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Niosome: A Novel Drug Delivery System

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A R T I C L E I N F O

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A B S T R A C T

Over decades analysts are endeavoring to utilize the medications in an effective way to treat different infectious disease. The productive use can be clarified as diminished portion, decreased symptoms, and decreased dose recurrence, more prominent patient consistence and most extreme centralization of the medication at the site of activity in order to lessen the undue presentation to the whole body. A niosome is a non-ionic surfactant-based liposome. Niosomes are formed mostly by incorporation of cholesterol as an excipient. The surfactant molecule arrange themselves in such a way that hydrophilic head in outward direction and hydrophobic tail faced towards each other to form the micelles. Niosomes are one of the best carrier system for drug targeting. Niosomes are biodegradable, nontoxic, more stable than liposomes and inexpensive, an alternative to liposomes. This article focus on introduction of niosomes, composition of niosomes, difference between niosome and liposome, different method of preparation, characterisation of niosome and application of niosome.

1. Introduction

1.1. Definition

A niosome is a non-ionic surfactant-based liposome. Niosomes are formed mostly by incorporation of cholesterol as an excipient. Niosomes are structurally similar to liposomes , both having bilayer, however, the materials used for preparation of niosomes make them more stable and thus niosomes are more stable than liposomes. The niosomes are microscopic having nanometric scale. The particle size ranges from 10 nm-100 nm [1-3]. Bilayer vesicles can be divided into unilamellar and multilamellar vesicles. The particle sizes of small unilamellar vesicles (SUV) in the range of 10–100 nm, large unilamellar vesicles (LUV) 100–3000 nm, and multi-lamellar vesicles (MLV) greater than 5 μm reported [4-7].

1.2. Advantages of Niosomes

1. Niosomes are osmotically active and stable.
2. The stability of the entrapped drug increased by niosome.
3. Handling and storage of surfactants do not require any special storage conditions
4. Oral bioavailability of drugs can be increased by niosome.
5. They enhance the penetration of drugs through skin.
6. Niosomes can be used for oral, parenteral as well topical.
7. The surfactants used in niosomes are biodegradable, biocompatible, and non-immunogenic.

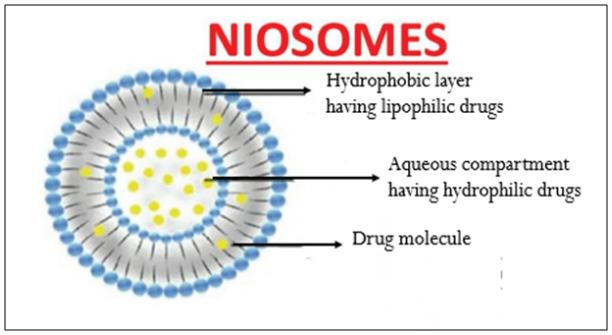

Figure 1: Structure of Niosome

1.3. Disadvantages of Niosomes

1. Niosomes are physically unstable.
2. Aggregation of particle occurs.
3. Leakage of entrapped drug.
4. Hydrolysis of encapsulated drugs leads to limiting the shelf life of the dispersion.

1.4. Compositions of Niosomes [8-10]

1. The two significant segments utilized for the arrangement of niosomes are

1. Cholesterol
2. Nonionic surfactants

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1.4.1. Cholesterol

Cholesterol is used in the formulation which gives rigidity and proper shape, conformation to the niosomes preparations. Presence of cholesterol make significant changes in bilayer fluidity and permeability. Cholesterol a waxy steroid metabolite is usually added to the non-ionic surfactants to provide rigidity and orientational order. It does not form the bilayer itself and can be incorporated in large molar ratios. Cholesterol is an amphiphilic molecule; it orients its OH group towards aqueous phase and aliphatic chain towards surfactant's hydrocarbon chain. Rigidization is provided by alternative positioning of rigid steroidal skeleton with surfactant molecules in the bilayer by restricting the movement of carbons of hydrocarbon.

1.4.2. Nonionic surfactants

The non ionic surfactants possess both hydrophilic head as well as hydrophobic tail. A wide range of surfactants and their combinations in different molar ratios have been used to entrap many drugs in niosomes of varying features such as size:

E.g. Spans (span 60, 40, 20, 85, 80); Tweens (tween 20, 40, 60, 80) and Brijs (brij 30, 35, 52, 58, 72, 76).

