NIOSOME: A Novel Trend in Herbal Drug Delivery

Ms. Shruti R. Rupnar*, Ms. Mayuri S. Bhadalekar[1], Ms. Mayuri V. Bhosale[1], Dr. Nilesh B. Chougule[2], Mr. Nitin G. Gudphale, Mr. Rahul S. Koli
Assistant Professor Ashokrao Mane Institute of Pharmacy Ambap, Maharashtra, India, 416112
Principal Ashokrao Mane Institute of Pharmacy Ambap, Maharashtra, India, 416112

Abtsract: It has been claimed that employing proactive and plant selections, unique herbal formulations such as polymeric nanoparticles, nanocapsules, liposomes, phytosomes, animations, microspheres, transfersomes, and ethosomes have been created. Novel formulations of plant actives and extracts are said to have notable advantages over traditional formulations, including improved solubility, bioavailability, and protection from toxicity; increased pharmacological activity; increased stability; improved tissue macrophage distribution; sustained delivery; and protection from physical and chemical degradation. To achieve controlled and targeted drug delivery, a number of novel drug delivery systems have been reported through various routes of administration. To achieve controlled and targeted drug delivery, a number of novel drug delivery systems have been reported through various routes of administration. It is frequently designed to allow the development and maintenance of any concentration at the target spot for prolonged periods of time. Niosomes is one such method of medication targeting. The research of the niosomes is the main objective of this review.

Keywords: Herbal Drugs; Herbal novel drug delivery system; Niosomes; Non-ionic surfactant.

INTRODUCTION

Herbal medicines are gaining popularity in the modern world because they can be used to treat a wide range of illnesses with less hazardous side effects.[1] People use natural extracts and herbal treatments to treat a variety of illnesses. Numerous phytochemicals found in these herbal treatments are combating the disease at the same time. [2] The majority of biologically active phytoconstituents made of flavonoids, phenolics, and glycosidic aglycones have poor water solubility and have a low level of bioavailability in the cellular medium. [3] Due to its aesthetic appeal, increased patient compliance, and pronounced therapeutic results, the use of herbal medicines has drawn attention on a global scale. The conservation of traditional medical practices, the preservation of biodiversity, and the advancement of the health care system all benefit from ethnobotanical knowledge of these plants and how indigenous cultures use them. The medications are produced in an appropriate formulation that takes into account the safety, acceptability, and efficacy of other substances. This preparation is frequently referred to as a dosage form or drug delivery system. [4] The dosage forms have evolved from straightforward mixtures and pills to extremely complex technologies, intensive drug delivery systems, or NDDSs, as a result of advancements in all fields of science and engineering. By delivering the treatment only to the area of the patient's body that is afflicted, novel herbal drug carriers treat specific diseases. NDDS is useful in that it releases the herbal medication at a predetermined rate and delivers the medication directly to the area of action, minimising adverse effects while increasing bioavailability.[1] One of the innovative drug carriers, niosomes are generated by the self-association of nonionic surfactants and cholesterol in an aqueous phase. They have a bilayer structure. Niosomes are biocompatible, non-immunogenic, and biodegradable. [5]

NOVEL HERBAL DRUG DELIVERY SYSTEM

The limitations of the conventional drug delivery methods are addressed by the innovative drug delivery system, which is a novel method of drug administration. Our nation possesses a wealth of Ayurvedic knowledge, but only recently has its full potential been recognised. However, the traditional and antiquated drug administration method utilised to give the patient the herbal medicine causes a reduction in the drug's effectiveness. [6] This sort of noisome (100-3000 nm) has a high aqueous phase-to-surfactants compartment ratio; as a result, the

bioactive material can be captured with a very economical use of membrane surfactants if the revolutionary drug delivery method is utilised in herbal medicine. This particular noisy (100–3000 nm) has a high aqueous phase–to–surfactants compartment ratio, allowing for highly efficient entrapment of the bioactive substance. It might aid in boosting the potency and minimising the negative effects of various herbal ingredients and herbs. [7] This is the fundamental rationale behind the use of innovative medication delivery systems in herbal medicines. In order to treat increasingly severe disorders, it is crucial to combine cutting-edge drug delivery systems with Indian Ayurvedic treatments. To achieve targeted and regulated drug delivery, new herbal drug delivery systems have arisen, incorporating a variety of administration modalities. One such system that contributes to extending the duration of a drug in systemic circulation and reducing toxicity through selective uptake is drug encapsulation in vesicles. Numerous vesicular drug delivery systems, including liposomes, niosomes, and provesicular systems like proliposomes and proniosomes, have been created based on this approach. In new herbal drug delivery technology, drug distribution is controlled by putting the medication into a carrier system or by altering the drug's molecular structure. [3]

NIOSOMES

Colloidal niosomes are produced from self-liposomal structures. non-ionic surfactant assemblage in aqueous medium Closed bilayer structures are produced as a result of niosomes' alleviation of the accompanying drawbacks. Niosomes act as drug depots in the body, releasing the drug through its bilayer in a controlled manner to provide prolonged release of the contained drug. [8] Niosomes can also be used to deliver drugs specifically to the body part where they are needed for a therapeutic effect. decreasing the amount of medication needed to produce the intended result. In contrast to liposomes, which are more prone to oxidation, are more expensive, and are more difficult to obtain in high purity levels that affect size, shape, and stability, niosomes are mostly composed of non-ionic surfactants, giving them the advantage of being more stable. Niosoms can accommodate a vast variety of pharmaceuticals with a wide range of solubilities because they are amphiphillic, or both hydrophilic and lipophillic in nature. [9]

ADVANTAGES OF NIOSOMES

1) It is possible to achieve targeted drug delivery and Increases the drug's stability while it is entrapped.
2) By modifying the composition of the vesicle, size lamellarity, surface charge, tapped volume, and concentration, vesicle characteristics can be changed. [10]
3) They can release the medicine gradually and deliberately.
4) Surfactants are non-toxic, non-immunogenic, biodegradable, and biocompatible. [11]
5) Increase the oral bioavailability of poorly absorbed medications and increase drug penetration through the skin.
6) By delaying clearance from the blood, shielding the drug from the biological environment, and limiting the effects to the target cells, niosomes enhance the therapeutic performance of drug molecules. [12]
7) Niosomes can speed up medication absorption and normal vesicle administration in the nonaqueous exterior phase. [13]
8) When compared to alternative distribution systems, patient compliance is higher. [14]

