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Niosomes as Novel Drug Delivery System: Review Article

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ABSTRACT
Niosomes composed of non-ionic surfactant vesicles they are prepared by hydrating mixture of cholesterol and non-ionic surfactant. They can be used as the carriers of amphiphilic and lipophilic drug. Niosomes is the type of delivery system in which medication is encapsulated in a vesicles. Niosomes exhibit various properties that is they are biodegradable, biocompatible non-immunogenic and has flexibility in their structure. Motive of preparing this review is that we have to enlighten the various applications of niosomes they are used to treat number of disease. In this review article we will study about different aspects of niosomes. That is their Method of preparation , mechanism of action , how neosomes helps in drug permeation , their use in permeation enhancer, their application how we can use niosomes to treat different type of disease and their toxicity and how we can treat their toxicity by the help of surfactants.
Keywords: Niosomes , method of preparation , Encapsulation, Surfactant , vesicles and Application, Toxicity.

I. INTRODUCTION

In the year 1909 the researcher name Paul Ehrlich started the work of establishment of targeted delivery when he thought that a Drug Delivery mechanism that would target directly to infective cells. We will now study what is drug targeting . The drug targeting can be elobrated as the ability to direct a therapeutic agent to a desired specific site to show the action on targeted tissue. In niosomes as a novel drug delivery the medication is encapsulated in a polymer matrix as a vesicles [2] these vesicles basically contain a double layer of non-ionic surfactant hence the name given to them as niosomes. The vesicles that are amphiphilic in nature are non-surfactant such as span-60 which is usually stabilized by addition of cholesterol and ample amount of anionic surfactant such as dicetyl phosphate [3]

Merits Of Niosomes

- The less amount of dose is effective to get the proper effective effect
- Niosomes are stable as we use hydrophilic system because of hydrophilic in nature they are osmotically active .
- Due to hydrophilic in nature the drug that they entrapped they tend to increase their stability
- Can enhance the skin penetration of drugs
- The vesicles present in the suspension are hydrophilic that's why they show high amount of patient acceptance over oil based system
- Vesicles act as depot to release the drug slowly

Demerits of niosomes

- May require specialized equipment
- High production cost
- Inefficient drug loading
- Fusion
- Aggregation
- Leaking of entrapped drugs
- The demerits of hydrolysis on the encapsulated drugs results into limiting the shelf life of the paticular formulation

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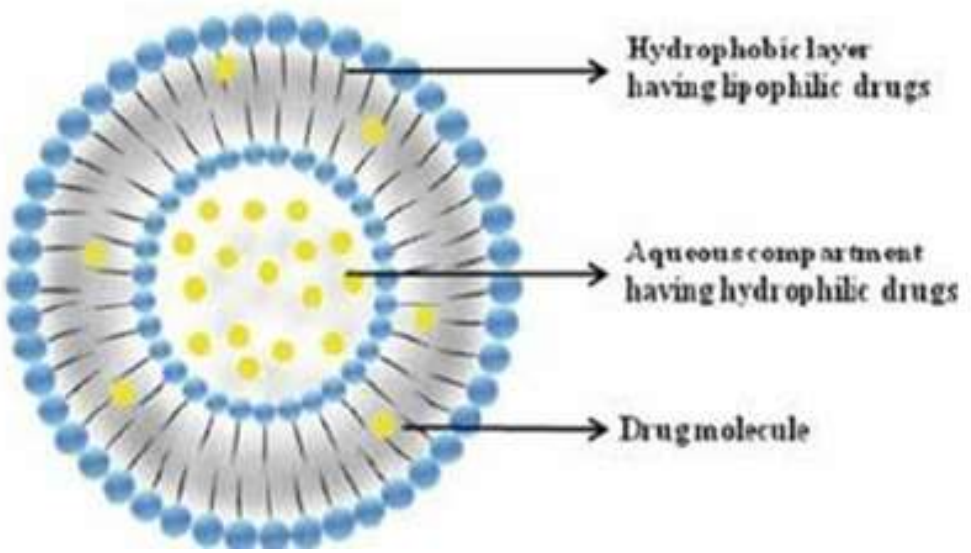

Structure of Typical Niosomes

STRUCTURE OF NIOSOMES[1]

The vesicles of niosomes that is amphiphilic is non-ionic surface acting agent such as span -60 this is stabilized by the addition of cholesterol and ample amount of anionic surfactant such as dicetyl phosphate which are used to stabilizing the niosomes vesicles .

