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A Novel Drug Delivery System: Niosomes Review

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***Abstract*: Niosomes are microscopic vesicles of non-ionic surfactant that are created when the surfactant self- assembles. One intriguing novel drug delivery strategy is niosomal delivery. Liposomes and niosomes are different chemically, yet they share comparable morphological characteristics. Non-ionic surfactants form niosomal vesicles, while lipids form liposomal vesicles. Because surfactants have a stronger chemical stability than lipids, niosomes are superior than liposomes. The notion of niosomes, their benefits advantages, disadvantage, and their composition, their preparation process, the variables affecting niosomal formulation and characterisation, and their applications are the main topics of this review paper. Numerous illnesses, including Parkinson's disease, cancer, migraines, psoriasis, and leishmaniasis, can be treated with niosomes. Niosomes are a useful tool for diagnosis.**

***Keywords*: niosomes, surfactant, bilayer, method of preparation, vesicles, application.**

1. Introduction

When Paul Ehrlich, a researcher, conceived of a drug delivery system that would target infectious cells directly in 1909, he began the process of establishing targeted delivery. We shall now examine the concept of drug targeting. The capacity to direct a therapeutic medication to a desired precise spot to demonstrate the action on targeted tissue can be expanded upon as drug targeting [1]. Niosomes are tiny vesicles of non-ionic surfactant that are created when the surfactant self-assembles. A promising new medicine delivery strategy is niosomal drug delivery. Although their chemical makeup is different, niosomes and liposomes share comparable physical characteristics. Liposomal vesicles are made of lipids, whereas niosomal vesicles are made of non-ionic surfactants. Since surfactants have a higher chemical stability than lipids, niosomes are preferable than liposomes. When non-ionic surfactant of thealkyl or dialkylpolyglycerol ether class is mixed with cholesterol and then hydrated in aqueous medium, niosomes are created [2]. The method of preparation technique utilized to create niosomes can determine either they are unilamellar or multilamellar [3]. Therefore, the hydrophobic drugs are embedded in the bilayer itself, while the hydrophilic substance are held inside the space comprised in the vesicle. Niosomal technology has a broad range of applications and is useful in the treatment of certain illnesses. Niosomes have the potential to direct drugs and vaccines into the reticulo-endothelial system, which is one of their most advantageous properties. Niosomal vesicles are selectively taken up by the reticulo-endothelial system (RES). Circulating serum factors known as opsonins regulate noisome uptake by marking them for clearance.

A. *Merits of Niosomes*

- To get the desired benefits, a lower dose is more effective.
- Due to their hydrophilic character, niosomes are osmatically active and the stable form of our hydrophilic systems.
- The medicine they entrapped tends to get more stable because of its hydrophilic character.
- Can improve how well medications penetrate the skin.
- Vesicles serve as a depot for the drug's steady release.

B. *Demerits of Niosomes*

- Might need particular instruments
- High cost of production
- Blending
- Leakage of medication that is trapped

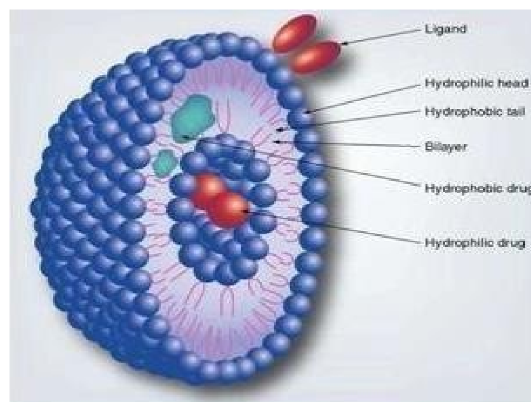

Fig. 1. Structure of Niosomes [39]

The amphiphilic niosome vesicles, which act as non-ionic surface acting agents like span - 60, are stabilized by the addition of cholesterol and a certain quantity of anionic surfactant, like diacetylphosphate [5].

