WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 13, 674-686. Research Article ISSN 2277– 7105

NIOSOME: A PROMISING NOVEL DRUG DELIVERY SYSTEM FOR THE NATURAL DRUG THROUGH BLOOD BRAIN BARRIER

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Article Received on
27 August 2020,
Revised on 17 Sept. 2020,
Accepted on 07 October 2020
DOI: 10.20959/wjpr202013-18920

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ABSTRACT

Niosomes are considered as novel drug delivery systems (NDDS), are non-ionic surfactant vesicles produced by hydrating blend of cholesterol and nonionic surfactants. It can be utilized as carriers of amphiphilic and lipophilic drug. In niosomes drug delivery system, the medication is encapsulated in a vesicle. Niosomes are exhibit flexibility in their structural characterizations, main property is biodegradable, biocompatible non-immunogenic. Can enhance the solubility, stability of pharmaceutical molecules. They are invented to provide targeting and controlled release of natural pharmaceutical compounds. the preparation method, type and amount of surfactant, drug entrapment, temperature of lipids hydration, and nature of drug molecules are some major factor which can influenced drug targeting, therapeutic application of noisome. The main objective of this article is the application of niosome technology is used to treat a number of diseases, niosome are have excellent good opportunity in research and beneficial for pharma industries. It also provides recent data about the various types of ligand agents which are able to give active targeting drug delivery to the central neuron system.

KEYWORDS: Niosomes, Compositions, Methods of Preparation, applications, characterization.

INTRODUCTION

Several brain and Central nervous system disorder are associated with mortality like neurological disorders (meningitis, encephalitis, viral, bacterial, protozoan, and fungal and worm infections), neurological disorder (epilepsy, seizures, trauma, Parkinson, Alzheimer, mono-neuropathy, polyneuropathy, and myopathy), and brain tumors (cerebral tumors). These problems required proper drug delivery for treatment.[1] Most organs in our body, apart from the brain and spinal cord, are perfused by capillaries lined with endothelial cells which required small pores to deliver the small molecules move rapidly into the organ interstitial fluid from the circulation Several approaches to create novel CNS drug-delivery systems are primarily due to the anatomical and physiological characteristics of the blood- brain barrier (BBB).[2–4]

In the brain arteriole the, ECs are connected to each other by zonula occludens (continuous tight junctions TJs), which are cover Para cellular pathway.[6, 7] This can efficiently obstruct the free polar solutes from Para cellular pathways and so throw away the admission to brain interstitial fluid. Therefore, the BBB let the small particles to pass over the brain through the blood stream such as those that pass in the brain by an active transport apparatus, mainly with crucial nutrients, precursors, and.[8–11] Drug can be transported into the brain endothelium by mechanism namely as BBB peptide transport mechanisms. Generally, there are three ways for deliver drug into the brain[8, 12] containing intra- cerebroventricular (ICV) administration, systemic absorption through BBB, nasal administrations there are many other disadvantage also found of various route of administration which re enlisted blow.

A. Systemic absorption[2,7]

1. In the central nervous system the therapeutics level concentration does not get achieved.
2. There is the chance of the systemic toxicity / side effect inside the body.
3. Mainly in the body the occurrence of the hypoxia like condition is occurring.
4. In the neurodegenerative disorder the delivery of the drug across blood brain barrier reduced so brain mucosa is getting damaged which directly restrict or obstruct the drug delivery.

B. Nasal administration[11,13]

1. The drug efficiency getting reduced
2. Due to the use of the frequent, rapid use of the nasal route the nasal mucosa is getting damaged
3. By the large molecular weight of the drug compound the therapeutic delivery is getting reduced.
4. Nasal congestion occurs.

C. Intracerebro ventricular route[13,15]

1. many time it is found that the large frequent administration of the large volume of the fluid is given within very less time.
2. There is the devolvement of the more intolerable pain which can produced mainly due to the high intracranial pressure so which can affect the drug delivery.
3. Reduction into therapeutic effect due to the lower concentration of the active compound the body.

