



# **Proniosomes: Non-Ionic Surfactant Coated Vesicular Carrier Systems with Effective Drug Targeting**

**Santosh Kumar Rada <sup>a†</sup> and Gokula Brijitha <sup>a#</sup>**

<sup>a</sup> *GITAM Institute of Pharmacy, GITAM (Deemed to be University) Visakhapatnam, Andhra Pradesh, India.*

## **Authors' contributions**

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

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## **ABSTRACT**

Proniosomes is one of the unique drug delivery technology wherein the medicament is enclosed in a vesicle and have a variety of medicinal and cosmetic applications. Vesicular drug delivery reduces the treatment cost by increasing the bioavailability of the drug, especially for sparingly soluble compounds. Proniosomes are easier to create and less expensive than other innovative formulations. Proniosomes improve medication stability and give significant accessibility in dosage, distribution, passage, and storage, demonstrating that proniosomes stand as a very promising drug carrier technology. This study emphasizes proniosome preparation procedures in general, and also its submissions in drug delivery and targeting. As well, this review broadly elucidates the potential of proniosomes in delivering drugs via different routes, such as oral, oral mucosal, dermal and transdermal, ocular, parenteral, pulmonary, intranasal, and vaginal. Lastly, a comparison of proniosomes versus niosomes demonstrates the fundamental differences between them. According to the findings, this system seems to be a prospective forthcoming drug carrier that might be scaled up for commercial use with physicochemical stability.

<sup>†</sup>Assistant Professor;

<sup>#</sup>M.Pharmacy student

<sup>\*</sup>Corresponding author: E-mail: [srada@gitam.edu](mailto:srada@gitam.edu);

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## 1. INTRODUCTION

Proniosomes are non-ionic surfactant-coated carrier systems that instantly create niosomes when moistened. It is a granular, dry, free-flowing substance that gets wet shortly before use. They can administer a variety of hydrophilic and hydrophobic medicines in a variety of ways. This novel developing concept has shown promise in terms of increasing oral bioavailability, directing medications to specific sites, and achieving regulated release and preventing drug-related toxicity, drug penetration across the stratum corneum is used. Proniosome technology provides a novel solution for pharmaceuticals that are poorly soluble. Many of the issues connected with aqueous niosome dispersions, as well as the issue of physical stability, would be avoided. Peptidosomes are a versatile delivery strategy because they are easy to disperse, measure, transfer, and store [1].

## 2. ADVANTAGES

- Physical stability concerns, such as aggregation, leakage, and fusion can be avoided.

- This system avoids hydration of encapsulated medicine, resulting in a reduction of the dispersion's shelf life.

- Proniosomes are carrier particles that are soluble in water which adds to the benefit of transit, distribution, and storage of the drug.

- In these types of preparations, non-acceptable solvents are avoided. Without the need for vesicle dispersion in a polymeric matrix, the systems can be made into transdermal patches right away.

- The vesicles could operate as a drug repository, slowly releasing the medicine.

- The stability of the medication that is entrapped by being osmotically active and stable is increased.

- It is non-immunogenic, biodegradable, and biocompatible with the human body [2].

- Drug molecules' therapeutic efficiency is improved by delaying their removal from the bloodstream, shielding them from the extracellular environment, and restricting their effects to target cells.

- They increase the uptake of medication through the skin, improving the oral bioavailability of poorly absorbed drugs.

- They can be administered orally, parenterally, or topically to reach the targeted site.

- Because of their exclusive design, which contains hydrophilic, hydrophobic, and amphiphilic components, they may take medicinal compounds with a variety of solubilities.

## 3. STRUCTURE

Proniosomes are microscopic lamellar structures. Based on the method of preparation, they are either unilamellar or multi-lamellar. They combine a non-ionic surfactant of the alkyl or dialkyl polyglycerol ether and cholesterol followed by hydration in aqueous media. The surfactant molecule directs themselves such that the hydrophilic ends orient outward, while the hydrophobic ends are in the opposite direction to form the bilayer. Like liposomes, proniosomes are also made up of a bilayer of non-ionic surface-active agents [3]. The vesicle holds hydrophilic drugs within the space enclosed in the vesicle and the hydrophobic drugs are embedded within the bilayer [4].

