes and are non-toxic because of these surfactants. In addition to non-ionic surfactants, they may also contain cholesterol or its derivatives and charged molecules.



- They are less toxic due to their non-ionic nature.
- The large-scale production of niosomes does not require any special conditions.

of the formulation when compared to liposomes.

- Niosomes contain non-ionic surfactants, whereas liposomes contain phospholipids which are neutral or charged.

Comparison between Niosomes and Liposomes

- Niosomes are less expensive than liposomes.
- Niosomes does not require any special conditions or methods for storage and handling

TRANSFEROSOMES

A transferosome carrier is an artificial vesicle designed to be such as a cell vesicle or a cell engaged in exocytosis and thus suitable for controlled and potentially targeted drug delivery.

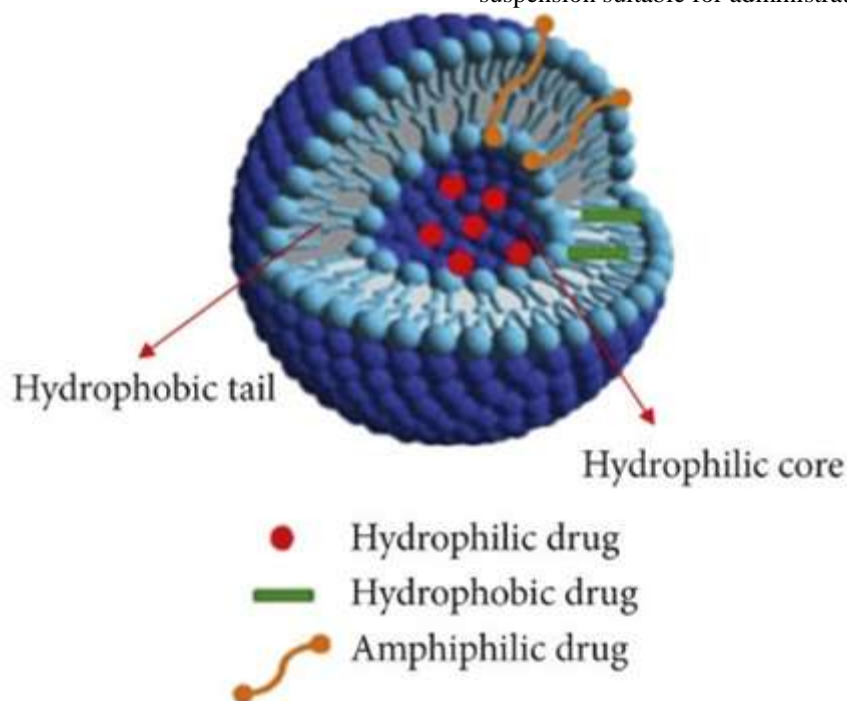
PROTEASOMES

Proteasomes are cytoplasmic organelles consisting of a central cylindrical particle connected at both ends by two regulatory molecules responsible for the degradation of endogenous proteins. Proteins targeted for destruction are recognized by proteasomes thanks

to the presence of ubiquitin conjugated to the lysine residue of the target protein.

PRONIOSOMES

Proniosomes are dry, flowable preparations of a surfactant-coated carrier that, when rehydrated by stirring in hot water, form a multilamellar niosome suspension suitable for administration.



Nonionic surfactant vesicles, called niosomes, are microscopic lamellar structures formed by mixing nonionic surfactant, cholesterol, and diacetyl phosphate followed by hydration in an aqueous environment. Proniosomes offer a novel and versatile concept for drug delivery via vesicles with potential for transdermal drug delivery. Why proniosomes form niosomes when rehydrated with skin water under appropriate conditions. Proniosomes minimize niosome problems such as aggregation, fusion and loss, as well as problems related to transport, storage and dosing. The transdermal therapy system offers significant advantages over non-invasive parenteral drug therapy. Avoids the first intestinal transit and reduces the side effects of liver metabolism. Probubble systems have attracted researchers as an alternative strategy for transdermal drug delivery because of non-toxicity and penetration effect of surfactant.

