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Proniosomal gel: transdermal drug delivery: A review

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ABSTRACT

Drug delivery systems using colloidal particulate carriers such as liposomes or niosomes have distinct advantages over conventional dosage forms because the particles can act as drug containing reservoirs. Modification of the particle composition or surface can adjust the affinity for the target site and the drug release rate, and the slowing drug release rate may reduce the toxicity of drug.Transdermal is a non-invasive mode of drug delivery route. It is an attractive route of drug administration to maintain drug levels in the blood for a sustained period of time locally and systemically.Proniosomes are well documented for transdermal drug delivery and preferred over other vesicular systems because they are biodegradable, biocompatible, non-toxic, possess skin penetration ability and prolong the release of drugs by acting as depot in deeper layers of skin.Proniosomes are dry formulation of water-soluble carrier particles coated with surfactant which can be dehydrated to form niosomal dispersion immediately before use on brief agitation in hot aqueous media within minutes.The review provides an idea about the design and development of proniosomal gel (PNG)and its properties.

Keywords: Proniosomes, Non-ionic surfactants, Transdermal delivery.

1. INTRODUCTION

Though the oral route is the most favorable route for delivery of drugs, it has limited importance especially in the treatment of skin diseases. Among the topical drug delivery systems the proniosomal gels are becoming more popular due to ease of application and better percutaneous absorption, than other semi solid preparations. Transdermal delivery systems are becoming better alternatives to oral delivery because it exhibits better control of plasma drug levels, no hepatic first-pass metabolism, a decreased systemic toxicity and a higher degree of patient compliance .Number of permeation enhancers has been introduced to establish a therapeutically effective plasma drug levels in case of poorly permeable drugs.Proniosomes are non-ionic surfactant coated dry forms, converted in to niosomes by hydration to yield an niosome dispersion having the capability of delivering drugs in a sustained manner for enhanced bioavailability and therapeutic effect. Proniosomes are superior to niosomes by displaying high physical and chemical stability, improved drug targeting with less production cost. Proniosmal drug delivery system is more advantageous by overcoming the drawbacks of liposomes and liposomal drug delivery by using in various drug delivery systems and having low formulation cost, long shelf life, better drug targeting at specified site in a sustained manner, permeation enhancement of drug and minimizing physical stability problems such as fusion, leaking, aggregation . The non-ionic surfactants are preferred in the proniosomes preparation than cationic, anionic and ampholytic surfactants because they have ability to enhance solubility which helps in increasing solubility and bioavailability of poorly water soluble drugs[1].

1.1. Ideal properties of drug to develop proniosomes

- Low aqueous solubility
- High dosage frequency
- Short half life
- Controlled drug delivery
- High adverse drug reaction

1.2. Mechanism of drug absorption through skin

Proniosomes should be hydrated to form niosomal vesicles before the drug is released and permeates across skin.It depends on nature and type of drug,vesicles formed and hydration temperature for conversion of proniosomes to niosomes.Since proniosomes contain both non-ionic surfactant and phospholipids it improve the permeation.The lipids used act as a carrier that will form depot at the site and sustains the action [2].

1.3. STURCTURE OF PRONIOSOMES

Proniosomes are microscopic lamellar structures. They combine a non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and cholesterol followed by hydration in aqueous media. The hydrophilic ends of the non-ionic surfactant orient outward, while the hydrophobic ends are in the opposite direction to form the bilayer. Like liposomes proniosomes are also made up of a bilayer. In proniosomes the bilayer is made of non-ionic surface active agents. On the basis of method of preparation proniosomes are unilamellar or multi-lmellar.

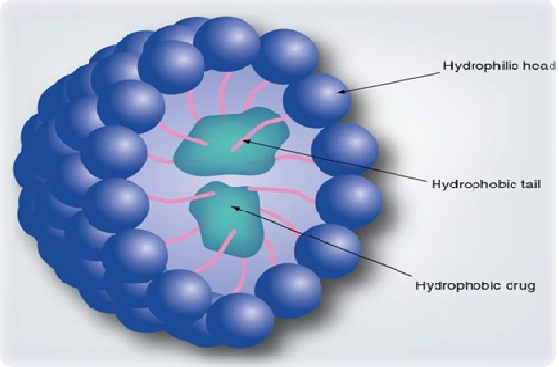

Figure - 1: Structure of Proniosomes.

1.4. TYPES OF PRONIOSOMES

According to the type of carrier and method of preparation of proniosomes they are of two types.

1.4.1. Dry granular proniosomes

Sorbitol based proniosomes

Sorbitol based proniosomes is a dry formulation that involves sorbitol as a carrier, which is further coated with non-ionic surfactant and is used as a noisome within minutes by the addition of hot water followed by agitation.

Maltodextrin based proniosomes

Maltodextrin based proniosomes are prepared by fast slurry method. Maltodextrin is a polysacride easily soluble in water which is used as a carrier in proniosome preparation. Maltodextrin particles are used to increase in gain in surface area. The higher surface area results in thinner surfactant coating which is suitable for rehydration process[3].

Liquid crystalline proniosomes

This type of proniosomes is reservoirs for transdermal delivery of the drug. The transdermal patch involves an aluminum foil as a baking material along with a plastic sheet. Proniosomal gel spread evenly on the circular plastic sheet followed by covering with a nylon mesh[4].

