EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 6
Issue: 4
85-90
Year: 2019

REVIEW ON PRONIOSOMES AS A NOVEL CARRIER FOR NOVEL DRUG DELIVERY SYSTEM

Dr. Shaikh Siraj N.*, Irshad Ahmad Mohd. Salim, Dr. G. J. Khan, Band Afzal Abdul Razzak and M. Y. Khalifa

Department of Pharmaceutics, Ali-Allana College of Pharmacy Akkalkuwa, Nandurbar, Maharashtra, India-425415.

***Corresponding Author: Dr. Shaikh Siraj N.**

HOD Pharmaceutics, Department of Pharmaceutics, Ali-Allana College of Pharmacy Akkalkuwa, Nandurbar, Maharashtra, India-425415.

Article Received on 31/01/2019 **Article Revised on 21/02/2019** **Article Accepted on 14/03/2019**

ABSTRACT

Proniosomes are liquid crystalline compact niosome hybrids which upon hydration form niosomes. It is drug with larger physical and chemical stability and potentially scalable for commercial viability. Proniosomes overcome the disadvantages associated with niosomal and liposomal drug delivery systems. It can act as drug reservoirs and the rate of drug release can be controlled by change of their composition. Proniosomes have presented benefits as drug carriers such as less charge, small toxicity. Proniosomes are used as carrier in novel drug delivery system, in which the medication is encapsulated in a vesicle and provide various pharmaceutical and cosmetic presentations. Proniosomes are generally made by spraying surfactant in organic solvent onto carrier and then evaporating the solvent. Proniosomes are dry preparation of water-soluble carrier particles that are coated with surfactant and can be hydrated to form niosomal dispersion directly before use on brief excitement in hot aqueous media within actions. Proniosomes are superior to niosomes by showing high physical and chemical stability, developed drug targeting with less manufacturecost. Many types of drug deliveries can be possible using proniosomes based niosomes like targeting, ophthalmic, topical, parenteral, oral vaccine. This review focus on advantages, types Proniosomes and their preparation, characterization and their applications in Novel drug delivery.

KEYWORDS: Surfactants, Enhances, Liquid Crystalline, Biodegradable, Carrier.

INTRODUCTION

Recently Nanotechnology has brought a revolution in the Pharmaceutical sector by development of novel dosage forms such as Proniosomes, niosomes, andliposomes.

Liposomes, niosomes also have physical stability problems such as leakage, fusion, aggregation and Sedimentation.[1] Proniosomes overcomes the above disadvantages associated with niosomal and liposomal drug delivery systems. Proniosomes is liquid crystalline compact niosome hybrids which upon hydration form niosomes.

It offers novel solution for poorly soluble drug. Proniosomes is a dry free following, granular product that could be hydrate d directly before use and would avoid many of the difficulties associated with aqueous noisome dispersion and difficulty of physical stability.[2]

The Proniosomes approach decreases these difficulty by using dry, free flowing product, which is extra stable through sterilization and storage.[3]

Proniosomes are generally made by spraying surfactant in organic solvent onto carrier and then evaporating the solvent.[4] Proniosomes can act as drug reservoirs and the rate of drug release can be controlled by change of their composition. Proniosomes have presented benefits as drug carriers such as less charge, small toxicity.[5] Compared to liposome or niosomes, proniosomes are very promising as drug carriers and compared to liposome and niosome suspension, proniosome represents a significant improvement by eliminating physical stability problems, such as aggregation or fusion of vesicles and leaking of entrapped drug's during long time storage.[6]

I) Advantages of Proniosomes

1. Increase the stability of entrapped drug.
2. Surfactants use as a biodegradable.
3. The surfactants customare biocompatible and non-immunogenic.
4. Noexact condition is compulsory for handling and storage of surfactants
5. Avoidingdifficulty of physical stability like aggregation, fusion, leaking.
6. Progress of oral bioavailability of poor absorbed drug.
7. Improvement of enhance skin penetration of drug.
8. It is the dry and free flowing powder[1]

2) Types of Proniosomes

Two types of Proniosomes.

A. Liquid crystalline proniosomes

B. Dry granular proniosomes

A) Liquid Crystalline Proniosomes

Surfactants molecule are saved in contact with water, these are three types.

1) Increasing temperature at Kraft point
2) Addition of solvent which dissolve lipids
3) Use of both temperature and solvent.[1]

- **Advantages of Liquid Crystalline Proniosomes**[7]
- Stability
- High entrapment efficiency
- As a penetration enhancer
- Easy to scale up as no lengthy process is involved

B) Dry Granular Proniosomes[2,8,9]

These are type of carrier.

