World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(REVIEW ARTICLE)

Innovative Niosomal technologies: Advantages, challenges and future trends

Sneha V *, J Adlin Jino Nesalin, Ganesh N S and Vineeth Chandy

Department of Pharmaceutics, T John College of Pharmacy, Bengaluru-83, Karnataka, India.

World Journal of Biology Pharmacy and Health Sciences, 2025, 21(02), 372-379

Publication history: Received on 03 January 2025; revised on 13 February 2025; accepted on 16 February 2025

Article DOI: https://doi.org/10.30574/wjbphs.2025.21.2.0184

Abstract

Noisomes are tiny, bubble-like vesicles made from non-ionic surfactants, and like liposomes, they have a bilayer structure, which allows them to carry both water-soluble and fat-soluble drugs, either in their inner watery core or within their lipid bilayer. They are being widely explored as a cost-effective, non-biological alternative to liposomes and as drug carriers that can influence how medications are distributed and released in the body. What makes niosomes particularly valuable is that they offer all the benefits of liposomes such as controlled drug release and targeted delivery at a lower cost. They are also more stable, easier to store, and do not rely on phospholipids, which can be expensive. Due to these advantages, niosomes have been extensively studied for use in treating cancer, viral infections, and bacterial diseases.

To create noisome, a specific type of surfactant is combined with water. Cholesterol is often added to strengthen the vesicle walls and minimize leakage, while stabilizers help prevent the vesicles from clumping together by creating repulsive or protective barriers. Advancements in niosomes include discomes, proniosomes, elastic and polyhedral niosomes. Among these, proniosomes are superior over other vesicular carriers. Proniosomes are dry formulations of water-soluble nonionic surfactant coated carrier system which immediately forms niosomes upon hydration. They have the capability to overcome the instability problems associated with niosomes and liposomes and have the potential to improve solubility, bioavailability, and absorption of various drugs. Furthermore, they offer versatile drug delivery concept for enormous number of hydrophilic and hydrophobic drugs. They have the potential to deliver drugs effectively through different routes at specific site of action to achieve controlled release action and reduce toxic effects associated with drugs.

Keywords: Noisome; Proniosomes; Non-ionic surfactant; Vesicles

1. Introduction

Over the past decade, vesicle-based systems have gained significant attention in the field of drug delivery. These systems, such as liposomes, noisomes, transferosomes, pharmacosomes, and ethosomes, offer innovative ways to improve how drugs are delivered in the body. Among them, niosomes are particularly promising due to their nonionic nature, making them effective tools for advanced drug delivery solutions. Creating a novel drug delivery system (NDDS) requires meeting two essential criteria: releasing the drug at a controlled, predictable rate and ensuring the drug reaches the target site in a therapeutically effective amount. Unfortunately, traditional drug delivery methods often fail to achieve these goals. L'Oreal was the first industry (cosmetic) which produced niosomes. Later on, its applications were explored in the pharma industry.

Noisomes are unique, non-ionic surfactant-based vesicles that can be multilamellar or unilamellar. They work by encapsulating a water-based solution within a bilayer membrane formed by organized surfactant molecules. These vesicles are created by hydrating a non-ionic surfactant film, which absorbs or traps the surrounding aqueous solution.

* Corresponding author: Sneha V

The main purpose of niosomes is to improve drug delivery by controlling the release of the drug, altering its distribution in the body, and ensuring it reaches specific target sites effectively[1].

Noisomes are highly advantageous due to their stability, cost-effectiveness, and ease of production. They do not require hazardous solvents, making them safer for large-scale manufacturing. These characteristics have positioned niosomes as a promising platform in pharmaceutical and therapeutic applications[2].

Niosomes provide controlled, sustained, and targeted drug release. While liposomes were the first vesicular carriers, they have several downsides, including toxicity, high costs, and instability at different pH levels. Because of these limitations, researchers turned their attention to niosomes.

Niosomes come in different forms, including unilamellar, oligolamellar, and multilamellar vesicles. They are made from non-ionic surfactants, which is why they are called "niosomes." These surfactants not only make them non-toxic but also enhance their stability. Cholesterol or its derivatives are often added to strengthen their structure, while charged molecules help maintain stability. Niosomes form naturally when non-ionic surfactants self-assemble, creating a structure capable of carrying both hydrophilic (water-soluble) and hydrophobic (fat-soluble) drugs. Niosomes can deliver multiple drugs at the same time. For example, they've been used to simultaneously deliver doxorubicin and curcumin, two powerful anticancer agents[3].

