WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 14, 1322-1333. Review Article ISSN 2277– 7105

A REVIEW ON PRONIOSOMES DRUG DELIVERY: AN INNOVATIVE APPROACH

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Article Received on
19 Sept. 2020,

Revised on 09 October 2020,
Accepted on 29 October 2020

DOI: 10.20959/wjpr202014-19169

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ABSTRACT

The main aim of drug therapy is to provide therapeutic effect of drug to precise site in the body instantly achieve and then preserve desired drug concentration in order to produce preserve effect. conventional pharmaceutical dosage forms are incapable of controlling the rate of drug delivery to the target site, that result the substantial distribution of drugs in the non- target tissue and body fluids required therapeutic doses that could far exceed the amount necessary in target cells, that was the higher dosage usually lead to dangerous for health during treatment and after treatments. A novel drug delivery system, It is delivers the drug at fixed rate as it's requirement. Drug encapsulation in the vesicles is one such system which helps to prolong drug duration in systemic circulation and decrease the toxicity by selective uptake vesicles drug delivery system e.g. niosomes, proniosomes, liposomes, pharmocosomes etc. To overcome the limitation associated with liposomes and proliposomes, niosomes have gained attention as drug carriers and drug targeting agents. Proniosomes are the functional drug delivery system, Ease of transfer, Feasibility, distribution, storage, and high drug loading capacity, fewer side effects, high efficacy, & concentration of surfactant affect. Encapsulation efficiency & drug release rate. as compared to other novel formulation proniosomes increase the stability profile, problems involved with niosomes such as leakage, fusion, aggregation, and provide convenience in dosing, distribution, transportation and storage showing improved result. This review complies merits and demerits of vesicular drug delivery, over the conventional dosage form, Proniosomes definition types and its method and applications.

KEYWORDS:- vesicular drug delivery, Niosomes, proniosomes, proniosomal gel.

INTRODUCTION

Proniosomes are dry formulation of water soluble carrier particles that are coated with surfactant. They are rehydrated to form niosomal dispersion immediately before agitation in hot aqueous media within minutes. The fundamental object of development controlled and targeted release dosage form is that improve the therapeutic effect of drug improve drug safety margin of high potency drugs by the increases plasma concentration, and also decrease side effects.[1] Main object of Novel vesicular drug delivery system is that drug rate work on need of body throughout the period of treatment and controlled and targeted effect on the site of action, drug are encapsulated in to vesicles That manner prolonged drug action. Biological origin of these vesicles was first reported in 1965 by Bingham bodies. Targeted drug delivery is mode of delivering the therapeutic agent to the tissue of interest. Drug targeting means the delivery of drugs to receptor organs or any other specific part of body.[2] Various type of carriers are utilized to carry drugs at the target site in the body part like tissue organ which include, Niosomes, proniosomes, liposomes, microsphere, electrosomes, phytosomes etc. These type of vesicular drug delivery targeted drug in to the site of action.[3] Vesicular drug delivery like a colloidal particles in which amphiphilic molecule made a concentric bilayer covered by a aqueous compartment. The amphiphilic molecules like surfactants (nonionic), phospholipid (phasphotidylcholine, phasphotidylserin etc,) are add combination or separately with cholesterol.[4] Proniosomes evaded the problems associated with niosomes like fusion, aggregation, physical stability, sedimentation, aggregation leakage of drug. pronisomes are dry free- flowing formulation of surfactants- coated carrier, which can be rehydrated by brief agitation is hot water to form multillamellar niosomes.[5] Proniosomes have some advantages over the niosomes and liposomes, these are ease in transportation, sterilization, distribution, storage. Compare the conventional niosomes, proniosomes derived niosomes and proniosomes release profile express that both are more stable.[4] Niosomes structure and properties similar with liposomes. Proniosomes are dry formulation so it was hydration was easy and reduce the problems which associated with niosomes dispersions.[6] Pronoisomes were studied as alternatives to liposomes and other carrier system for entrapping both polar and nonpolar or hydrophobic and hydrophilic drugs. Maltodextrin proniosomes formulation was recently developed and delivered by both types of drug like hydrophobic and amphiphilic, in this formulation surfactant support carrier so easily adjust and surfactant to carrier with highest mass proniosomes prepared.[7]

