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NIOSOMES- VERSATILE NANO VESICLES FOR ENHANCED DRUG DELIVERYSYSTEM

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ABSTRACT

The concept of Targeted drug delivery system was proposed by Paul Ehrlich in the year 1909. The Various carrier systems include liposomes, serum proteins, microspheres and niosomes. Among these Niosomes are vesicular delivery systems which enable effective Bioavailability With controlled release for prolonged period of time .The vesicular system of niosomes withbilayer structure obtained by hydrating mixture of non- ionic surfactant and cholesterol. Niosomes are utilized for Drug delivery to specific sites to achieve desired therapeutic effects. Niosomes containing non-ionic surfactants improve solubility of poorly water soluble active substances. In Niosomes, a vesicle is amphiphilic I nature which is non-ionic surfactant such as span-60 promotes their efficiency in encapsulating drugs. Cholesterol used to maintainthe rigidity of Niosomes. Niosomes are spherical in shape and consists lamellar structures atmicroscopic level. They are categorized into 2 group's i.e Unilamellar and Multilamellar vesicles .Niosomes have various advantages over other delivery systems. Niosomal formulations used in many diseases like Neoplastic, Acquired immune deficiency syndrome, lung diseases, bacterial and fungal infections, inflammation. This review article is about the role of Niosomes as drug delivery system and information of their structure, preparation and applications.

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INTRODUCTION

Niosomes are a type of Novel drug delivery system. In which medication is encapsulated ina vesicle. Niosomes obtained by hydrating the mixture of non- ionic surfactant and cholesterol. They are non-ionic in nature, Biodegradable Biocompatible, non-toxic and non-immunogenic able to exhibit flexibility in their structural properties.Niosomes are versatile Carrier system that can be administer through various routes IV,IM,Transdermal ,ocular. non -ionic surfactants improve solubility of poorly water soluble active substances. They have both polar and non-polar segments. Therefore they can encapsulate both hydrophilic and hydrophobic active substances or drugs[1].Niosomes are considered promising drug Carriers as they improve and prolong the residence time of drug's in systemic circulation and increase the therapeutic efficacy of drugs and permits targeted drug delivery [2].

STRUCTUREOF CARRIER SYSTEM

The vesicular system of Niosomes with bilayer structure which is composed of non-ionic surfactants, may strengthen a drug's bioavailability to a specific region for a set duration oftime.A vesicle forming amphiphilic surfactantsuch as span -60 which is tend to held steadyby addition of cholesterol and a small amount of an anionic surfactant likedactyl phosphate, which also aids in stabilizing the vesicle [3].

Niosomes are spherical in shape and consist of microscopic lamellar structures, I.e. unilamellar or multilamellar structures.

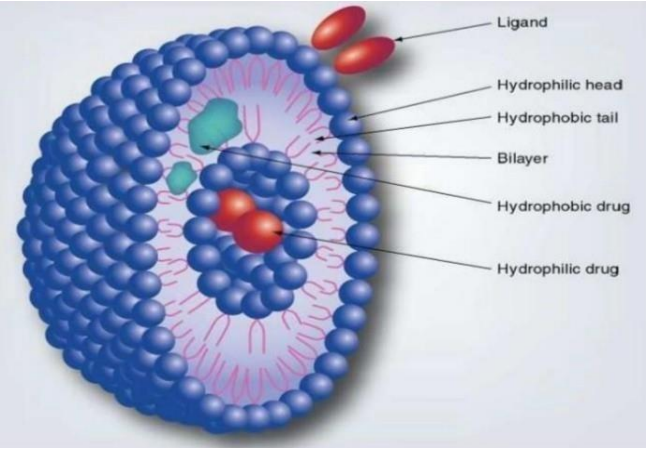

Figure no : 1 Structure of Niosomes.

Ref : Manoj kumar Mishra, Niosomes:An approach towards targeted drug delivery system ,Nanomedicine,2016.

COMPOSITION OF NIOSOMES[3]: The two primary compounds used for ensuring niosomesare

1. Cholestrol and
2. Nonionic surfactants

1. cholestrol : cholesterol which is a steroidal derivative , utilized to provide rigidity and suitable shape.
2. Nonionic surfactants: the following non ionic surfactants are typically employed in niosome preparation .Example: spans [span 60.40, 20.85, 80]

Tweens [tweens 20, 40, 60, 80]

Brijs [brij 30, 35, 52, 58, 72, 76].