To suggest an alternative drug-delivery system, two provisions must be considered. The drug must be released in a steady rate and it must be release in an adequate quantity of the active component at the required site. However, as it is mentioned above, systemic absorption through the BBB is easier than the other methods. The previous methods do not fulfil these requirements. To fulfil these requirements, nanostructures are a promising approach to improve natural drug delivery through the brain. The nanostructure could able to change the properties and the behavior of the natural drugs inside the body after administration. It can prevent drugs from deterioration.[16-17] and transporting them to their site of action.[17] Also, enhancement of blood circulation period.[18] Improvement of drug deposition in the pathological tissues[19], and reducing the toxicity can organize the application of the nanostructure for numerous pharmaceutical uses.[22] Amongst all above listed systems, especially liposomes and niosomes are most commonly utilized for the treating pathological disease sufficiency can be enhanced by passes through tissues via blood vessels targeting permeable components.[20, 21] Depending on the polymer material and morphology of the drug-delivery system, various nanoparticles can be prepared from polymers, metals, and colloidal systems. Vesicular systems include vesicular drug- delivery system that has containing liposome's, twosomes, transfersomes, bilosomes, and noisome.[23, 24] Paul Ehrlich, in 1909, began the era of improvement for targeted delivery when he visualized drug delivery

mechanism that would target directly to diseased cell. The ability to direct a therapeutic agent exactly to desired site of action with little or no interaction with non-target tissue is known as Drug targeting. In niosomal drug delivery system the medication is surrounded in a vesicle.[25] The vesicle is composed of a bilayer of non-ionic surfactants and hence the name noisome. In noisome, the vesicles are composed of the amphiphilic, non-ionic surfactant such as Span – 60 which is usually fixed by addition of cholesterol and small amount of anionic surfactant such as dicetyl phosphate.[26]

Table 1:- advantage and disadvantage.

Advantages of noisome	Disadvantages of noisome
1. The characteristics such as size, lamellarity etc. of the vesicle can be varied depending on the requirement.	1. Fusion
2. The vesicles can act as a depot to release the drug slowly and offer a controlled release.	2. Aggregation
3. Since the structure of the noisome offers place to accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.	3. Leaking of entrapped drug
4. The vesicle suspension being water based offers greater patient compliance over oil based systems	4. Physical instability
5. They are osmotically active and stable.	5. Hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.
6.They increase the stability of the entrapped drug	

STRUCTURE OF NIOSOME

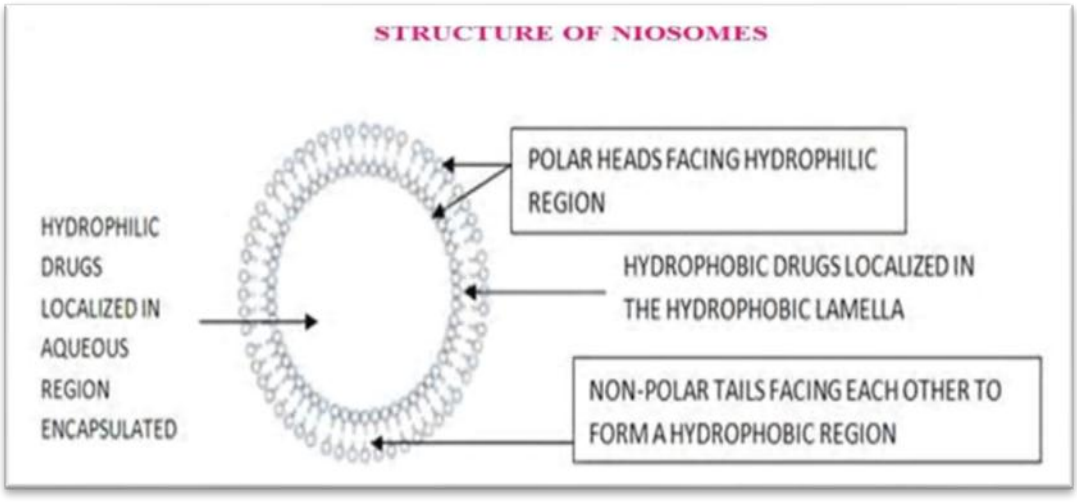

Fig: - 1 structure of noisome.

