



Review on Proniosomal Transdermal Drug Delivery System

Saba Khan^{1*}, Jaya Agnihotri², Alina Bi Shaikh³, Mahnaz Sayyed³,
Masnoon Khan³ and Arif Khan³

¹HKCP, Masters Research Student, Department of Pharmaceutics, Mumbai,
Maharashtra, India

²HKCP, Associate Professor, Department of Pharmaceutics, Mumbai, Maharashtra,
India

³HKCP, Final Year Student, Mumbai, Maharashtra, India

*Corresponding Author: Saba Khan, HKCP, Masters Research Student,
Pharmaceutics, Mumbai, Maharashtra, India.

Received: September 14, 2023

Published: December 06, 2023

© All rights are reserved by Saba Khan., et al.

Abstract

Scientists dedicated their efforts to enhancing drug delivery methods while preserving the integrity of these methods' undesirable traits. This dedication ultimately resulted in the creation of proniosomes, a revolutionary medication delivery system. Due to their unique benefits, proniosomes stand out from niosomes and liposomes. These proniosomes are made of non-ionic, water-soluble dry formulations that are added to a carrier system. Upon hydration, these proniosomes transform into niosomes, effectively addressing the instability issues associated with traditional delivery systems. Niosomes, in turn, exhibit tremendous potential for improving the dissolution, accessibility, and absorption of a wide range of medications, whether they are hydrophilic or hydrophobic. Additionally, proniosomes offer a versatile approach to drug delivery, enabling precise medication delivery to the desired target site. The risk of unwanted side effects is reduced by this regulated release technique. Recognizing and understanding the limitations of each study is imperative since each research approach possesses its unique set of advantages and drawbacks. Observational studies can employ a variety of design methodologies, including ecological, prospective, retrospective, case-control, case-crossover, or cross-sectional cohort designs. In the realm of diagnostic research, a critical subset of observational experiments is dedicated to comparing the accuracy of different diagnostic methods and tests against established diagnostic benchmarks. It is essential to underscore that biomedical research heavily relies on data collected through rigorously validated scientific methodologies and employs appropriate statistical methods to derive meaningful insights. Consequently, selecting a robust study strategy is paramount in ensuring an objective and impartial evaluation of research inquiries. This comprehensive review encompasses a wide array of facets related to proniosomes, encompassing their advantages, preparation techniques, mechanisms of action, materials and specifications, study designs, as well as characterization and evaluation parameters.

Keywords: Proniosomes; Carrier; Transdermal; Skin Permeation; Application

Introduction

Proniosome

In a dry formulation, proniosomes represent carrier particles coated with surfactants that possess water solubility. When agitated within a hot water solution, these proniosomes rapidly rehydrate, forming a niosomal dispersion suitable for the application.

One noteworthy characteristic of proniosomes is their ability to maintain physical stability during storage and transportation.

Medications enclosed within the vesicular structure of proniosomes experience several benefits. They enjoy an extended shelf life within the bloodstream, achieve enhanced tissue penetration,

and exhibit reduced toxicity. From a technical standpoint, niosomes emerge as highly appealing drug carriers due to their superior chemical stability and the absence of various drawbacks associated with liposomes, including elevated production costs and variability in phospholipid purity [1-4].

Proniosomes have attracted the attention of researchers since the early 1980s, primarily due to their potential applications as both pharmacological carriers and targets. These applications offer numerous advantages compared to conventional medication delivery methods while effectively addressing associated disadvantages [5].

Mechanism of action

Proniosomes are niosomes in an inactive state that must be transformed into active niosomes by a procedure known as hydration. There are two different ways that this hydration can take place.

According to the figure, the proniosome is a stage amid niosome production. There are two strategies to transform the proniosome formulation into niosomes [6-8].

- **Skin-Driven Hydration:** The proniosome formation and conversion to niosomes are hydrated by the water in the skin. This hydration is accomplished by the skin itself.
- **Solvent-Mediated Hydration:** Proniosomes are transformed into niosomes using aqueous solutions, such as pure water, saline solution, and buffers, with or without agitation and sonication [9-11].

Methods for delivering medication through the skin, known as transdermal delivery methods, utilize various strategies to effectively penetrate the skin. These techniques capitalize on the unique properties of the skin to ensure proper absorption of medications. Here are a few important approaches [12-15].