Advantages of Proniosomes over the other vesicular systems

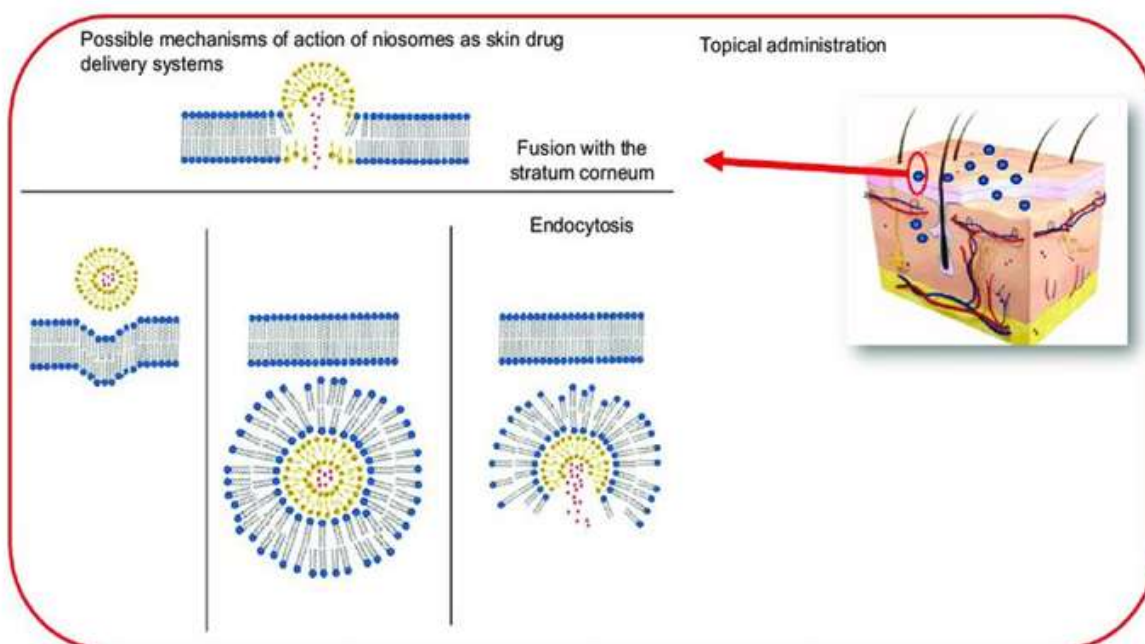
1. It shows controlled, targeted and sustained release of drugs due to the formation of depots.
2. It can capture both hydrophilic and hydrophobic drugs.
3. It is biodegradable, biocompatible and non-immunogenic for the organism.
4. The shape, size, composition and flowability of the proniosomal drug can be controlled if necessary.
5. Proniosomes avoid physical stability problems such as fusion, aggregation, sedimentation and losses during storage.
6. Avoid chemical stability problems such as hydrolysis of encapsulated drugs, which limit the stability of the dispersion.
7. Drug delivery improves bioavailability and minimum side effects.

Action of Proniosomes

The mechanism of drug transport across the skin via vesicles shows contradictory results. Therefore, it is unclear which factors influence skin-vesicle interactions and determine the

efficiency of drug transport through the skin. However, it is clear that the pro-vesiclesystem converts into vesicles before the drug must be released and penetrates through the skin. The Bilayer present in the vesicles acts as a limiting barrier to the action of drugs. In addition, it contains surfactants (nonionic) and Phospholipids,

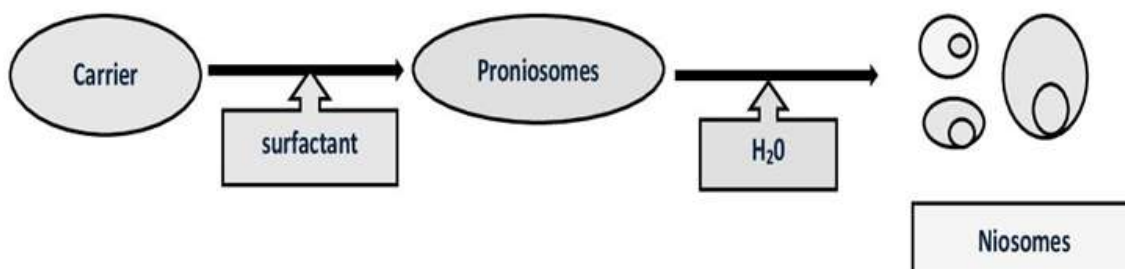
both of which act as penetration enhancers and can increase penetration power. Lots of drugs, penetration enhancers influence vesicles to reduce the barrier properties of the stratum corneum. Another possible mechanism is to modify the structure of the stratum corneum to penetrate the drug Encapsulated in the vesicles.



Formation of Niosome from Proniosomes

Niosomes can be prepared from proniosomes by adding various types of aqueous

phase of drug to the proniosomes with brief mixing. And niosome production by the proniosome.



Composition of Proniosomes

The essential components for the delivery system are as follows :

1. Surfactant

Surfactants are surfactants, mostly organic compounds, that naturally have hydrophobic and

hydrophilic groups. Therefore, surfactants contain both a water-insoluble (hydrophobic) component and a water-soluble (hydrophilic) component. They can act as wetting agents, emulsifiers, solubilizers and permeability enhancers.

Type of non-ionic surfactant	Examples
Fatty alcohol	Cetyl alcohol, stearyl alcohol, cetostearyl alcohol, oleyl alcohol
Ethers	Brij, Decyl glucoside, Lauryl glucoside, Octyl glucoside, Triton X-100, Nonoxynol-9
Esters	Glyceryl laurate, Polysorbates, Spans
Block copolymers	Poloxamers

2. Membrane stabilizer

Cholesterol and lecithin are mainly used as preservatives for cell membranes. Steroids are important components of the cell membrane and their presence in the membrane leads to significant changes in the stability, fluidity and permeability of the bilayers. Cholesterol is a natural steroid used as a membrane additive. Cholesterol prevents the aggregation of the preparation through steric or electrostatic repulsion effects. It leads to the transformation from a gel state to the liquid phase in the vesicular systems. Phosphatidylcholine is the main component of lecithin. It has low water solubility and can form liposomes, bilayer layers or lamellar structures depending on hydration and temperature. Depending on the source from which they are obtained, they are called egg lecithin and soy lecithin. It act as a stabilizing as well as enhancers.

