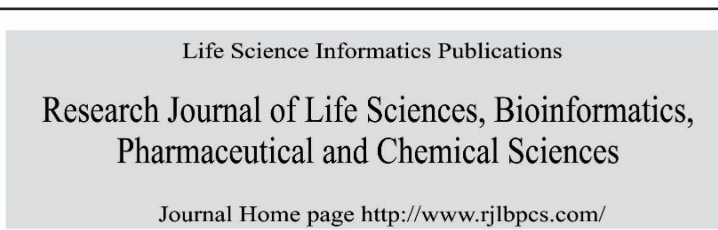

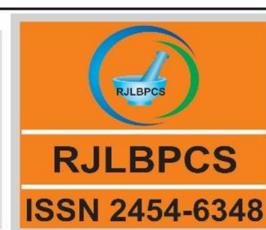

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NIOSOMES: A VERSATILE DRUG DELIVERY SYSTEM

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ABSTRACT: Drug delivery systems are defined as formulations aim for transportation of a drug in the desired area of action within the body. Niosomes are thought to be the better candidate's drug delivery system due to the various factor like cost, stability, etc. various types of drug delivery is possible using Niosomes like targeting drug action, ophthalmic, parenteral. etc. In recent years, Niosomes have become the vesicles of choice in drug delivery. Niosome vesicles are found to be of value in immunology, membrane biology and diagnostic techniques. A number of Novel drug delivery system has been reported through various route of administration, to achieve controlled and targeted drug delivery. Often formulated to permit the establishment and maintenance of any concentration at target site for longer intervals of time. One such technique of drug targeting is Niosomes. In a vesicle. This review also gives relevant information regarding various applications of niosomes in gene delivery, vaccine delivery and anticancer drug delivery.

KEYWORDS: Niosomes, Targeted Drug Delivery, Vesicles, NDDS.

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1.INTRODUCTION

Novel drug delivery system aims to delivery drug at a rate directed by the needs of the body during the period of treatment and channel the active entity to the site of action.

In the past few decades, considerable attention has been focused on the development of new drug delivery system (NDDS). The NDDS should ideally fulfill two prerequisites. Firstly, it should deliver the drug at a rate directed by the needs of the body, over the period of treatment. Secondly, it should channel the active entity to the site of action. Conventional dosage forms including prolonged release dosage forms are unable to meet none of these. At present, no available drug delivery system behaves ideally, but sincere attempts have been made to achieve them through various novel approaches in drug delivery.[1] The aim of Novel Drug Delivery System is to provide a therapeutic amount of drug to the appropriate site in the body to accomplish promptly and then maintain the desired drug concentration. The drug- delivery system should deliver drug at a rate control by the necessarily of the body over a specified term of treatment. The particulate carrier systems also known as colloidal carrier system, it includes lipids particles, microspheres, polymeric micelles and various vesicular systems. In recent years, vesicles systems are highly ordered assemblies of one or several concentric lipid bilayers formed when certain amphiphilic building blocks are confronted with water. The various types of vesicular system include liposomes, Niosomes, transfersomes and pharmacosomes[2-5]. A Niosomes are the non ionic surfactant vesicle having a bilayer structure formed by self assembly of cholesterol and non ionic surfactant. They are the ideal drug delivery system providing the targeted site of action[6-8].

Vesicular systems have certain advantage over conventional dosage form:

- Vesicles can play a major role in modeling biological membranes, and in the transport and targeting of active agents.
- Encapsulation of drug within the vesicular system prolongs the systemic circulation and also can be targeted to site of infection which reduces the toxicity with no adverse effect[8]
- It also reduces the cost of therapy by improved bioavailability of medication especially in case of poorly soluble drugs.
- They can incorporate both hydrophilic and lipophilic drugs.
- Vesicular drug delivery systems delay drug elimination of rapidly metabolizable drugs, and function as sustained release systems.
- This system solves the problems of drug insolubility, instability, and rapid degradation.