DISADVANTAGES:

1) Processing calls for specialised equipment. [14]
2) Entrapped drug leakage.
3) It takes time. [15]
4) The shelf life of niosome aqueous solutions may be shortened as a result of the fusion, aggregation, and hydrolysis of drugs that are enclosed in capsules.
5) Complicated preparatory process. [10]

COMPOSITION OF NIOSOMES

Niosomes resemble liposomes structurally in that they are likewise formed of a bilayer. Instead of phospholipids, as is the case with liposomes, the bilayer within niosomes is made of non-ionic surface active substances. [13] It includes 3 major components:

1] Non-ionic surfactants: The surface-active agent serves as the main ingredient in the formulation of the noisome. HLB value is used to determine the surfactant to use. HLB numbers between 4 and 8 were discovered to be compatible with vesicle formation

because they are an excellent indicator of any surfactant's ability to form vesicles. They have a polar head and a non-polar tail and are amphiphilic in nature. Because they don't carry any charge, these substances are more stable, compatible, and non-toxic than other surfactants like anionic, cationic, and amphoteric surfactants. These substances lessen cellular surface irritation and hemolysis. They can be used as emulsifiers and wetting agents. A hydrophilic head and a hydrophobic tail are features of the non-ionic surfactants. [14]

Egs. Spans (span 60, 40, 20, 85, 80), Tweens (tween 20, 40, 60,80). Brijs (brij 30, 35, 52, 58, 72, 76). [16]

2. Cholesterol: As an amphiphilic molecule, cholesterol directs its OH group toward the aqueous phase and its aliphatic chain toward the hydrocarbon chain of the surfactant. The non-ionic surfactants are typically supplemented with cholesterol, a waxy steroid metabolite, to increase stiffness. Additionally, cholesterol is known to stop the transition from the gel to liquid phase, which prevents leaking. [17]

3. Charge inducing molecule: These assist in adding surface charge to the produced vesicles, boost vesicle stability by avoiding vesicle fusion brought on by repulsive forces of the same charge, and offer larger zeta potential values. Positive charge inducers include sterylamine and cetyl pyridinium chloride, whereas negative charge inducers include dicetyl phosphate dihexadecyl phosphate, lipoamine acid, and others. [18]

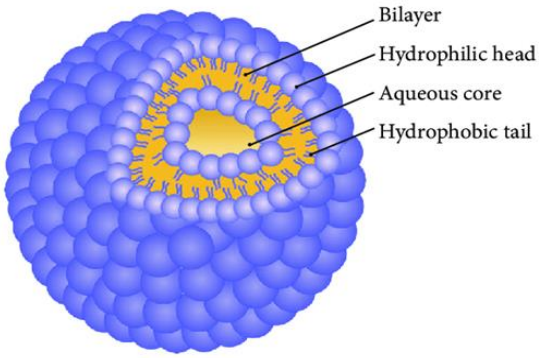


Fig. Structure of Niosomes

CLASSIFICATION OF NIOSOMES

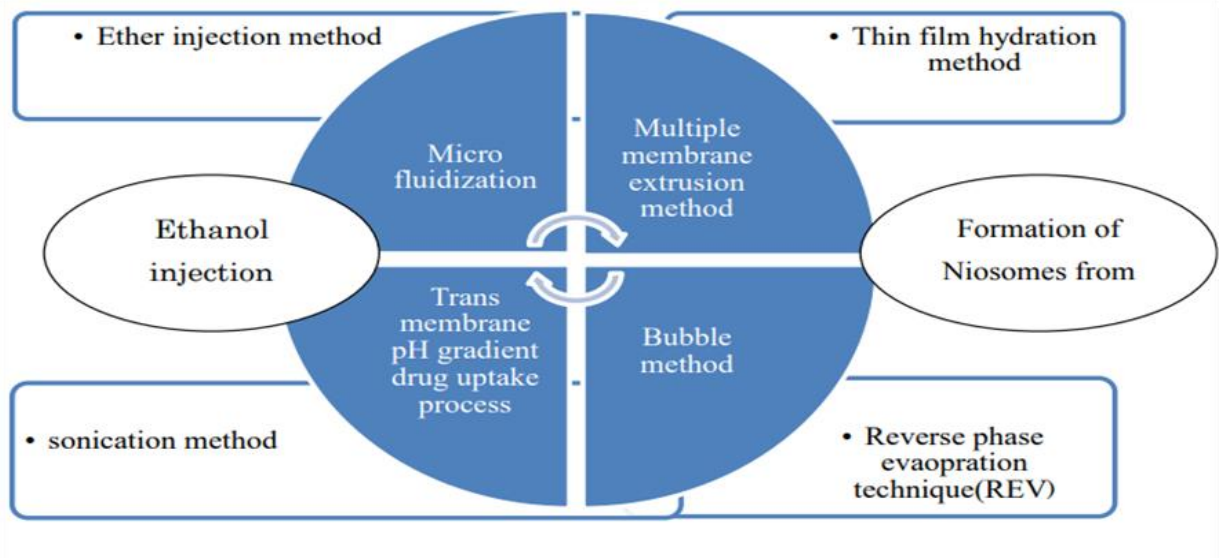
The niosomes are also classified according to the number and size of bilayer which is as follows,

1)Multilamellar Vesicles (MLV): The aqueous lipid compartment is surrounded by a variety of bilayers that make up MLV. These vesicles range in diameter from 0.5 to 10 micrometres. The aqueous lipid compartment is surrounded by a variety of bilayers that make up MLV. These vesicles range in diameter from 0.5 to 10 micrometres.

ii) Large Unilamellar Vesicles (LUV): This particular noisy (100–3000 nm) has a high aqueous phase–to–surfactants compartment ratio, allowing for highly efficient entrapment of the bioactive substance.

iii) Small Unilamellar Vesicles (SUV): Most often, the multilamellar vesicles are converted into very tiny unilamellar vesicles using the extrusion, French press, and sonication methods. [19]

METHODS OF PREPARATIONS



1) Thin Film Hydration method: In this procedure, an organic solvent (diethyl ether, chloroform, or methanol) is used to dissolve the surfactants, cholesterol, and some additions, such as charged molecules. The organic solvent is then eliminated using a rotary vacuum evaporator to produce a thin coating on the flask's interior wall. The dry film is hydrated above the surfactant's transition temperature (Tc) for a predetermined amount of time while being constantly shaken. Using this method, conventional multilamellar niosomes are created. [5]