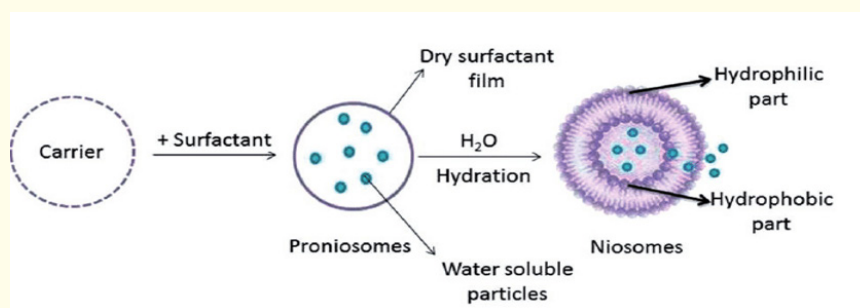


Figure 1

Transfers

Transfers represent a type of transdermal delivery method that is characterized by their ability to deform without causing harm. This flexibility enables them to navigate through the outer layer of the skin and efficiently deliver medications.

Ethosomes

Ethosomes offer another approach utilized in transdermal drug delivery. These vesicles composed of lipids are specifically designed to disrupt the dense structure of the epidermis upon entry into the body. Through this mechanism, they facilitate penetration of medications, thereby ensuring effective absorption occurs.

Proniosomes and Niosomes

Proniosomes and niosomes are innovative delivery systems that utilize surfactants. These surfactants help improve the penetration of medications into the skin. They aid in the transportation of medications through the layers of the skin and improve the solubility of pharmaceuticals.

Any molecule applied topically must first get beyond the skin's barrier, which is made up of the Stratum Corneum (SC) and the viable epidermis, regardless of the precise method used. Successful transdermal distribution hinges on successfully overcoming this barrier, which serves as the first line of defence.

In conclusion, transdermal medication delivery methods employ various techniques to ensure the efficient and safe absorption of drugs through the skin. Each approach has its unique characteristics and advantages, making them valuable options for delivering

medications to the body. However, it is crucial to consider the specific needs of the patient and the medication being administered when choosing the most suitable transdermal method.

Advantages of proniosomes transdermal drug delivery tool

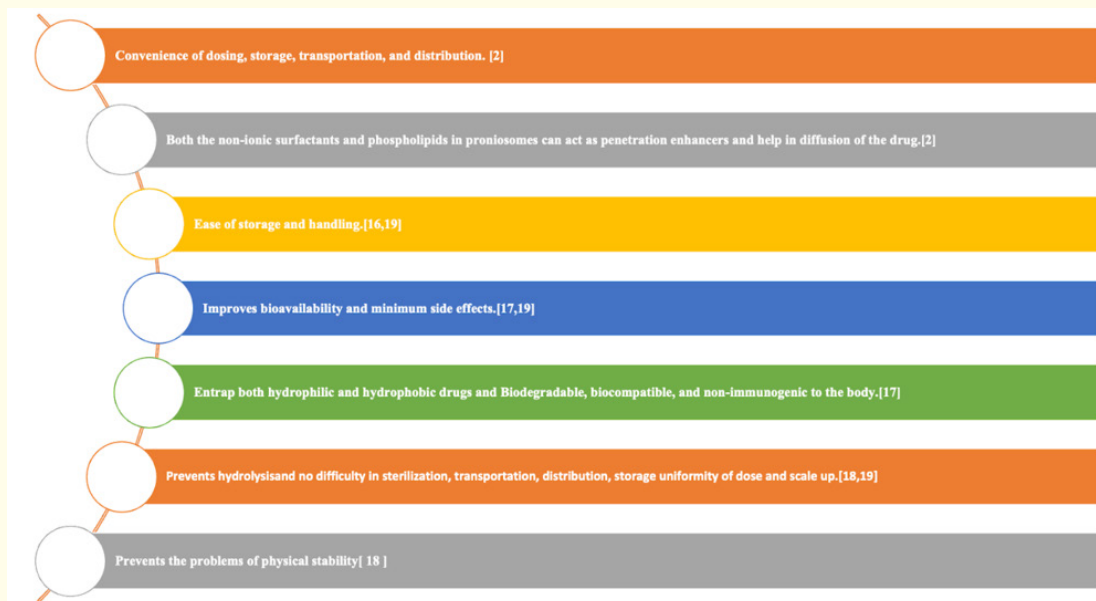


Figure 2

Structure of proniosomes

Lamellar tiny structures make up proniosomes. They mix cholesterol with a non-ionic surfactant of the alkyl or dialkyl polyglycerol ether type, then hydrate it in water. To create the bilayer, the surfactant molecules direct themselves such that the hydrophilic ends of the non-ionic surfactant face outward and the hydrophobic ends face inside. Proniosomes include a bilayer, just like liposomes do. Proniosomes have a bilayer comprised of substances with non-ionic surface activity [20,21].