3. Carrier Material

Assisting in the preparation of proniosomes, this allows the formulation to be flexible in terms of the ratio of surfactant to other ingredients included. In addition, this increases the surface area and thus the effective load. Carriers must be safe and non-toxic, free-flowing, and have low solubility in the loaded mixture solution and good water solubility to facilitate hydration.

4. Solvent and Aqueous phase

Alcohol is used in the preparation of proniosomes because it has a strong influence on

the size of vesicles and the penetration rate of the drug. Bubbles formed from various alcohols, with ethanol having a water solubility greater than , resulting in the formation of the larger vesicle size instead of isopropanol , which forms the smaller vesicle size due to the presence of a branched chain. Phosphate buffer pH 7.4, 0.1% glycerin, hot water, used as aqueous phase in the production of proniosomes .

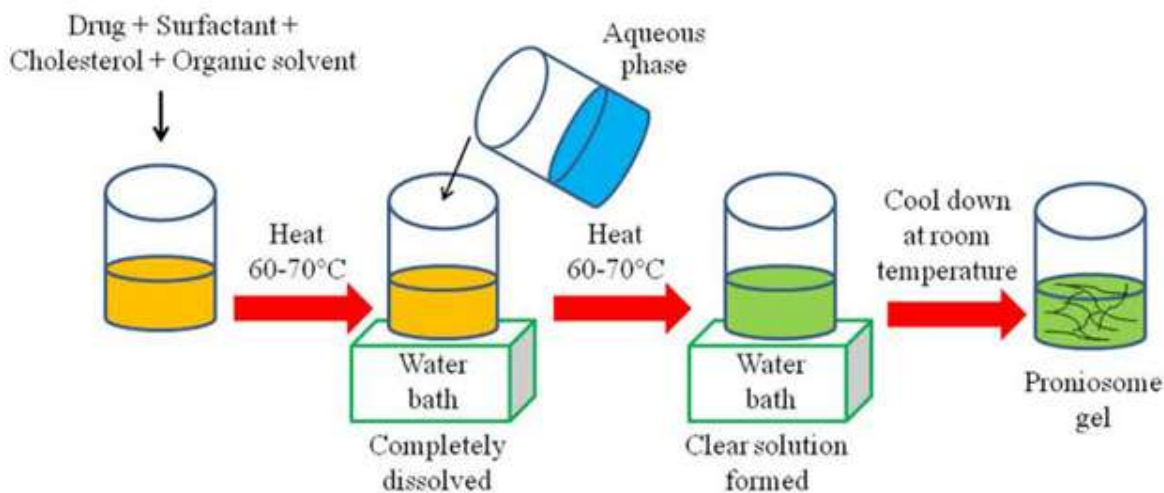
Methods of Preparation of Proniosomes

Proniosomal formulations may be prepared by,

1. Slurry method.
2. Coacervation phase separation method
 - a) Modified coacervation method
 - b) Handshaking method
3. Slow spray coating method.

1. Slurry Method

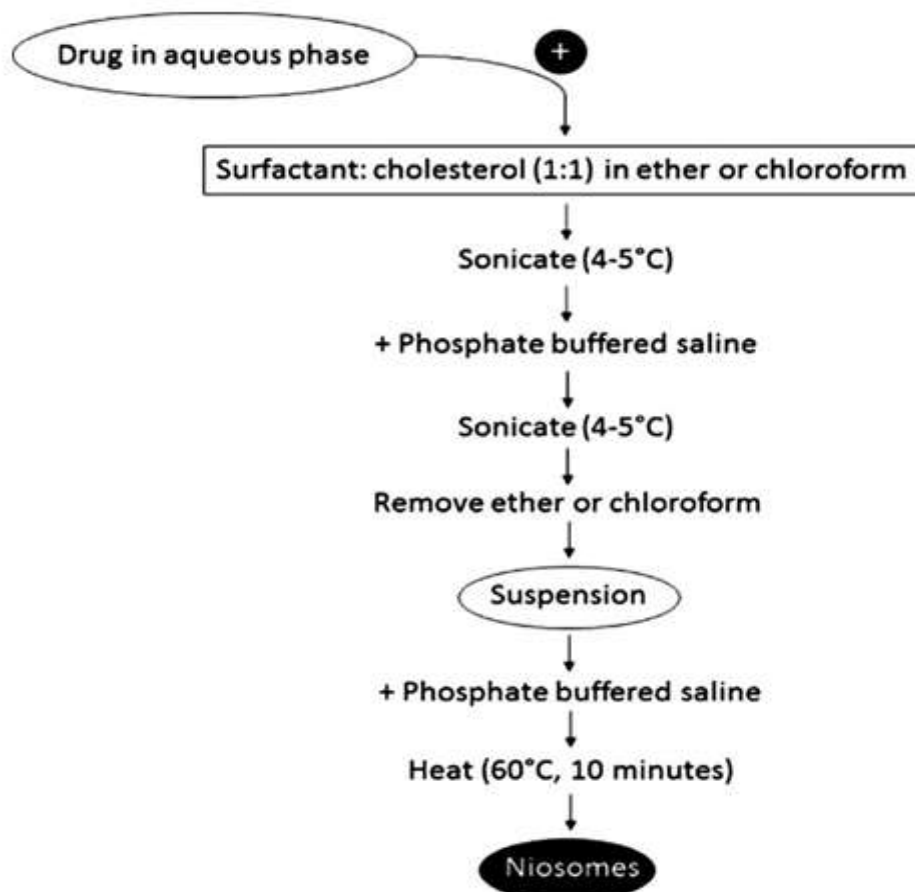
Proniosomes were prepared by the slurry method. Briefly, a weighed amount of surfactant and cholesterol was dissolved in an appropriate solvent. The resulting solution was transferred to a round bottom flask containing the vehicle. If the surfactant level is lower, more solvent can be added to create a suspension. The flask was connected to a flash rotary evaporator and the organic solvent was evaporated under reduced pressure to ± 20 °C. In the bottle you will receive dry and dissolved proniosomes. Finally, they were stored in a tightly closed container until further evaluation.