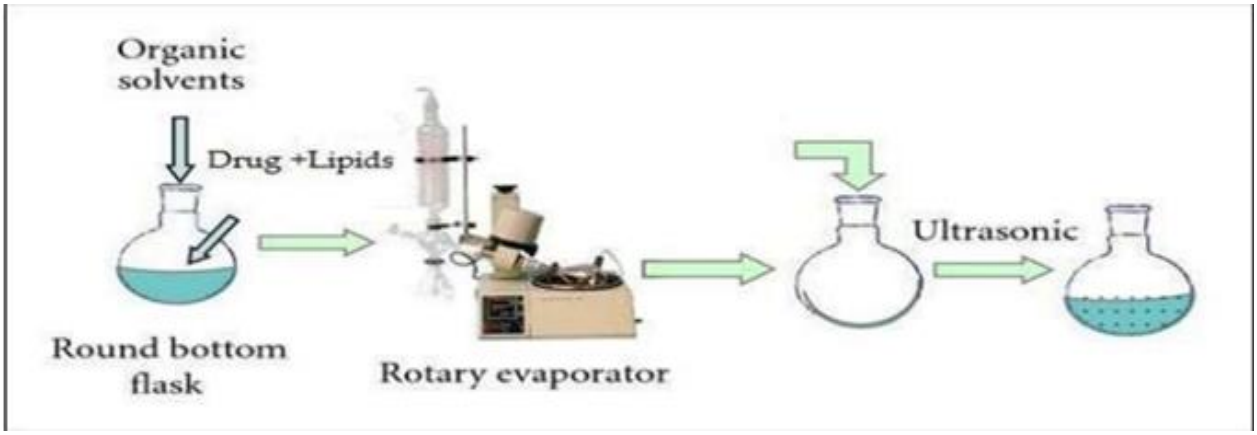


Fig 4 : Thin film hydration Method Of Niosomes Preparations

2) Ether injection method: The surfactant and other components are dissolved in ether (diethyl ether) and slowly injected into an aqueous solution that is kept at 60°C using a needle in the ether injection method. As a result of this addition, ether evaporates and single-layered vesicles are created. By adjusting the needle size and other factors, this approach has the advantage of allowing for size control. It has the drawbacks of low material solubility in ether and difficulties removing ether from the finished formulation. [9]

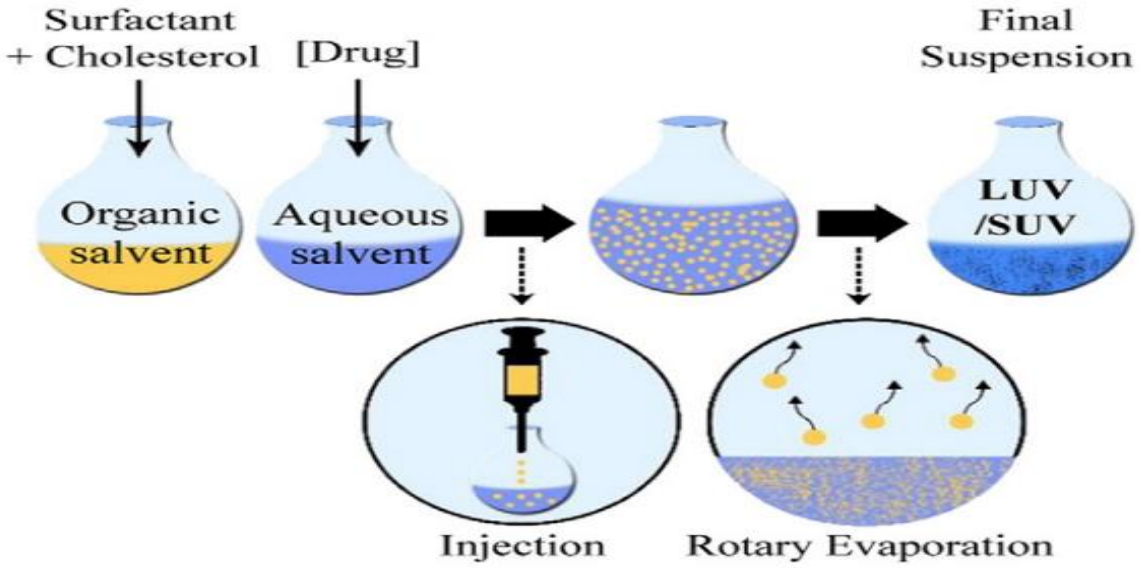


Fig. Protocol for niosome preparation through ether injection method.

3) Sonication: Baillie et al. generated niosomes for the first time in 1986 using the sonication technique. In this procedure, a mixture of surfactant and cholesterol (150 micromoles) was dissolved in a 2 ml aqueous introduction vial. Spread is heated to 600 °C for three minutes while being subjected to probe sonication. These systems combine to generate MLVs that are vibrated at ultrasonic frequencies. Sonicators come in two varieties: Probe and Bath. When the sample volume is small, a probe sonicator is used, and when the sample volume is high, a bath sonicator is used. [13]

A) Bath sonicator B) Probe sonicator

Fig 5 : Sonication technique

4) Heating method (HM): Surfactants and some additives, like cholesterol, were individually hydrated in PBS (pH = 7.4) for an hour at room temperature in a nitrogen atmosphere. The solution is then heated (to a temperature of around 120 °C) on a hot-plate stirrer to dissolve the cholesterol after roughly 15-20 minutes. The temperature is then lowered to 60 °C, and while stirring for an additional 15 minutes, the additional ingredients—surfactants and other additives—are added to the buffer in which the cholesterol has been dissolved. The niosomes produced at this stage are stored at 4-5 °C under a nitrogen environment until usage, after which they are kept at ambient temperature for 30 min. [21]