C. *Various types of Niosomes*

Niosomes can be categorized into three types according to the size of their vesicles. The vesicles inconsideration are classified as small (SUV, size = 0.025-0.05 µm), large (LUV, size = 0.10 µm), and multilamellar (MLV, size = 0.05 µm).

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D. Composition of Niosomes

The following are some of the components that are used in the preparation of niosomes:

1. Cholesterol
2. Non ionic surface acting agent

1) Cholesterol

These are the derivatives of steroids that are utilized to give the right amount of stiffness, flexibility, and shape [5].

2) Non ionic surface acting agent

A specific non-ionic surfactant example that is used in the niosome synthesis process. Eg. Spans (span 20, 40, 60, 80, 85)

Tweens (tween 20, 40, 60, 80)

Brijs (brij 30, 35, 52, 58, 72, 76

There is a hydrophilic head and a hydrophobic tail to the non-ionic surfactant [5].

E. Method of Preparation

The vesicles' membrane permeability, entrapment effectiveness of the aqueous phase, size, size distribution, and number of bilayers are all influenced by the preparation method.

1. Sonication
2. Micro fluidisation method
3. Hand shaking method (Thin film hydration technique)
4. Trans-membrane pH gradient (inside acidic) drug uptake process (remote loading)
5. Reverse phase evaporation technique (REV)
6. Ether injection method
7. Multiple membrane extrusion method
8. The bubble method

F. Preparation of Small Unilamellar Vesicles

1) Sonication

Cable describes the process of sonicating a solution to produce vesicles. In a 10 ml glass vial containing amixture of surfactant and cholesterol, an aliquot of drug-containing buffer solution is added. To create niosomes, the mixture is then sonicated for three minutes at 60ºC in a sonicator equipped with a titanium probe [6].

2) Micro fluidisation method

Within the interaction chamber, two fluidized streams flow forward through a carefully defined microchannel and interact at extremely high velocities. In this case, a common gateway is set up so that the energy fed into the system stays in the region where niosomes form. Better reproducibility, reduced size, and increased uniformity are the end results [7].

G. Preparation of Multilamellar Vesicles

1) Hand shaking method (Thin film hydration technique)

In a volatile organic solvent such as menthol, diethyl ether, or chloroform, surfactant and cholesterol are dissolved. A small layer of solid mixture remains on the flask wall after the organic solvent is evaporated using a rotating flash evaporator at room temperature (20ºC). After that, the dried surfactant film is gently agitated and rehydrated with an aqueous medication solution at the temperature of the surfactants employed for the designated amount of time (the "time of hydration"). This process forms multilamellar niosomes. The process of creating thermosensitive niosomes involves evaporating an organic solvent at 60ºC, leaving a thin coating on the rotary flask evaporator's wall. Next, the drug- containing aqueous solution is gradually added while shaking at ambient temperature and then subjected to sonication [8].

2) Trans-membrane pH gradient drug uptake process

Chloroform dissolves cholesterol and surfactant. To create a thin layer on the round-bottom flask wall, the solvent is then evaporated at a lower pressure. Through vortex mixing, 300 mM citric acid (pH 4.0) is added to the film to hydrate it. After three cycles of freezing and thawing, the multilamellar vesicles are subjected to sonication. An aqueous solution containing 10 mg/ml of the medication is vortexed and added to this niosomal suspension. After that, 1M disodium phosphate is added to the sample to bring its pH up to 7.0–7.2. In order to create the necessary multilamellar vesicles, this mixture is later heated at 60°C for 10 minutes [9].

H. Preparation of Large Unilamellar Vesicles

1) Reverse phase evaporation technique (REV)

Utilizing a mixture of ether and chloroform, cholesterol and surfactant are dissolved in this process. Thisis combined with a drug-containing aqueous phase, and the two resultant phases are sonicated at 4-5°C.A tiny quantity of phosphate buffered saline is added, and the clear gel that has formed is subsequently subjected to more sonication. Under low pressure and at 40°C, the organic phase is eliminated. To produce niosomes, the resultant viscous niosome suspension is heated in a water bath at 60°C for 10 minutes after being diluted with phosphate-buffered saline [10].