1) Sorbitol based proniosomes
2) Maltodextrin based proniosomes

1 **Sorbitol based Proniosomes**[2,7] It is a dry preparation that includes sorbitol as the carrier since the sorbitol carrier is soluble in organic solvent, the procedure is necessary to be repeated till the desired surfactant coating has been achieved.[8] There are made by the spraying surfactant mixture prepared in organic solvent in to sorbitol powder and then evaporating the surfactant.

2 Maltodextrin based Proniosomes

Maltodextrin based proniosomesnew development and has potential application in delivery of hydrophilic or amphiphilicdrug. It is prepared by the slurry method. The method of obtaining noisome from such a proniosomes for the drug delivery is very simple. The greater surface area outcome in thinner surface coating, which make the hydration process efficient.[1]

III) Components of Proniosomes[9,10]

The essential components of the delivery system as follows.

a) Surfactants
b) Carrier material
c) Membrane stabilizers
d) Solvent and aqueous phase
e) Drug
f) Hydration medium
g) Nature of encapsulated drug

a) Surfactants

Surfactants are the surface active agent'scommonly organic compounds that are amphiphilic in nature. They have variety of function containing as solubilizers, wetting agents, emulsifiers and permeability enhancer. Surfactant molecule contains both a waterinsoluble andwater soluble components. Selection of surfactant should be done on the basis of HLBvalue On the basis of dangerous packing parameters of surfactants can predicate geometry of vesicle to be formed. Dangerous packing parameters can be defined using equation.

$$Cpp = V/1c \times ao$$

Where,

Cpp = 0.5-1 spherical vesicles form
Cpp = 1 in verted vesicles form
V = hydrophilic group volume
1c = the critical hydrophobic group length
ao = the areav of hydrophilic head group

Table 1: List of surfactants used in proniosomes formulation.

Non-ionic amphiphilic	Examples
Alkyl ethers and alkyl glycerol Ethers	Polyoxyethylene 4 lauryl ether (Brij30)
Polyoxyethylenecetyl ethers	Brij 52, 56, 58
Polyoxyethylenestearyl ethers	Brij 72, 76
Sorbitan fatty acid esters	Span 20, 40, 60, 80
Polyoxyethylenesorbitan fatty acid esters	Tween 20, 40, 60, 80

b) Carrier materials

Carrier when used in the proniosomesformulation permits the flexibility in the ratio of surfactant and other components that incorporated.

Table 2: Carriers used for the preparation of proniosomes.[2]

Sr.No	Carrier materials
1	Maltodextrin
2	Sorbitol
3	Mannitol
4	Spraydried lactose
5	Glucose monohydrate
6	Lactose monohydrate
7	Sucrose stearate

c) Membrane stabilizer

Cholesterol and lecithin are mostly used as membrane stabilizer. Steroids are main components of cell membrane and their presence in membrane and bring about importance changes with regard to bilayer stability, fluidity and permeability. It prevents aggregation by the inclusion of aggregate by repulsive steric or electrostatic effects. Cholesterolgrowth or losses the percentage encapsulation efficiency depending on either the variety of the surfactants or its concentration within the formula. It acts as stabilising as well as penetration enhancer. It is found those vesicles composed of soya lecithin probably due to the change in the intrinsic composition.[7,8,9]

d) Solvent and aqueous phase

Alcohol used in Proniosomes has a great effect on vesicle size and drug permeation rate. vesicle formed different alcohol are different size and they follow the order, Ethanol > propanol >Butanol> Isopropanol[1]. Ethanol are the better solubility in aqueous solution hence leads to development of larger size of vesicles instead of isopropanol which is forms smaller size of vesicles due to branched chain present.[7] Phosphate buffer pH 7.4, 0.1% glycerol, boiling water is used as aqueous phase in preparation of proniosomes.[9]

In comparison to other drug delivery system.

a) The Proniosomal system is passive, non-invasive and is available for immediate commercialization.
b) Proniosomes composition is safe, effective and the components are accepted for pharmaceutical and cosmetically use.

e) Model drug selection criteria[10]

Drug selection criteria based on the following expectations.