The non ionic surfactants consists of hydrophilic head and hydrophobic tail **.**

ADVANTAGES [4,5,6,7]

1. Niosomes are stableand osmatically active.
2. It has increased dermal penetration and oral bioavailability.
3. Targeted drug delivery can be achieved using Niosomes,the drug is delivered directly to the body part when the therapeutic effect is required.
4. Lowdose is required to achievethedesired effect.
5. Niosomes are amphiphilic i.e. both hydrophilic and lipophilic in nature and can accommodate a large number of drugs with widerange of solubility's.
6. It can be administered through various routes viz.oral , parenteral, topical, ocular.
7. Niosomes have characteristics such as non-toxic, Biocompatible, Biodegradable and non-immunogenic.
8. Non-ionic carriers are safer.
9. They release the drug slowly and give a controlled release wherevesicles act as depot.
10. The therapeutic efficacy of drugs is improves by reducing the clearance rate, targeting to the specific site and byprotecting the encapsulated drug.
11. Nospecial requirements needed for handling and storage of surfactants and Niosomes.
12. The Bilayers of the Niosomes protect the enclosed API from variousfactorsinside andoutside the body.
13. Niosomes have improved therapeutic performance of drug.

DISADVANTAGES [4,5,6]

1. Niosomes require specialized equipment .
2. Time consuming process.
3. Physical instability.
4. Inefficient drug loading.
5. Production cost is high.
6. Aqueous suspension of noisome exhibit fusion, aggregation, leaching of entrapped drug, thus limiting the shelf life of noisome dispersion.
7. Extrusion and sonication approach takes time and requires specialized equipment.

TYPES OFNIOSOMES

Proniosomes :

These are the niosomal formulation containing carrier and surfactant, which requires to be hydrated. Proniosomes decreases the aggregation, leaking and fusion problem associated with niosomal formulation.

Aspasomes :

Aspasomes are combination of acorbyl palmitate, cholesterol and highly

Charged lipid diacetyl phosphate leads to formation of vesicle called Aspasomes. They are used to increasethetransdermalpenetrationof drugs.

Vesicles in water andoil system(v/w/o): it is the emulsification of an aqueous Niosomes,

Into an oil phase from vesicle in water and in oil emulsion (v/w/o). This prepared by addition of Niosome suspension formulated from mixture of sorbitol mono stearate, cholesterol and solution to oil phase at 60 ° C . it results in formation of vesicle in water inoil emulsion by cooling to room temperature forms vesicle in water in oil gel .This vesicles can entrap protein drugs and protect from enzymatic degradation and have controlledrelease.

Niosomes in carbopol gel:

Niosomes prepared using Drug, s p a n s and cholesterol.The Niosomes thus obtained were incorporated in carbopol gel base containing propylene glycol and glycerol

Niosomes of Hydroxyl propyl methyl cellulose:

In this,a base containing 10% glycerin of Hydroxypropyl methyl cellulose was first prepared and then Niosomes incorporated in it [8].

Overall, the objective of the review article is to elucidate the role of niosomes as an effective drug delivery system, providing readers with a thorough understanding of their structure, preparation, and diverse applicationsin therapeutic medicine.

METHODOFPREPARATIONS

Ether injection method:

This method is based on slow injection of surfactant: Cholesterol solution in either through 14 gauge needle into a preheated aqueous phase maintained at 60 ° C. Vaporization of ether resulting into a formation of ether gradient at ether -water interface which leads to formation of single layered vesicles. The particle size depends upon the conditions used , the diameter of the vesicle range from 50 to 1000 nm[2].