## 4. PRONIOSOME ACTION

Fig. 2 shows a proniosome, which is in the intermediate of the niosome production process. There are two methods for converting proniosome formulation into niosomes [5,6].

1. Skin-based hydration: It occurs when water in the skin is used to hydrate the proniosome formulation and change to niosomes.
2. Solvent-based hydration: Proniosomes are converted to niosomes using aqueous solutions, such as pure water, saline solution, and buffers, with or without agitation and sonication [7,8].

## 5. DIFFERENT TYPES OF PRONIOSOMES

### 5.1 Dry Granular Proniosomes

Dry granular proniosomes are made by covering a water-soluble carrier with a surfactant, such as sorbitol or malt dextrin.

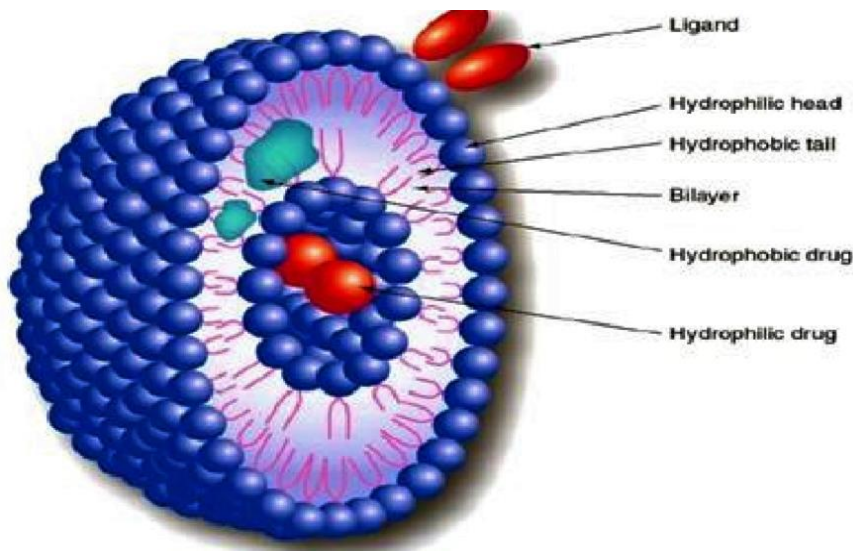


Fig. 1. Structure of proniosome

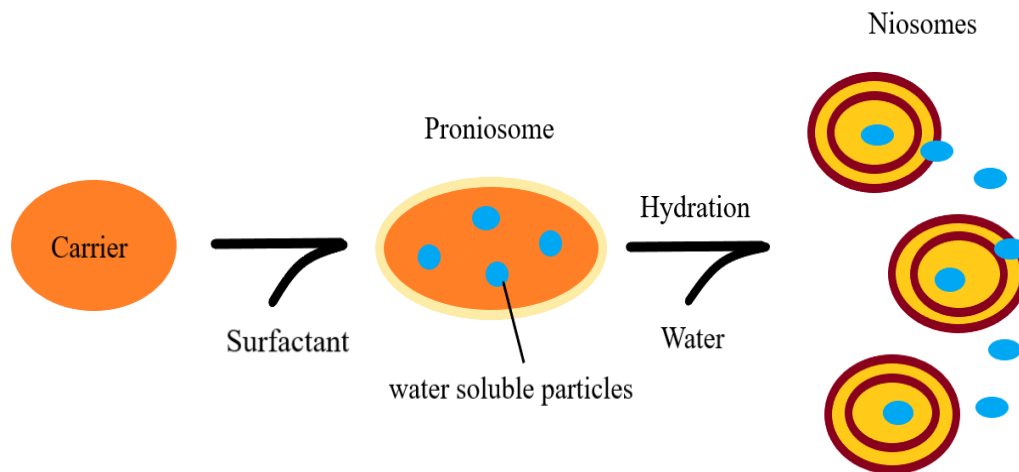


Fig. 2. Show the action and conversion of Proniosome into Niosome

**a) Proniosomes based on sorbitol:** This is also a dry formulation that uses sorbitol as the carrier, that is subsequently coated with a nonionic surfactant and may be used as niosomes in a few minutes by agitating it with warm water.