1. Short half-life
2. Higher adverse drug reaction drugs
3. Small aqueous solubility of drug
4. Controlled drug delivery proper drug
5. High dosage frequency of drug

f) Hydration medium

a) Phosphate buffer having several pH's are commonly used hydration medium for preparation of proniosomes derived niosomes. The hydrating is used to make niosomes should be usually above the gel to liquid phase transition temperature of the system.

g) Nature of encapsulated drug

The specific factor in the consideration is the influence of an amphiphilic drug on vesicle preparation. The extra drug is added the increase in its encapsulation could be the result of saturation of the medium increase in the drug concentration presented an increase in the both percentage encapsulation efficiency and the quantity of drug encapsulated per mole total lipids upon hydration and preparation of Niosomes.[7]

IV) Methods of preparation of Proniosomes[11]

The Proniosomes are prepared by the following methods.

1. Spraying method / spray coating method
2. Slurry method
3. Coacervation phase separation method

1. **Spraying method / spray coating method**

Spray coating method is developed by the Hu and Rhodes in (1999) in which round bottom flask containing sorbitol are attached on the rotary evaporator.[1] a mixture and cholesterol should be ready and introduced in to round bottom flask on rotary evaporator by sequential spraying of aliquots in to carrier's surface.[3] evaporator has to be avacuated and rotating flask can be rotated in water bath in vacuum at 65-70 c for 10-20 min. surfactants coating on the carrier is very thin and hydration of this coating allows multilamellar vesicle to form as the carrier dissolves. The main advantage of this method is to provide a means to formulate hydrophobic drugs in a lipid suspension with or without problem with instability of the suspension or susceptibility of active ingredient to hydrolysis.[10] proniosomes derived niosomes dispersion is obtained by hydrating proniosomes preparation with 80 ^{0}c distilled water and vertex mixing for 2 min.[12]

Advantages[7]

It's a very simple method suitable for hydrophobic drug without concerns of instability or susceptibility of active pharmaceutical ingredient to hydrolysis.

Disadvantages

a) ThisMethod is time consuming and includesparticular equipment with vacuum and nitrogen gas.
b) The thin film approach allows only for a predetermined lot sizes so material often wasted so minute quantities or minor dose batch can be tedious one.

2. Slurry method

"Almira, I and Blazek-Walsh et al in (2001)" established slurry method to produce proniosomes using Maltodextrin as a carrier. Slurry method that entire volume of surfactant solution is added to Maltodextrin powder in rotary evaporator and vacuum applied the powder appears to be dry and free flowing.[8] The powder should be stored at 4 ^{0}c in a closed container. The time required to produce Proniosomes is independent on the ratio of carrier material to surfactant solution.[13]

Advantages of slurry methods[7]

1) Higher surface area result in thinner surfactant coating makes the re hydration procedure efficient.
2) Maltodextrin like polysaccharide which is simply soluble in water.
3) It's used as carrier material they were simply coating by easily adding surfactant with organic solvent to dry Maltodextrin.

Disadvantages of slurry methods

1) Method is time consuming and includesparticular equipment with vacuumand nitrogen gas.
2) Thin film approach allows only for a pre determine lot sizes so material obtain wasted.

3) Coacervation phase separation method

Weight correctly or particular amount of surfactant, carrier (lecithin), cholesterol and drug can be taken in a clean and dry wide mouthed glass vial (5ml) and solvent should be added to it.[11] Ingredients are all heated and after heating all ingredient should be mixed with glass rod. It's the open end of glass vial are essential covered with a lid.

Advantages

1) This method is simple and without time consumable so it does required any specific equipment's
2) Special adopted for gel preparation
3) Less quantities or less dose preparation can be prepared on lab scale.[12,13]
4) **IV) Characterisation of Proniosomes.**[14,15,16]

Table 3: Characterization parameters of proniosomes.[7]

PARAMETER	INSTRUMENT/METHOD USED
Vesicle morphology	Scanning electron microscopy, Laser microscopy.
Figure and surface Morphology	Optical microscopy, Scanning microscopy, Transmission microscopy.
Angle of repose	Funnel method
Encapsulation efficiency	Centrifugation method, Dialysis method
Drug release kinetic data analysis	Higuchi's model, Peppa's model.
In-vitro methods for assessment drug release from Proniosomes	Dialysis tubing, Reverse dialysis, Franz diffusion cell.
In-vitro permeation study	Franz diffusion cell, Kesharychien diffusion cell

The characterisation of Proniosomes is supported by different ways.

a) Scanning electron microscope
b) Measurement of angle of repose
1. Funnel method
2. Cylinder method

c) Optical microscopy
d) Entrapment efficiency

a) Scanning electron microscope

Using through scanning electron microscopy the surface morphology and size distribution of proniosomes can be studied. Proniosomes were spread on to the double sided tape that was attached on aluminium stubs. The aluminium stub was located in vacuum chamber of a scanning electron microscope and was made electrically conductive by coating a thin layer of gold and scanning electron microscopepictures were noted at 15ev accelerating voltage.