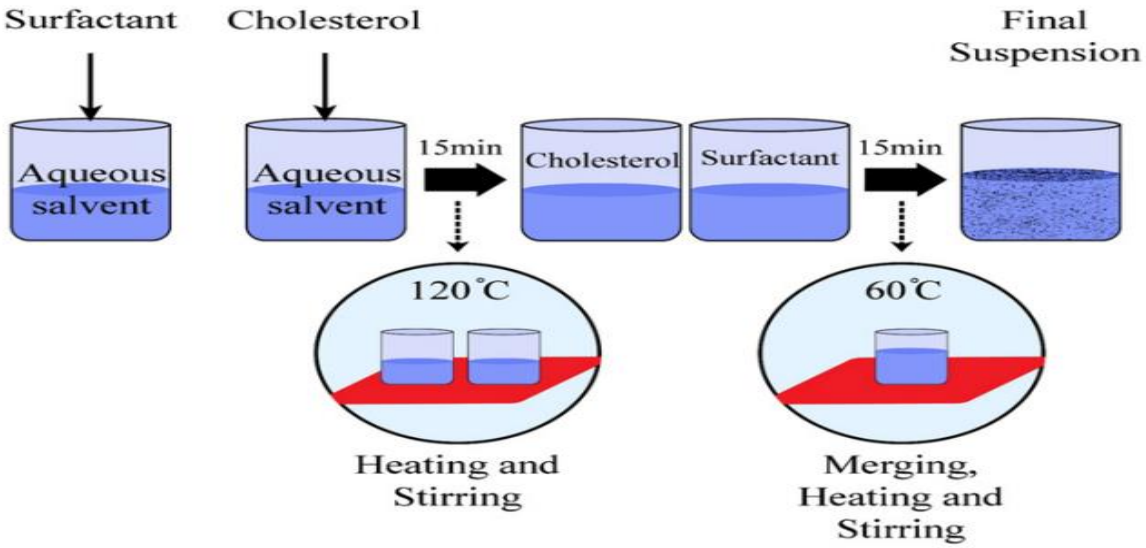


Fig. Protocol for niosome preparation through heating method.

5)Multiple Membrane Extrusion Method: By using a rotary evaporator, a surfactant, cholesterol, and dicetyl phosphate mixture in chloroform creates a thin film. Aqueous drug polycarbonate membranes hydrate the film. Extrusion of the solution and the resulting suspension through a polycarbonate membrane is done in a series of up to eight passages. For controlling niosome size, it works well. [22]

6) MICROFLUIDIZATION: This is a new method for making small MLVs. The fluid is pumped at an extremely high pressure using a micro fluidizer (10,000 psi). In micro channels within an interaction chamber, the two phases are permitted to interact at extremely high speeds. Niosomes are formed uniformly and in small numbers as a result of the high speed impact and energy involved. High repeatability is a strength of this technique. [20]

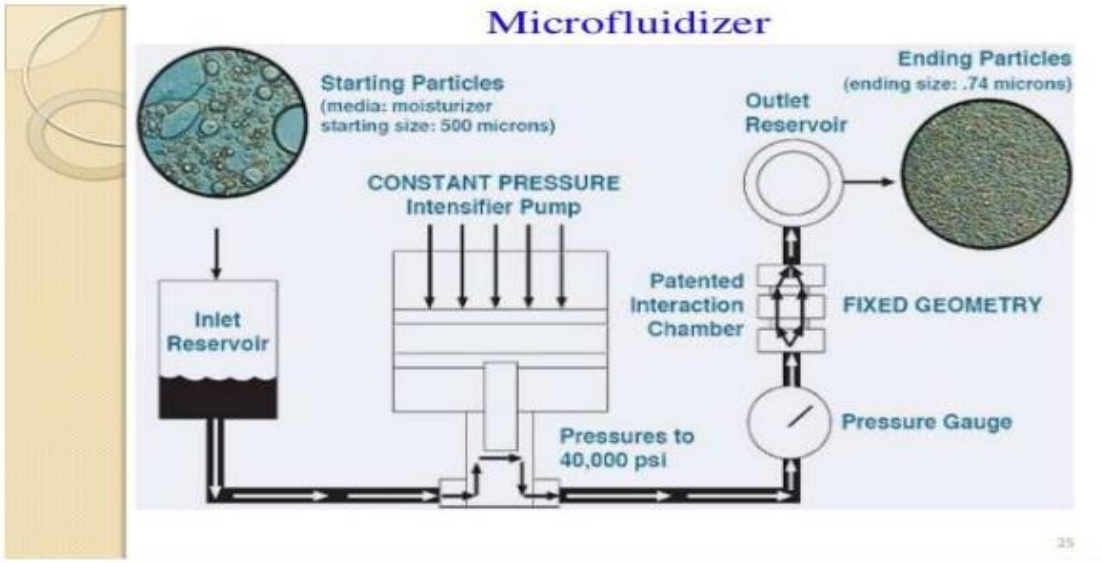


Fig.Microfludisation method

7) The Bubble Method: Niosomes are made using this technique in a single step without the need for an organic solvent. The components are all mixed together in a buffer, and the mixture is then poured into a flask with a flat bottom and submerged in a controlled-temperature water bath. The flask has three necks that are connected to the thermometer, nitrogen supply, and water-cooled reflux. To create niosomes, the dispersion is bubbled with nitrogen in this assembly after being mixed with a shear homogenizer for 15 seconds. [9]