2. Difference between Liposome and Niosome

Table 1: Difference between Liposome and Niosome

Sr No	Liposomes	Niosomes
1	Vesicles made up of concentric bilayer of phospholipid	Vesicles made up of surfactant with or without cholesterol
2	A naturally occuring type of vesicles	A type of synthetic vesicles
3	Consist of phospholipid bilayer	Consist of non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class
4	Size ranges from 10-3000nm	Size ranges from 10-100nm
5	Comparatively expensive	Inexpensive
6	Special storage condition required	No such condition requirement.
7	Phospholipids used are unstable	Non-ionic surfactants are stable
8	More toxic	Less toxic

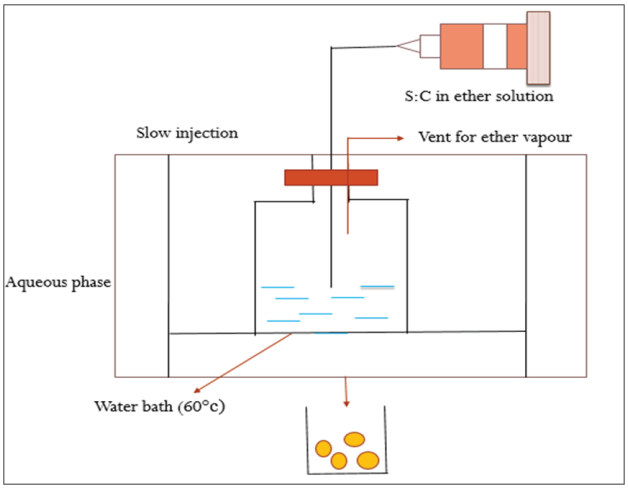

Figure 2: Diagrammatic presentation of ether injection method

3. Preparation Of Niosomes [11-17]

The arrangement techniques ought to be picked by the utilization of the niosomes, since the planning strategies impact the quantity of bilayers size, size appropriation, and entrapment efficiency of the watery stage and membrane permeability of the vesicles.

3.1. Ether Injection Method

In this method, niosomes are prepared by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C. The surfactant blend in ether is infused through 14-measure needle into a fluid arrangement of material. Ether vapourize leads to formation of single layered vesicles. Depending upon the conditions used during formulation the diameter of the vesicle range from 50 to 1000 nm.

3.2. Hand Shaking Method (Thin Film Hydration Technique):

In Hand shaking method, the cholesterol and surfactant were dissolved in a volatile organic solvent (diethyl either, chloroform or methanol) in a round bottom flask. The organic solvent is removed at room temperature (20°C) by using rotary evaporator which gives a thin layer of solid mixture which is deposited on the wall of the flask. The dried surfactant film can be rehydrated with watery stage at 0-60°C with delicate tumult. This procedure structures niosomes with multilamellar structure.

3.3. Sonication Method

In this method, the drug is dissolved in buffer .The small quantity of buffer drug solution is added to the surfactant/cholesterol mixture in a 10-ml glass vial. The mixture is probe sonicated at 60°C for 3 minutes by using a sonicator. The resultant vesicles are formed of small unilamellar type niosomes.