Various types of Niosomes:

Based on the vesicle size, niosome can be divided into three groups. These are small unilamellar

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vesicles (SUV, size=0.025-0.05 μm), multilamellar vesicles (MLV, size=>0.05 μm), and large unilamellar vesicles (LUV, size=>0.10 μm).

Advantage of Novel drug delivery system:

1) Improves the therapy by increasing the duration of action and reducing the side effects.
2) Increases the patient compliance and provides convenient route of administration.
3) Achieve the targeting of drugs to a specific site which reduces the unwanted side effects and obtain maximum efficacy.
4) Reduces the dose and thus reduces the side effects of drugs.
5) Reduction in the total amount administered over the period of drug treatment.
6) Maximizing availability with minimum dose.
7) Protections from the first pass metabolism and gastro intestinal tract degradation.
8) Safety margin of high potency drugs can be increased.
9) Targeting the drug molecule towards the tissue or organ reduces the toxicity to the normal tissues.
10) Improved patient compliance.

Disadvantages of Novel drug delivery system:

1) Administration of sustained release medication does not have prompt termination of therapy.
2) The physician has less flexibility in adjusting dosage regimen.
3) The various physiological factors such as gastro-intestinal pH, enzyme activities, food, which interfere with the absorption of the drug system.

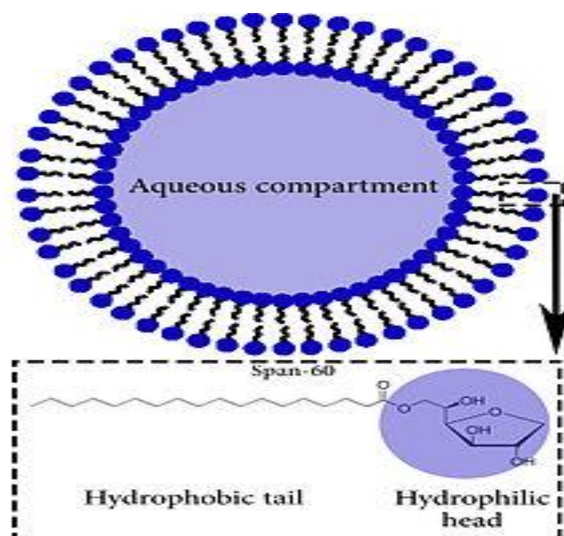

Figure1. : Niosomes (Non- ionic surfactant vesicles)