2. Structure

Niosomes are tiny, spherical structures made up of one or more layers, which can be either single layered (unilamellar) or multi-layered (multilamellar). These layers are formed using nonionic surfactants, and they may also contain cholesterol and charge-inducing molecules to improve their stability and performance[4]. Nonionic surfactants play a crucial role in the formulation of niosomes, which are bilayer vesicles widely used in drug delivery, drug targeting, and cosmetics. These surfactants are amphiphilic molecules, which means they have both hydrophilic (water-loving) and hydrophobic (water-repelling) parts, enabling the formation of stable bilayer structures. Their selection is vital in determining the stability, efficiency, and functionality of niosomes[5]. Choosing the right surfactant is crucial while formulating niosomes, as it significantly impacts their formation and stability. A key factor in this selection is the Hydrophilic-Lipophilic Balance (HLB) value of the surfactant. The HLB value indicates the degree to which a surfactant is hydrophilic (water-attracting) or lipophilic (oil-attracting). For niosome formation, surfactants with HLB values between 4 and 8 are generally preferred, as they facilitate the self-assembly of molecules into stable bilayer structures. Surfactants with HLB values higher than 8 tend to be more hydrophilic, which can hinder their ability to form stable bilayers necessary for vesicle formation. However, incorporating cholesterol into the formulation can mitigate this issue, allowing the formation of stable niosomes even with surfactants possessing higher HLB value[6].

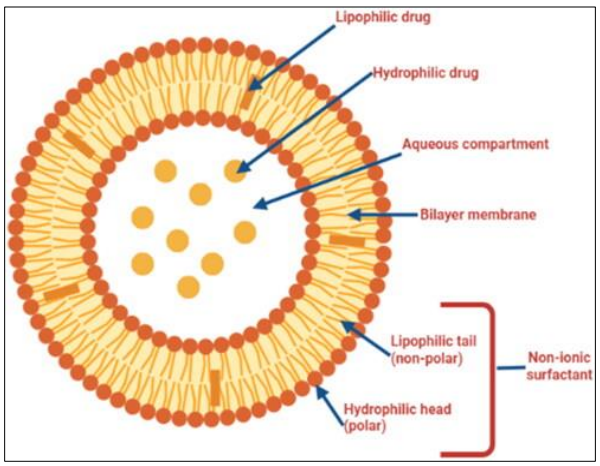

Figure 1 Structure of niosome

3. Classification of niosomes

Niosomes are primarily categorized based on the number of bilayers and their size, which are influenced by the preparation method. The main types of niosomes include:

Table 1 Classification of niosomes

1.Multilamellar Vesicles (MLV):	These consist of multiple bilayers surrounding aqueous compartments. Typically, MLVs have diameters ranging from 0.5 to 10 mm. They are commonly used in niosomal preparations and are particularly suitable for encapsulating lipophilic (fat-loving) compounds.
2. Large Unilamellar Vesicles (LUV):	Featuring a single bilayer, LUVs have sizes between 100 and 3000 nm. They possess a high aqueous-to-lipid ratio, making them efficient for entrapping larger volumes of bioactive materials with economical use of membrane lipids.
3. Small Unilamellar Vesicles (SUV):	These are also single-bilayer vesicles but are smaller in size, typically ranging from 10 to 100 nm. SUVs are often produced from MLVs through methods like sonication or extrusion. Their small size makes them suitable for delivering drugs that require rapid absorption.

Each type of niosome offers unique advantages, and the choice among them depends on the specific requirements of the drug delivery system, such as the nature of the drug to be encapsulated and the desired release profile[7].

4. Salient features of niosome

- Niosomes can entrap solutes.
- Niosomes are osmotically active and stable.
- Niosomes have an infra-structure comprising hydrophobic and hydrophilic for the foremost part together thus likewise oblige the medication atoms with a thorough kind of dissolvability.
- Niosomes discharge the medication in a controlled way by means of its bilayer which give supported arrival of the encased medication, so niosomes fill in as medication warehouse in the body.
- They improve the solubility and oral bioavailability of poorly soluble drugs and also enhance the skin permeability of drugs when applied topically.
- Niosomes show flexibility in their structural characteristics and should be designed according to the required situation
- Better availability to the actual site, just by protecting the drug from biological environment.
- Niosomes increase the steadiness of the entrapped drug[8,9,10].