2. Coacervation phase separation method

Precisely weighed or required amounts of surfactant, cholesterol and drug were mixed with organic solvent in glass vials and heated in a water bath. Shake the glass vials until the ingredients

are completely dissolved. The mixtures were allowed to cool to room temperature and it was observed whether a clear, translucent solution or a creamy white proniosome gel was formed. The resulting gel was mixed with stabilizer and then stored in the dark for characterization.



a) Modified Coacervation method

This is a modified coacervation method. According to the formula, the precisely weighed drug containing cholesterol, lecithin and surfactant was mixed with the solvent in a wide mouth glass tube. The open end of the glass tube was covered with a lid and the mixtures were heated in a water bath at $65 \pm 3^\circ\text{C}$ for 5 min. Phosphate buffer pH 7.4 was then added and the mixture was further heated in a water bath until a clear solution was formed. The mixture was allowed to cool until the dispersion turned into a proniosome gel.

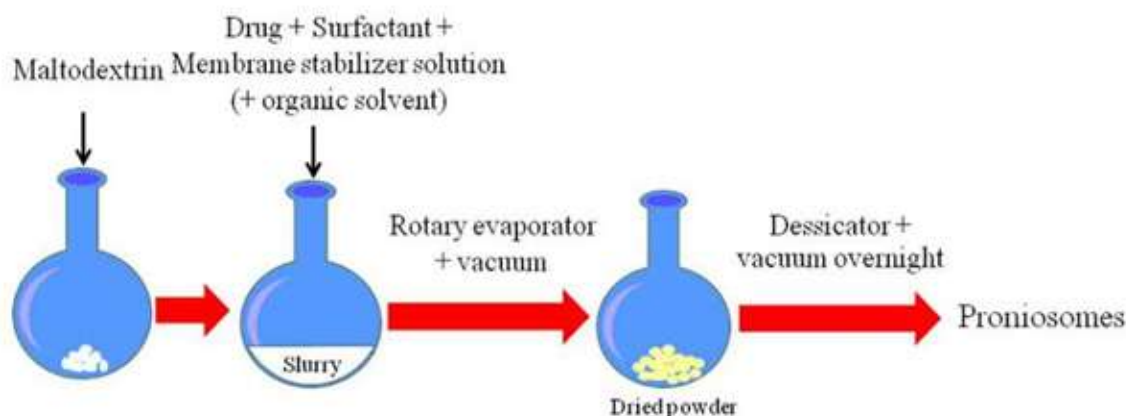
b) Handshaking method

Bubble-forming ingredients such as cholesterol and surfactants are dissolved in a round-bottomed flask containing an organic solvent. The resulting solvent mixture is evaporated in a flash rotary evaporator at room temperature. A thin layer of the dried solid mixture is deposited on the walls of the flask. The dried solid film can be rehydrated with the aqueous phase at $0-60^\circ\text{C}$ with gentle stirring. This method creates typical multilamellar

niosomes.

3.Slow spray coating method

Proniosomes are prepared by spraying a surfactant in organic solvents onto a support and then evaporating the remaining solvent. For this purpose, a mixture of surfactants, cholesterol and diacetyl phosphate is placed in a flask containing the desired amount of carrier. On a rotary evaporator by continuously spraying portions of onto the surface of the support at a controlled application rate of . Transfer the bottle to a water bath at $65-70^\circ\text{C}$ and rotate the bottle after adding the final portions of add vacuum until the powder is completely dry. Repeat the process until the surfactant level reaches the desired value. So you get a very thin coating carrier, a surfactant, and the hydration of the coating allows the carrier to dissolve. The material is then dried overnight in a vacuum dryer. A dry, liquid preparation of "proniosomes" is created, which is then used for characterization and preparation.