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METHODS OF PREPARATION

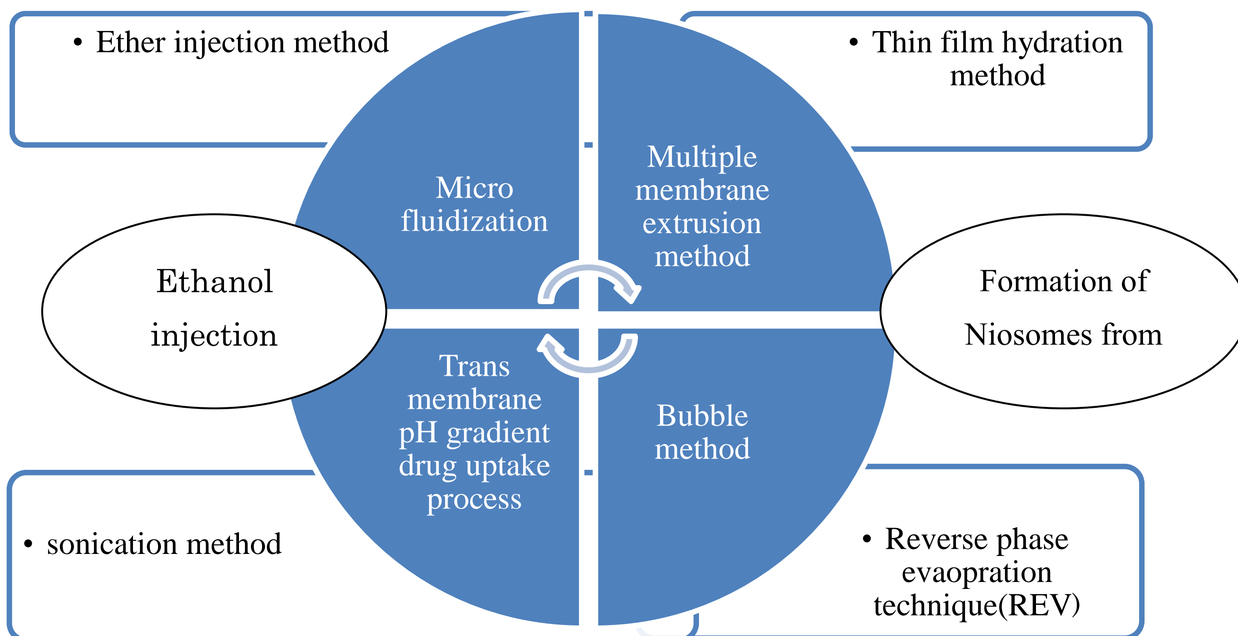

Figure 2. : Various methods for Niosomes preparation

Ether injection method:

The injection of an organic solution of surfactants: lipids through a 14 gauze needle at a rate approximately 0.25 ml/m in to a preheated aqueous solution of the drug maintained at 60°[09-11].Subsequent removal of residual ether under vacuum leads to the formation of small unilamellar vesicles.

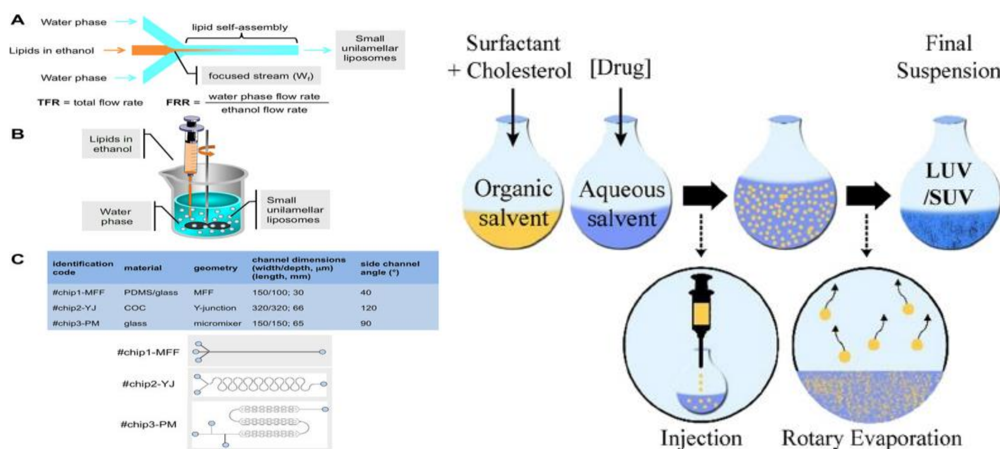

Figure 3. : Ether injection method for Niosomes preparation

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Thin film hydration method: (Hand shaking Method)

Lipid and non-ionic surfactant are dissolved in an organic solvent in round bottom flask. The organic solvent is removed by means of rotary evaporator at reduced pressure, multilamellar vesicles are formed spontaneously when an excess volume of aqueous buffer is added into dry lipid and shaken by hand or vortex mixer. The size and encapsulating efficiency of multilamellar vesicles depends on the duration and intensity of shaking, the presence of change inducing agents in the bilayer, ionic strength of aqueous medium and lipid concentration.