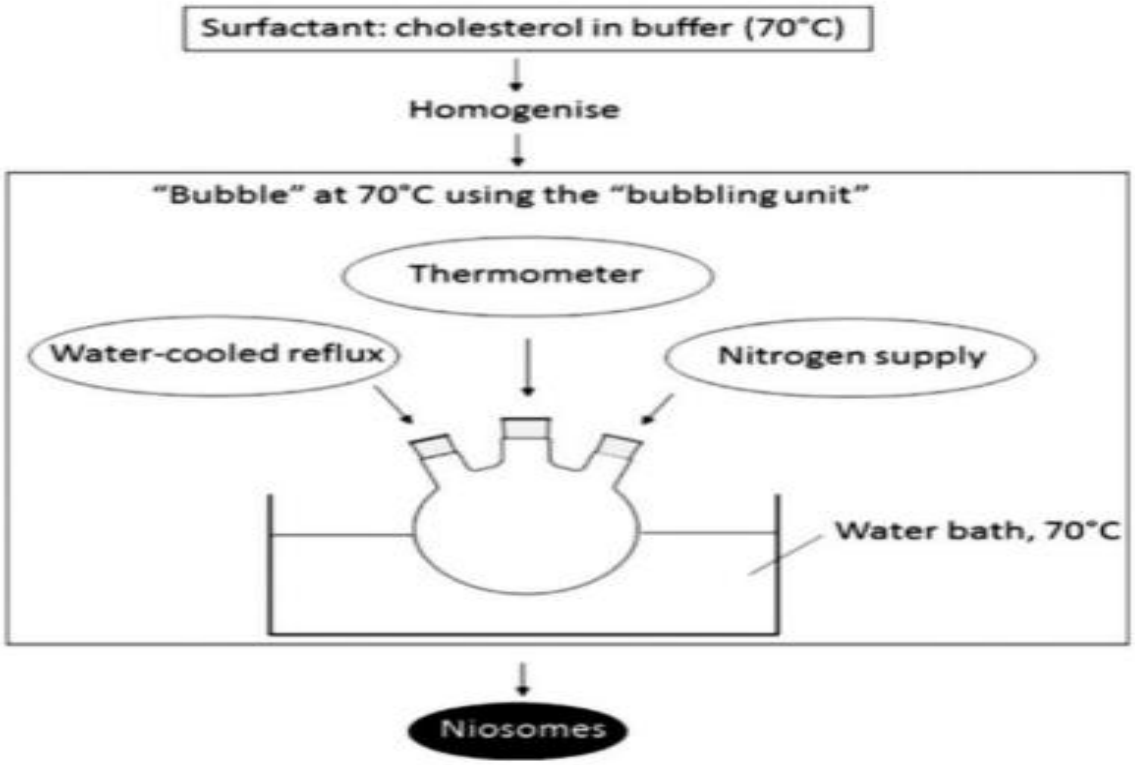


Fig.The bubble method

8) Reverse Phase Evaporation Technique (REV): A combination of ether and chloroform is used to dissolve the cholesterol and surfactant (1:1). This is combined with an aqueous phase that contains a medication, and the resulting two phases are sonicated at 4-5°C. A small amount of phosphate buffered saline is added, and then the transparent gel that has formed is further sonicated (PBS). Low pressure and 40°C are used to eliminate the organic phase. Niosomes are produced by diluting the resulting viscous niosome suspension with PBS and heating it on a water bath at 60°C for 10 min. Tween 85 was reportedly used in the manufacture of DiclofenacSodium Niosomes. [23]

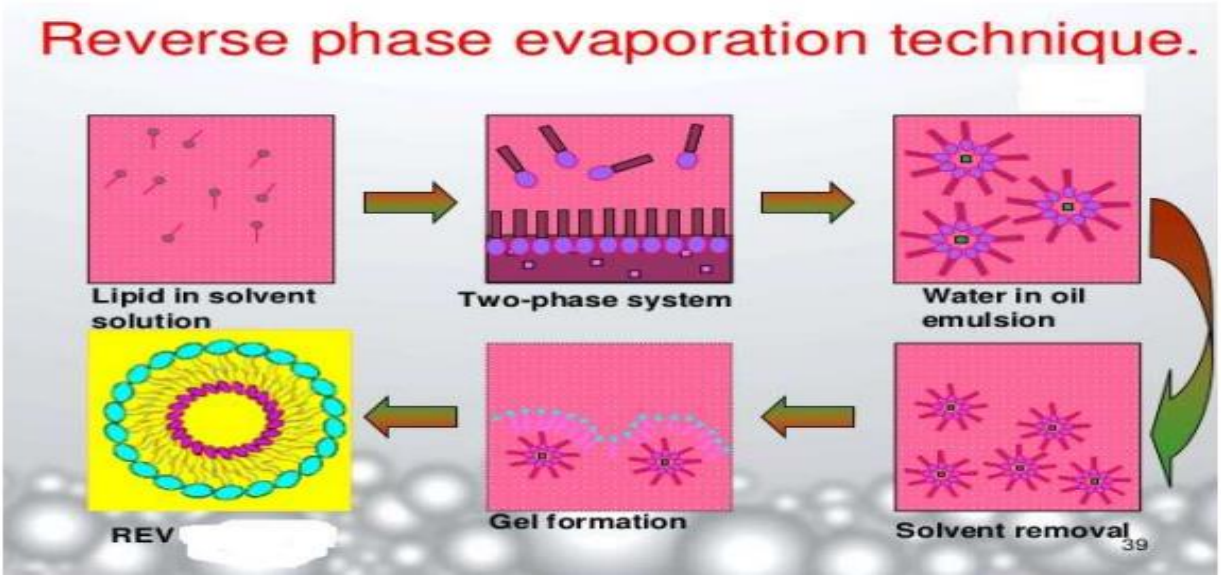


Fig. Reverse Phase Evaporation Technique

10) Formation of niosomes from proniosomes: Using the pronesome technique, a surfactant-coated water-soluble carrier, such as sorbitol or mannitol, is used. A dry formulation is created as a result of the coating process. This substance is known as "Proniosomes," and it must be hydrated before usage. The inclusion of the aqueous phase results in the formation of the niosomes. This approach offers convenience in dosing, distribution, transportation, and storage and reduces physical stability issues including the aggregation, leakage, and fusing problem while producing better outcomes than traditional niosomes. [5]

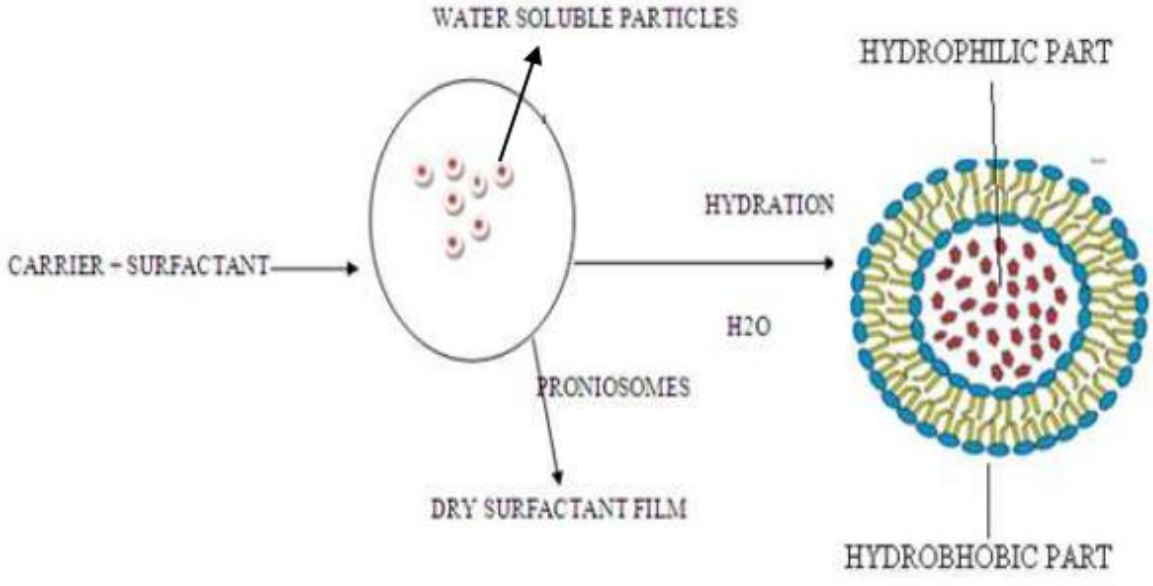


Fig. Niosome formulations from proniosome.