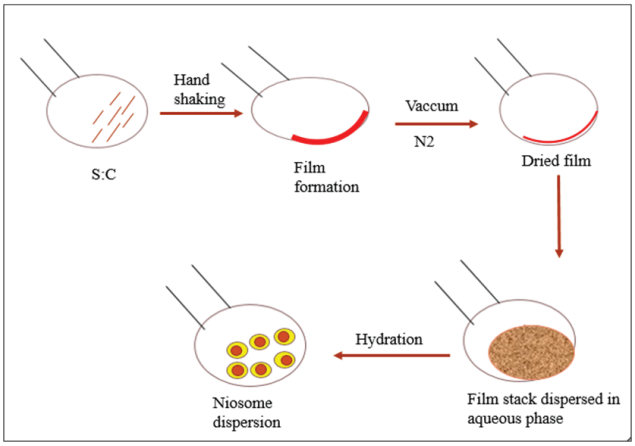

Figure 3: Diagrammatic Presentation of Hand Shaking Method

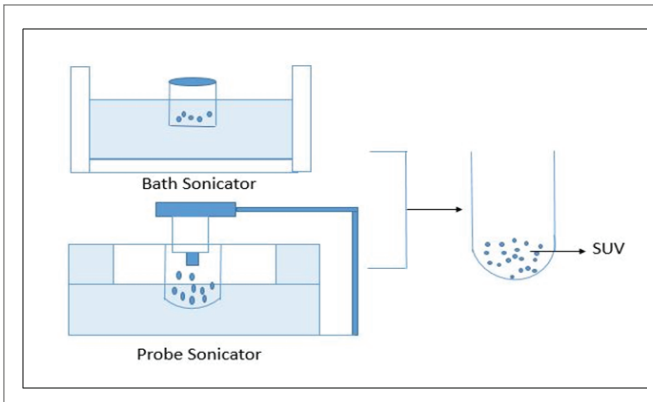

Figure 4: Diagrammatic Presentation Sonication Method

3.4. Multiple Membrane Extrusion Method [18]

Mixture of surfactant, cholesterol and dicetyl phosphate dissolved in chloroform and made into thin film by evaporation of solvent. The film is hydrated with watery medication polycarbonate layers, arrangement and the resultant suspension expelled through which are put in arrangement for upto 8 entries. The multiple membrane extrusion method is good for controlling niosome size.

3.5. Reverse Phase Evaporation Technique (REV) [19-21]

Surfactant and cholesterol (1:1) are dissolved in a mixture of ether and chloroform. Drug is dissolved in an aqueous phase. This aqueous phase is added to organic phase which resulting two phases sonicated at 4-5°C. The reasonable gel shaped is further sonicated after the expansion of a modest quantity of phosphate buffer saline solution (PBS).The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with PBS and heated on a water bath at 60°C for 10 min to yield niosomes.

3.6. Bubble Method

Bubble method involves preparation of niosomes only in one step without addition organic solvent. All the components are dispersed in buffer and this dispersion is placed in a round bottom flask which is immersed in a water bath with controlled temperature. The flask has three necks which are water cooled reflux, thermometer and nitrogen supply. The dispersion is mixed with a shear homogenizer for 15 seconds and then bubbled with nitrogen in this assembly gives the niosomes.

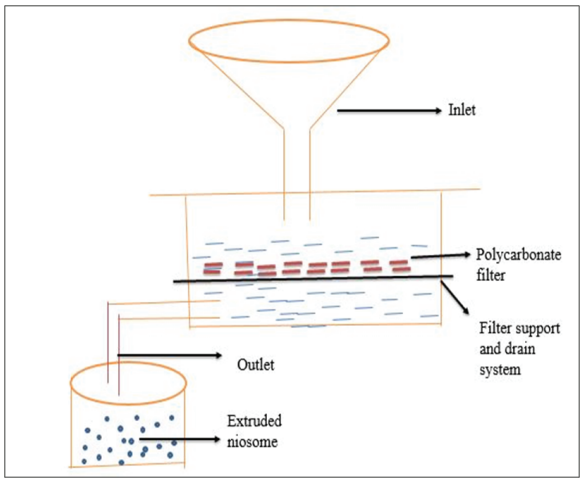

Figure 5: Diagrammatic Presentation of Multiple Membrane Extrusion Method

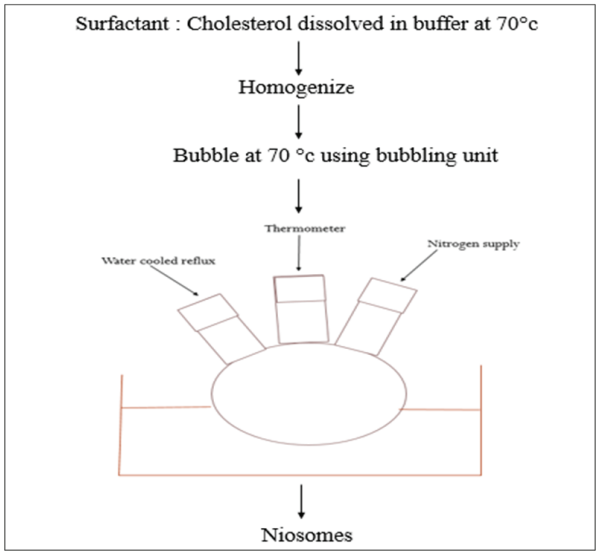

Figure 6: Diagrammatic Presentation of Bubble Method

3.7. Proniosomes [20]

Another strategy for creating niosomes is to cover a water-dissolvable transporter, for example, sorbitol with surfactant. The consequence of the covering procedure is a dry plan. In which each water-dissolvable molecule is secured with a flimsy film of dry surfactant. This planning is name "Proniosomes".