**b) Proniosomes based on maltodextrin:** A maltodextrin-based proniosome formulation has been introduced recently so that it could be utilized to deliver hydrophobic or amphiphilic medications. The formulations with the best results used hollow particles with a wide surface area. The bigger the surface area, the thinner the surfactant coating is appropriate for the

rehydration process. The fundamental benefit of this formulation is that it allowed the quantity of carrier required to sustain the surfactant to be easily adjusted, resulting in proniosomes with exceptionally high surfactant-to-carrier mass ratios [9,10].

## 5.2 Liquid Crystalline Proniosomes

Surfactant lipophilic chains can convert into a disordered liquid state called lyotropic liquid crystalline state in three ways when kept in contact with water (neat phase). The following are the three options:

- Raising kraft point temperature (Tc)
- Lipids are dissolved by adding a solvent.
- Temperature and solvent are both used.

The next phase, also known as the lamellar phase, exists within the intervening aqueous layer and is made up of bilayer sheets stacked on top of one other. These structures form thread-like bi-refringent patterns under a polarised microscope.

## 6. MATERIALS AND METHODS

### 6.1 Components

#### 6.1.1 Surfactants

Surfactants are organic compounds with both hydrophobic (water-insoluble) and hydrophilic (water-soluble) groups that act as a surface-active agents.

They have a variety of functions, such as solubilizers, wetting agents, emulsifiers, and permeability enhancers [11]. Alkyl ethers, alkyl esters, alkyl amides, and fatty acid esters are the most commonly used non-ionic amphiphiles for vesicle formation [12].

#### 6.1.2 Carrier material

When utilized in the creation of proniosomes, the carrier allows for greater freedom in the surfactant and other components ratios.

It increases the surface area of the loading area, allowing for more efficient loading. The carriers must be non-toxic, safe, and effective, as well as free-flowing, have a low solubility in the loaded mixed solution, and have a high water solubility for convenient hydration [14,15].

#### 6.1.3 Membrane stabilizers

The most widely utilised membrane stabilisers are Cholesterol and Lecithin.

Cholesterol is a steroid that occurs naturally and is employed as a membrane addition. It prevents aggregation by including molecules that stabilize the system and avoid the formation of clusters as a result of repulsive steric or electrostatic interactions.

Lecithin contains a lot of phosphatidylcholines. It has a low water solubility and, depending on hydration and temperature; bilayer sheets, liposomes, lamellar structures, and micelles can all be formed [16].

#### 6.1.4 Solvent and Aqueous Phase

Alcohol, which is used in this formulation, has a considerable effect on the size of vesicles and the rate of drug permeation. The size of vesicles produced by different alcohols varies, and they are sorted in this order: Propanol, butanol, and isopropanol follow ethanol.

Ethanol has a higher water solubility than other alcohols, it creates the largest vesicles, whereas isopropanol generates the smallest vesicles due to the presence of a branched chain.

The aqueous phase in the formulation of proniosomes is phosphate buffer of pH 7.4, hot water, and glycerol (0.1%) [17].

#### 6.1.5 Drug

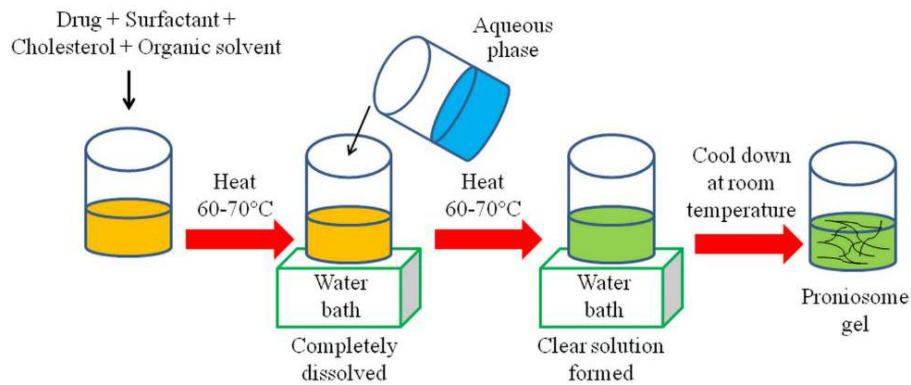
- Drugs to be choosed with
- High dosing frequency
  - Low water solubility.
  - Drug delivery in a controlled fashion.
  - A higher rate of adverse medication reactions.
  - Very brief half-life.