Characterization of Proniosomes

Evaluation Studies are further carried out for the prepared proniosomes in order to find out the :

- Measurement of angle of repose
- Scanning electron microscopy (SEM)
- Optical microscopy
- Measurement of vesicle size
- Drug content
- Entrapment efficiency
- In-vivo release studies
- Stability Studies

1. Measurement of Angle of repose

Funnel method : The funnel was fixed in a suitable position and the proniosomal powder was poured in such that the outlet of the funnel was 10 cm above the surface level. The powder flowed out of the funnel and formed a cone on the surface. The angle of repose was calculated by measuring the height of the cone and the diameter of its base.

The formula for calculating the angle of repose is $\tan^{-1}(2h/d)$. In this formula, h is the height of the pile of powder and d is the diameter.

2. Scanning Electron Microscopy (SEM)

The particle size of proniosomes is a primary factor. The surface morphology and size

distribution of the proniosomes. They were examined using SEM. Double-sided adhesive tape was attached to the Aluminum and Proniosomal powder sections. The aluminum piece was placed in the Vacuum chamber of a scanning electron microscope (XL 30 ESEM from EDAX, Philips, Netherlands). The morphological characteristics of Samples were observed using a Gas secondary electron detector (operating pressure 0.08 Torr, acceleration voltage – 30.00 KV) XL 30, (Philips, Netherlands).

3. Optical microscopy

The niosomes were mounted on glass slides and viewed under a microscope. The microscope has a 1200x magnification and, after sufficient dilution, is used for morphological observations. A micrograph of sample was taken with a microscope using a Digital reflex camera.

4. Measurement of Vesicle size

Vesicle dispersions were diluted approximately 100-fold in the same medium used for their preparation. The size of vesicle was measured using a particle size analyzer. The device consists of a 632.8 nm He-Ne laser beam that focuses using a Fourier lens

(R-5) to a minimum power of 5 MW to a spot at the center of the multi-element detector and a small sample volume becomes contained in the cell. Samples were mixed using a mixer before bubble size determination.

5. Drug content

The proniosomes corresponding to 100 mg were collected in a standard volumetric flask. They were lysed with 50 mL of methanol by the method of stirring for 15 minutes. The solution was diluted to 100 ml with methanol. Subsequently, 10 ml of this solution was diluted to 100 ml with phosphate-buffered saline at a specific pH. Samples were taken and the absorption at a specific wavelength was measured and the active ingredient content was calculated from the calibration curve.

6. Entrapment efficiency

Separation of the untrapped drug from the niosomal suspension was achieved by exhaustive dialysis and centrifugation. The dialysis suspension was collected in a dialysis tube, to which an osmotic cellulose membrane was attached on one side, in the tube the dialysis fluid was

suspended in 100 ml of salt buffer with a specific pH, which was stirred on a magnetic stirrer. The niosomal suspension and the unencapsulated drug were redistributed in the medium through an osmotic cellulose membrane. After 6 hours of exhaustive dialysis, optical density values were recorded and assessment of entrapped drug was performed using UV spectrophotometry.

7. In-vivo release studies

Drug release from proniosomal Preparations was achieved using various techniques such as Franz diffusion cell, Keshary-Chien diffusion chamber, cellophane dialysis membrane, United States Pharmacopoeia (USP) Type 1, porous molecular spectrum or tubular membrane certainly. Drug release from proniosome-derived niosomal vesicles may occur by one or more of the following Mechanisms: desorption from the vesicle surface or diffusion of the drug from the bilayer membrane or combined mechanisms of desorption and diffusion.

8. Stability studies

Stability studies were carried out by storing the prepared proniosomes under different temperature conditions such as refrigeration temperature (2-8°C), room temperature (25° ± 0.5°C) and elevated temperature (45° ± 0.5°C) of the period from 1 month to 3 months. The drug content and the variability of the mean follicle diameter were monitored regularly. International Conference on Harmonization (ICH) Guidelines suggest that stability studies of dry proniosome powders intended for reconstitution be accelerated stability at 40°C/75% relative humidity in accordance with climates and international climatic conditions should be tested (WHO, 1996). For Long-term stability studies, the temperature is 25°C/60% relative humidity for countries in Zones I and II and for countries in Zones III and IV the temperature is 30°C/65% relative humidity RH. The product must be evaluated for appearance, color, marking, pH, preservatives, particles, sterility and pyrogenicity.

Applications Of Proniosomes

1. Targeting of Bioactive agents

One of the most useful aspects of proniosomes is their ability to target drugs to a specific area. Proniosomes can be used to target drugs to the reticuloendothelial system. The reticuloendothelial system “RES” prefers proniosomal vesicles. The uptake of proniosomes is

controlled by circulating factors called opsonins in the serum. This drug site is used to treat tumors in animals known to metastasize to the liver and spleen. This healing position can also be used to treat parasitic infections of the liver. Proniosomes can also be used to target drugs to organs other than the RES. Transport system "like antibodies"; They can be attached to proniosomes (since immunoglobulin readily binds to the lipid surface of the nose) to target them to a specific organ.