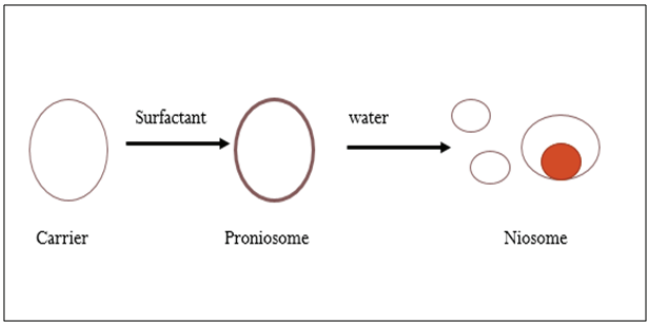

Figure 7: Diagrammatic presentation of Proniosomes

4. Separation of Unentrapped Drug

The expulsion of unentrapped solute from the vesicles can be cultivated by different strategies, which include:

4.1. Dialysis [22]

The aqueous dispersion of noisome is dialyzed in a dialysis tubing against phosphate buffer or normal saline or glucose solution.

4.2. Gel Filtration [23,24]

The unentrapped drug in niosomal dispersion is removed by gel by using Sephadex-G-50 column and elution with phosphate buffered saline or normal saline.

4.3. Centrifugation [25,26]

The niosomal suspension is centrifuged and the supernatant liquid is separated. The pellet is washed and afterward resuspended to get a niosomal suspension free from unentrapped sedate.

5. Method of Characterization of Niosomes [27-31]

Table 2: Method of Characterization of Niosomes

S.No	Niosome Parameters	Measurement
1.	Size	DLS, SEM, AFM, STM, CLS
2.	Encapsulation efficiency	The amount of loaded drug is determined by HPLC, UV.
3.	Z potential	DLS
4.	Stability	DLS

6. Application [35,22]

6.1. Niosomes as Drug Carriers

The niosomal embodiment of Methotrexate and Doxorubicin builds sedate conveyance to the tumor and tumoricidal action of the medication.Niosomal system can be used as diagnostic agents.

6.2. Ophthalmic Drug Delivery

Bioadhesive-covered niosomal plan of acetazolamide which is set up from surfactant length 60, cholesterol stearylamine or dicetyl phosphate displays progressively inclination to lessen the intraocular pressure when contrasted with promoted detailing (Dorzolamide).

6.3. Immunological Application of Niosomes

Niosomes have been used for studying the nature of the immune response produced by antigens.

6.4. Transdermal Delivery

Slow penetration of drug through skin is the major disadvantage of transdermal route of delivery. When drug incorporated in niosomes, penetration rate of drug in increased.

6.5. Delivery of Peptide Drug

There are several limitation associated with oral peptide delivey as breakdown of peptide. By using niosomal preparation, peptides are protected from gastrointestinal peptide breakdown.

6.6. Sustained Release

Drugs which having low water solublity and low therapeutic index are formulated in niosomal preparation for its sustained release action [37].

7. Conclusion

Niosomes appeared to be a well preferred drug delivery system over liposome as niosomes being stable and economic. They present a structure similar to liposome and hence they can represent alternative vesicular systems with respect to liposomes, due to the niosome ability to encapsulate different type of drugs within their multienvironmental structure.

Conflict Of Interest

None.

Acknowledgements

None.

Table 3: Application of Niosomes

S.No	Surfactant	Method	Loaded drug	Encapsulation rate	Administrated	Application	Ref No
1.	Pluronic L64	REV	Doxonrubicin	38.73	-	Anti cancer	[38]
2.	Span 60 Tween 60	REV	Ellagic acid	38.73	Transdermal-	Antioxidant	[39]
3.	Tween 20	THF and Sonication	Curcumin	74.5		anticancer	[40]
4.	Tween 61	THF and Sonication	Tyrosinase plasmid	-	transdermal	vitiligo	[41]
5.	Tween 80 squalene	REV	pCMSECAP	-	Ocular	Gene delivery	[42]
6.	Polyoxyethylene alkyl ether	THF	Insulin	-	oral	Diabetes	[43]

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