## 7. PREPARATION METHODS

Non-ionic surfactants, coating carriers, and membrane zstabilizers make up the majority of proniosome preparation. The following procedures can be used to manufacture the formulation. They are:

**Table 1. Common non-ionic surfactants [13]**

| SL. NO. | Non-ionic Surfactants                  | Examples  |
|---------|--|---|
| 1       | Alkyl ethers and alkyl glyceryl ethers | Polyoxyethylene4laurylether<br>Polyoxyethylenecetylethers<br>Polyoxyethylene stearyl ethers |
| 2       | Sorbitan fatty acid esters             | Span 20,40,60,80  |
| 3       | Polyoxyethylene fatty acid esters      | Tween 20,40,60,80   |



**Fig. 3. Schematic diagram showing coacervation phase separation method**

#### A. Slurry method

Proniosomes are manufactured by combining the carrier and the entire solution of surfactant in a round-bottomed flask attached to a rotating flash evaporator, then vacuuming the mixture to form a dry, free-flowing powder. Finally, the mixture must be kept chilled and exposed to light in a properly sealed container. This approach protects the active compounds and surfactants from hydrolysis and oxidation due to the homogenous coating on the carrier. In addition, the increased surface area leads to a thinner surfactant layer, which increases the rehydration process efficiency [18].

#### B. Method of spray coating

The rotating evaporator can be connected to a 100ml round bottom flask with the required carrier. Before placing the rotating flask in a water bath at 65-70°C for 15-20 minutes under vacuum, the evaporator must be purged. This method is repeated until all of the surfactant solutions have been administered. Evaporate the powder until it is dried completely [19].

#### C. Phase separation by coacervation

It is the most popular method for making proniosomal gel. Weighed amounts of medication, fat, and surfactants are added to a dry wide-mouthed glass beaker, followed by the addition of solvent. The ingredients are mixed well and heated in a water bath at 60–70°C until the surfactant mixture is completely dissolved [20]. During the process, extreme caution must be exercised to prevent any solvent from evaporating. Following that, the aqueous phase is added to the mixture and warmed in a water bath. Proniosomal gel is created by chilling the fluid overnight.

## 8. CHARACTERIZATION OF PRONIOSOMES

The manufactured proniosomes are next subjected to evaluation procedures to determine the

- The angle of repose measurement
- SEM (Scanning Electron Microscopy) is a type of microscopy that uses electron (SEM)
- Optical microscopy is a type of microscopy that uses light to magnify
- Vesicle size measurement
- The presence of drugs
- Effectiveness of entrapment
- Experiments on in vivo release
- Research on stability

**Angle of Repose Measurement:** The angle of repose is calculated by the following equation;

$$\text{Angle of repose} = \tan^{-1} (h/r)$$

**By Cylinder Method:** This method involves pouring proniosomal powder into a cylinder that was fixed at a height of 10cm above a leveled surface. The powder is then flowed down in the cylinder to form a cone on the surface, and the angle of repose is calculated by measuring the height of the cone and the diameter of its base [21].

**By Funnel Method:** The funnel was fixed in position, and the proniosomal powder was poured into it until the exit of the funnel which was 10 cm above the surface level. The powder flowed down from the funnel to form a cone on the surface, and the angle of repose was obtained by measuring the height and base diameter of the cone [22].

**SEM (Scanning Electron Microscopy):** The size of proniosome particles is an important factor. The surface appearance and size distribution of proniosomes were examined using SEM. The proniosomal powder was applied on aluminum stubs using double-sided tape. The aluminum stub was placed in the vacuum chamber of a scanning electron microscope (XL 30 ESEM with EDAX, Philips, Netherlands). The morphological characterization of the materials was seen using a gaseous secondary electron detector (working pressure of 0.8 torrs, acceleration voltage-30.00 KV) XL 30, (Philips, Netherlands) [23].

**Optical Microscopy:** Niosomes were put on glass slides and examined under a microscope using optical microscopy (Medilux-207R11, Kyowa-G enter, Ambala, India). After appropriate dilution, the microscope's magnification is 1200, which is employed for morphological examination. A digital Single-lens reflex (SLR) camera was used to capture a photomicrograph of the preparation taken under the microscope.