4.1. Advantages

- Improved bioavailibility.
- Niosomes increase the invigorative performance of the medication particles by postponed relaxation from the diffusion, shielding the medication from natural condition and limiting efficacy to focus on cells.
- Niosomal dispersion during an aqueous phase are often emulsified during a nonaqueous phase to manage the delivery.
- Niosomes can increase the rate of drug and administered normal vesicle in external nonaqueous phase.
- They are osmotically active and stable, also as they increase the steadiness of entrapped drug.
- They improve oral bioavailability of poorly absorbed drugs and enhance skin penetration of medicine[11,12].

4.2. Disadvantages

- Physical instability
- Aggregation
- Fusion
- Leaking of entrapped drug
- Hydrolysis of encapsulated drugs which limits the shelf life of the dispersion.

4.3. Applications

- Niosomes are used for studying the character of the immune reaction provoked by antigens.
- It is used as drug Targeting.
- It is used as Anti-neoplastic Treatment i.e. Cancer disease.
- It is used as Leishmaniasis i.e. Dermal and Mucocutaneous infections e.g. Sodium stibogluconate.
- Niosomes as carriers for Hemoglobin.
- It is more suitable for delivery of peptide drugs.
- It is used in Studying Immune Responses[13,14].

5. Advancements (proniosomes)

One of the key advantages of proniosomes is their superior physical and chemical stability compared to conventional niosomes and liposomes. They effectively minimize common issues such as aggregation, fusion, and leakage of the encapsulated drug, thereby extending shelf life. Additionally, being in a dry, free-flowing state, proniosomes are more convenient to store, transport, and handle, eliminating the need for special storage conditions required for liquid-based vesicular systems[15]. Upon hydration, proniosomes form niosomes that can encapsulate a variety of drugs, enhancing their bioavailability and therapeutic efficacy. This versatility makes them suitable for delivering both hydrophilic and hydrophobic drugs. Moreover, the production of proniosomes is relatively straightforward and cost-effective, making them a practical choice for large-scale manufacturing. Their stability also reduces costs associated with storage and transportation[16].

In summary, proniosomes represent a significant advancement in drug delivery systems, offering improved stability, ease of use, and efficient delivery of a wide range of therapeutic agents[17].

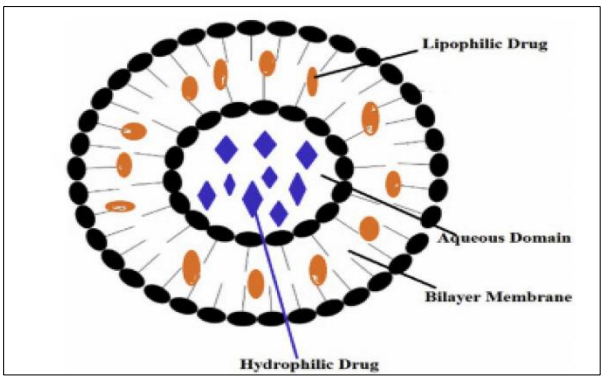

Figure 2 Structure of Proniosome

6. Methods of preparation

Different methods are reported for the preparation of proniosomes, such as

- Slurry method
- Coacervation phase separation method
- Spraying method

- **Slurry method**: This method involves preparation of slurry in a round bottom flask using carrier and surfactant solution. Additional amount of organic solvent can be added if desired to obtain slurry. The slurry is dried by applying vacuum to get free-flowing powder of proniosomes. The powder should be stored at 4 °C in a sealed container. The time required to produce proniosomes is independent on the ratio of carrier material to surfactant solution[18,19,20].

- **Coacervation phase separation method:** This is the widely used method to prepare proniosmal gel. Weighed quantities of drug, lipid and surfactants are taken in a dry wide-mouthed glass beaker followed by the addition of solvent. The ingredients are mixed well and warmed over water bath at 60–70 °C until the surfactant mixture dissolves completely. During the process care must be taken to prevent loss of any solvent due to evaporation.

Finally, the aqueous phase is added to the mixture and warmed on water bath. The resultant solution is cooled overnight to obtain proniosomal gel[21,22].