FACTORE AFFECTING PHYSICO-CHEMICAL PROPERTIES OF NIOSOMES

Various factors that affect the physico-chemical properties of niosomes are discussed further.

1) Nature of Surfactants: Because surface free energy decreases with increasing surfactant hydrophobicity, a rise in the HLB value of the surfactant results in an increase in the mean size of niosomes. Both a liquid and a gel state are possible for the niosome bilayers. It is dependent on the temperature, surfactant type, and cholesterol. In the gel state, alkyl chains are well organised; in the liquid state, they are chaotic. The surfactant's gel-to-liquid phase transition temperature (TC) influences entrapment effectiveness. [22]

Eg.For instance, a span 60 with a higher TC shows improved entrapment.

2) Nature of Encapsulated Drug: The medication interacts with the head groups of the surfactant and produces a charge that causes mutual repulsion between the surfactant bilayers, increasing vesicle size. The charge generation on the bilayer prevents the agglomeration of vesicles.

3) Membrane Composition: In addition to surfactants and medications, many additives can be used to create niosomes. Niosomal system's addition of cholesterol molecule gives membrane stiffness and lessens medication leakage from niosome. Cholesterol improves the hydrodynamic diameter and trapping effectiveness of niosomes. In general, cholesterol acts in two ways: on the one hand, it boosts the chain order of bilayers in the liquid state, and on the other, it lowers the chain order of bilayers in the gel state. A higher cholesterol concentration in the bilayers results in a slower rate of material release, which increases the stiffness of the resulting bilayers. The increase in entrapped volume is caused by the presence of charge, which also tends to increase the interlamellar distance between succeeding bilayers in multilamellar vesicle structures. [25]

4) Resistance to osmotic stress: Niosomes are reduced in diameter when a hypertonic salt solution is added to a suspension of niosomes. Faster release may be caused by mechanical loosening of vesicles structure under osmotic stress after an initial slow release with minor enlargement of vesicles in hypotonic salt solution.[15]

5) Temperature of Hydration: The size and form of the niosome are influenced by hydration temperature. It should be above the system's gel to liquid phase transition temperature for optimal conditions. Surfactant vesicle assembly is impacted by niosomal system temperature changes, which also lead to changes in vesicle shape. [24]

6) Method of Preparation: Comparing the hand shaking method to the ether injection method, larger vesicles (0.35-13 nm) are produced. Reverse phase evaporation can be used to create small niosomes. Greater homogeneity and tiny vesicles are produced using the micro fluidization technique. The trans membrane pH gradient (inside acidic) drug absorption procedure produced niosomes that had higher drug entrapment and retention rates. [25]

7) Stability Study: The optimised batch was kept in hermetically sealed vials at various temperatures to gauge the stability of niosomes. Since instability of the formulation would reflect in drug leakage and a decline, surface features and percentage of drug retained in niosomes and niosomes formed from proniosomes were chosen as parameters for evaluation of the stability. in terms of the medication retention rate. The niosomes were taken at regular intervals (0,1,2,and 3 months) and examined for surface characteristics, colour change, and drug retention.[26]

EVALUATION OF NIOSOMES

1. Size: Niosomal vesicles are thought to be spherical in shape, and the laser light scattering method can be used to measure their mean diameter. Electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy, and freeze fracture electron microscopy can all be used to measure the diameter of these vesicles.[25]

2)Entrapment Efficiency (EE): It is described as the proportion of the medication that the niosome has caught. First, a suitable approach is used to separate the medication that is not entrapped in order to determine the effectiveness of entrapment (e.g. by centrifugation method). The resultant solution is then divided, and the liquid supernatant is gathered. The collected supernatant is then diluted as needed and estimated using the right technique as described in the drug's monograph. Both the method of production and the physicochemical characteristics of the medication affect the entrapment efficiency (EE) and yield of niosome. [27] The formulation process and the

inclusion of cholesterol, which makes the niosomes less leaky, affect the number of double layers, vesicle size and distribution, aqueous phase entrapment efficiency, and permeability of vesicle membranes. The existence of a net charge in this process, whether positive or negative, can enhance water absorption within the double layer. Such hydration causes an increase in loaded hydrophilic molecules relative to uncharged vesicles, which are likely found both within the bilayer and in the centre of aggregated formations. [28]

3)Bilayer Rigidity and Homogeneity: The existence of a net charge in this process, whether positive or negative, can enhance water absorption within the double layer. Such hydration causes an increase in loaded hydrophilic molecules relative to uncharged vesicles, which are likely found both within the bilayer and in the centre of aggregated formations. [29]

4) Number of lamellae: Number of lamellae of niosomes are determined by nuclear magnetic resonance (NMR) spectroscopy, X-ray scattering and electron microscopy. [25]

5) In-vitro release: Dialysis tubing is a tool used in in-vitro release rate studies. distilled water is used to clean and soak a dialysis sac. A bag constructed of tubing is pipetted with the vesicle suspension solution and then sealed. The vesicles are contained in the bag and are incubated at a temperature of 25°C or 37°C in a 250ml beaker containing 200ml of buffer solution with constant shaking. The buffer is subjected to periodic drug content analysis using the appropriate test method. [30]