2) Ether injection method

In this approach, surfactant that has been dissolved in diethyl ether is added to warm water that is kept at 60 degrees Celsius. Using a 14-gauge needle, the ether solution containing surfactant is injected into an aqueous solution of the substance. Ether vaporization results in the formation of single-layered needles. The vesicle's diameter ranges from 50 to 1000 nm, depending on the circumstances [11].

I. Miscellaneous

1) Multiple membrane extrusion method

This procedure can be used to prepare the vesicles to the desired size. Up to eight channels can be created by connecting polycarbonate membranes in sequence. Evaporation is used to create a thin coating of the mixture of dicetyl phosphate, cholesterol, and surfactant. After that, the drug-containing aqueous solution is used to rehydrate the film. Using C16G12, the final solution is extruded through a polycarbonate membrane (0.1µm nucleophore) [12].

2) The bubble method

It is an innovative approach for producing niosomes in a single step without the use of organic solvents. The temperature of the bubbling unit is controlled by three necks on a round-bottomed flask that is submerged in water. Water-cooled reflux is located in the first neck; a thermometer is located in the second neck; and a nitrogen supply is located in the third neck. At 70ºC, cholesterol and surfactant are distributed in a PH 7.4 buffer. A high shear homogenizer is used for 15 seconds to

blend the dispersion. At 70ºC, nitrogen gas instantly bubbles [13].

3) Niosomes preparation using polyoxyethylene alkyl ether

Alternative methods can be used to modify characteristics such as the quantity and size of bilayers of polyoxyethylene alkyl ethers and vesicles containing cholesterol. Large multilamellar vesicles can be generated from small unilamellar vesicles when the temperature rises beyond 600°C, and multilamellar vesicles can be converted back into unilamellar ones by vigorous shaking at ambient temperature. Since it is known that polyethylene glycol (PEG) and water higher temperatures demix due to a breakdown of hydrogen bonding between water and PEG moieties, it is the characteristics for polyoxythelene alkyl ether surfactants to transformation from unilamellar to multilamellar vesicles at higher temperature [14].

J. Separation of Entrapped Drug

The unentrapped medication can be extracted from the niosomal vesicles using a number of methods, including,

1. Dialysis
2. Gel filtration
3. Centrifugation

1) Dialysis

Dialysis of the aqueous niosomal dispersion is performed using normal saline, phosphate buffer, orglucose solution in dialysis cellophane tubing [15], [16].

2) Gel filtration

By running the drug through a sephadex G50 column and eluting it with either normal saline or phosphate buffered saline, the unentrapped drug from the niosomal dispersion is eliminated.

While thefree medication remains on the column, the vesicles percolate down it [17], [18].

3) Centrifugation

In either water or saline, the niosomal dispersion is centrifuged. When a niosomal suspension free of unentrapped medication is obtained, the sedimented pellet of niosomes is cleaned and resuspended. The medication that is not entrapped in the supernatant is separated [19].

K. Characteristics of Niosomes

1. Size
2. Vesicles charge
3. Bilayer formation
4. Number of lamella
5. Membrane rigidity and homogeneity
6. Entrapment efficiency
7. In vitro drug release
8. Stability studies

1) Size

when it is assumed that niosomal vesicles have a spherical shape, a number of methods, including laser light scattering, electron microscopy, molecular sieve chromatography, ultracentrifugation, photon correlation microscopy, optical microscopy, and freeze fracture electron microscopy, can be used to determine their mean diameter [20]-[22].

2) Vesicles Charge

A significant factor affecting the stability and behavior of niosomes is the vesicle surface charge. In terms of stability against aggregation and fusion, charged niosomes are reported to be more stable than uncharged niosomes. The zeta potential obtained through dynamic light scattering or micro electrophoresis can be used to assess the surface potential of niosomes. As an alternative, PH-sensitive fluorophores can be employed [23].