**Measurement of Vesicle Size:** By diluting the vesicle dispersions 100 times in the same solution that was used to make them, the size of the vesicles could be determined. A particle size analyzer was used to measure the vesicles' dimensions. A 632.8 nm He-Ne laser beam is focused through a Fourier lens (R-5) to a point at the center of a multi-element detector and a small volume sample holding cell with a minimum power of 5Mw. Before evaluating the vesicle size, the ingredients were mixed using a stirrer [24].

**Composition of the drug:** 100 mg of peptidosomes were put into a standard volumetric flask. To lyse them, 50 mL methanol was shaken over them for 15 minutes. To dilute the solution to 100mL, methanol was added. The solution was then diluted to 100 ml using a saline phosphate buffer at a specific pH. After removing aliquots and measuring absorbance at a specific wavelength, the drug content was calculated using the calibration curve.

**Entrapment efficiency:** Using an intensive dialysis procedure and centrifugation, the unentrapped medicine was removed from the niosomal suspension. Theniosomal solution was placed in a dialysis tube with an osmotic cellulose membrane securely attached to one side and suspended in 100 mL of pH-controlled saline buffer agitated on a magnetic stirrer. An

osmotic cellulose membrane was used to separate the unentrapped medication and niosomal suspension from the media. Optical density measurements were collected after 6 hours of dialysis, and the amount of medication trapped was estimated using a UV spectrophotometric technique. The below formula was used to calculate Entrapment Efficiency [25].

Entrapment efficiency = Amount of entrapped drug x 100/Total Amount of drug

**In vivo release studies :** The drug release from proniosomal formulations was investigated using several techniques such as the Franz diffusion cell, Keshary-Chien diffusion cell, Cellophane dialyzing membrane, USP dissolving apparatus Type-1 [26,27], and spectra/or molecular porous membrane tubing. Desorption from the surface of vesicles, drug diffusion from a bilayered membrane, or a combination of desorption and diffusion mechanisms can all be used to release drugs from proniosome-derived niosomal vesicles [28].

**Stability research:** For 1 to 3 months, the proniosomes were maintained at several temperatures, including refrigeration (2°-8°C), room temperature (25° 0.5°C), and high temperature (45° 0.5°C). Regularly regularly, drug content and average vesicle diameter variation were examined [29].

Stability tests for dry proniosomes powder intended for re-formation should be conducted at 75% relative humidity in compliance with international climatic zones and standards, according to ICH regulations.

## 9. CLINICAL APPLICATIONS

**Applications in Cardiology:** Proniosomes are employed as carriers for the transdermal release of captopril for the treatment of hypertension in cardiology. The medicine is released more slowly in the body. Sorbitan esters, cholesterol, and lecithin are used to encapsulate the drug [30].

**In Diabetes application:** Span, soya, lecithin, diacetyl phosphate, and cholesterol were employed to study the skin penetration mechanism of furosemide proniosomes. Overall, the data imply that proniosomes are used to distribute furesamide in a non-invasive manner [31].

**Delivery of Peptide drugs:** The enzymes that would otherwise break down the peptide and

protein connections are bypassed in oral peptide medication administration. The peptides were successfully protected against gastrointestinal peptide breakdown using niosomes. Oral administration of a vasopressin derivative entrapped in niosomes resulted in a considerable improvement in the peptide's stability [32].

**Niosomes as hemoglobin carriers:** Many carrier proteins can be found in the blood. Hemoglobin can be carried by niosomes in the bloodstream. Because the niosomal or proniosomal vesicle is permeable to oxygen, it serves as a hemoglobin carrier in patients. In cardiac diseases, hormone treatment, and antibiotic therapy, proniosomes are also employed as a carrier system [33].

**Hormone replacement treatment (HRT):** Proniosome-based transdermal administration of levonorgestrel, an emergency contraceptive, has been studied. The niosome has a liquid crystalline compact hybrid structure. Particle size, encapsulation efficiency, stability, and in vivo and in vitro studies were all performed on the system. In addition, a bioassay for progestational activity was carried out. It includes an endometrial assay and inhibition of corpora lutea development [34].