As shown in the above figure there are basically two building or fundamental blocks are found which can play the very crucial role in the development of the vesicles and it can give all desire property to the niosome.

A. cholesterols :- basically it is consider as the good vesicles should bear the good property like the appropriate size, shape, unbending nature, flexibility and it can mainly provided by the cholesterols molecule.
B. Non ionic surfactants: - the main component is the non ionic surfactant which is basically hydrophilic head and hydrophobic tail portion which can play main role in the development of the niosome. They are non charge materials and it was found that the there is limited number of the hydrophobic tail moiety but there is large availability of the hydrophilic head group. Example is polyglycerol alkyl ether, twins, and span. etc.

Table 2:- surfactant examples.

Non ionic surfactants	Examples
Twins	40 , 60
Spans	20 ,40
Brijis	

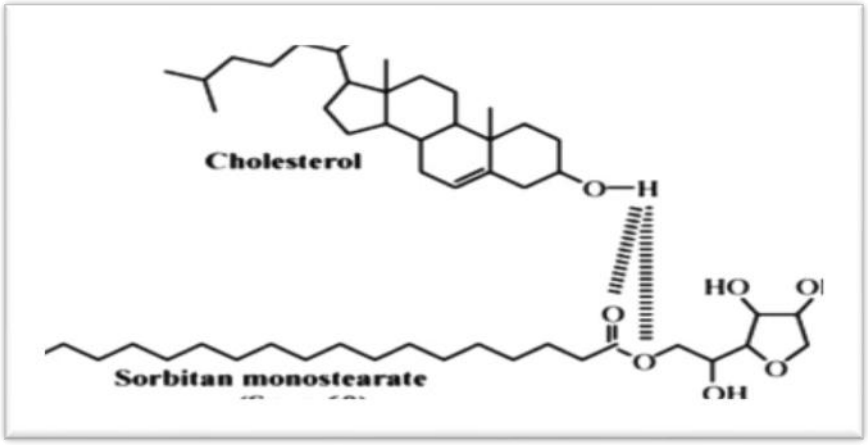

Fig 2:- Structural interaction between Span 60 and cholesterol.

Types of niosome

Mainly these are vesicles which consider as the novel drug delivery system containing vesicular structure in which drug is getting loaded has various functions, shapes. Has which can produce by the various method of preparation. Mainly it can found the 3 main types.

Table: - 3 types of noisome.

Types	Property
SUV (small unilamellar vesicles)	These are unilamallar vesicles having the size

	10-100nm, single coating compound which produced by the sonication, extrusion, method.
MLV (multiple lamellar vesicles)	It contains multiple layers of coating into which the drug is getting loaded and employes simple method for development. Size 100-1000nm.
LUV (LARGE unilamellar vesicles)	It the largest vesicular structure in which the more bioactive material loaded. Size 100-250 nm.

Fig 2- types of niosome.

Method of preparations

A. Ether injection method

The mixture of surfactant, cholesterol and active pharmaceutical ingredients, is dissolved in diethyl ether and by using suitable a gauze needle injected gradually into an aqueous phase. By rotary evaporator above the boiling point of the organic solvent ether solution is evaporated. After complete evaporation of the organic solvent, the large vesicles are additionally exposed to decrease the size to give single-layered vesicles.[28]

B. Trans membrane pH Gradient Method

Surfactant and cholesterol are mixed in chloroform and evaporated under reduced pressure then stream of nitrogen passed to give a small lipid film on the wall of a round-bottom flask. By using an acidic compound (usually citric acid) the obtained lipid film is hydrated. The

resulting preparation is exposed to freeze-thaw cycles.[31-34] The pH of the sample is then elevated to 7.2.[41]

C. Reversed-Phase Evaporation

The surfactants are dissolved in a mixture of ether and chloroform and added into water phase containing the drug to yield w/o emulsion. The resulting mixture is homogenized, and then, organic phase is evaporated.[29] The surfactant forms a gel first and then hydrates to form spherical stable uniform vesicles.[29, 30]

D. Sonication

In the sonication the surfactant cholesterol mixture is distributed in water phase that contains the drug in flax. Then by using probe sonication mixture is subjected for 3 minutes at 60°C until formation of multilamellar vesicles.[42]

Characterization of Niosomes

1. Measurement of Angle of repose

The angle of repose of dry powder was measured by a funnel method. The noisome powder was poured into a clean dry funnel which was fixed at a position using tripod stand. The powder flows down from the funnel to form a cone on the surface and the angle of repose was then calculated by measuring the height of the pile of powder and the diameter of its base.