APPLICATION

1) Niosomes as drug delivery systems: A targeted drug delivery system's main goals are to lessen the medication's toxicity and increase selectivity toward the targeted tissue. Paul Ehrlich created a drug delivery system in 1909 that allows the drug to be delivered directly to diseased cells and tissues. Various systems such as Immunoglobulins, liposomes, microspheres and Niosomes were employed as a means of delivering the medicine to the intended tissues and cells. Due to their distinctive qualities and stability characteristics, liposomes and niosomes received particular attention among these. Drugs that are lipophilic and hydrophilic can both be captured by niosomes. Niosomes function better as a medication delivery system to tumours, the liver, and the brain because they include non-ionic surfactant and lipid. In order to treat cancer, parasite, viral, and other microbial disorders more effectively, they are frequently utilised nowadays. [10]

2) Magnetic Niosomes: Niosomes have potential for use in different applications, particularly in the treatment of cancer, when combined with magnetic targeting and drug delivery.[31] The fundamental idea behind employing magnetic materials in cancer therapy is to use extracorporeal magnets to steer drug-loaded magneto-niosomes toward a particular organ or tissue in the body.[32] A excellent illustration of this capability of niosomal systems is the formulation of ocaliz in magnetically controlled drug targeting of doxorubicin.[33]

3)Delivery of Peptide Drugs: It has long been difficult to avoid the enzymes that would break down peptides used in oral medication administration. It is being researched if niosomes may successfully shield peptides from gastrointestinal peptide degradation. An in vitro investigation using oral administration of a vasopressin derivative trapped in niosomes revealed that drug entrapment dramatically improved the peptide's stability. [34]

4)Transdermal drug delivery by niosomes: The main disadvantage of transdermal drug delivery systems is how slowly the drug permeates the skin; however, this disadvantage can be overcome through transdermal drug delivery of drugs contained in niosomes. Erythromycin was found to penetrate the skin more quickly when administered as niosomes to hairless mice during transdermal application. The results of the confocal microscopy study and data from various evaluating parameters showed that non-ionic vesicles targeted the drug to the pilo sebaceous glands, resulting in an earlier effect. [35]

5)Leishmaniasis: A parasite from the genus Leishmania infects the liver and spleen cells to cause leishmaniasis, a disease. Niosomes were used in tests to demonstrate that it was possible to administer higher doses of the medication without causing the side effects, allowing for greater therapeutic efficacy.

6) Immunological application of niosomes: For research into the nature of the immune response triggered by antigens, niosomes have been employed. Drugs can be directed at organs other than the reticulo-endothelial system via niosomes. Niosomes can be directed to particular organs by attaching a carrier system (such as antibodies) to them because

immunoglobulins bind to the lipid surface of niosomes with ease. [36]

7) Niosomes as carriers for Hemoglobin: Niosomes are capable of transporting haemoglobin. Niosomal suspension's visible spectrum is placed on free hemoglobin's. Because vesicles are oxygen permeable, they can change the haemoglobin dissociation curve much like unencapsulated haemoglobin may. [15]

8) To Increase Oral Bioavailability: According to reports, the formulation of niosomes increased the oral bioavailability of griseofulvin and acyclovir compared to the drug alone. Similar to this, when given to rats as a micellar solution along with the POE-24- cholesteryl ester, poorly absorbed peptide and ergot alkaloid can have their absorptivity increased.[37]

9) Ophthalmic drug delivery: Due to tear formation, the impermeability of the corneal epithelium, non-productive absorption, and transient residence time, it is challenging to achieve optimal bioavailability of drugs from ocular dosage forms as ophthalmic solution, suspension, and ointment. However, several vesicular systems, such as niosomes and liposomes, are suggested for usage in experimental settings in order to attain optimal drug bioavailability. [23]

10)Localized Drug Action: Since their size and low porosity through connective tissue and epithelium keep the drug isolated at the site of administration, Niosome drug delivery is one method to achieve ocalize pharmacological action. The efficacy and potency of the medicine are increased as a result of ocalize pharmacological action, and its systemic harmful effects, such as Mononuclear cells take up antimonials that are contained within niosomes, which causes the medication to ocalize, increase in potency, and then reduce both in dose and toxicity24. Niosomal drug delivery technology is in in its early stages of development, although it has showed promise in leishmaniasis treatment and cancer chemotherapy. [38]

CONCLUSION

Since ancient times, herbal medicines have been used extensively around the world. Both doctors and patients now realise their superior therapeutic value due to the fact that they have less side effects than modern medications. By combining ayurvedic medicines into contemporary dose forms, they can be used more effectively and in better form. However, in order to maximise patient compliance and prevent recurrent administration, phytotherapeutics require a scientific strategy to distribute the components in a novel way. The herbal medications can be included in NDDS, allowing us to deliver the right dosage to the target site. We can therefore draw the conclusion that NDDS for herbal medications will be a ground-breaking application in the traditional herbal formulations, saving time in preparation and improving patient compliance. Niosomes may increase the bioavailability and targeting of medications, as well as lessen their toxicity and side effects. It is possible to improve the niosome's capacity for drug delivery by using cutting-edge ideas like proniosomes.

REFERENCE

[1] Chauhan Pradeep, Tyagi Bharat Kumar Herbal Novel Drug Delivery System and Transforsomes Journal of Drug Delivery & Therapeutics. 2018; 8(3): 162-168

[2] S. Rajalakshmi, Niraj Vyawahare, Current development in novel drug delivery systems of bioactive molecule plumbagin 2018, VOL. 46, NO. S1, S209–S218

[3] RABIA NUR UN, F. BARIS BARLAS 2 Phytoniosomes: In Vitro Assessment of the Novel Nanovesicles Containing Marigold Extract. International Journal of Polymeric Materials and Polymeric Biomaterials, [Dicle University] at 23:24 23 June 2015

[4] Prajakta N. Dongare 1, Anuja S. Motule 1, Recent development in novel drug delivery systems for delivery of herbal drugs: An updates, GSC Advanced Research and Reviews, 2021, 08(02), 008–018

[5] Didem Ag Seleci, Muharrem Seleci, Niosomes as Nanoparticular Drug Carriers: Fundamentals and Recent Applications, Institute for Technical Chemistry, Leibniz University Hannover, 30167 Hannover, Germany Volume 2016, Article ID 7372306, 13 pages.

[6] Suvarna G. Bhokare*1 , Chaitali C. Dongaonkar2 ,Herbal Novel Drug Delivery-A Review, WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCE ,Volume 5, Issue 8, 593-611 ,2016.