COMPOSITION OF NIOSOMES: [1]

There are various components used for the preparation of niosomes they are as follows.

1. Cholesterol
2. Non-ionic surface acting agent

1.CHOLESTEROL:

These are the derivative of steroids which is used to provide the flexibility , rigidity and to give appropriate shape .

2.NON-IONIC SURFACE ACTING AGENT

The examples of certain non-ionic surfactant that are incorporated for the preparation of niosomes

Eg. Spans (Span20,40,60,80,85)

Tweens (tween 20,40,60,80)

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

The non ionic surfactant consist of a hydrophilic head and hydrophobic tail .

PREPARATION OF NIOSOMES:

Sonication Method:

There are different sort of system is utilized to arrange niosomes this may be the type of system during which the sample of drug solution is added within the buffer system and this mixture of buffer and drug is added in to the surfactant or cholesterol mixture in an exceedingly glass vial which is 20ml . The mixture is sonicated at a temperature of 60°C for 3 minutes employing a sonicator with a titanium probe to yield niosomes

Hand shaking method (Thin film hydration techniques): [4]

Surfactant along with cholesterol are dissolved during a volatile organic solvent as an example diethyl either , chloroform and methanol in an exceedingly very round bottom flask . the natural dissolvable is eliminated at temperature (20°C) utilizing turning evaporator leaving a slim layer of strong blend kept on the mass of the jar. The surfactant which is dried a movie are often rehydrated with watery stage at 0-60°C with delicate fomentation to yield multilamellar niosomes.

Micro fluidization method [6]

It is a recent technologies used to prepare unilamellar vesicles of well defined size distribution. the tactic of micro fluidization depends on the principle of two fluidized streams which are at ultra high velocity which they're interacting with each other . The impingement of the thin liquid sheet along a customary front is arranged specified the energy supplied to the system remains within the realm of niosomes formation. The results may be a greater uniformity smaller size and better reproducibility of niosomes formed.

Reverse Phase Evaporation Technique (REV) [7]

The 1:1 ratio of cholesterol and surfactant mixture is dissolved within the mixture of same

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organic material they're chloroform and ether. The drug is dissolved within the aqueous phase is added within the above mixture which they form two phase which they're sonicated at 4-5°C . a transparent gel is formed and further sonicated after the addition od phosphate buffered saline . there's presence of organic phase which is removed at the temperature of 40°C and so the pressure is low. The Niosomes solution now present is in viscous form and it's diluted with the help of buffer of phosphate and also the diluted solution is heated in water bath for 10 min under the temperature of 60°C which at the highest yield Niosomes.

The Bubble Method [8]

The foaming unit comprises of the round-lined flagon with three neck , and this will be situated in an exceedingly very water shower to manage the temperature. within the primary and second neck the thermometer and water cooled reflux is placed and at the third neck the nitrogen supply is given. Cholesterol along with the surfactant are dispersed together within the buffer (PH 7.4) at 70°C the dispersion mixed for 15 second with high shear homogenizer and immediately afterward bubbled at 70°C using nitrogen gas to yield niosomes [12]

FACTORS AFFECTING NIOSOMES FORMULATION[13]

- DRUGS
- NATURE AND TYPE OF SURFACTANT
- CHOLESTEROL CONTENT AND CHARGE
- RESISTANCE TO OSMOTIC STRESS
- TEMPERATURE OF HYDRATION

1.Drugs

When the drugs in the niosomes is entrapped it influence the charge and rigidity of the niosomes bilayers. The hydrophilic and lipophilic balance of the drugs is disturbed the degree of entrapment .

2.Nature And Type Of Surfactant [9]

The size of the niosomes is directly proportional to the HLB of the surfactant this means that size of the niosomes will increases proportionally with the increase in the HLB of the surfactant like span 85 because the surface free energy decreases with an increase in hydrophobicity of surfactant. A surfactant must always contain a hydrophilic head and hydrophobic tail. The hydrophobic part of the surfactant contain one or two alkyl or perfluoroalkyl group or in some situations it may contain a single steroidal group.

3.Cholestrol content and charge[10,21]

The entrapment efficiency and hydrodynamic diameter of niosomes is increased by the help of cholesterol. It enables membrane stabalizing activity and decrease the leakiness of membrane. If the cholesterol content of bilayer increase it may result in a decrease in the release rate of encapsulated material and therefore an increase of the rigidity of the bilayers obtained. The presence of charge will increase the interlamellar distance between successive bilayers in multilamellar vesicle structure and leads to greater overall entrapped volume

4.Resisitance to osmotic stress

By the addition of hypertonic salt solution to the niosomes suspension by this addition their diameter is reduced

5.Temperature of Hydration

The shape and size of the niosomes is dependent on hydration temperature.