- **Spraying coating method**: In this method, proniosomes are prepared by spraying surfactant in organic solvent onto a carrier/coating material followed by evaporation of solvent. The surfactant forms a thin film on the carrier and subsequent hydration causes formation of multi-lamellar vesicles[23,24].

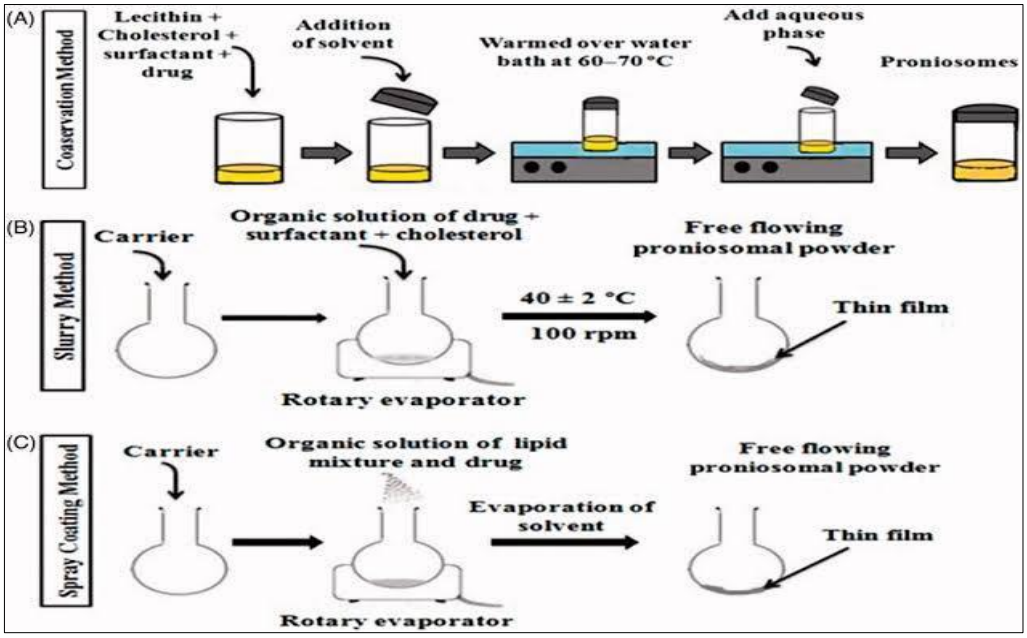

Figure 3 Preparation of proniosomes; a) Coacervation method; b) Slurry method; c) Spray coating method

7. Characterization of proniosomes

- Particle size analysis: Particle size of proniosomes is a very important characteristic. Size distribution and surface morphology (smoothness, roundness and aggregates formation) of particles can be studied by scanning electron microscopy (SEM). The vesicle formation by the procedure can be confirmed by optical microscopy. The niosome suspension must be placed over a glass slide and dried at room temperature, the dry thin film of niosome suspension formed has to be observed for the formation of vesicles.
- Measurement of zeta potential: Another characteristic of proniosomes that is of extreme interest is zeta potential. It is a measure of the particle charge, the larger the zeta potential absolute value the larger the amounts of surface charge. Logically, the zeta potential is an index for particle stability. In case of charged particles with increase in zeta potential, the repulsive interactions also increase leading to the more stable particle formation with a more uniform size distribution. A physically stable proniosomal formulation solely stabilized by electrostatic repulsion will have a ± 30 mV of minimum zeta potential and this stability helps in preventing aggregation.
- Osmotic shock: This study helps to determine the changes in the vesicle size. Thes niosomal formulations have to be incubated for 3 h with hypertonic, isotonic, hypotonic solutions and should be observed under optical microscope for vesicle size changes[25,26].
- Separation of free (untrapped) drug: The free drug can be separated from the entrapped drug using techniques as mentioned below.

7.1. Dialysis

Using suitable dissolution medium, the aqueous niosomal dispersion has to be dialyzed in dialysis tubing at room temperature. At appropriate time intervals, the samples should be withdrawn from the medium, centrifuged and analyzed for drug content using suitable method UV spectroscopy, HPLC, etc.

7.2. Gel filtration

Gel filtration is another method used for separation of unentrapped drug from niosomal dispersion using a Sephadex-G-50 column, eluted with suitable mobile phase and analyzed with suitable analytical techniques[20,22].