[7] Venkata Ramesh Yasam, Satya Lavanya Jakki, A review on novel vesicular drug delivery: proniosomes, Drug Delivery, 21:4, 243-249, 2014.
[8] Ali Bagheri, Boon-Seang Chu and Harisun Yaakob, Niosomal Drug Delivery Systems: Formulation, Preparation and Applications, World Applied Sciences Journal 32 (8): 1671-1685, 2014
[9] Anchal Sankhyan and Pravin Pawar, Recent Trends in Niosome as Vesicular Drug Delivery System Journal of Applied Pharmaceutical Science 02 (06); 2012: 20-32
[10] Chanchal Joy, Smitha K. Nair*, Niosomes as Nano-carrier Based Targeted Drug Delivery System, Journal of Drug Delivery & Therapeutics. 2021; 11(4-S):166-170
[11] Harini Chowdary Vadlamudi, 1 M. Sevukarajan, Niosomes Drug Delivery System- A Review Indo American Journal of Pharmaceutical Research. 2012:2(9)
[12] Madhav NVS* and Saini A, Niosomes A Novel Drug Delivery System, IJRPC 2011, 1(3)
[13] Kamlesh Maurya1, Arpita Singh1, Niosomes: Classification, preparation and application Int J Indig Herbs Drugs 2021; 6(1):29–32
[14] Kauslya Arumugam1*, Borawake Payal D1, Niosomes: A Novel Carrier Drug Delivery System, Journal of Drug Delivery & Therapeutics. 2021; 11(1):162-170
[15] Patil Abhishek S.* ; Shaikh Bilal J.; Niosomes-A Promising Drug Delivery carrier, Int. Journal of Pharmaceutical Sciences and Medicine (IJPSM), Vol.6 Issue. 6, June- 2021, pg. 15-27
[16] Rageeb Md. Usman*, Prasanna R, NIOSOMES: A NOVEL TREND OF DRUG DELIVERY Md. ejbps, 2017, Volume 4, Issue 7, 436-442.
[17] Sanklecha VM1 *, Pande VV1, Review On Niosomes, Austin Pharmacol Pharm - Volume 3 Issue 2 – 2018
[18] *Nazia Khanam1, Md. Irshad Alam, RECENT TRENDS IN DRUG DELIVERY BY NIOSOMES: A REVIEW, Asian Journal of Pharmaceutical Research and Development Vol.1 (3) May– June 2013:115-122
[19] Rohit, S. C. Arora, Rashmi Manchanda* and Rajesh Manchanda, Natural Polysaccharides Based Niosoms: A Promising Drug Delivery System, world journal of pharmaceutical research, Volume 11, Issue 3, 768-784.
[20] NareshKalra, G. jeyabalan2Niosomes: A Versatile Drug Delivery System. SunRise University, Alwar, Rajasthan, India. 2016 Nov-Dec RJLBPCS 2(4) Page No.44
[21] Saeid Moghassemi , Afra Hadjizadeh Nano-niosomes as nanoscale drug delivery systems:An illustrated review, Journal of Controlled Release 185 (2014) 22–36
[22] Kaur Dhanvir*, Kumar Sandeep Niosomes: Present scenario And Future Aspects Journal of Drug Delivery & Therapeutics. 2018; 8(5):35-43
[23] Sudhir Kumar Ray1, Nargish Bano1, Tripti Shukla*1 Niosomes: as novel vesicular drug delivery system, Journal of Drug Delivery & Therapeutics. 2018; 8(6):335-341
[24] Jessy Shaji1 and Akshay Shah1 Niosoms:A Novel Drug Delivery System, world journal of pharmaceutical research Volume 4, Issue 6, 853-876.
[25] Sultan Ahmad, Deepak Teotia and Kapil Kumar*, Niosoms-A Promising carrier for drug delivery July - August 2018; 7(4): 3015-3021
[26] V. Pola Chandu1*, A.Arunachalam1 Niosoms:A novel drug delivery system International Journal Of Novel Trends In Pharmaceutical Science , Volume 2 | Number1 | Feb| 2012.
[27] Sahin N. O., Nanomaterials and Nanosystems for Biomedical Applications, Chap. 4, ed. by Mozafari M. R., Springer, The Netherlands, 2007, pp. 67—81.
[28] Bhaskaran S., Lakshmi P. K., Acta Pharm. Sci., 51, 27—32 (2009).
[29] Pravina Gurjar, NiveditaNaik, Sujay Chouksey Niosomse:A Promising Pharmaceutical Drug Delivery, Int.J.Pharm Anal Vol: 2 Issue:5 Page:425-431
[30] Sharma Rajni1*, Dua Jagdeep Singh 1, Advancement in Novel Drug Delivery System: Niosomes,Journal of Drug Delivery & Therapeutics. 2019; 9(3-s):995-1001
[31] Kong, M., H. Park, C. Feng, L. Hou, X. Cheng and X. Chen, 2013. Construction of hyaluronic acid noisome as functional transdermal nanocarrier for tumor therapy. Carbohydrate Polymers, 94(1): 634-641.
[32] Widder, K., G. Flouret and A. Senyei, 1979. Magnetic microspheres: synthesis of a novel

parenteral drug carrier. Journal of Pharmaceutical, 68(1): 79-82.

[33] Tavano, L., M. Vivacqua, V. Carito, R. Muzzalupo, M.C. Caroleo and F. Nicoletta, 2013. Doxorubicin loaded magneto-niosomes for targeted drug delivery. Colloids and surfaces. B, Biointerfaces, 102: 803-807.

[34] Navneet Kumar Verma, Asha Roshan,Niosomes and Its Application- A Review, IJRPLS, 2014, 2(1): 182-184

[35] *Nazia Khanam1, Md. Irshad Alam2, Recent Trends In Drug Delivery By Niosoms: A Review, Asian Journal of Pharmaceutical Research and Development Vol.1 (3) May– June 2013:115-122

[36] V. Kusum Devi, Nimisha Jain, Kusum S. Valli, Importance of novel drug delivery systems in herbal medicines, Pharmacognosy Reviews | January-June 2010 | Vol 4 | Issue 7

[37] Rampal RAJERA, Kalpana NAGPAL, Shailendra Kumar SINGH,Niosomes: A Controlled and Novel Drug Delivery System Biol. Pharm. Bull. 34(7) 945—953 (2011)

[38] V.Shakya, B.K.Bansal Niosoms: A Novel Trend In Drug Delivery International Journal of Research and Development in Pharmacy and Life Sciences June - July, 2014, Vol. 3, No.4, pp 1036-1041