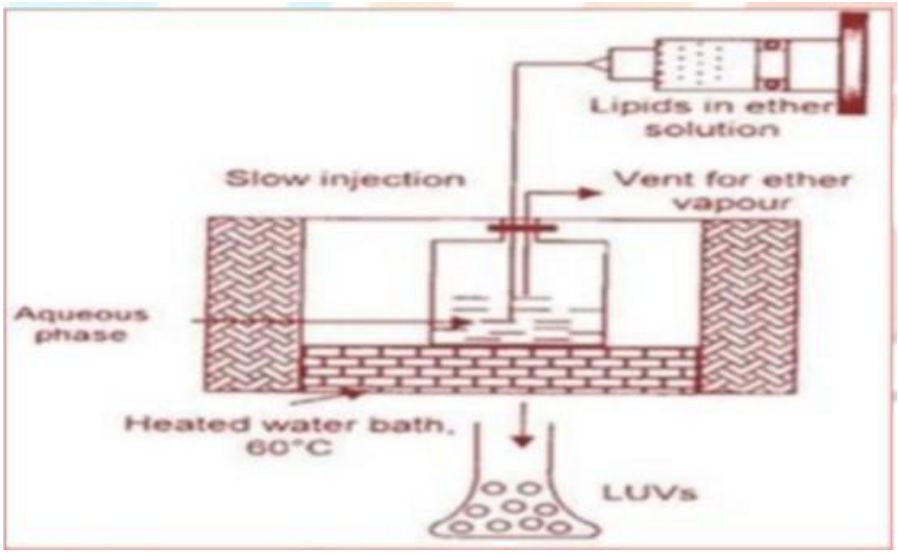

Figure no : 2 Ether Injection Method.

Ref : Sidramappa basawaraj shirsand , Recent advances in niosomal drug delivery system :A Review, 2019.

1. **Sonication:** In this method, an aliquot of drug solution in buffer is added to the surfactant/ cholesterol mixture in a 10ml glass vial. The mixture is probe sonicated at 60 °C for 3 minutes using a sonication. The resultant vesicles are of small unilamellar type Niosomes.[3].

2. **Handshaking Method:** (Thin film hydration technique) surfactant and cholesterol are dissolved in a volatile organicsolvent (diethyl ether, chloroform or methanol) in a roundbottom flask. The organic solvent is removed under vacuum at room temperature usingrotary evaporator leaving a thin layer of solid mixture deposited on the wall of the flask. The dried surfactant film can be rehydrated with aqueous phase at temperature slightly above the gentle agitation .This process formslarge multilamellar Niosomes [4].

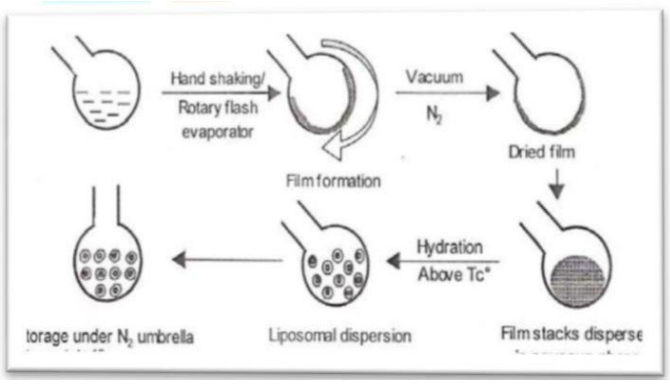

Figure no : 3 Hand Shaking Method.

Ref : Thushar Rukari Niosomal drug delivery system – Promising Drug carriers , 2013.

3. **The Bubble Method:**It is a Novel technique for the one step preparation of Liposomes andNiosomes without the use of organic Solvent.The bubbling unit consists of round bottom flask with three necks positioned in water bath to control the temperature. Water cooled reflux and thermometer is positioned in the first and second neck, nitrogen supply through the third neck. Cholesterol and surfactants are dispersed together in this buffer(pH-7.4)70◦ C,the dispersion mixed for 15 seconds with High shear homogenizer and immediately bubbled at 70◦C using nitrogen gas[5].