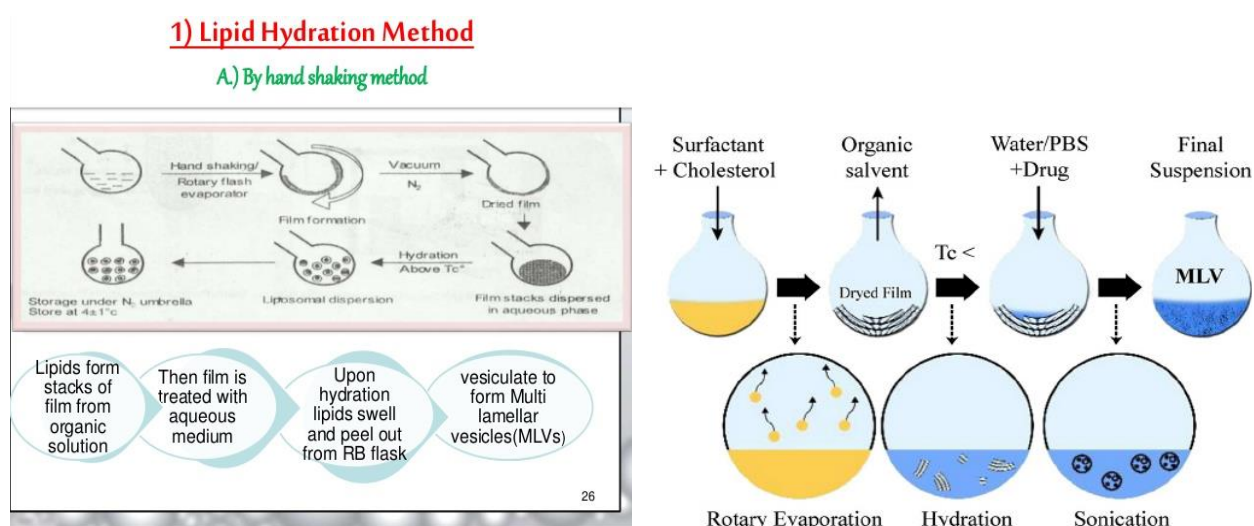

Figure 4. : Thin Film Hydration method.

Ethanol injection method:

Lipids dissolved in ethanol are rapidly injected in to an excess of buffer solution or other aqueous medium through a fine needle. The force of the injection is usually sufficient to achieve complete mixing, so that the ethanol is diluted almost instantaneously in water and lipid molecules are dispersed evenly throughout the medium.

Sonication method:

The multilamellar vesicles and large unilamellar vesicles are sonicated with a bath type or probe sonicator, under an inert atmosphere (usually nitrogen gas) to get the small unilamellar vesicles. During Sonication the multilamellar vesicles structure is broken down to form small unilamellar vesicles[12-14]

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Figure 5. : Sonication method.

Micro fluidization:

This is recent technique to prepare small MLV's. A micro fluidizer is used to pump the fluid at a very high pressure (10,000 psi). The two phases are allowed to interact at ultra high speed in micro channels in an interaction chamber. The high speed impingement and the energy involved leads to formation of uniform and small Niosomes. This method has a high degree of reproducibility[15].