Proniosomes can be either unilamellar or multi-lamellar depending on the preparation procedure. The proniosome is composed of a surfactant bilayer with hydrophilic ends exposed on the exterior and interior of the vesicles and hydrophobic chains facing one another within the bilayer. Thus, hydrophilic medications are

held within the vesicle’s confined region, and hydrophobic drugs are incorporated within the bilayer [22,23].

Proniosomal gel has a unique structural makeup and might appear as a transparent, translucent, or semisolid gel. Due to the presence of a small amount of solvent, these proniosomes exhibit a variety of liquid crystal phases, including lamellar, hexagonal, and cubic.

Surfactant sheets are arranged in a bilayer configuration during the lamellar phase. While the cylindrical structure of the hexagonal phase is firmly packed and structured in a hexagonal pattern. A continuous, curved lipid bilayer that extends in three dimensions is present in the cubic phase [24].

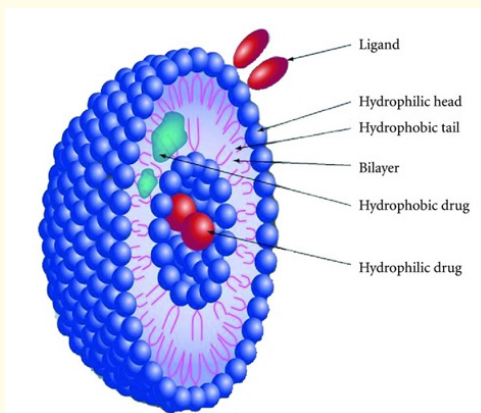


Figure 3

Application

Sr no	Application	Reference
1	<p>Niosomes in Cosmetics</p> <p>Niosomes have shown superior efficacy in delivering enoxacin compared to liposomes or standalone active components. This suggests that niosomes can be a valuable tool for delivering larger molecules to the skin, particularly when the skin's barrier function is slightly compromised.</p>	Wu, X., <i>et al.</i> [2]
2	<p>Niosomes for the Delivery of Ingredients to Prevent Scarring</p> <p>In terms of improving papain penetration, promoting transdermal absorption, and lessening scarring, elastic niosome particles fared better than normal nanomaterials. Gallic acid's chemical stability and epidermal penetration were both improved by these annoying particles, indicating their viability as anti-ageing drug carriers.</p>	Chen, S., <i>et al.</i> [26], Cerqueira-Coutinho, C., <i>et al.</i> [27]
3	<p>Application on the Hair</p> <p>The utilization of niosomes not only ensures that the hair maintains a healthy, non-greasy, and silky feel but also aids in the repair of damaged hair. Furthermore, it restores the hair's natural tone, resulting in a shinier and more vibrant appearance.</p>	Abu Hajleh., <i>et al.</i> [28]
4	<p>Prolonged release</p> <p>Niosomal encapsulation can be used to provide medications that have a poor therapeutic index and low water solubility with the prolonged release action of proniosome so that the drugs remain in circulation for a longer period.</p>	Biju SS., <i>et al.</i> [29]
5	<p>Uses For Understanding Immunological Response</p> <p>Niosomes were used for an immune response investigation because of their immunological selectivity, low toxicity, and higher stability.</p> <p>The greatest tools for examining the nature of the immune response triggered by antigens are niosomes and protoniosomes.</p>	Kakr R., <i>et al.</i> [30], Chandra A., <i>et al.</i> [31]
6	<p>Peptide medication delivery</p> <p>Niosomes were used to circumvent a significant problem of oral peptide medication delivery—bypassing the enzymes, which causes a breakdown of peptide and protein bonds.</p> <p>It was successful in preventing gastrointestinal peptide breakdown and preserved the peptides.</p>	Akhilesh D., <i>et al.</i> [32]