**Cosmetics and Cosmeceuticals:** Proniosomes are available in two forms, depending on the manner of preparation: semisolid liquid crystal gel and dry granular powder. The proniosome gel is the most often utilized for topical/transdermal usage. Because of their precise features, proniosome gel can be employed as an effective delivery vehicle for cosmetics and Cosmeceuticals [35]. Proniosomes gel formulation has benefits in terms of regulated drug administration, increased bioavailability, fewer adverse effects, and trapping of both hydrophilic and hydrophobic drugs [36].

## 10. PRNIOSONES IN DRUG DELIVERY AND TARGETING

**Oral Delivery:** Oral administration is the highly favored and most common way of drug administration. Many medications are provided parenterally to increase their bioavailability due to certain issues associated with drugs administered orally, such as limited gastrointestinal tract stability, pre-systemic drug breakdown by acidic or enzymatic action, and low permeability through the intestinal epithelium. Several studies have found that proniosomal

powders taken orally can improve the solubility and bioavailability of poorly soluble compounds [37]. Song et al. (2015) proved that proniosomes are a promising carrier in industrial manufacturing by constructing free-flowing and stable proniosomes of the weakly water-soluble drug vinpocetine to boost its oral bioavailability and gastrointestinal absorption [38]. The outcomes of the study revealed that the greater bioavailability of vinpocetine in proniosomes was due to two mechanisms. First, there are the niosomes that are generated when proniosomes are hydrated in the gastrointestinal tract. The gastrointestinal tract has a bioadhesive feature that allows it to stick to the gastric wall, which is followed by endocytosis. Second, there are niosomes that possibly improve the lymphatic movement that was previously possible of avoiding the first-pass effect and, as a result, higher bioavailability.

**Oral Mucosal Delivery:** The oral mucosa is a more available and permeable route compared to the skin; it is self-administrable, has a substantial blood supply, is less sensitive to irritants, provides a moist environment for drug solubility, and allows for fast systemic drug delivery. An orodental and anti-inflammatory mucoadhesive proniosomal gel containing lornoxicam was created, which transported the medication directly to the site of action in the oral cavity in patients suffering from dental pain and inflammation absorption [39]. This technique can be utilized to boost the therapeutic efficacy of lornoxicam for dental administration, resulting in improved patient compliance and fewer gastrointestinal side effects. According to the findings of the study, oral mucoadhesive proniosomal gels are a promising approach for lornoxicam transmucosal delivery into the oral cavity [40].

**Dermal and Transdermal Delivery:** Dermal administration has several advantages, including high concentrations at the site of action, decreased systemic absorption, and fewer side effects. Furthermore, the transdermal technique also has various advantages, including a noninvasive procedure, avoiding first-pass hepatic metabolism, which increases drug bioavailability, overcoming gastrointestinal degradation, maintaining steady-state plasma levels, and enhancing patient compliance [41,42]. Besides, the transdermal technique has considerable limitations, such as restricted drug permeability through the skin due to the stratum corneum, which is a major barrier to absorption.

The vesicular medicine administration strategy has been proved to be a feasible alternative to physically or chemically circumventing epidermal barriers [43]. Proniosomes are a versatile vesicular drug delivery technology capable of delivering drugs transdermally. Moreover, topical use of these vesicles as cutaneous drug delivery systems has the potential to improve treatment efficacy while reducing side effects [44]. They also have a predisposition for attaching to the stratum corneum, being converted to niosomes after hydration, and penetrating the skin through the stratum corneum, resulting in greater skin permeation [45]. These vesicular carriers function as drug reservoirs, and the rate of drug release can be controlled by altering the composition or surface of the carriers [46].

## 11. OCCULAR DELIVERY

One of the most unusual and difficult routes for formulation scientists is the ocular medication delivery system. Because of the blinking reflex, decreased eye capacity, nasolacrimal drainage, and the corneal and conjunctival epithelial barriers, ocular drug delivery methods have low bioavailability and restricted absorption in the intraocular area, which limits the retention duration of drug molecules in the eye. As a result, many additional ocular drug delivery techniques, such as in situ gels, liposomes, nanospheres suspensions, in situ nanosuspensions, nanoparticles, nanoemulsions, and niosomes, have recently been researched to overcome the drawbacks of traditional eye preparations.