Advantages of proniosomes over the niosomes include

1. Niosomes have some drawback like aggregation, fusion, leakage, physical stability to overcome these type of drawback we have to developed the formulation of proniosomes or proniosomal gel.[5]
2. Drug entrapped in vesicles in proniosomes, vesicles work like a repository which helps to prolong release.[4]
3. Proniosomal gel for ocular delivery full fill necessities and increase contact time and also save the degradation of drug from the metabolic enzymes which was present in tear.[8]
4. Drug which have limiting shelf life can be overcome by hydrolysis of entrapped drug.[7]
5. One of best parameter of proniosomes powder ease of use, dry powder form is further produce capsules beads also.[4]
6. Proniosomes also overcome the problems associated with liposomes such as sedimentation, storage, oxidation, hydrolysis.[9]
7. Compared the other semisolid dosage form proniosomal gel better percutaneous absorption.[10]
8. Proniosomes offer a promising drug delivery and also improve skin recovery rate.[10]
9. Storage of proniosomes this advantage with proniosomes so, proniosomes is a versatile drug delivery system.[11]
10. Proniosomes and proniosomal gel components are work as membrane stabilizer, lecithin work as penetration enhancer and cholesterol change the fluidity of buffer.[12]

Components of proniosomes[13]

S, No.	Class	Example	Use
1	Surfactant	Span20, 40,60,80,85, Tween 20,40,80	To increase drug flux rate across the skin
2	Cholesterol	Cholesterol	To prevent leakage after drug formulation
3	Lecithin	Soya lecithin, egg lecithin	Penetration enhancer
4	Solvent	Chloroform, ethyl, methyl alcohol,	Work as penetration enhancers

1. **Surfactant:-** Sorbitan esters and polysorbate are used pharmaceutical formulations as lipophilic nonionic surfactant.when sorbitan used alone, sorthebitan esters (3-8 HLB) produce stable water -in- oil and micro emulsion but they are sometime used with combined different ratio of a polysorbate (8-16 HLB) to produce water -in- oil or oil -in- water emulsion. They act as permeability enhancers. HLB value of surfactant among 4-8

small, spherical shape vesicles form while greater the HLB value increase the size of vesicles. Sorbitan ester.

Sorbitan monolaurate (span 20).

Sorbitanmonopalmitate (Span 40).

Sorbitan monostearate (Span60).

Sorbitan monooleate (Span 80).

Polysorbate (PolyoxyethyleneSorbitan fatty acid ester) .

Tween 20.

Tween 40.

Tween 60.

Tween 80[14]

2. **Cholesterol:-** Cholesterol used as a fluidity buffer, and also changes permeability presence in the membrane. cholesterol have amphipathic nature, OH group bind with the aqueous phase while aliphatic changed with parallel with hydrocarbon. Entrapment efficiency of drug depends on the concentration of cholesterol, if concentration increase drug leaks because its effects on vesicles.[10]

3. **Lecithin -** It is a complex mixture of acetone- insoluble phosphatides, consist of mainly phospholipids like phosphatidyilcholin, phosphatidylehanolamine, phosphatidylserin, combination of triglycerides, fatty acids, and carbohydrate. Soya lecithin vesicles are larger than egg lecithin, that was difference between soya lecithin vesicles and egg lecithin vesicles. Lecithin increase entrapment efficiency of drug. avoid the problem of leakage of drug.[14]

4. **Solvent-** Alcohol (Ethanol, propanol, Butanol, Isopropanol) Pronisomes having great effect on vesicles and permeability of drug by the alcohol Following. Order of alcohol form different type of vesicles that is, Ethenol> Propanol> Butanol> Isopropanol. Solubility effect the vesicles Size greater solubility like Ethenol in water due to this maximum size vesicles formed and low solubility of Isopropanol in water minimum size vesicles formed.[4]

Drug - Selection of drug depends on some parameters

1. Solubility of drug is low
2. Drugs have higher toxic effect

3. Dosing frequency high
4. Drug have short half life
5. Control and targeted drug delivery suitable[1]

Method of preparation of proniosomes

Slurry method- In a round bottom flask prepared a slurry, usually solvents are used for prepared the slurry and maltodexrtin as a carrier. To found the free flowing powder of proniosomes applied vacuum for during slurry, first take a round bottom flask containing carrier (Maltodextrin, lecithin), to evaporate the solvent flask attached to the rotary evaporator to 50-60 rpm at temperature 45-47 °C. to find the dry free flowing product, reduced the pressures 600 mm Hg and found the dry formulation, store tightly closed container under refrigeration.[5]