7	Proniosomes as haemoglobin carriers Niosomes can also be used as carriers for haemoglobin inside the blood, according to research (Moser P. and Marchand Arvier M. in 1989). The niosomal vesicle can be used as a carrier of haemoglobin in anaemic patients since it is oxygen permeable.	Sudhamani T [33], Kakar R 34, Sankar V., <i>et al.</i> [35]
8	Hormone delivery Work has been done on the transdermal delivery of the emergency contraceptive levonorgestrel using proniosomes. The corpora lutea was blocked and endometrial samples were tested as part of the bioassay study's progestational activity.	Vora B., <i>et al.</i> [36]
9	Proniosomes in phytochemical drugs (curcumin) Proniosomes encapsulated Curcumin for transdermal administration Curcumin offers diverse therapeutic benefits, but its poor solubility in acidic environments hinders oral absorption and bioavailability. Transdermal drug delivery, specifically using SPAN80-based proniosomal systems, can address these issues and enhance Curcumin's therapeutic effects. Cholesterol aids in dissolving Curcumin and improves drug penetration, while higher SPAN-80 concentrations boost encapsulation efficiency.	Kumar K and Rai AK., <i>et al.</i> [37]
10	Anti-neoplastic Treatment The encapsulation of drugs like Doxorubicin and Methotrexate in niosomes has shown significant benefits compared to untrapped or uncoated drugs. These advantages include a slower rate of body clearance, higher plasma drug levels, and a slower rate of tumour multiplication.	Sudhamani Tet al [33], Kakar R., <i>et al.</i> 34, Sankar V., <i>et al.</i> [35]

Table 1

Material and Methodology

Material

Sr no	Material	Role	Action	References
1.	Span, tween	Non-ionic surfactant	Maintains the Hydrophilic-Lipophilic Balance (HLB) level, increases the rate at which drugs are absorbed via the skin	Vora B., <i>et al.</i> [36], Politis S., <i>et al.</i> [38], Friston KJ., <i>et al.</i> [39]
2.	Cholesterol, Soya lecithin	Stabilizers	The permeability and stability of vesicles are significantly modulated by cholesterol. Soya Lecithin serves as an enhancer for penetration. Lecithin's primary function is to maintain the stability, permeability, and structural integrity of vesicles, resulting in improved penetration properties.	Solanki AB., <i>et al.</i> [40], Amaro E., <i>et al.</i> [41]
3.	Glucose monohydrate, lactose monohydrate, Sucrose stearate, Mannitol, Polyols, and Maltose	Carriers	It holds the drug	Solanki AB., <i>et al.</i> [40], Amaro E., <i>et al.</i> [41]
4.	Methanol, chloroform, ethyl alcohol	Organic solvent	Impact drug vesicle and penetration	Solanki AB., <i>et al.</i> [40]

Table 2

Various method used for preparation [42-46]

Method of coacervation phase separation

To generate a transparent dispersion, a mixture of lipids, a surfactant, and medication is blended with a solvent and subjected to heating in the temperature range of 60 to 70°C using a water bath.

Product type

Translucent gel.

Slurry technique

An organic solution is prepared by combining cholesterol, surfactants, and medication. This mixture is then poured over a carrier

medium to generate a slurry. To achieve proniosomes with optimal flow properties, it is advisable to employ rotary evaporators for efficient solvent evaporation.

Product type

Powder.

Method of spray coating

A rounded-bottom flask connected to a rotary evaporator is utilized to sequentially spray organic solutions containing cholesterol, surfactants, and medication onto a carrier material.

Product type

Powder.