CHARACTERIZATION OF NIOSOMES [11]

1.Measurement Of Angle Of Repose

Angle of repose of dry powder niosomes can be calculated by the help pf funnel method. The powder of niosomes is poured into the funnel which was fixed at certain position so that the 13mm outlet orifice of the funnel is 5cm above a level black surface . the Powder will flows down from the full to form a little mountain like structure on the surface and the angle of repose was then calculated by measuring the height of the mountain and the diameter of its base

2.Scanning electron microscopy [14]

The size of the particles of niosomes is very important characteristics . the surface morphology (roundness, smoothness, and formation aggregate) and the size distribution of niosomes were studied by scanning electron microscopy (SEM). Sprinkle the niosomes on the double sided tape that was affixed on the aluminium stubs. The aluminium stub was placed in the vaccum chamber of the scanning electron microscope. The sample was observed for morphological Characterization using a gaseous secondary electrondetectors.

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3.Osmotic shock[14]

If the size of the vesicles changes it can be determined by the osmotic studies. The formulation of niosomes are incubated with the hypotonic , isotonic , hypertonic solution for 3 hours. After the time interval we can see the changes in the size of the vesicles in the formulation are viewed under optical microscopy.

4.Stability Studies [15]

If we have to find out the stability of the niosomes, the optimized batch was stored in airtight sealed vials at different temperatures. The surface characteristics and percentage drugs retained in niosomes and niosomes derived from proniosomes were selected as parameters for the evaluation of stability. if the formulation is instable it can be reflect in drug leakage .

5. Zeta Potential analysis[16]

We have to do zeta potential analysis because to know the colloidal properties of the formulation that we have prepared . the diluted Niosomes that is derived from proniosomes dispersion was determined using zeta potential analyzer based on electrophoretic light scattering and lasser doppler velocimetry method .the temperature set at 25°C charge on vesicles and their mean zeta Potential values with standard deviations of measurement were obtained directly from the measurements.

IN-VITRO METHOD FOR NIOSOMES[18]

In vitro drug release can be studied by following ways

- Dialysis Tubing
- Reverse dialysis
- Franz diffusion cell

1.Dialysis Tubing

In-vitro drug release can be achieved by using dialysis tubing. The niosomes is placed in a prewashed dialysis Tubing which can be hermetically sealed . dialysis sac is then dialyzed against a suitable dissolution medium at room temperature,after some intervals of time the sample can be withdrawn from the medium . the maintenance of sink condition is essential [17]

2.Reverse Dialysis [19]

This is the technique in which a small Dialysis as containing 1ml of dissolution medium are placed in proniosomes. The proniosomes then displaced into the dissolution medium. We can do direct dilution of the proniosomes by the help of this method . however the rapid release cannot be qauntified using this method [20]

3.Franz diffusion cell

Franz diffusion cell method can also be used to study the

In-vitro diffusion study. Proniosomes can be placed in the donor chamber of the franz diffusion cell fitted with a cellphane membrane. At room temperature the proniosomes can be dialyzed against a suitable dissolution media. At regular intervals of time the sample is withdrawn and analyzed for drug content using suitable method (UV, spectroscopy, HPLC etc) the maintenance of the sunk condition is essential [10,21]

APPLICATIONS OF NIOSOMES [10,21]

- It has been used to study the immune response provoked by antigen
- It is widely used to study the Drug targeting
- We can use it as anti-neoplastic Treatment that is in treatment of cancer
- Niosomes can be used as Carriers for hemoglobin
- Nowadays it can be used as delivery of peptide Drugs
- It can give good therapeutic effect on opthalmic drug delivery
- It widely can used as diagnostic agent

Immunological Application Of Niosomes [22]

Basically niosomes can be used for studying the nature of the immune response that is stimulted by antigens. Niosomes can also be used for targeting drugs for organs other than the Reticulo-endothelial system. A carrier system is attached to the niosomes to target the specific organs of the body.

Sustained Release [22]

The action of sustained release can be applied to the drugs which have low therapeutic index and have solubility which is low .

Localized Drug Action[22]

Drug delivery through niosomes is the modern approaches to achieve localized drug action since their size and low penetrability through epithelium and connective tissue keeps the drug localized at the site of administration.