3) Bilayer Formation

The creation of x-cross during the assembly of non-ionic surfactants under light polarization microscopy is a characteristic of bilayer vesicle formation [24].

4) Number of Lamella

Small angle X-ray scattering, electron microscopy, and NMR spectroscopy are used to determine the number of lamellae in vesicles [25].

5) Membrane Rigidity and Homogeneity

Niosome biodistribution and biodegradation are influenced by the stiffness of the membrane. It is possible to estimate the bilayer stiffness of vesicles by measuring the fluorescence probe's mobility in relation to temperature. P-NMR, differential scanning calorimetry (DSC), Fourier transform-infrared spectroscopy (FT-IR), and fluorescence resonance energy transfer (FRET) can all be used to determine the homogeneity of a membrane [26].

6) Entrapment Efficiency

As mentioned above unentrapped drug is separated by dialysis, centrifugation, gel filtration, and/or after niosomal dispersion is prepared. full vesicle disruption with 0.1% Triton X-100 or 50% n-propanol is carried out to estimate the amount of medication that remained trapped in niosomes, and the reaction mixture is subsequently examined using the suitable assay technique for the drug. The definition of entrapment efficiency (EF) is as follows: [27]

EF = (quantity entrapped/total quantity) x 100.

7) In Vitro Drug Release

- *Dialysis*

It is the most simplest technique for figuring out the drug's niosomal-loaded release kinetics invitro. Tubing for dialysis is utilized. The dialysis sack is hermetically sealed and filled with niosomal suspension. To do dialysis, immerse the sack in 200 milliliters of buffer solution at either 25 or 27 degrees Celsius while stirring continuously. Samples are taken out on a regular basis, and an appropriate technique is used to analyze the drug content [28].

- *Reverse Dialysis*

Niosomes are added to several tiny dialysis tubes along with 1 milliliter of dissolving liquid. Following that, the niosomes are removed from the dissolving media [28].

- *Franz Diffusion*

In a Franz diffusion cell, niosomes are dialyzed against appropriate dissolving fluid across a cellophane membrane at ambient temperature. The samples are taken out on a regular basis, and their drug content is determined by analysis. FRET is now utilized to track the release of material enclosed inniosomes [28].

8) Stability Studies

Constant drug concentration and particle size of the encapsulated drug are signs of niosome stability. Cholesterol is a surfactant whose type and concentration affect niosome stability. 29 For example: At normal temperature, sonicated spherical niosomes remain stable. Atambient temperature, sonicated polyhedral niosomes are unstable; however, at the phase transition temperature, they become stable.

L. Factors Affecting Niosomes Formulation

1. Drug
2. Nature and type of surfactant
3. Cholesterol content and charge
4. Resistance to osmotic stress
5. Temperature of hydration

1) Drug

When a drug is trapped in niosomes, the size of the vesicle rises, most likely due to an increase in the charge and mutual repulsion of the surfactant bilayers or an interaction between a solute with head groups of surfactants. While a medication gets trapped in the longer PEG chains. Thus, there is less of a tendency for vesicles coated with polyoxyethylene glycol (PEG) to enlarge in size. The drug's hydrophilic lipophilic balance influences the degree of entrapment [29].

2) Nature and Type of Surfactant

The mean size of niosomes increases with an increase in the hydrophilic-lipophilic balance (HLB) of surfactants, such as Span 85 (HLB 1.8) to Span 20 (HLB 8.6).

Proportionately, as the surface free energy of surfactants falls as their hydrophobicity rises. The bilayers of the vesicles are either in the so-called liquid state or the gel state, depending on temperature, the kind of lipid or surfactant, and the presence of additional components like cholesterol. The bilayers will be in the liquid state when their structure is chaotic and in the gel state when alkyl chains are present in a well-organized structure. The phase transition temperature of surfactants has an impact on entrapment efficiency as well; for instance, Span 60 has a higher [30].

3) Cholesterol Content and Charge

Cholesterol incorporation enhances the niosomes' hydro-dynamic diameter and entrapment efficiency. There are two ways that cholesterol works.