Evaluation of proniosomes

Sr no	Parameters	Technique	References
1.	Angle of repose	Funnel approach Cylinder approach	Raymond CR., <i>et al.</i> [47], Radha GV., <i>et al.</i> [48]
2.	Particle/vesicle size and size distribution	The Malvern master size, Coulter submicron size analyzer, optical microscopy, photon correlation, laser diffraction particle size analyzer	Sankar V., <i>et al.</i> [35], Nasr M [49]
3.	Aerodynamic behavior	Twin stage impingement	Abd-Elbary A., <i>et al.</i> [50]
4.	entrapment efficiency	Using alcohol and propylene glycol to lyse vesicles	Sankar V., <i>et al.</i> [35]
5.	Shape and surface morphology	Transmission electron microscopy, optical microscopy, and scanning electron microscopy	Sankar V., <i>et al.</i> [35]
6.	Sieve fractionation	Fritsch analysts sieve shaker	Waghmode M., <i>et al.</i> [51]
7.	Spontaneity	Neubauer chamber	Parthibarajan R., <i>et al.</i> [52]
8.	Separation of untrapped drug	Centrifugation, ultracentrifugation, gel filtration, and exhaustive dialysis	Yadav K, Yadav D., <i>et al.</i> [53]
9.	<i>In vitro</i> drug release studies	Keshary-chein diffusion cells, Franz diffusion cells, Dialyzing membrane made of cellophane, molecular porous membrane tubing called Spectarpor, USP dissolving device, <i>in vitro</i> skin permeation studies	Prakash SG., <i>et al.</i> [54]
10.	<i>In vivo</i> studies	Different types of animals, such as rats, mice, rabbits, and guinea pigs, can be used for <i>in vivo</i> investigations.	Fang SC., <i>et al</i> [55], Raymond CR., <i>et al.</i> [56]
11.	Stability studies	According to ICH recommendations, at various temperatures including refrigeration (2°-8°C), room temperature (25°C 0.5°C), and increased temperature (45°C 0.5°C) for a period of one to three months.	Anchal Sankhyan., <i>et al.</i> [56]

Table 3

Conclusion

Proniosomes are surfactant-coated carrier particles that dissolve in water. Just before use, they can be immediately hydrated, producing an aqueous niosomal dispersion. Compared to niosomes and liposomes, pheniosomes are more stable. They have several outstanding qualities that make them useful for transdermal medication delivery, including the capacity to encapsulate both lipophilic and hydrophilic medicines. Due to their simple and affordable production scaling procedure, proniosomes have

become a popular dosage form for transdermal medication administration. Proniosomes have successfully solved stability issues, such as fusion and aggregation during storage, that are frequently encountered with niosomes and liposomes.

Future Scope

Proniosome-derived niosomes have revolutionized pharmaceutical research, offering targeted therapeutic benefits. The potential for these carriers extends to nutraceuticals, herbal compounds,

cosmetics, and peptide delivery, addressing enzymatic degradation challenges. Proniosomes also hold promise for vaccines, minimizing adverse drug effects, and treating anaemia. To realize their full potential, further research and industrial-scale studies are needed, but challenges must be met to establish their suitability for diverse drug and product deliveries.

Source of Funding

"There are no sources of funding to declare".

Conflict of Interest

"The author(s) declare no conflict of interest".