Coacervation phase separation- In a stopper glass vials required amount of surfactants, cholesterol and lecithin mixed with solvent stopper used to prevent the loss of solvent. This mixer was heated and then mixed by a glass rod after complete mix all ingredients small amounts of buffer solutions was added to the prepared mixture and heat again on water bath for 10 minutes, Than found a clear solution, this solution left for 24 hour at room temperature clear solution converted in to proniosomal gel.[14]

Spray coating method- In this method carrier take in a round bottom flask and attached with rotary evaporator and then prepared a mixture by required amount of cholesterol and surfactant and spray on the carrier the evaporator evacuated and kept in rotating flask and temperature maintain 65-70°C under the vaccum for 15-20 minutes. Evaporation continued and all surfactants are add till the dry powder of proniosomes were not prepared.[10]

Niosomes prepared from proniosomes

To formulate the niosomes from proniosomes aqueous phase adding with drug and proniosomes with a brief agitation at mean transition temperature and higher than it surfactant.

Evaluation parameter

In vitro studies

1. Shape and surface morphology - Scanning electron microscopy (SEM), transmission electron microscopy (TEM), and Optical microscopy method use in surface and shape morphology like, spherical shape, round shape, after formation of aggregation.[4]
2. Mesurment of angle of repose- prepared dried pronisomes for the angle of repose, here two methods for measurement of angle of repose

a) funnel method

b) cylinder method

A. In the cylinder method powder of proniosomes flow in the cylinder powder, make a pile, to find out the angle of repose, measure heap of pile and radius.

B. Funnel method- Take a funnel and, funnel fixed at height and dried pronisomes poured in it that way make a pile measured hight and radius to find out angle of repose.[4]

Vesicles morphology:- Proniosomes vesicles Related with the vesicles morphology like shape and size. Two condition suitable for the measurement without agitation and with agitation. Result of largest vesicles Size found in hydration without agitation. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) used in vesicles morphology.[13]

Drug content:- Content of drug calculated by calibration curve. proniosomes measured in a volumetric flask about 100 mg and add methanol and shaking for 15-20 minutes, again mix 100 mg methanol for dilute the solution after dilution take 10 ml part of this solution for dilution at certain PH with saline phosphate buffer. Take solution in cuvete to take of absorbance at any wavelength, then measured drug content through calibration curve.[9]

Encapsulation efficiency-To calculated % Encapsulation Efficiency used following formula

$$\%\text{Encapsulation Efficiency} = \frac{\text{Total drug - Free dug}}{\text{Total drug}} \times 100$$

First proniosomes converted in to niosomes to add distilled water and worm water, than centrifuge the prepared dispersion system. a clear fraction take and determined by spectroscopy of drug content.[15]

Stability studies:- used this parameter for proniosomes Object is that how long time formulation stand and what temperature so we three temperature to check out, first is room temperature (25±2°c), second is refrigerator (4-8°c) and third is oven temperature (45-2°c). To perform this practical proniosomal gel fill in a glass vial and covered with aluminium foil, after a time period sample withdrawal after an interval after one or two months, to check crystal formed stature solid or liquid both , particle and entrapment efficiency also analyze.[10]

Application of proniosomes

As a drug carrier- To overcome the problems associated with niosomes liposomes proniosomal gel advantages as good drug carrier compare to other conventional drug delivery. problem associated with niosomes stability aggregation, proniosomes does not these types occurs problems.

Transdermal drug delivery systems- Proniosomes increase the mechanism of action of drugs through the skin. cosmetics mainly used this proniosomal technology. In comparison to Un - Entrapped drug penetration increases by proniosomal gel, and also greatly work on weak immune system. Now proniosomal vaccine for Transdermal drug delivery also researched.[4]

Targeted drug delivery - One of the best advantages of vesicular drug delivery is targeted effect on site of the action. Proniosomes produce targeted effect on reticulo - endothelial system, reticulo endothelial system take up proniosomes vesicles. Circulating serum factor controlled the uptake of proniosomes that factor is opsonines that type utilization of drug targeted to metastasize tumors which was occurs in the animal liver, spleen.[7]

Ocular drug delivery - In the ocular drug delivery of proniosomal gel, full fill the problems those are face in ocular drug delivery, maintain the drug activity. That solve metabolism problem and also save degradation of drug by metabolic enzyme which is available in tear and corneal epithelial surface and other advantage is increase contact time and retention of drug also improve. Lomefloxacin proniosomal gel good for bacterial conjunctivitis compare the conventional eye drops.[8]