Transdermal delivery of drugs by niosomes[22]

The drugs which have slow penetration of drugs through skin is the major drawback for the transdermal drugs delivery. An enhanced rate of

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transdermal drug delivery can be achieved by the help of niosomes. Topical niosomes can be served as a solubilization matrix as a local depot for sustained release of dermally active compounds, as a enhancers of penetration .

Leishmaniasis[22]

Leishmaniasis is type od disease in which a parasite of the genus leishmania enters the cell of the liver and spleen. Use of niosomes is done to achieve high level of the drugs incorporated in to the body without triggering the side effects .

ROUTE OF APPLICATION OF NIOSOMES DRUGS [1]

Intravenous route

Exmaple: Doxorubicin, comptothecin , insulin, zidovodin,

Inhalation

Examples: All trans-retonic acids

Transdermal route

Examples: piroxicam, estradiol, nimesulide

Ocular route

Exmaples: timolol maleate, cyclopentol

Nasal route

Exmaples: sumatriptan ,influenzaviral vaccine

TOXICITY OF NIOSOMES:

Niosomes toxicity is related to different types of components i.e non-ionic surfactant has high amount of biocompatibility and they are less toxic that of anionic , amphoteric and cationic . when the equivalent amount of Surfactant are present in the form of vesicular system the properties of niosomes strongly decrease[23]. Hofland et al[38]studied and evaluated the toxicity of different type of surfactants used in niosomal formulation to human keratinocytes. And he explained proposed a demonstration on ester type of surfactants which are less toxic due to enzymatic degradation of bonds in ether . hemolytic test has been used to predict the toxicity of a surfactant and in vesicular system has been derived from them[24].As of late, it has been exhibited that the capacity of niosomes to disturb erythrocytes relies upon the length of the alkyl chain in the surfactant and on the size of the colloidal totals in arrangement. Apparently, a more limited carbon chain intercalates better into the layers oferythrocytes, destructing their sub-atomic association; niosomes have more trouble to interface with natural films, coming about in significant hemolysis[25].Niosomes arranged with bolaform surfactants showed empowering security and bearableness information both in vitro in human keratinocytes and in vivo in human volunteers, who showed no skin erythema when topically treated with a medication free bolaform niosome definition.[26]

Niosomes As Percutaneous Enhancers:

While applying niosomes to the skin, one needs to separate what sort of impact is required, ie, a nearby impact inside the skin (dermal medication conveyance) or a fundamental impact joined by saturation through the skin (transdermal medication conveyance)[27] .Arriving at the circulatory system is the point of transdermal focusing on, and is turning into a focal point of interest for some, drug research bunches concentrating on sicknesses like aggravation, disease, psoriasis, alopecia, and acne[28].The transdermal course enjoys a few upper hands over the ordinary courses of medication organization: pinnacle and box levels in serum (a danger and bother of intravenous treatment) are kept away from; first-pass hepatic digestion and gastrointestinal debasement (pH, enzymatic action, and communications with food, refreshments, and other orally regulated medications), are kept away from, prompting an expansion in drug bioavailability and viability; and it can fill in as an option in contrast to oral medication organization when that course is unacceptable (eg, spewing and looseness of the bowels). Different benefits of the transdermal course incorporate the openness of the skin, the moderately huge surface region for assimilation, and the way that it is painless, making the patient more agreeable.Notwithstanding, the transdermal course of medication organization has a significant drawback, ie, a low entrance rate through the skin. Just a predetermined number of medications can be figured as transdermal conveyance frameworks because of the impact of the layer corneum, which fills in as a rate restricting advance during drug saturation. This layer is extremely particular regarding the sorts of particle that it permits to be moved through the skin; along these lines, just atoms with explicit physicochemical properties can cross the skin adequately.[29]

Drug move across the layer corneum is mostly an inactive interaction and can happen by means of three courses: intercellular, transcellular (paracellular), and transappendageal. Whenever it has crossed the epidermis, a compound might be taken out by the dermal dissemination or be moved to more profound tissues[30]. Many systems have been surveyed for their capacity to conquer the

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boundary capacity of the layer corneum and to further develop drug transport into the skin. Specifically, infiltration enhancers might act by at least one of three expected components as per the lipid-protein-parceling hypothesis: they can adjust the intercellular lipid structure between the corneocytes to build diffusivity; and they can change intracellular protein areas inside the horny layer and may expand apportioning of the medication into the skin tissue[31]. During the last decade, niosomes have gone through escalated examination for transdermal medication conveyance, and appear to be encouraging vehicles for dynamic substances and focusing to the skin layer. Niosomes are becoming well known in the field of skin drug conveyance because of their remarkable qualities and the properties prompted by their essence in a definition, for example, upgraded drug entrance, neighborhood stop for supported medication discharge and a rate-restricting layer for adjustment of fundamental medication retention through the skin[32].