2. Anti-neoplastic treatment

Most cancer drugs cause serious side effects. Proniosomes can alter metabolism; They extend the circulation and half-life of the drug, thereby reducing the side effects of the drug. Probiosomal trapping of doxorubicin and methotrexate has shown beneficial effects compared to non-capturing drugs, such as reduced tumor proliferation rates and higher plasma concentrations with simultaneous slower elimination.

3. Leishmaniasis

Leishmaniasis is a disease in which a parasite of the genus *Leishmania* attacks the cells of the liver and spleen. Medications commonly prescribed for treatment include antimony derivatives (antimonials), which in higher concentrations can cause damage to the heart, liver, and kidneys. The use of niosomes in the studies carried out has shown that it is possible to administer higher doses of the drug without causing side effects, allowing greater effectiveness of treatment.

4. Transdermal drug delivery

The main disadvantage of transdermal administration is the slow penetration of the drug through the skin, while an increase in the penetration rate was achieved by transdermal administration of the drug incorporated into niosomes.

5. Cosmetic delivery

The first report of nonionic surfactant vesicles comes from cosmetic applications developed by L'Oréal. Niosomes were developed and patented by L'Oréal in the 70s and 80s. The first Niosome product was launched by Lancôme in 1987. The benefits of using niosomes in cosmetic and skin care applications include their ability to increase the stability of entrapped drugs,

improve the bioavailability of poorly absorbed ingredients, and improve skin penetration.

6. Ocular drug delivery

When administering the drug into the eye in the form of a proniosomal gel, it is necessary to completely solve the problems arising during ocular administration of the drug while maintaining the effect of the drug. They solve the problem of metabolism and also prevent the breakdown of the drug by the metabolic enzyme present on the surface of the tear epithelium and cornea. Another advantage is to increase contact time and improve drug retention.

7. Proniosomes as a carrier for Haemoglobin

Proniosomes can be used as carriers for haemoglobin within the body particularly in anaemic patients, because of these vesicles are permeable to oxygen.

8. Other Applications

a) Sustained Release

Administration of the drug in proniosomal capsules with low water solubility, a prolonged action of the drug in a brimonidine tartrate-based proniosomal gel improves the bioavailability of the drug in the eye, increases the residence time of the drug and improves the functionality of the eye contact time of the drug and allows prolonged release of the drug.

b) Localized drug action

Drug delivery via niosomes is one way to achieve local pharmacological effects, as their large size and low permeability through the epithelium and connective tissue result in the drug being localized to the site of administration. The local action of the drug increases the effectiveness of the drug and at the same time reduces, among other things, its systemic toxic effects. Antimony encapsulated in niosomes is taken up by mononuclear cells, which localize the drug, increasing its effectiveness and thus reducing both dose and toxicity. The development of niosomal drug delivery technology is still in its infancy, but this type of drug delivery system has shown promise in cancer chemotherapy and anti-leishmania therapy.

II. CONCLUSION

Proniosomes niosomes are very promising as drug carriers. Compared to liposomes of natural or synthetic phospholipids; niosomes have the

advantage that chemical degradation problems, such as oxidation and hydrolysis, may be largely alleviated. Compared to liposome or niosome suspensions, proniosomes represent a significant improvement by eliminating physical stability problems, such as aggregation or fusion of vesicles and leaking of entrapped drugs during long-term storage. Compared to niosomes prepared by conventional means, proniosome-derived niosomes are superior in their convenience of storage, transport and dosing. The release data indicate that proniosome-derived niosomes are at least as effective as conventional niosomes in their release characteristics, and may therefore offer improved bioavailability of some drugs with poor solubility, controlled release formulations, or reduced adverse effects of some drugs. Because proniosomes are a dry powder, further processing is possible. To provide convenient unit dosing, the proniosome powder may be processed to make beads, tablets, gel or capsules. One of the greatest advances offered by proniosomes is their ease of use. Proniosome derived niosome suspensions appear to be as good as or better than conventional niosome preparations, and may be an appropriate preparation to use as a hydrophobic drug carrier.