1. It makes liquid state bilayers' chain order higher, and
2. It makes gel state bilayers' chain order lower.

Raising the cholesterol content makes the bilayers more stiff and slows the rate at which the encapsulated material releases [31].

4) Resistance to Osmotic Stress

Niosome mixtures observe a decrease in diameter when hypertonic salt solution is added. Most likely as a result of the eluting fluid's inhibition in the hypotonic salt solution vesicles, there is a gradual release at first, accompanied by a small enlargement of the vesicles; this could be because the vesicles' structure chemically loosens under osmotic stress [32].

5) Temperature of Hydration

The temperature of hydration has an impact on the niosome's size and shape. The temperature at which gel liquid phases change should be higher than the hydration temperature. The assembly of surfactants into vesicles and the alteration of vesicle shape are impacted by temperature changes. The alteration is also explained by the hydration time and medium volume. When the hydration temperature, duration, and medium volume are not chosen properly, fragile niosomes and drug leakage issues may occur [33].

M. Application of Niosomes

- It has been performed to study the immunological response that antigens elicit.
- It's commonly used to study medication targets.
- It can be used as an anti-neoplastic in the treatment of cancer.
- Hemoglobin can be carried by niosomes.
- It is generally applicable as a diagnostic tool.
- It can provide effective treatment and delivery of drugs for the retinal artery.

N. Immunological Application of Niosomes

Niosomes have been utilized to explore the nature of the immune response induced by antigens. According to reports, niosomes are an efficient adjuvant for immunological stability, less toxicity, and selectivity [33].

1) Sustained Release

It can occur to use the action of sustained release to medications with low therapeutic index and low solubility [34].

2) Localized Drug Action

Because of niosomes' small size and low penetration into connective tissue and epithelium, niosomal dosage forms are one method for achieving localized pharmacological action at the site of administration. This results in enhancing of efficacy and potency of the drugs and also minimizes its systemic harmful effects e.g. Mononuclear cells absorb the anti monials contained in niosomes, which causes the drug to localize, become more potent, and hence become less toxic and dose-related [35], [36].

O. Transdermal Delivery of Drugs by Niosomes

Transdermal drug administration using niosomes has increased the penetration rate because the main cause of the drug's extended skin penetration drawback of the transdermal delivery system for different dose forms. Using hairless mice, different formulations of erythromycin, including niosomes, were evaluated for topical distribution. Through confocal microscopy and the results of the investigations, it was found that non-ionic vesicles could be designed to specifically target pilosebaceous glands [37].

P. Leishmaniasis Therapy

The majority of medications directed to treat leishmaniasis are derivatives of antimony. At larger dosages, these medications can cause liver, heart, and renal problems. Utilizing niosomes as a drug delivery system demonstrated that side effects could be overcome at larger concentrations as well, leading to increased treatment efficacy [38].

Q. Routes of Application of Niosomes Drugs

Intravenous route:

Examples: Doxorubicin, Methotrexate, insulin, Cisplantin, Hydrochloride.

Inhalation:

Examples: All trans-retionic acids.

Transdermal route:

Examples: Ketoconazole, Piroxicam, Estradiol, Enoxacin.

Ocular route:

Examples: Timolol maleate, Cyclopentolate.

Nasal route:

Examples: Sumatriptan, Influenza viral vaccine.

2. Conclusion

The niosomal drug delivery system indicates the significant innovations in drug delivery systems. The concept of using drugs to target the niosomes and integrate them into them Researchers and academicians generally agree that niosomes are particular to the place. In comparison to liposomes, they are alternative vesicular systems that offer a number of benefits, including affordability and stability. A lot of study needs to be done to properly investigate the potential of this novel drug delivery system, as niosomes offer a promising drug delivery systems.

References

[1] Buckton G. Switzerland: Academic Publishers; 1995. Interfacial phenomena in Drug Delivery and Targeting; pp. 154–5.