MECHANISM OF ACTION OF NIOSOMES AS PERMEATION ENHANCERS:

There is no single component that can adequately clarify the capacity of niosomes to build drug move through the skin, and a few systems have been proposed, including: adjustment of the hindrance capacity of the layer corneum, because of reversible irritation of lipid organization[33]. decrease of transepidermal water misfortune, which expands hydration of the layer corneum and releases its intently pressed cell structure[34]. and adsorption or potentially combination of niosomes on the outer layer of the skin, as uncovered by freeze crack electron microscopy and little point X-beam dispersing, prompting a high thermodynamic action slope of medication at the connection point, which is the main thrust for saturation of a drug[35].Adsorption of niosomes onto the cell surface happens with practically zero disguise of either fluid or lipid parts; it might occur either because of drawing in actual powers or because of restricting by explicit receptors to ligands on the vesicle layer and move of medication straightforwardly from vesicles to the skin. Then again, niosomes may meld with the cell layer, bringing about complete blending of the niosomal substance with the cytoplasm. At long last, niosomes might be overwhelmed by the cell (endocytosis), with lysozymes present in the cytoplasm corrupting or processing the membranous construction of the niosome, in this manner delivering the entangled material into the medium.[36,37]

II. CONCLUSION:

Niosomal drug delivery system is one of the greatest exmaples in the field of pharmacy and a great evolution in drug delivery technologies and nanotechnology . it the most acceptable dosage form as compared to the other dosage form because the niosomes are economical and stable in nature. There is a lot of scope for the encapsulated toxic anticancer drugs , anti-infective , anti-AIDS etc .niosomes is used because with the help of niosomes we can achieve better bioavailability and targeting properties and they can be used to reduce the toxicity and the side effects of the drugs .the concept of incorporation of the niosomes into the dosage form to target specific tissues and body.

REFERENCE:

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

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

[3]. Hunter CA, Dolan TF, Coombs G, Baillie AJ. Vesicular frameworks (niosomes and liposomes) for conveyance of sodiumstibogluconate in exploratory murine instinctive leishmaniasis. J Pharm Pharmacol 1988; 40:161-5.

[4]. Khandare JN., Madhavi G., Tamhankar BM., Niosomes Novel Drug Delivery System. The Eastern Pharmacist.1994, 37: 61-64.

[5]. http//en.wikipedia.org/wiki/Niosomes, design of niosomes.

[6]. Rogerson A., Cummings J., Willmott N., Florence AT., The circulation of doxorubicin in mice following organization in niosomes. J. Pharm. Pharmacol. 1988, 40: 337-34

[7]. Biju SS., Talegaonkar S., Misra PR., Khar RK., Vesicular frameworks: An outline. Indian J. Pharm. Sci. 2006, 68:141-153.

[8]. Ijeoma F., Uchegbu., Suresh P., Vyas., Non-ionic surfactant based vesicles (niosomes) in drug conveyance. Int. J.Pharm. 1998; 172: 33–70.