7.3. Applications

- Behavior of proniosome derived niosomes will be similar to liposomes showing advantages as drug carriers, comprising lower cost and toxicity, easy storage and handling, increased stability[25].
- Encapsulation of drug in proniosomal formulations reduces the toxicity in various therapies and applications and also prolongs the encapsulated drug circulation time and changes drug distribution in the body[26,27].
- Proniosomes as drug delivery vesicles, increases absorption of some drugs through cell membranes and cellular uptake via endocytosis and so confines the drug in tissues and targeted organs and also helps to evade the reticulo-endothelial system[16,28,29].

8. Future trends

Proniosomal formulations have gained increasing attention as versatile and efficient drug delivery systems due to their advantages, including enhanced stability, ease of preparation, and controlled release of active ingredients. However, despite their proven potential, opportunities remain to expand their application in various fields such as cosmetics, nutraceuticals, herbal actives, and synthetic formulations.

In the field of cosmetics, proniosomes could enhance the delivery of bioactive compounds like anti-aging agents, antioxidants, or moisturizers by improving their skin penetration and stability. For nutraceuticals, proniosomes can offer targeted delivery and improve the bioavailability of vitamins, minerals, and dietary supplements, potentially addressing issues like degradation in the gastrointestinal tract.

When it comes to herbal ingredients, proniosomes could overcome common challenges like poor solubility and stability, unlocking their full therapeutic potential. With more research and development, particularly focusing on scaling up production, these innovative systems could pave the way for groundbreaking applications in both natural and synthetic formulations[30].

9. Conclusion

Proniosomes have emerged as promising drug carriers with significant potential for future applications. As precursors to niosomes, they offer a range of advantages over liposomal vesicular systems, including superior physical and chemical stability, enhanced scalability for commercial production, and ease of formulation. The ability to incorporate amphiphilic drugs further broadens their application scope.

One of the most notable areas where proniosomes excel is transdermal drug delivery. They provide significant benefits such as non-toxicity, surfactant-mediated penetration enhancement, and the ability to modulate drug release effectively. These attributes make them ideal for delivering therapeutic agents through the skin with improved efficacy and patient compliance.

Additionally, the dry powder form of proniosomes enhances their versatility, making them suitable for unit dosage forms like tablets, capsules, and beads. This property not only facilitates dosage precision but also contributes to their stability and long shelf life.

Despite their demonstrated advantages, there remains considerable scope for further research. Investigating new carrier materials for proniosome preparation and exploring their applications across diverse drug delivery routes and therapeutic areas could unlock their full potential. Enhanced studies into scaling up processes, safety, and compatibility with various drug classes will further solidify proniosomes as a key drug delivery platform in the pharmaceutical field.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Rajera R, Nagpal K, Singh SK, Mishra DN. Niosomes: a controlled and novel drug delivery system. Biol. Pharm. Bull. 2011 Jul 1;34(7):945-53.

[2] Sahin NO. Niosomes as nanocarrier systems. BNMS. 2007;16(7):67-81.

[3] Bhardwaj P, Tripathi P, Gupta R, Pandey S. Niosomes: A review on niosomal research in the last decade. J. Drug Deliv. Sci. Technol. 2020 Apr 1;56(1):28-44.

[4] Yeo PL, Lim CL, Chye SM, Ling AP, Koh RY. Niosomes: a review of their structure, properties, methods of preparation, and medical applications. Asian Biomed. 2017 Aug 1;11(4):301-14.

[5] Mawazi SM, Ge Y, Widodo RT. Niosome Preparation Techniques and Structure-An Illustrated Review. Pharm. 2025 Jan 6;17(1):67.

[6] Umbarkar MG. Niosome as a Novel Pharmaceutical Drug Delivery: A Brief Review Highlighting Formulation, Types, Composition and Application. IJPER. 2021 Jan 2;55(2):1-18.

[7] Verma AK, Bindal JC. A vital role of niosomes on Controlled and Novel Drug delivery. IJNDD. 2011 Oct;3(56):238-46.

[8] Makeshwar KB, Wasankar SR. Niosome: a novel drug delivery system. Asian J. Pharm. Res. 2013 Jun;3(1):16-20.

[9] Sankhyan A, Pawar P. Recent trends in niosome as vesicular drug delivery system. J. Appl. Pharm. Sci. 2012 Jun 30;2(19):20-32.