[2] Handjani-Vila RM, Ribier A, Rondot B, Vanlerberghe G. Dispersions of lamellar phases of non-ionic lipids in cosmetic products. Int J Cosmetic Sci. 2003;1:303–14.

[3] Weissman G, Bloomgarden D, Kaplan R, Cohen C, Hoffstein S, Collins T, et al. A general method for the introduction of enzymes, by means of immunoglobulin-coated liposomes, into lysosomes of deficient cells. Proc Natl Acad Sci. 1975;72:88–92.

[4] Baillie AJ., Florence AT., Hume LR., Muirhead GI., RogersonA., The arrangement and properties of niosomes non ionic surfactant vesicles. J. Pharm. Pharmacol. 1985, 37:863-868.

[5] Gayatri Devi S, Venkatesh P, Udapa N. Niosomal sumatriptan succinate for nasal organization.Int J Pharm Sci 2000;62:479-81.

[6] Baillie AJ, Florence AT, Hume LR, Muirhead GT, Rogerson A. The preparation and properties of niosomes-non-ionic surfactant vesicles. J Pharm pharmacol. 1985;37:863-868.

[7] Khandare JN, Madhavi G, Tamhankar BM. Niosomes novel drug delivery system. East Pharmacist. 1994;37:61–4.

[8] Vijay S Jatav, Santosh K Singh, Pankaj Khatri, Ashish K Sharma, Rambir Singh. Formulation and in-vitro evaluation of Rifampicin-Loaded Niosomes. J. Chem. Pharm. Res. 2011; 3(2):199-203.

[9] Mayer LD, Bally MB, Hope MJ, Cullis PR. Uptake of antineoplastic agents into large unilamellar vesicles in response to a membrane potential. Biochem Biophys Acta. 1985;816:294–302.

[10] Naresh RA, Chandrashekhar G, Pillai GK, Udupa N. Anti-inflammatory activity of Niosome encapsulated diclofenac sodium with Tween-85 in Arthitic rats. Ind J Pharmacol. 1994;26:46–8.

[11] Suggy S, Murari CR, Ahmad. Niosomes- A review. Biopharm. 2004,24-37.

[12] Srinivas S, Anand kumar Y, Hemanth A, Anitha M. Preparation and evaluation of niosomes containing aceclofenac. Dig J Nano Mat and Biostr. 2010;3(2):199-203.

[13] Chauhan S, Luorence MJ. The Preparation of Polyoxyethylene Containing Non-Ionic Surfactant Vesicles. J Pharm Pharmacol. 1989; 41:46.

[14] Kaneshina S, Shibata O, Nakamura M: The effect of pressure on the mutual solubility of anonionic surfactant water system. Bull Chem Soc Japan, 1982, (55), 951-952.

[15] Hao Y, Zhao F, Li N, Yang Y, Li K. Studies on a high encapsulation of colchicine by a niosome System. Int J Pharm. 2002; 244: 73–80.

[16] Muzzalupo R, Trombino S, Iemma F, Puoci F, Mesa CL, Picci N. Preparation and characterization of bolaform surfactant vesicles. Colloids Surf B. Biointerfaces. 2005; 46(2): 78–83.

[17] Yoshioka T, Sternberg B, Florence AT. Preparation and properties of vesicles (niosomes) of sobitan monoesters (Span 20, 40, 60, and 80) and a sorbitan triester (Span 85). Int J Pharm. 1994; 105: 1-6.

[18] Gayatri DS, Venkatesh P and Udupa N. Niosomal Sumatriptan Succinate for Nasal Administration. Int J Pharm Sci. 2000; 62(6):479-481.

[19] Yoshida H, Lehr CM, Kok W, Junginger HE, Verhoef JC, Bouwstra JA. Niosomes for oral delivery of peptide drugs. J Cont Rel. 1992; 21: 145-154.

[20] Biswal S, Murthy PN, Sahu J, Sahoo P, Amir F: Vesicles of Non-ionic Surfactants (Niosomes) and Drug Delivery Potential. International Journal of Pharmaceutical Sciences and Nanotechnology, 2008, (1), 1-8.