[9]. Malhotra M., Jain N.K., Niosomes as Drug Carriers. Indian Drugs. 1994, 31(3): 81-866.
[10]. Alsarra A., Bosela A,, Ahmed S.M,, Mahrous G.M., Proniosomes as a medication transporter for transdermal conveyance of ketorolac. Eur. J. Pharm. What's more Biopharm. 2004; 2(1): 1-6.
[11]. Hu C., Rhodes D.G., Proniosomes: a clever medication transporter planning. Int. J. Pharm. 1999, 185: 23-35.
[12]. Breimer DD and Speiser R. Points in Pharmaceutical Sciences. Elsevier Science Publishers, New York, USA.1985;291.
[13]. Handjani VRM. Scattering of Lamellar Phases of Nonionic Lipids in Cosmetic Products. Int J Cosmetic Sc.1979;30.
[14]. Sternberg B, Uchegbu IF, Florence AT and Murdan S. 1998.
[15]. Theresa MA. Drugs distributed by ADIS global Ltd. 1998; 56(5):747-756.
[16]. Buckton G and Harwood. Interfacial Phenomena in Drug Delivery and Targeting Academic Publishers, Switzerland. 1995;154-155.
[17]. Shahiwala An and Misra A. Studies in Topical Application of Niosomally Entrapped Nimesulide. J Pharma Sci.2002;220.
[18]. Reddy DN and Udupa N. Definition and Evaluation of Oral and Transdermal Preparation of Flurbiprofen what's more Piroxicam Incorporated with Different Carriers. Drug Dev Ind Pharm. 1993; 843.
[19]. Satturwar P M. Plan and Evaluation of Ketoconazole Niosomes. Ind J Pharm Sci. 2002; 155.
[20]. Azmin MN, Florence AT, Handjani-Vila RM, Stuart JF, Vanlerberghe G, Whittaker JS. The impact of non-ionic surfactant vesicle (niosome) capture on the retention and appropriation of methotrexate in mice. J Pharm Pharmacol 2005;37:237-42.
[21]. Weissman G, Bloomgarden D, Kaplan R, Cohen C, Hoffstein S, Collins T, et al. An overall technique for the presentation of proteins, through immunoglobulin-covered liposomes, into lysosomes of lacking cells. Proc Natl Acad Sci 1975;72:88-92.
[22]. Navneet Kumar Verma, Asha Roshan. Niosomes and its application:A Review, IJRPLS, 2014; 2(1): 182-184
[23]. Sahin NO. Niosomes as nanocarrier systems. In: Mozafari MR, editor. Nanomaterials and Nanosystems for Biomedical Applications. New York, NY, USA: Springer; 2007.
[24]. Pape WJ, Pfannenbecker U, Hoppe U. Validation of the red blood cell test system as in vitro assay for the rapid screening of irritation potential of surfactants. Mol Toxicol. 1987;1:525–536.
[25]. Tavano L, Infante MR, Abo Riya M, et al. Role of aggregate size in the hemolytic and antimicrobial activity of colloidal solutions based on single and gemini surfactants from arginine. Soft Matter. 2013;9:306–319.
[26]. Paolino D, Muzzalupo R, Ricciardi A, Celia C, Picci N, Fresta M. In vitro and in vivo evaluation of bola-surfactant containing niosomes for transdermal delivery. Biomed Microdevices. 2007;9:421–433.
[27]. Walker RB, Smith EW. The role of percutaneous penetration enhancers. Adv Drug Deliv Rev. 1996;18:295–301
[28]. Thakur V, Arora S, Prashar B, Vishal P. Niosomes and liposomes – vesicular approach towards transdermal drug delivery. International Journal of Pharmaceutical and Chemical Sciences. 2012;1:981–993.
[29]. Barry BW. Lipid protein partitioning theory of skin penetration enhancement. J Control Release. 1991;15:237–248
[30]. Schreier H, Bouwstra J. Liposomes and niosomes as topical drug carriers: dermal and transdermal drug delivery. J Control Release. 1994; 30:1–15.
[31]. Karande P, Mitragotri S, Enhancement of transdermal drug delivery via synergistic action of chemicals. Biochim Biophys Acta. 2009; 1788:2362–2373.
[32]. Bouwstra JA, Honeywell-Nguyen PL. Skin structure and mode of action of vesicles. Adv Drug Deliv Rev. 2002;54:41–55
[33]. Manconi M, Sinico C, Valenti D, Lai F, Fadda AM. Niosomes as carriers for tretinoin. III. A study into the in vitro cutaneous delivery of vesicle-incorporated tretinoin. Int J Pharm. 2006;27:11–19
[34]. Abdelkader H, Alani AW, Alany RG. Recent advances in non-ionic surfactant vesicles (niosomes): self-assembly fabrication, characterization, drug delivery applications and limitations. Drug Deliv. 2014;21:87–100
[35]. Mali N, Darandale S, Vavia P. Niosomes as a vesicular carrier for topical administration of minoxidil: formulation and in vitro

assessment. Drug Deliv Transl Res. 2013;3:587–592.
[36]. Cevc G. Lipid vesicles and other colloids as drug carriers on the skin. Adv Drug Deliv Rev. 2004;56:675–711.
[37]. El Maghraby GM, Barry BW, Williams AC. Liposomes and skin: from drug delivery to model membranes. Eur J Pharm Sci. 2008;34:203–222.
[38]. Hofland HE, Bouwstra JA, Verhoef JC, et al. 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.