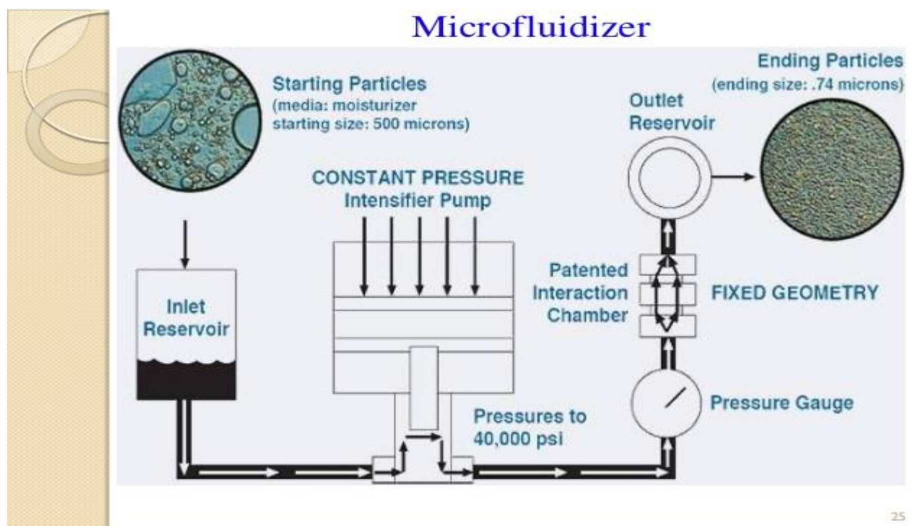

Figure 6. : Microfludisation method.

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Multiple membrane extrusion method:

The basic principle involves extrusion that is forced passage of mixture/suspension/emulsion of the components through polycarbonate membranes repeatedly to obtain niosomes of desired size. The organic phase is dried in a rotary evaporator and is hydrated by aqueous phase; the resultant is extruded through the membrane[16].

Trans membrane pH gradient drug uptake process:

The organic phase with dissolved components is evaporated to form a thin layer and hydrated with citric acid, multilamellar vesicles are formed which are freeze thawed 3 times and sonicated. To this Niosomal suspension aqueous solution with drug is added, vortexed and pH is raised upto 7.0-7.2 with 1M disodium phosphate. The mixture is later heated at 60 °C for 10 minutes to get drug loaded niosomes[17, 18].

Bubble method:

It is novel technique for the one step preparation of liposomes and Niosomes without the use of organic solvents. The bubbling unit consists of round bottomed flask with three necks positioned in water bath to control the temperature. Water cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through third neck .cholesterol and surfactant are dispersed together in this buffer(pH7.4) at 70ºC, the dispersion mixed for 15 seconds with high shear homogenizer and immediately afterwards "bubbled" at 70ºC using nitrogen gas.

Reverse phase evaporation technique (REV):

The surfactants are dissolved in a mixture of ether and chloroform to which an aqueous phase Containing the drug is added. The resulting two-phase system is then homogenized and the Organic phase evaporated under reduced pressure to form Niosomes dispersed in the aqueous Phase[19].

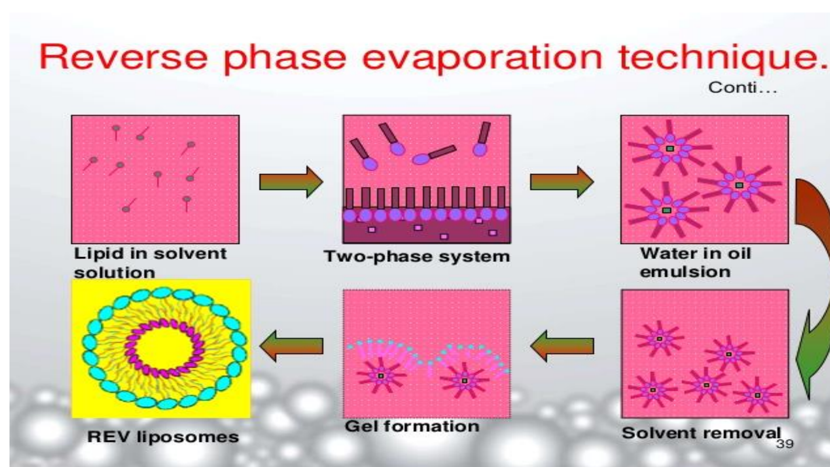

Figure 7. Reverse phase evaporation technique

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Formation of Niosomes from proniosomes:

Coat a water- soluble carrier such as sorbitol with surfactant obtained a dry formulation. In which each water soluble particle is covered with a thin film of dry surfactant. The preparation is termed "Proniosomes".