Peptide drugs delivery - In comparison to conventionall peptide drug, that has drawback peptide proteins break down by passing enzyme, niosomes protected in gastrointestinal peptide breakdown drug which entrapped in vesicles so stability increase.[9]

Sustained drug release- Proniosomal encapsulated drug delivery applied with low water solubility, prolong drug action in brimonidine tartrate based proniosomal gel improve ocular bioavailability of drug prolong residence time and improve ocular contact time in of drug and also provide sustained release of drug.[12]

Some research work of proniosomes

Research	Authors	Result
Design and development of proniosomal Transdermal drug delivery system for captopril	Ankur gupta, Sunil kumar Prajapati et al.,[16]	gel possesses high entrapment efficiency and utilizes alcohol which itself can act as penetration enhancer.
Proniosomal gel - derived niosomes: an approach to sustain and improve the ocular delivery of Brimonidine tartrate; formulation, in vitro characterization and in vivo pharmacodynamic study	Alaa Emad Eldeeb, Salwa Salah and Mahmoud Ghorab[12]	Proniosomal of BRT were successfully prepared by coacervation phase separation method, a promising ocular drug delivery vehicle for BRT in treatment of glaucoma with a sustained release manner, high entrapment of BRT and sustained release profile over 24 h.and also improve bioavailability drug release from prepared vesicles.
Single intravenous dose of novel flurbiprofen-loaded proniosomes formulation provides prolonged systemic exposure and anti inflammatory effect	Preeti verma, Sunil kumar prjapati[17]	This report is the first to demonstrate prolonged systemic exposure and therapeutic effect parenteral delivery. A promising approach to treat acute pain and inflammation that seen surgery and injury. Drug entrapment efficiency was also increase with increasing span 80 to span 20 ratios, a single intravenous bolus dose to provide a sustained therapeutic effect.
Improved bioavailability and antitumor effect of Docetaxel by TPGS modified proniosomes: in vitro in vivo evaluation	Helong Liu, Liangxing Tu et al.,[18]	Particle size plays an important role on clearance and tumor uptake of nano particle. The in vitro release results showed that both DTX - TPGS -PN and DTX - PN niosomes totally released in 12 h and 8 h in simulated

		intestinal fluid and simulated gastrointestinal fluid respectively.
Transdermal delivery of oxybutynin chloride proniosomal gels for the treatment of overactive bladder	Rajan Rajabalaya, Sheba R David et al.,[19]	Proniosomal gel had most effective combination of surfactants, alcohol and aqueous phase. It also possessed the highest EE, drug permeation , therapeutic effect. Highly regenerative bladder surfaces and faster salivary secretion recovery
Optomization of aceclofenac proniosomes by using different carriers, part 1: Development and characterization	Rana M. F. Sammour, Muhammad Taher et al.,[20]	Aceclofenac proniosomes were prepared successfully by using different carriers such as glucose, Mannitol, Maltodextrin. Maltodextrin highest solubility, that may effect the bioavailability. The optimized aceclofenac
Formulation of tretinoin - loaded The encapsulation of TRT in topical proniosomes for treatment of acne: in vitro characterization, skin irritation test and comparative clinical study	Shawky Abbedlmalak Salwa Abbed Rahman, Nevine[21]	proniosomes provide the advantages and overcoming solubility and skin irritancy, problems. Enhance the penetration of the TRT across the stratum corneum, enhancing the acne treatment efficacy of TRT while reducing its side effects.
Development and optimization of boswellic loaded proniosomal gel	Meenu Mehta, Harish Dureja[22]	Proniosomal gel is a suitable carrier for the delivery of BAs with enhanced Transdermal delivery due to its small size and better encapsulation of drug within the vesicles. Proniosomal gel showed significantanti-inflammatory effect as compared to the standard voveran gel.

CONCLUSION

Proniosomes or proniosomal gel promising drug delivery for future with a great advantage and betterment comparison to other drug delivery. That delivery to overcome the drawback, those are faced in conventional and other dosage form. Many types delivery is possible by proniosomes such controlled, targeted, Transdermal, ocular, sustained etc, in the Transdermal delivery advantage is this produce non toxicity and penetration enhance. In the ophthalmic

drug delivery improve bioavailability of drug and increase residence time in epithelial surface and improve contact time. Dry proniosomes convenient and easy to handle and can further make new dosage form make capsule, beads, tablets. Proniosomes drug delivery effective and intended therapy.

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