REFERENCES

- [1]. Radha, G. V., Rani, T., & Sarvani, B. (2013). A review on proniosomal drug delivery system for targeted drug action. *Journal of Basic and Clinical Pharmacy*, 4(2), 42.
- [2]. Goudanavar, P. (2019). Review on Proniosomes. *Humanjournals.com*.
- [3]. 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. [Google Scholar]
- [4]. 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. [Google Scholar]
- [5]. Dua JS, Rana AC, Bhandari AK. Liposomes methods of preparation and applications. *Int J Pharm Stud Res*. 2012;3:14–20. [Google Scholar]
- [6]. Bhardwaj, P., Tripathi, P., Gupta, R., & Pandey, S. (2020). Niosomes: A review on niosomal research in the last decade. *Journal of Drug Delivery Science and Technology*, 56(101581), 101581.
- [7]. Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): physical and Pharmaceutical chemistry. *Adv Coll Int Sci* 1995; 58: 1–55.
- [8]. Uchegbu IF, Vyas SP. Non-ionic surfactant based vesicles (niosomes) in drug delivery. *Int J Pharm* 1998; 172: 33–70
- [9]. Carafa M, Santucci E, Lucania G. Lidocaine loaded non-ionic surfactant vesicles: Characterization and in-vitro permeation studies. *Int J Pharm* 2002; 231: 21–32.
- [10]. Alsarra IA, Bosela AA, Ahmed SM, et al. Proniosomes as a drug carrier for transdermal Delivery of ketorolac. *Eur J Pharm Biopharm* 2005; 59: 485–490.
- [11]. Rai K, Gupta Y, Jain A, Jain SK. Transfersomes: Self-optimizing carriers for bioactives. *PDA J Pharm Sci Technol*. 2008;62:362–79. [PubMed] [Google Scholar].
- [12]. Kish-Trier E, Hill CP. Structural biology of the proteasome. *Annu Rev Biophys*. 2013;42:1.1–121. [Google Scholar]
- [13]. Hu C, Rhodes DG. Proniosomes: a novel drug carrier preparation. *Int J Pharm* 1999; 185: 23–35.
- [14]. Mahmoud Mokhtar, Omaima A. Sammour, Mohammed A. Hammad, et al. Effect of Some formulation parameters on flurbiprofen encapsulation and release rates of niosomes prepared from proniosomes. *Int J Pharm* 2008; 361: 104–111.
- [15]. Kumar S. Proniosomal gel of flurbiprofen: formulation and evaluation. *Journal of drug delivery and therapeutics*. 2012 Jan 19;2(1).
- [16]. Kumar K, Rai AK. Development and evaluation of proniosomes as a promising drug carrier to improve transdermal drug delivery. *IRJP* 2011;2:71-4
- [17]. Bachhav AA. Proniosome: A novel non-ionic provesicules as a potential drug carrier. *Asian Journal of Pharmaceutics (AJP): Free full-text articles from Asian J Pharm*. 2016 Sep 10;10(03).
- [18]. Touitou E, Junginger HE, Weiner ND, Nagai T, Mezei M. Liposomes as carriers for topical and transdermal delivery. *J Pharm Sci* 1994;83(9):1189-203.[Crossref] [Google Scholar] [Pubmed]
- [19]. Sinico C, Fadda AM. Vesicular carriers for dermal drug delivery. *Expert Opin Drug*