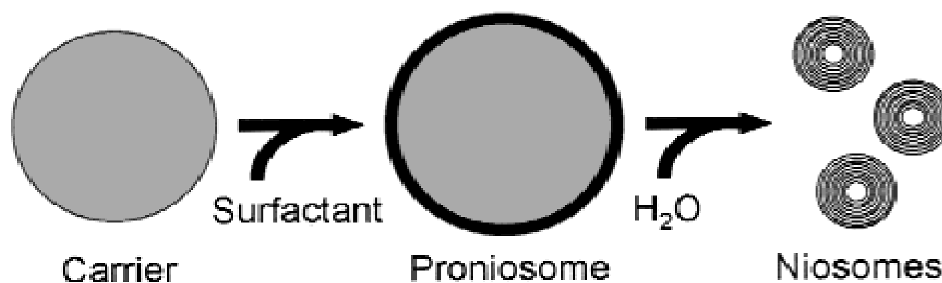

Figure 8. Formation of Niosomes from proniosomes:

Characterization of Niosomes:

1. **Vesicles Diameter**

The diameter of Niosomes can be determined using light microscope, photon correlation microscopy. Various other technique which are used to determine the vesicles the diameter are Scanning electron microscopy(SEM), Salad-1100 laser diffraction particle size analyzer, Coulter submicron particle size analyzer, .Klotz® particle sizer & Anderson cascade impactor.

2. **Entrapment efficiency**

After preparing the niosome, unentrapped drug is separated by dialysis, centrifugation & gel chromatography. The remaing entrapped drug in niosomes is determined by lysing the vesicles. The percentage of drug entrapped is calculated using the following formula:

$$\% \text{ Entrapment efficiency} = \frac{\text{Amount of drug entrapped}}{\text{Total amount of drug}} \times 100.$$

3. ***In vitro* release rate**

   Release of the drug can be monitored by dialyzing Niosomal suspension against the buffer at definite temperature and determing the drug content of dialysate[20].

4. **Osmotic shrinkage**

   Osmotic shrinkage of vesicles can be determined by monitoring reductions in vesicle diameter, initiated by addition of hypertonic salt solution to suspension of niosomes.

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Niosomes prepared from pure surfactant are osmatically more sensitive in contrast to vesicles containing cholesterol.

5. **Physical stability of vesicles at different temperature**

   Aggregation of fusion of vesicles as a function of temperature was determined as the changes in vesicles diameter by laser light scattering method. The vesicles were stored in glass vials ate room temperature or kept in refrigerator (4°C) for 3 months.

6. **Turbidity measurement**

   The niosomes were diluted with bidistilled water to give a total lipid concentration of 0.312mM. After rapid mixing by Sonication for 5 min, the turbidity was measured as the absorbance with an UV diode array spectrophotometer[21].

Table No.1 Methods of Evaluation of Niosomes

Sr. No.	Evaluation Parameter	Method/ Instrument
1.	Size distribution, Polydispersity index	Scanning electron microscopy(SEM), Malvern Mastersizer, Anderson cascade impactor, Dynamic light scattering particle size analyzer, Optical microscopy, Klotz® particle sizer.
2.	Morphology	Optical microscopy, SEM, TEM, freeze fracture tech Phase Contrast microscopy, Quasi elastic light scattering technique, Small angle X-ray diffraction (SA-XRD).
3.	Thermal analysis	DSC, DTA, Hot stage microscopy
4.	Zeta potential	Malvern Zetasizer (zetameter), Microelectrophoresismeter.
5.	Lamellarity	Optical microscopy, TEM
6.	Membrane microstructure	Negative staining TEM
7.	Viscosity	Low shear rheoanalyser, Oswalt-U-tube
8.	Entrapment efficacy	Dialysis, gel chromatography, Centrifugation
9.	Conductivity	Conductometer
10.	*In-vitro* release study	Dialysis membrane
11.	Permeation study	Franz diffusion cell

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4. CONCLUSION

Niosomes is prominent tool (drug carrier) for sustained release drug delivery system. Niosomes are novel drug delivery system which offers a large number of advantages over other conventional and vesicular delivery systems there is lot of scope to encapsulate toxic anti-cancer drugs, anti-viral drugs, anti-infective drugs, anti-AIDS drugs, anti-inflammatory etc. in Niosomes. Thus Niosomes present itself as a versatile tool in therapeutics.