1.5. Formulation of proniosomes

Non-ionic surfactants

A wide range of surfactants are available and the selection of surfactants should be done on the basis of Hydrophilic Lipophilic balance. The HLB in between 4 to 8 was found to be compatible with vesicles formulations [5]. Degree of entrapment is affected by HLB number. Transition temperature of surfactants also affects entrapment of drug in vesicles. Spans have highest phase transition temperature provides the highest entrapment for the drug [6]. Span 40 and span 60 produces vesicles of larger size with higher entrapment of drug. The drug leaching from the vesicles is reduced due to high phase transition temperature and low permeability. The encapsulation efficiency of tween is low as compared to span because of the larger size of vesicles and less lipophilic nature of tween. When span is used it also increases the lipophilicity of drug [7].

Lecithin

Phosphotidyl choline is the major component of lecithin. The name basically depends upon their source of origin such as soya lecithin from soya beans and egg lecithin from egg yolk. Phosphotidyl choline has low solubility in water [8]. Incorporation of lecithin in proniosomes may act as permeation enhancer, prevents the leakage of drug and enhanced the percent drug entrapment due to high phase transition temperature. The vesicles composed of soya lecithin are of larger size then vesicle composed of egg lecithin due to difference in the intrinsic components. On the basis of penetration capability the soya lecithin is considered as a good candidate as it contains unsaturated fatty acids, oleic and linoleic acid while egg lecithin contains fatty acids [9].

Cholesterol

Cholesterol is an essential component of vesicles. Incorporation of cholesterol influence vesicles stability and permeability[10] . Concentration of cholesterol plays an important

role in entrapment of drug in vesicles. The entrapment efficiency and permeation increases with increasing cholesterol content and by the usage of span 60 which has higher transition temperature [11].

Solvent

Selection of solvent is another important aspect as it has great effect on vesicle size and drug permeation rate [12]. Vesicles formed from different alcohols are of different sizes and they follow the order: ethanol > propanol > butanol > isopropanol. Higher size of vesicles in case of ethanol is due to its greater solubility in water and smallest size of isopropanolol, may be due to branched chain present in it [13]. Ethanol may cause the reduction of lipid polar head interactions within the membrane, thereby increased the skin permeation [14] .

Aqueous phase

Phosphate buffer 7.4, 0.1% glycerol and hot water are mainly used aqueous phase for proniosomes. pH of the hydrating medium also play important role in entrapment efficiency. The aqueous medium might influence the tactness of proniosomes, thus affecting their entrapment efficiency [15].

Table - 1: Components of proniosomes

Components	Examples	Uses
surfactants	Tween(20,40,60,80), span(20,40,60)	To increase drug flux across the skin
Cholestrol	cholestrol	To prevent leakage of drug formulation
Lecithin	Soya and egg lecithin	Penetration enhancer
Sugar	Maltodextrin, sorbitol	Provides flexibility in surfactant and other component ratio alters the drug distribution
Solvent	Ethanol,methanol,propanol, isopropanol	Skin permeation
Aqueous phase	Hot water,buffer,glycerol	Entrapment efficiency

1.6. METHOD OF PREPARATION

The proniosomes can be prepared by

- Spraying method.
- Slurry method.
- Coacervation phase separation method.

Spraying method

Proniosomes are prepared by spraying the surfactant in organic solvent onto sorbitol powder and then evaporating the solvent. Because the sorbitol carrier is soluble in the organic solvent, it is necessary to repeat the process until the desired surfactant load has been achieved. The surfactant coating on the carrier comes out to be very thin and hydration of this coating allows multilamellar vesicles to form. Accurately weighed quantity of the carrier is transfer into a round bottom flask and keep it in a rotary evaporator. After that add required quantities of Surfactant and Cholesterol mixture by spraying these onto carrier material and evacuate. Then keep the round bottom flask in a water bath under 65-70^{0}C for 20 minutes. Repeat the process till all the surfactants added, and continue the evaporation to get a free flowing proniosome powder. Then this powder mixed with suitable gelling agent [1-2%][16].

Slurry method

In a round-bottomed flask carrier powder and followed by surfactant solution is added to form slurry. If the surfactant solution added is less in volume, then to form slurry additional amount of organic solvent can be added. By using rotary vaccum evaporator the slurry in the flask made dry and free flowing. The flask was removed and kept overnight under vaccum. The proniosome powder formed is collected and sealed in containers and stored at 4°C [17].

Coacervation phase separation method

Accurately weighed or required amount of surfactant, carrier (lecithin), cholesterol and drug can be taken in a clean and dry wide mouthed glass vial (5 ml) and solvent should be added to it. All these ingredients has to be heated and after heating all the ingredients should be mixed with glass rod. To prevent the loss of solvent, the open end of the glass vial can be covered with a lid. It has to be warmed over water bath at 60-700 C for 5 minutes until the surfactant dissolved completely. The mixture should be allowed to cool

down at room temperature till the dispersion get converted to a proniosomal gel[18].

2. CONCLUSION

Proniosomes represent a promising drug delivery system. When compared to niosomes, proniosomes are better candidates for drug delivery due to cost, stability, etc. Various types of drug deliveries can be possible using proniosomes based niosomes like targeting, ophthalmic, topical, parenteral, vaccine etc.These systems can be used as an alternate strategy for delivery of drugs through skin because it reduces the toxicity and enhances penetration effect of surfactants. So, based on various studies proniosomal system would be an efficient drug carrier for the future.

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