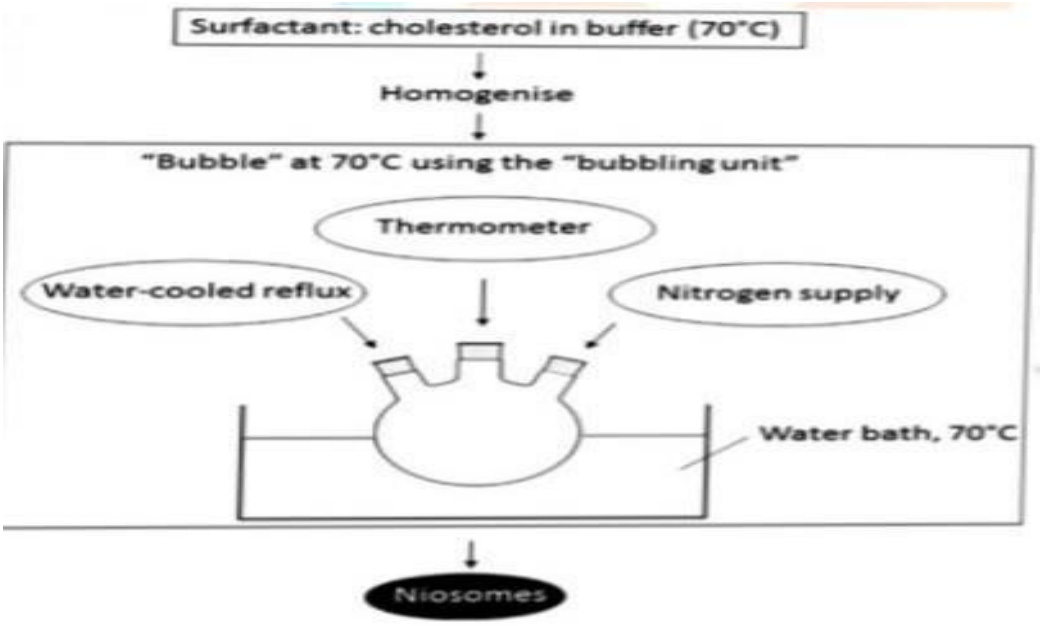

Figure no 4 : The Bubble Method.

Ref: Pei ling yeo, Niosomes :A Review of their structure , properties ,Methodas of preparation , and medical Applications,2018.

4. **Micro Fluidization Method :** In this method two fluidized streams (one containing drug and other surfactant) interact at ultra-high velocity, in precisely defined micro channelswithin the interaction chamber in such a way that energy supplied to the system remains in the area of Niosomes formations.It results in better uniformly, smaller size and reproducibility in the formulation of Niosomes.This is called submerged jel principle[2,5].

5. **Reverse Phase Evaporation Technique :** Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this andthe resulting two phases are sonicated at 4-5◦C. The Clear gel formed is further sonicated after the addition of a small amount of phosphate buffered saline.The organic phase isextracted at 40 ◦ C under low pressure. The resulting viscous Niosome suspension is diluted with phosphate buffered saline and heated on a water bath at 60 ◦C for 10 minutesto yield Niosomes[6].

Figure no 5 Reverse phase evaporation technique.

Ref Ayushi Joshi , Niosomes, Aquosomes, Electrosomes, Phytosomes , 2020.

CHARACTERIZATION OF NIOSOMES

Characterizations of Niosomes are required to evaluate the quality of the produced vesicles and their application[15,21].

1. **Entrapment Efficacy**: The Entrapment Efficacy determines the amount of drug within the Niosomes. The amount of free drug (or) medication in the supinated can be measured after centrifuging the loaded niosomal solution and this may be calculated using an equation[9,12].

2. **Stability studies**: To assess the niosomes stability. The batch which was optimized andkept in sealed airtight vials at varying temperatures. Percentage of drug retained in niosmoes , surface characteristics and niosomes obtained from proniosomes were selected as parameters for determination of the stability. If the formulation is instable would reflect in drug leakage[9].

3. **Osmotic Shock**: Through osmotic studies, the Change in vesicle. Size can be determined. Niosomes formulations are incubated for 3 hours with hypotonic, isotonic, hypertonic solutions. After certain time interval the change in vesicle size are viewed under opticalmicroscopy[9,20].

4. **Zeta Potential analysis**: To determine the colloidal properties of prepared formulations, Zeta Potential analysis is used. The diluted niosomes which derived from proniosomes dispersion was determined using Zeta Potential analyzer. Based on electrophoretic light scattering and laser Doppler velocimetry method. The temperature was set at 25°C charge on vesicles and their mean Zeta Potential values with standard deviation of measurements wereobtained directly from the measurement[10].