Proniosomes, in particular, hold a lot of potential for topical ocular drug administration. Proniosomes can form niosomes after hydration in the ocular canal, and both nonionic surfactants and phospholipids in proniosomes work as penetration enhancers. Proniosomal gels as an ocular formulation can increase drug residence time in the corneal cavity, offer prolonged and sustained action, suppress enzymatic metabolism in tears, and improve ocular bioavailability by preventing enzymatic metabolism on the corneal epithelial surface. Among those who have contributed to this work are Li et al (2014) has created a proniosomal system for ophthalmic delivery of tacrolimus, which resulted in the creation of niosomes after hydration in the oral cavity. As tacrolimus-loaded proniosomes were tested in vitro on newly excised rabbit corneas, they showed improved penetration due to higher tacrolimus retention in

the cornea when compared to standard ointments [47].

A proniosomal gel method was developed by encapsulating Lomefloxacin HCl to improve its ocular bioavailability for the treatment of bacterial conjunctivitis in another investigation. The developed optimized system extends the medication's retention period in the cornea, increases local action, improves penetration, and regulates drug release, resulting in higher antibacterial therapeutic benefits.

## 12. PARENTERAL DELIVERY

Parenteral administration is a common style for pharmacological agents with low bioavailability and a narrow therapeutic index. It has several benefits in situations, counting ease of access, rapid onset of action, and suitability for conditions where the oral route is inconvenient, There have been significant advancements in the field of vesicular system, which have the latent to maintain sustained drug release via parenteral administration while avoiding the subjects associated with traditional parenteral drug delivery systems, predominantly for drugs with a narrow therapeutic index and poor bioavailability [48]. Proniosomes are among the vesicular drug carriers that can be utilized to deliver pharmaceuticals via the parenteral route since they can be stored, transported, disseminated, sterilized, and separated into units dosages for parenteral administration [49]. A parenteral proniosome formulation could improve efficacy and reduce toxicity by avoiding frequent injections or continuous intravenous infusions. Flurbiprofen's anti-inflammatory activities were increased by producing a free-flowing proniosome formulation and administering it intravenously after reconstitution. The blood concentration was maintained using this formulation by minimizing drug changes in plasma levels as a result of numerous administrations, and its anti-inflammatory and analgesic activities were eventually strengthened.

## 13. PULMONARY DELIVERY

Because of the large surface area of the alveoli, high blood flow in the lungs, the presence of tiny diffusion channels between the blood and the alveoli, and the lack of first-pass hepatic impact; the lungs are a good way to enter the systemic circulation. Also, the use of portable inhalers makes this method more pleasant for patients.



Because of breakthroughs in nanotechnology, the treatment of several lung illnesses by inhalation has improved. Several nano-drug delivery methods are utilized to target certain tissues and cells to achieve greater effects and prevent harmful effects of the treatment in the lungs and other organs. By using beclomethasone dipropionate (BDP) as a model medication, nebulize proniosome delivery devices were successfully developed. Aeronex pro and Omron Micro air vibrating-mesh nebulizer and Pari LC Sprint air-jet nebulizer are the two systems that have been created.

After hydration of proniosomes, the aerosol properties of the niosomes generated were investigated. BDP entrapment in proniosomes was higher than in normal niosomes, according to the findings. Furthermore, aerosols made from both nebulizable systems produced high drug yield and fine particle fraction (FPF). As a result, the proniosomal system emerged as a viable way for delivering BDP-niosomes using vibrating mesh and air-jet nebulizers.

#### 14. INTRANASAL ROUTE

Intranasal delivery, which avoids the blood-brain barrier, is a promising noninvasive strategy for delivering medications directly to the CNS (BBB). The nasal epithelium's high permeability, porous endothelium membrane, wide surface area, and high blood flow allow for rapid medication absorption in the nasal mucosa. Nasal administration, on the other hand, has some drawbacks, including rapid drug removal due to the mucociliary clearance system, mucosal injury from frequent use, nasal discomfort, nasal congestion, and partial breakdown by the nasal peptidase enzyme system. The creation of nanocarriers with sizes ranging from 1 to 100nm that may easily pass the brain endothelium is presently the most sophisticated and advantageous noninvasive strategy for delivery to the cerebrum.