Bibliography

- Radha G., *et al.* "A review on proniosomal drug delivery system for targeted drug action". *Journal of Basic and Clinical Pharmacy* 4.2 (2013): 42.
- Arunothayanun P., *et al.* "The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether". *International Journal of Pharmaceutics* 201.1 (2000): 7-14.
- Mittal S., *et al.* "Proniosomes: The effective and efficient drug-carrier system". *Therapeutic Delivery* 11.2 (2020): 125-137.
- Paolino D., *et al.* "Improved in vitro and in vivo collagen biosynthesis by asiaticoside-loaded ultradeformable vesicles". *Journal of Controlled Release* 162.1 (2012): 143-151.
- Paolino D., *et al.* "Paclitaxel-loaded ethosomes®: Potential treatment of squamous cell carcinoma, a malignant transformation of actinic keratoses". *European Journal of Pharmaceutics and Biopharmaceutics* 81.1 (2012): 102-112.
- Cserháti T. "Alkyl ethoxylated and alkylphenol ethoxylated nonionic surfactants: Interaction with bioactive compounds and biological effects". *Environmental Health Perspectives* 103.4 (1995): 358-364.
- Hofland HEJ., *et al.* "Interactions of non-ionic surfactant vesicles with cultured keratinocytes and human skin in vitro: A survey of toxicological aspects and ultrastructural changes in stratum corneum". *Journal of Controlled Release* 16.1-2 (1991): 155-167.
- Fang JY., *et al.* "In vitro skin permeation of estradiol from various proniosome formulations". *International Journal of Pharmaceutics* 215.1-2 (2001): 91-99.
- Gupta A., *et al.* "Design and development of a proniosomal transdermal drug delivery system for captopril". *Tropical Journal of Pharmaceutical Research*, 6.2 (2007).
- Kaur Prabhjot and Kaur Loveleenpreet. "Niosomes Used as Targeting Drug Delivery System: A Overview". *Asian Journal of Research in Chemistry* 7.7 (2014): 687-692.
- McCrudden M T., *et al.* "Strategies for enhanced peptide and protein delivery". *Therapeutic Delivery* 4.5 (2013): 593-614.
- Muzzalupo R and Tavano L. "Niosomal drug delivery for transdermal targeting: Recent advances". *Research and Reports in Transdermal Drug Delivery* 23 (2015).
- Khatoon M., *et al.* "Proniosomes derived niosomes: Recent advancements in drug delivery and targeting". *Drug Delivery* 24.2 (2017): 56-69.
- Ammar H O., *et al.* "Proniosomes as a carrier system for transdermal delivery of tenoxicam". *International Journal of Pharmaceutics* 405.1-2 (2011): 142-152.
- Akhilesh D., *et al.* "Proniosomes - A propitious provesicular drug carrier". *International Journal of Pharmaceutical Sciences and Research* 1 (2011): 98-103.
- Kumar K and Rai AK. "Development and evaluation of proniosomes as a promising drug carrier to improve transdermal drug delivery". *IRJP* 2 (2011): 71-74.
- ND Shukla and M Tiwari. "Proniosomal Drug Delivery System-Clinical Applications". *International Journal of Research in Pharmaceutical and Biomedical Sciences* 2.3 (2011): 880-887.
- AK Jha., *et al.* "Vesicular System -Carrier for Drug Delivery". *Der Pharmacia Sinica* 2.4 (2011): 192-202.
- Sagar G H., *et al.* "Self-assembled surfactant nano-structures important in drug delivery: a review" (2007).
- Walve J R., *et al.* "Transfersomes: a surrogated carrier for transdermal drug delivery system" (2011).

21. Sudarshan Upadhye S and Rafik IN. "Proniosomes: A novel vesicular drug delivery system". *American Journal of PharmTech Research* 10.2 (2020): 260-273.
22. Comelles F, et al. "Influence of ionic surfactants on the formation of liquid crystals in oleic acid/glycol/water systems". *Journal of Surfactants and Detergents* 10.3 (2007): 137-144.
23. Murdan S. "Interaction of a nonionic surfactant-based organogel with aqueous media". *International Journal of Pharmaceutics* 180.2 (1999): 211-214.
24. Wu X and Guy R H. "Applications of nanoparticles in topical drug delivery and cosmetics". *Journal of Drug Delivery Science and Technology* 19.6 (2009): 371-384.
25. Chen S, et al. "Recent advances in non-ionic surfactant vesicles (niosomes): Fabrication, characterization, pharmaceutical and cosmetic applications". *European Journal of Pharmaceutics and Biopharmaceutics* 144 (2019): 18-39.
26. Cerqueira-Coutinho C, et al. "Niosomes as nano-delivery systems in the pharmaceutical field". *Critical Reviews™ in Therapeutic Drug Carrier Systems* 33.2 (2016): 195-212.
27. Abu Hajleh MN, et al. "The revolution of cosmeceuticals delivery by using nanotechnology: A narrative review of advantages and side effects". *Journal of Cosmetic Dermatology* 20.12 (2021): 3818-3828.
28. Biju S, et al. "Vesicular systems: an overview". *Indian Journal of Pharmaceutical Sciences* 68.2 (2006).
29. Kandpal N, et al. "Proniosomes: A pro vesicular system in ocular drug delivery". *Journal of Advanced Biotechnology and Experimental Therapeutics* 6.3 (2023): 622.
30. Chandra A and Sharma P K. "Proniosome-based drug delivery system of piroxicam". *African Journal of Pharmacy and Pharmacology* 2.9 (2008): 184-190.
31. Akhilesh D, et al. "Comparative study of carriers used in proniosomes". *International Journal of Pharmaceutical and Chemical Sciences* 3 (2012): 6-12.
32. Sudhamani T, et al. "Proniosomes—a promising drug carriers". *International Journal of PharmTech Research* 2.2 (2010): 1446-1454.
33. Kakar R, et al. "Proniosomes: An emerging vesicular system in drug delivery and cosmetics". *Der Pharmacia Lettre* 2.4 (2010): 227-239.
34. Sankar V, et al. "Proniosomes as drug carriers". *Pakistan Journal of Pharmaceutical Sciences* 23.1 (2010): 103-107.
35. Vora B, et al. "Proniosome-based transdermal delivery of levonorgestrel for effective contraception". *Journal of Controlled Release* 54.2 (1998): 149-165.
36. Kumar K and Rai A. "Development and evaluation of proniosome- encapsulated curcumin for transdermal administration". *Tropical Journal of Pharmaceutical Research* 10.6 (2011).
37. N Politis, et al. "Design of experiments (DoE) in pharmaceutical development". *Drug Development and Industrial Pharmacy* 43.6 (2017): 889-901.
38. Friston K J, et al. "The trouble with cognitive subtraction". *NeuroImage* 4.2 (1996) 97-104.
39. Solanki A B, et al. "Formulation and optimization of piroxicam proniosomes by 3-factor, 3-level box-behnken design". *AAPS PharmSciTech* 8.4 (2007).
40. Amaro E, et al. "Study design in fMRI: Basic principles". *Brain and Cognition* 60.3 (2006): 220-232.
41. Mujoriya RZ and Bodla R. "Niosomthe the -challenge in preparation for pharmaceutical scientist". *International Journal of Applied Pharmaceutics* 3 (2011): 11-15.
42. Noordzij M, et al. "Study designs in clinical research". *Nephron Clinical Practice* 113.3 (2009): c218-c221.
43. Biberstein M and Parker B A. "Enema-induced hyperphosphatemia". *The American Journal of Medicine* 79.5 (1985): 645-646.
44. Bello A K, et al. "Population-based screening for microalbuminuria among relatives of CKD patients: The Kidney Evaluation and Awareness Program in Sheffield (KEAPS)". *American Journal of Kidney Diseases* 52.3 (2008): 434-443.
45. Ibeiez L, et al. "Case-control study of regular analgesic and nonsteroidal anti-inflammatory use and end-stage renal disease". *Kidney International* 67.6 (2012): 2393-2398.