5. **Morphology of Niosomes**: Morphology of Niosomes includes microscopic methods like transmission electron microscopy (TEM), Scanning electron microscopy and atomicforcemicroscopy to analyze niosomal vesicles [9].

6. **Scanning electron microscopy (SEM) :** The niosomes particle size, the surface morphology and size distribution were studied by scanning electron microscopy. Niosmoes was sprinkled on the double sided tape which was affixed on aluminum stubs. The stub was placed in vacuum chamber of SEM using gaseous secondary electron detectors, the sample was observed for morphological Characterization[10,20].

APPLICATIONS[1,2,3,11,17,19]

Localized DrugAction

Niosomal formulation have localized Drug Action because of their size and low penetrability through connective and epithelial tissues.

DrugTargeting

Most useful aspect of niosomal Drug Delivery is having ability to Target drugs. Niosomes can able to Target drugs to ReticuloEndothelial systemand organs.

Transdermaldelivery ofdrugs

Drugs having low penetration through skin are major disadvantage of transdermal route ofdelivery. By incorporating transdermal delivery of drugs with niosomes increases the penetration rate of the drugs.Because of desirable properties of niosomal formulation they have been used in therapeutic applications.

Neoplasia

Niosomal formulation can be used as antineoplastic treatment incancertherapy .

Leishmaniasis

It is a type of disease in which genus leishmania parasite enters the cell of spleen and liver. The drugs commonly used for leishmaniasis treatment have side effects on the other organs of body, to avoid such side effects they are incorporatedwith niosomes.

Carrier for hemoglobin

The niosomal hemoglobin suspension was found to give superimposable curve on freehemoglobin curve. Niosomes play a key role as carrier in hemoglobin.

Nasaladministration

Drugs incorporated to Niosomal system Improve direct transport percentage, drug Targeting effectiveness, brain bioavailability and brain absorption through direct nose to brain Channel showing Improved central nervous system Targeting.

Niosomes used in cosmetics Suitable for skin moisturizing and tanning products with increased permeation through skin.

CONCLUSION

Niosomal Drug delivery system is one of the best approaches to achieve desired therapeuticefficacy withreduced toxic Drug effects. It is known to be most efficient system amongnovel technologies. Drugs which incorporate into niosomal Drug delivery system can achieve better Bioavailability and therapeutic performance to the targeted organs and tissues with less side effects. Niosomes are stable in nature and they are economical. No Special requirements Are required for storage and handling of Niosomes. Niosomal system is best among other delivery systems and it was found that Niosomes are useful inpharmaceutical field as they offer structural characteristics Like composition, size and can be designed as desired. It was concluded that Niosomes are effective drug delivery tools for targeting of various therapeutically Active substances.

SUMMARY

Niosomes can be represent as most effective tool for targeted drug delivery Of numerousdiseases and enableto provide improved therapeutic performance than other conventionaldrug delivery systems. It is the most acceptable dosage form compare to other form because of their desirable properties and they are stable in nature. Niosomes have important role in numerous drug deliveries like Drug targeting, transdermal, ophthalmic,and parenteral and topical drug delivery . Niosomal carriers are safer to target specific Sites in the body.

ABBREVIATIONS

NDDS (Novel Drug Delivery System),
TEM (Transmission ElectronMicroscopy),
SEM (Scanning Electron Microscopy) .

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Competing Interests:
The authors declare no conflict of interest.

Ethical matter: NIL

MARKETED FORMULATION OF NIOSOMES

Table no: 1 Marketed formulation of niosonmes.

BRAND NAME	GENERIC NAME	INDICATION	ROUTE OF ADMINISTRATION
Neutropin®	Somatropin	Growth deficiencies	Subcutaneous
Somatuline®	Lanreotide	Acromegaly	Intramuscular
Suprecur®	Buserelin	Endometriasis	Intramuscular
Arestin®	Minocycline	Periodontitis	Subgingival
Zoladex®	Goserelin acetate	Prostate cancer	Subcutaneous
Sandostatin®	Octreotide	Acromegaly	Intaveneous
Vivitrol®	Naltrexone	Alcohol dependence	Intamuscular

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