- Deliv 2009;6(8):813-25.[Crossref] [Google Scholar] [Pubmed]
- [20]. Junginger HE, Hofland HJ, Bouwstra JA. Liposomes and niosomes: Interactions with human skin. *Cosmet Toilet* 1991;106(8):45-50.[Google Scholar]
- [21]. R Rao, R Kakar, G Anju, N Sanju. Proniosomes: An Emerging Vesicular System in Drug Delivery and Cosmetics. *Der Pharmacia Lettre* 2010; 2(4): 227-239.
- [22]. K Kumar, AK Rai. Development and Evaluation of Proniosomes as a promising drug carrier to improve transdermal drug delivery. *IRJP* 2011; 2 (11): 71-74.
- [23]. K Yadav, D Yadav, K Saroha, S Nanda, P Mathur. Proniosomal Gel: A provesicular approach for transdermal drug delivery. *Der Pharmacia Lettre* 2010, 2(4): 189-198.
- [24]. Akhilesh D, Faishal G, Kamath JV. Comparative study of carriers used in proniosomes. *Int J Pharm Chem Sci.* 2012;3:6-12.
- [25]. N Pandey. Proniosomes and Ethosomes: New Prospect in Transdermal and Dermal Drug Delivery System. *IJPSR* 2011; 2(8): 1988-1996.
- [26]. Mehta M, Garg M. Proniosomal gel: A promising drug carrier for boswellic acids. *J Med Sci.*;15(3), 2015, 130-134.
- [27]. Singla S, Hari Kumar SL, Aggarwal G. Proniosomes for penetration enhancement in transdermal system. *Int J Drug Dev Res.* 4, 2012,1-3.
- [28]. Kumari R, Verma K, Verma A, Yadav GK, Maurya SD. Proniosomes: a key to improved drug delivery. *Journal of Drug Delivery and Therapeutics.* 2014, 56-65.
- [29]. Solanki AB, Parikh JR, Parikh RH. Formulation and optimization of piroxicam proniosomes by 3-factor, 3-level Box-Behnken design. *AAPS PharmSciTech.* 8(4), 2007, 43.
- [30]. B. Swathi, K. Yashaswini, A. Yashvitha, k. Thulasi, Mariyam Ahmed, Muna Yousuf Ali. Formulation and Evaluation of Nebivolol Proniosomal gel. *International Journal of Pharma Science and Research.* Vol. 8(5), 2017.
- [31]. Ramkanth S, Chetty CM, Sudhakar Y. Development and in vitro permeation studies of proniosomal based transdermal delivery System of Atenolol. *Pak J Pharm Sci.* 27(1), 2014, 115-120.
- [32]. Fang JY, Yu SY, Wu PC, Huang YB, Tsai YH. In vitro skin permeation of estradiol from various proniosome formulations. *International Journal of pharmaceutics.* 215(1-2), 2001, 91-99.
- [33]. Radha GV, Rani TS, Sarvani B. A review on proniosomal drug delivery system for targeted drug action. *Journal of basic and Clinical pharmacy.*; 4(2), 2013, 42.
- [34]. El-Laithy HM, Shoukry O, Mahran LG. Novel sugar esters proniosomes for transdermal delivery of vinpocetine: preclinical and clinical studies. *European journal of pharmaceutics and biopharmaceutics.*; 77(1), 2011, 43-55.
- [35]. Bachhav AA. Proniosome: A novel non-ionic provesicules as potential drug carrier. *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm.* 10(03), 2016, 10.
- [36]. Kakkar R, Rao R, Kumar DN. Formulation and characterisation of valsartan proniosomes. *Maejo Int J Sci Technol* 2011;5:146-58.
- [37]. Pavala Rani N, Suryaprakashand TN, Senthamarai R. Formulation and evaluation of rifampicin and gatifloxacin niosomes on logarithmic phase cultures of mycobacterium tuberculosis. *Int J Pharm Biol Sci* 2010;1:379-86.
- [38]. 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.
- [39]. Kapil S, Rao R, Saini V. Preparation and evaluation of lornoxicam niosomal gel. *Int Res J Pharm* 2012;3:378-83.
- [40]. Kumar GP, Rao PR. Nonionic surfactant vesicular systems for effective drug delivery – An overview. *Acta Pharm Sinica B.* 2011;1:208-19.
- [41]. Gyati Shilakari, Davinder Singh, Abhay Asthana (2013), Novel vesicular carriers for topical drug delivery and their application's, *Int. J. Pharm. Sci. Rev. Res.*, 21(1), no. 14, 77-86.
- [42]. Shrishti Namdev, Preeti Jamkar, Satish Mandlik, Kishore Gujar (2014), recent trends in novel drug delivery for treatment of type I and II diabetes mellitus, *Asian Journal of Pharmaceutical Research and Development* Vol. 2 (3) 54-69.



- [43]. Trupti Anil Udasi, Vikrant P Wankhade, Latika, M. Ingle, Sandeep Atram, Kiran K. Tapar, proniosome: a novel approach to vesicular drugdelivery system, International Journal of Pharmacy and Pharmaceutical Science Research
- [44]. D. Nagasamy Venkatesh, V. Swetha Priyanka, K. Tulasi, K. Kalyani, Sheik Abid Ali (2014), Harikrishna Jilakara Proniosomes: A Superior Drug Delivery System, International Journal of Pharmaceutical Sciences and Drug Research; 6(3): 178-182.
- [45]. Ajay Solanki, Jolly Parikh, Rasjesh Parikh (2008), Preparation, Characterization, Optimization, and Stability Studies of Aceclofenac Proniosomes, Article in Iranian journal of pharmaceutical research (IJPR).
- [46]. Sahil Khindri, Geeta Aggarwal, SL Hari Kumar (2015), Role of niosomes and proniosomes for enhancing bioavailability of drugs, Khindri et al Journal of Drug Delivery and Therapeutics. 5(1):28-33.
- [47]. Anchal Sankhyan and Pravin Pawar (2012), Recent Trends in Niosome as Vesicular Drug Delivery System, Journal of Applied Pharmaceutical Science 02 (06); 20-32.
- [48]. Rawia M. Khalil, Ghada A. Abdelbary, Mona Basha, Ghada E. Awad, et al.(Design and evaluation of proniosomes as a carrier for ocular delivery of lomefloxacin) Journal of liposome research, 2016; 1532-2394
- [49]. Alaa Emad Eldeeb, Salwa Salah, Mahmoud Ghorab. (Proniosomal gel-derived niosomes : an approach to sustain and improve the ocular delivery of bromonidine tartrate; formulation, in-vitro characterization, and in- vivo pharmacodynamic study) Drug delivery, 2019; 26(1): 509-521.
- [50]. Didem Ag Selecı, Muharrem Selecı, Johanna-GabrielaWalter, Frank Stahl, and Thomas Scheper, Niosomes as Nanoparticulate Drug Carriers: Fundamentals and Recent Applications, Hindawi Publishing Corporation Journal of Nanomaterials Volume 2016, Article ID 7372306, 13 pages.
- [51]. Yasam Venkata Ramesh, N. Jawahar, Satya Lavanya Jakki (2013), Proniosomes: A Novel Nano Vesicular Transdermal Drug Delivery, J. Pharm. Sci. and Res. Vol.5(8), 153 – 158.