CONFLICT OF INTEREST

The authors declare that no competing financial interests exist.

REFERENCES

1. Li, V.H.K., Robinson, J.R. and Lee, V.H.L., In; Controlled Drug Delivery: Fundamentals and Applications, 2nd Edn., Vol 29, Marcel Dekker, Inc., NY, 1987, 7
2. Goldberg, E. P. Eds., In; Targeted Drugs, 2nd Edn., Wiley, New York, 1983, 312.
3. Gregoriadis, G., Nature, 1977, 265, 407.
4. Poste, G., Kirsch, R. and Koestler, T., In; Gregoriadis, G. Eds; Liposomes Technology Vol 3, CRC Press Inc., Baco Raton. Fl, 1983, 29.
5. Poznansky, M. J. and Juliano, R. L., Pharmacol. Rev., 1983, 36, 277.
6. Breimer D D and Speised R. 'Topics in Pharmaceutical Sciences'. Elsevier Science Publishers, Newyork, USA. 1985; 291.
7. Handjani VRM. Dispersion of Lamellar Phases of Nonionic Lipids in Cosmetic Products. *Int J Cosmetic Sci.1979*; 30.
8. Sternberg B, Uchegbu IF, Florence AT and Murdan S. 1998.
9 Niemec SM, Hu Z, Ramachandran C.et al. The effect of dosing volume on the disposition of cyclosporine A in hairless mouse skin after topical application of a non-ionic liposomal formulation.An in vitro diffusion study. STP Pharm. Sci. 1994;2:145–149.
10 Vanhal D, Vanrensen A, Devringer T.et al. Diffusion of estradiol from non-ionic surfactant vesicles through human stratum-corneum in vitro.STP Pharm. Sci. 1996;6: 72–78.
11 Jia-You Fang, Chi-Tzong Hong, Wen-Ta Chiu.et al. Effect of liposomes and niosomes on skin permeation of Enoxacin. Int. J. Pharm. 2001;219: 61–72.
12. Carter, KC, Baillie AJ, Alexender J, Dolan TF. The Therapeutic effect of sodium stibogluconate in BALB:c mice infected with Leishmania donovani is organ dependent. J. Pharma. Pharmacol., 1988,40,370-373.
13. Hofland H. E. J. Safety aspects of non-ionic surfactant vesicles-a toxicity study related to the physicochemical characteristics of non-ionic surfactants. J Pharm Pharmacol. 1992; 44:287-294.

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14 Yoshida H. et al. Niosomes for oral delivery of peptide drugs. J Control Release. 1992; 21: 145–153.
15. Khandare J. N., Madhavi G., Tamhankar B. M. Niosomes novel drug delivery system. The Eastern Pharmacist. 1994; 37: 61-64.
16. Anchal Sankhyan and Pravin Pawar, Recent Trends in Niosome as Vesicular Drug Delivery System, Journal of Applied Pharmaceutical Science 02 (06); 2012: 20-32.
17. Biju S. S., Talegaonkar S., Mishra P. R., Khar R. K. Vesicular systems: An overview. Indian J Pharm Sci. 2006; 68: 141-153.
18. Mayer L. D., Bally M. B., Hope M. J., Cullis P. R. Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. Biochem Biophys Acta. 1985; 816: 294-302.
19. Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes non-ionic surfactant vesicles. J Pharm Pharmacol., 1985; 37:863-8.
20. Yoshida H, Lehr CM, Kok W, junginger HE, Ver-hoef JC, Bouwstra JA. Niosomes for oral delivery of peptide drugs.J. control Rel., 1992, 21, 145-153.
21. Cook EJ and Lagace AP. US Patent, 1985,4,254,553.

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