[10] Gurjar P, Naik N, Chouksey S. Niosome: a promising pharmaceutical drug delivery. Int. J. Pharm Anal. 2014;2(5):425-31.

[11] Bagheri A, Chu BS, Yaakob H. Niosomal drug delivery systems: Formulation, preparation and applications. WASJ. 2014;32(8):1671-85.

[12] Madhav NV, Saini A. Niosomes: a novel drug delivery system. IJRPC. 2011;1(3):498-511.

[13] Alsarra IA, Bosela AA, Ahmed SM, Mahrous GM. Proniosomes as a drug carrier for transdermal delivery of ketorolac. Eur J Pharm Biopharm. 2005 Apr 1;59(3):485-90.

[14] Weissmann G, Bloomgarden D, Kaplan R, Cohen C, Hoffstein S, Collins T, Gotlieb A, Nagle D. A general method for the introduction of enzymes, by means of immunoglobulin-coated liposomes, into lysosomes of deficient cells. PNAS. 2016 Jan 23;72(1):88-92.

[15] Khatoon M, Shah KU, Din FU, Shah SU, Rehman AU, Dilawar N, Khan AN. Proniosomes derived niosomes: recent advancements in drug delivery and targeting. DDTR. 2017 Nov 1;24(2):56-69.

[16] Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes—non-ionic surfactant vesicles. J. Pharm. Pharmacol. 2006 Dec 16;37(12):863-8.

[17] Schreier H, Bouwstra J. Liposomes and niosomes as topical drug carriers: dermal and transdermal drug delivery. JCR. 2018 Apr 1;30(1):1-5.

[18] Blazek–Welsh AI, Rhodes DG. SEM imaging predicts quality of niosomes from maltodextrin-based proniosomes. Pharm. Res. 2001 May; 18(2):656-61.

[19] Perrett S, Golding M, Williams WP. A simple method for the preparation of liposomes for pharmaceutical applications: characterization of the liposomes. J. Pharm. Pharmacol. 1991 Mar;43(3):154-61.

[20] Solanki AB, Parikh JR, Parikh RH. Formulation and optimization of piroxicam proniosomes by 3-factor, 3-level Box-Behnken design. AAPS Pharmscitech. 2007 Oct; 8:43-9.

[21] Gupta A, Prajapati SK, Balamurugan M, Singh M, Bhatia D. Design and development of a proniosomal transdermal drug delivery system for captopril. Trop. J. Pharm. Res. 2007 Jul 31;6(2):687-93.

[22] Vora B, Khopade AJ, Jain NK. Proniosome based transdermal delivery of levonorgestrel for effective contraception. JCR. 1998 Jul 31;54(2):149-65.

[23] Biju S, Talegaonkar S, Mishra P, Khar R. Vesicular systems: an overview. Indian J. Pharm. Sci. 2006 Mar 1;68(2):84-91.

[24] Malhotra M, Jain NK. Niosomes as drug carriers. IDMA. 2006; 31:89-91.

[25] Uchegbu IF, Florence AT. Non-ionic surfactant vesicles (niosomes): physical and pharmaceutical chemistry. Adv. Colloid Interface Sci. 1995 Jun 27;58(1):1-55.

[26] Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The effect of non-ionic surfactant vesicle (niosome) entrapment on the absorption and distribution of methotrexate in mice. J. Pharm. Pharmacol. 2011 Apr;37(4):237-42.

[27] Ruckmani K, Jayakar B, Ghosal SK. Nonionic surfactant vesicles (niosomes) of cytarabine hydrochloride for effective treatment of leukemias: encapsulation, storage, and in vitro release. DrugDev. Ind. Pharm. 2000 Jan 1;26(2):217-22.

[28] Namdeo A, Jain NK. Niosomal delivery of 5-fluorouracil. J. Microcapsul. 2009 Jan 1;16(6):731-40.

[29] Devaraj GN, Parakh SR, Devraj R, Apte SS, Rao BR, Rambhau D. Release studies on niosomes containing fatty alcohols as bilayer stabilizers instead of cholesterol. J. Colloid. Interface Sci. 2002 Jul 15;251(2):360-5.

[30] Yasam VR, Jakki SL, Natarajan J, Kuppusamy G. A review on novel vesicular drug delivery: proniosomes. Drug Deliv. 2014 Jun 1;21(4):243-9.