2. Encapsulation Efficiency

Vesicles were digested with suitable organic solvents such as 50% n-propanol and examined with a suitable analytical method.[63]

The encapsulation efficiency (EE) percentage is calculated by the equation:

(Wt/Wi) ×100 %

Where, Wt = total amount of drug in the Nano vesicle suspension

WI = total quantity of drug added initially during preparation.

3. Osmotic shock

The change in the vesicle size can be determined by osmotic studies. In this method mainly the suspension is incubated with hypotonic, isotonic, hypertonic solutions for 3 hours. Then under optical microscopy the formulations are viewed for changes in the size of vesicles.[36]

4. Stability studies

Stability studies are more commonly done to prevent the sample form photo degradation, oxidation. The niosomes sample are taken at regular intervals of time, observed for color change, surface characteristics analyzed by suitable analytical methods.[37]

5. Zeta potential analysis

To determining the colloidal properties of the prepared formulations Zeta potential analysis is done. The suitably diluted noisome was determined using zeta potential analyzer which mainly based on electrophoretic light scattering. The temperature was set at 25°C. Charge on vesicles and their mean zeta potential values with standard deviation of measurements were obtained directly from the measurement.[38]

Table: - 4 evaluation parameter and techniques.

Evaluation Parameter	Generally used method in evaluation parameter
Morphology	SEM, TEM, freeze fracture technique
Size distribution, polydispersity index	Dynamic light scattering particle size analyzer
Viscosity	Ostwald viscometer
Membrane thickness	X-ray scattering analysis
Thermal analysis	DSC
Turbidity	UV-Visible diode array spectrophotometer
Entrapment efficacy	Centrifugation, dialysis, gel chromatography
In-vitro release study	Dialysis membrane
Permeation study	Franz diffusion cell

Application of noisome

There are numerous application of noisome are found some are listed below:

- It is used as Drug Targeting.
- It is used as Anti-neoplastic Treatment i.e. Cancer Disease.
- It is used as Leishmaniasis
- Noisome act as Carriers for Haemoglobin.
- It is used for Delivery of Peptide Drugs.
- Niosomal system can be used as diagnostic agents.

Table 5 -recent study of drug delivery using niosome as carriers.

application	surfactants	method	drug	route of administrations	reference
pulmonary delivery	twin 60	lipid layer hydration	ciprofloxacin	inhaler	[21]
chemotherapy	bola surfactant	lipid layer hydration	5-fluorouracil	topical	[31]
haemoglobins carriers	span 60	lipid layer hydration	haemoglobin	intravenous	
AIDS treatment	span 60	lipid layer hydration	stavudine		[37]

CONCLUSION

They have similar structure to liposome, to little same in property and hence they can represent alternative vesicular systems with respect to liposome's. Niosomes are thoughts to be better candidate drug delivery as compared to liposomes due to various factors like cost, stability etc. niosome have very important and key role in various types of drug deliveries; like targeting, topical, ophthalmic and parenteral. Niosome are somewhat similar to the liposome in structure, property hence it can mainly represent alternative vesicular system for carrier mediated drug delivery system. They are having ability to encapsulate various types of drug molecules within vesicles. They are mainly composed of nonionic surfactants and cholesterol, and their inside usually comprises a buffer solution at proper PH.

There are numerous approaches' are widely used for the preparation which can mainly effect the establishment and the properties of the medication, cholesterol amount, structure, type, and amounts of surfactant. Surface modification is comparatively easy on them, due to the functional groups that can add on their hydrophilic heads. Nonionic surfactant vesicles were introduced as an innovative and capable method to natural drug delivery. This system has an excellent upcoming future in pharmaceutical uses, mainly with the increasing availability of new approaches to overcome blood brain barriers and allow desire targeting into CNS. Niosomes are very useful in bright future for pharma industries.

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