Measurement of angle of repose

Two methods in which the angle of repose of dried proniosomes was measured.

1. Funnel method

The Proniosomalpowder was transferred into a funnel which was permanent at a position 10cm above alevel surface. The powder is poured from funnel to form a cone on the surface, and the angle of repose was then calculated by determining the height of the cone and diameter of its base.

2. Cylinder method

The Proniosomalpowder was transferred into a cylinder which was permanent at a position 10cm above a level surface. the powder is poured in a cylinder to form a cone on the surface, and the angle of repose was then calculated by determining the height of the cone and diameter of its base.

Angle of repose is calculated by the equation

$$Ø – Tan\text{-}1\ X\ (h/r)$$

b) Optical microscopy

Proniosomal powder was evaluated for number of vesicles formed after hydration. Proniosomal powder was subjected to hydration with phosphate buffer (ph 7.4) and the formed niosomes were counted by optical microscope using the haemocytometer.

c) Entrapment efficiency

The prepared niosomes were separated from entrapped drug by centrifugation. This method hydrated proniosomes were centrifugation at 14000rpm for 5 minutes using the refrigerated centrifuge and the supernatant were examined for free drug content. Entrapment efficiency was calculated using the given formula,

Entrapment efficiency = Total drug loaded –free drug ×100 Total drug

v) Applications of Proniosomes[1,8,17,18,19]

The application of Proniosomes technology is widely varied and can used to tried a number of diseases

1. Anti-neoplastic treatment
2. Leishmaniasis
3. Delivery of peptide drugs
4. Uses in studying immune response
5. Proniosomes as carriers for haemoglobin
6. Proniosomes used in cardiac disorders
7. Sustained release
8. Localized drug action
9. Antibacterial therapy
10. Hormonal therapy
11. Cosmetics
12. Nsaidappllication
13. As aniallergic

1) Preparation of vitamins

2) **Anti-neoplastic treatment**

Antineoplastic drug causes severe side effect. proniosome can alter the metabolism, prolong circulation and half- life of the drug decreasing the side effect of drug.

3) Treatment of Leishmaniasis

Leishmaniasis a disease in which a parasite of genus leishmania invades the cell of liver and spleen, use of proniosomes in tests conducted displayed that it was possible to administer higher levels of the drug without triggering of the side effect.

4) Delivery of peptide drugs[1]

Oral peptide drug delivery has long been faced with a task a bypassing the enzymes which would breakdown the peptide. Use proniosomes to successfully protect the peptide from gastrointestinal peptide breakdown is been investigating.

5) Uses in studying immune response

Proniosomes are the used in studying immune response due to their immunological selectivity. Proniosomes are being used to study the nature of the immune response provoked by antigens.

6) Proniosomes carriers for Haemoglobin

Proniosomes can be used as carriers for haemoglobin within the plasma. The proniosomal vesicle is permeable to oxygen and hence can act as a carrier for haemoglobin in anaemic patients.

7) **Proniosomes used in cardiac disorders**

Proniosmes are used as carriers for the transdermal delivery of cardiac active drugs. Mostly transdermal delivery of captopril for the treatment of hypertension. Proniosomal system causes lengthy release of the drug in body.

8) Sustained release

Character of liver as depot for methotrexate after proniosomes are taken of the liver cell. Azmin et al suggested that the role of liver.

9) Localisation drug action

Proniosomes is one of the approaches to achieve localised drug action, localised drug action result in enhancement of efficacy of potency of the drug and at the sometime decreases its systemic toxic effect Eg. Antimonial in capsulated within proniosomes are taken up by mononuclear cells result in localisation of drug increase in potency and hence reduce both in dose and toxicity.

10) Cosmetics

Proniosome gel used as-an effective delivery systems for cosmetics and Cosmeceuticals due to their single properties. For applying therapeutic and cosmetic agents onto or through skin involves a nontoxic, dermatologically suitable carrier, which not onlycontrol the discharge of the agent for prolong action but also enhances the penetration to the skin layer(Boddu M.et al., 2017).

ACKNOWLEDGEMENT

The authors are thankful to Hazrat Maulana G.M. Vastanvi Sahab, President, Jamia Islamia Ishaatul Uloom's Ali Allana College of Pharmacy Akkalkuwa, Dist-Nandurbar for providing the work facilities.