Vesicular drug delivery systems (liposomes and niosomes) are promising drug delivery carriers that can effectively deliver together small and large therapeutic agents to the CNS via the intranasal route, circumventing nasal delivery restrictions such as mucociliary clearance and enzymatic degradation, and increasing drug bioavailability [50]. Proniosomes have the potential to deliver medications via the intranasal route since they have enhanced penetration and

absorption capabilities. Proniosome delivery via the intranasal route has yet to be documented.

#### 15. VAGINAL DELIVERY

In most cases, the vaginal route of medication delivery is used to treat microbiological infections. Because it is highly vascularized and has great permeability, this route is widely employed for the transport of diverse compounds such as antimicrobials, antimycotics, sexual hormones, and peptides. Furthermore, it avoids hepatic first-pass metabolism and gastrointestinal absorption, making it an excellent route for mucosal drug delivery for both local and systemic applications. Tablets, solutions, foams, vaginal suppositories, and inserts have all been utilized in vaginal medicine delivery, although semisolid dose forms, particularly gels, are much favored [51]. Conventional vaginal surgery, on the other hand, there are some limitations to systems, like leakage and a limited residence time and disorder that innovative formulations can govern demonstrating optimal retention, release, and characteristics of diffusion.

Because of their high mucoadhesive properties and continuous drug release, pheniosomal gel systems are an effective carrier system for vaginal pharmaceutical administration. Abdou and Ahmed (2016) created a mucoadhesive vaginitis treatment that incorporates the antifungal medicine terconazole. The proniosomal system hydrates to produce niosomes, which are a good treatment for vaginitis because they allow the medicine to stay in the vaginal mucosa for a longer amount of time. A modified proniosomal formulation was added to carbopol gel to improve its mucoadhesive properties, and microbiological tests demonstrated that proniosomes are a viable vesicular system for mucosal drug administration [52].

#### 16. PRNOSOMES OVER NIOSOMES

Vesicular systems have been employed as drug delivery carriers for generations for a variety of reasons, including targeted drug administration, enhanced drug transport over varied biological barriers, and controlled drug release. Liposomes, niosomes, transfersomes, ethosomes, and other vesicular drug delivery systems are examples. Proniosomes have the potential to circumvent these constraints because they can be sterilized, kept at room temperature, and rapidly hydrated to form niosomal dispersion before distribution.

Proniosome powders have numerous advantages and are favored over lyophilized powders since lyophilization alters the drug's characteristics. Proniosomes were found to be superior to niosomes in several investigations.

A comparison of niosome and proniosome stability tests revealed that proniosomes can be effectively held at room temperature, with drug leakage from the proniosome vesicles decreased, which is the main concern with niosomes when stored at room temperature.

Similarly, proniosome stability can be assessed by testing proniosomal formulations containing tenoxicam for three months. Over 90 days, stability tests revealed higher entrapment efficiency and retention, as well as no significant change in mean particle size, when compared to freshly manufactured sucrose stearate niosome. In addition, when compared to niosomes, a proniosomal gel proved to be a potential technique for effectively administering estradiol via a transdermal route with higher skin permeability. The presence of nonionic surfactants and lecithin, both of which have penetration-enhancing properties, in proniosomes allows for the increased absorption of estradiol through the skin.

## 17. CONCLUSION

Proniosomes have enhanced physical and chemical stability, as well as the potential for economic sustainability, making them a promising drug carrier for the future. The system has the potential to successfully distribute amphiphilic medications. Proniosome-based niosomes can be utilised to administer a wide range of medications, including vaccinations that are targeted, ophthalmic, topical, parenteral, or oral. More research is being performed to understand the actual latent of this system. Proniosomes have sparked a lot of consideration for transdermal administration due to benefits such as surfactant penetration enhancement, no toxicity, and efficient drug release property modification. Proniosomes in a dry state provides for easy unit dosing because the powder can be processed further to produce beads, tablets, or capsules. The latest breakthroughs in research pave the path for the future use of diverse carrier materials that are biocompatible and suited for the creation of proniosomes. Future research should look at the compatibility of proniosomes with more drugs that have well-defined faults to provide the intended therapy more effectively and efficiently. Studies should be conducted to

evaluate the potential of various carrier materials to form proniosomes, as well as their ability to transport medicines via diverse pathways.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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