[21] Almira I, Blazek-welsh IA, Rhodes GD: Maltodextrin–Based proniosomes. AAPS Pharm Sci Tech,2001, (3), 1-8.

[22] Manosroi A: Characterization of Vesicles Prepared with Various Nonionic Surfactants mixed with Cholesterol. Colloids surf. Biointerfaces. 2003; 30: 129-138.

[23] Prabagar Balakrishnan, Srinivasan Shanmugam, Won Seok Lee, Won Mo Lee, Jong Oh Kim, Dong Hoon Oh, Dae-Duk Kim, Jung Sun Kimc, Bong Kyu Yoo, Han-Gon Choi, Jong Soo Woo, Chul Soon Yong. Formulation and in vitro assessment of minoxidil niosomes for enhanced skin delivery. Int J Pharm. 2009; 377: 1–8.

[24] Manosroi A. Characterization of Vesicles Prepared with Various Nonionic Surfactants mixed with Cholesterol. Colloids surf. Biointerfaces. 2003; 30: 129-138.

[25] Kreuter J. Colloidal Drug Delivery System of Niosome, Dekker series, Dekker publication.66:73.

[26] Muzzalupo R, Trombino S, Iemma F, Puoci F, Mesa CL, Picci N. Preparation and characterization of bolaform surfactant vesicles. Colloids Surf B. Biointerfaces. 2005; 46(2): 78–83.

[27] Alemayehu Tarekegn, Nisha M Joseph, S Palani, Anish Zacharia, Zelalem Ayenew: niosomes in targeted drug delivery: some recent advances. IJPSR, 2010, (9), 1-8.

[28] Arunothayanun P, Bernard MS, Craig DM, Uchegbu IF, Florence AT. The effect of processing variables on the physical characteristics of non-ionic surfactant vesicles (niosomes) formed from a hexadecyl diglycerol ether. Int J Pharm. 2000; 201: 7–14.

[29] Raja Naresh RA, Chandrashekhar G, Pillai GK, Udupa N: Antiinflammatory activity of Niosome encapsulated diclofenac sodium with Tween -85 in Arthitic rats. Ind J Pharmacol, 1994, (26), 46-48.

[30] Hunter CA, Dolan TF, Coombs GH, Baillie AJ. Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. J Pharm Pharmacol. 1988; 40: 161-165.

[31] Malhotra M, Jain NK: Niosomes as Drug Carriers. Indian Drugs, 1994, (31), 81-86.

[32] Rogerson A, Cummings J, Willmott N, Florence AT. The distribution of doxorubicin in mice following administration in niosomes. J Pharm Pharmacol. 1988; 40(5): 337-342.

[33] Brewer JM and Alexander JA: The adjuvant activity of non-ionic surfactant vesicles (niosomes) on the BALB/c humoral response to bovine serum albumin. Immunology, 1992, (75), 570-575.

[34] Navneet Kumar Verma,Asha Roshan . Niosomes and it's application:A Review, IJRPLS, 2(1):182-184, 2014.

[35] Chauhan S, Luorence MJ, The preparation of polyoxyethylene containing non-ionic surfactant vesicles. J Pharm Pharmacol, 1989, (41), 6.

[36] Hunter CA, Dolan TF, Coombs GH and Baillie AJ: Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. J Pharm Pharmacol, 1988, (40), 161-165.

[37] Jayaraman SC, Ramachandran C, Weiner N: Topical delivery of erythromycin from various formulations: An in vivohairless mouse study. J Pharm Sci, 1996, (85), 1082-1084.

[38] Hunter CA, Dolan TF, Coombs GH and Baillie AJ: Vesicular systems (niosomes and liposomes) for delivery of sodium stibogluconate in experimental murine visceral leishmaniasis. J Pharm Pharmacol, 1988, (40), 161-165.

[39] https://images.app.goo.gl/rWF358Zv4ybPVax89