46. D'Arcy P. "Handbook of pharmaceutical excipients". 2nd edn Ainley Wade and Paul J. Weller (Eds Joint publication of the american pharmaceutical association and the royal pharmaceutical society of great Britain, The Pharmaceutical Press, London, 1994. ISBN: 0 85369 305 6 (UK); 0 91730 66 8 (USA). Price £140; 672 pages. *International Journal of Pharmaceutics* 123.2 (1995): 301-302.
47. Radha G., *et al.* "A review on proniosomal drug delivery system for targeted drug action". *Journal of Basic and Clinical Pharmacy* 4.2 (2013): 42.
48. Nasr M. "In vitro and in vivo evaluation of proniosomes containing celecoxib for oral administration". *AAPS PharmSciTech* 11.1 (2010): 85-89.
49. Abd-Elbary A., *et al.* "Sucrose stearate-based proniosome-derived niosomes for the nebulisable delivery of cromolyn sodium". *International Journal of Pharmaceutics* 357.1-2 (2008): 189-198.
50. Maya W and Ashar S. "Proniosomal drug delivery systems: An overview". *International Journal of Pharmaceutical and Chemical Sciences* 1.3 (2012): 1044-1056.
51. Parthibarajan R., *et al.* "Formulation and evaluation of methotrexate proniosomal powder". *International Journal of Pharmacy and Pharmaceutical Sciences* 4.11 (2012): 175-178.
52. Yadav K., *et al.* "Proniosomal Gel: A provesicular approach for transdermal drug delivery". *Der Pharmacia Lettre* 2.4 (2010): 189-198.
53. Goudanavar P and Joshi VG. "An engineered specificity of Irinotecan loaded Proniosomes: Design and Characterization". *International Journal of Drug Delivery* 3.3 (2011): 472.
54. FShi B., *et al.* "Stealth PEG-PHDCA niosomes: Effects of Chain Length of PEG and Particle Size on Niosomes Surface Properties, In Vitro Drug Release, Phagocytic Uptake, In Vivo Pharmacokinetics and Antitumor Activity". *Journal of Pharmaceutical Sciences* 95.9 (2006): 1873-1887.
55. Pawar H., *et al.* "Novel vesicular drug delivery system for topical delivery of indomethacin". *Drug Delivery Letters* 5.1 (2015): 40-51.