CONCLUSION

Proniosomes are promising drug carriers for the future with larger physical and chemical stability and potentially scalable for commercial viability. Proniosomes overcome the disadvantages associated with niosomal and liposomal drug delivery systems. Many types of drug deliveries can be possible using proniosomes based niosomes like targeting, ophthalmic, topical, parenteral, oral vaccine etc. Proniosomes are a new and efficient approach to drug delivery. Researcher working on Proniosome can utilise it as a carrier in herbal drugs delivery, cosmetics, nutraceuticals, other formulations & promising drug delivery module.

REFERENCES

1. Sadanandan A, George B, Samuel J, Raj P, Thomas N, Daisy P, Carla B.A review on proniosomes: an innovative approach to vesicular drug delivery system. World journal of pharmacy and pharmaceutical sciences, 2017; 6(3): 1039-1035.
2. Sadiq M, Reddy K, kumar B, Nirosha K. Review on proniosome-a novel approach to vesicular system. International journal of novel trends in pharmaceutical sciences, 2014; 4: 97-100.
3. Kumar K, Rai A. Development and evaluation of Proniosomes as A promising drug carrier to improve Transdermal drug delivery. International Research Journal of pharmacy, 2011; 2(11): 71-74.
4. Malarkodi A. S, Srilakshmi C, Ganesan G. Proniosome Gel: An Effective Novel Therapeutic Topical Delivery System. International Journal of Pharm Tech Research, 2013; 5(4): 1754-1764.
5. Radha G, Chowdary C. Formulation and Evaluation of Ornidazole Proniosomal Gel.Indo american journal of pharmaceutical research, 2014; 4(4): 2657-2664.
6. Sudhamani T, Priyadarisini N, Radhakrishnan M.Proniosomes – A Promising Drug Carriers. Int.J. Pharm Tech Res., 2010; 2(2): 1446-1454.
7. Singh S, Chaudhari Y, Singh R, Kunwarpuriya A.Proniosomes: a recent advancement in vesicular drug delivery system. World Journal of Pharmaceutical Research, 2015; 4(5): 1671-1689.
8. Bharti N, Loona S, Khan M.Proniosomes: a recent advancement in nanotechnology as a drug carrier. International Journal of Pharmaceutical Sciences Review and Research, 2012; 12(1): 67-75.
9. Gupta R, Kumar S, Gupta N, Kumar A. The new advancement nanotechnology: proniosomes as a promising and potential drug carrier. International Journal of Research and Development in Pharmacy and Life Sciences, 2014; 3(6): 1258-1265.
10. Anil Udasi T. Proniosomes: A Novel Approach to vesicular drug delivery system. International Journal

of Pharmacy and Pharmaceutical Science Research, 2013; 3(1): 1-6.
11. Maya W, Ashar S.Proniosomal drug delivery systemsAn overview. International journal of pharmaceutical and chemical sciences, 2012; 1(3): 1044-1056.
12. Jadhav K, Pawar A Y, Bachhav A, Ahire A.Proniosome: A Novel Non-ionic Provesicules as Potential Drug Carrier. Asian Journal of Pharmaceutics, 2016; 10(3): 210-222.
13. Yasam V, Jakki S, Natarajan J, Kuppusamy G.A review on novel vesicular drug delivery: proniosomes. Drug delivery, 2013; 1-7.
14. Sulthana A A, George B J, Samuel J, Thomas N. Proniosomes a future Revolutionary drug delivery system. International Journal Of Pharmaceutical, Chemical And Biological Sciences, 2015; 5(4): 879-882.
15. Benipal G.Design, Development and Evaluation of Proniosomal Gel of an Antifungal Drug – Ketoconazole. I nternational Journal of Pharmaceutical Sciences Review and Research, 2015; 31(2): 265-272.
16. Srikanth, Kumar Y.A. Preparation and evaluation of Maltodextrin based Proniosomes containing Capecitabine. International Journal of Research and Development in Pharmacy & Life Science, 2017; 6(7): 2856-2861.
17. Sulthana A.A, George B.J, Samuel J. Proniosomes A Future Revolutionary Drug Delivery System. International Journal Of Pharmaceutical, Chemical And Biological Sciences, 2015; 5(4): 879-882.
18. Pradeepa N, Parthiban S, Kumar G.P.S. Proniosome A Promising Pulmonary Drug Delivery System. European Journal Of Pharmaceutical And Medical Research, 2018; 5(11): 609-618.
19. Boddu M, Choppari V, Rapalli V.K, et al. Formulation and Evaluation of Proniosomes of Felodipine. Drug Designing: Open Access, 2017; 6(3): 01-09.