Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2021, 13(7):01-07

Review Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

A Review on Proniosome: As a Drug Carrier

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ABSTRACT

A drug carrier is any substrate used in the process of drug delivery. The basic component of the drug delivery system is an appropriate drug carrier that sets out to improve the selectivity, effectiveness, and safety of drug administration. So, based on their biocompatible, biodegradable, and non-immunogenic structure, Proniosomes are promising drug carriers that are non-ionic surfactant-based multilamellar or unilamellar vesicle are now widely used as an alternative to the liposome. On the basis of structure, they are similar to liposomes in having bilayer but having chemical differences in monomer units which make Proniosomes stable. They can entrap both hydrophilic and lipophilic drugs of using either in an aqueous layer or in the vesicular membrane. Proniosomal carriers are suitable for the transdermal delivery of numerous pharmacological agents, including antioxidant, anticancer, anti-inflammatory, antimicrobial, and antibacterial molecules.

Keywords: Proniosome; Advantage; Application; Methodology; Drug carrier

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INTRODUCTION

This review provides a brief overview of using proniosome as a drug carrier by explaining its structure, advantage, application, and mode of action in the targeted site of the body. Colloidal particulate structures such as proniosome as drug delivery systems have distinct advantages over conventional dosage forms. These carriers can act as drug reservoirs and are primarily used to control the release of a drug into systemic circulation. This can be fulfilled either by slow release of drug over a long period of time or by activating release at the drug's target by stimulus, such as a change in pH and activation by light. Drug carriers are also used to improve the pharmacokinetic properties, specifically the bioavailability of many drugs with poor water solubility with poor solubility and membrane permeability.

Proniosomes are used as a drug carrier because they have benefits such as low cost, ease to formulate, good stability. They are much more stable because their forming materials are more stable than those of lipids both in terms of physical and chemical stability.

LITERATURE REVIEW

Nearly 25 odd years of continual and detailed research to reach the highest, the first formulation to be licensed for use in human beings is Liposome. However, liposomes have limited success in terms of oral delivery and suffer from physicochemical stability problems such as sedimentation, aggregation, fusion, phospholipid hydrolysis, and/or oxidation. To resolve these stability issues, proliposome approach has provided a major advancement by using the dry, free-flowing product, which is more stable during sterilization and storage [1].

Proliposome are the dry, free-flowing powder formulations containing water-soluble carrier particles coated with phospholipids which, upon the addition of water, disperse to form a multilamellar liposomal suspension. Despite these merits, proliposome preparation involves technical difficulties like usage of vacuum or nitrogen atmosphere during preparation and storage to prevent oxidation of phospholipids [2].

Niosomes are better alternatives to liposomes as promising drug carriers with greater chemical stability, entrapment efficiency of both hydrophobic and hydrophilic drugs and are less toxic due to their non-ionic nature. However, like liposomes, niosomes also have physical stability problems such as leakage, fusion, aggregation, and sedimentation [3]. These problems can be evaded by proniosomes.

Proniosomes are dry, free-flowing formulations of the surfactant-coated carrier, which can be rehydrated by brief agitation in hot water to form a multi-lamellar niosome suspension suitable for administration by oral or other routes [4].

Definition of Proniosome

Proniosomes are the dry formulation of water-soluble carrier particles that are coated with a surfactant. They are rehydrated to form niosomal dispersion immediately before use on agitation in hot aqueous media within minutes. Proniosomes are physically stable during storage and transport.

Advantages of Proniosomes

- Improvement in bioavailability and permeation of the drug.
- Enhances the skin permeation and develops a transdermal therapeutic system.
- Ease of manufacture and scale-up process.
- Avoid stability-related issues such as aggregation, fusion, and sedimentation.
- Used for targeted drug delivery of drugs.
- Fewer adverse drug reactions.

Structure of Proniosome

- Proniosomes are microscopic lamellar structures.
- The structural components present in proniosome are:

Cholesterol (a steroid derivative, which is used to provide rigidity and proper shape, conformation to proniosome form)

- The non-ionic surfactants used for the preparation of proniosome are-
- The alkyl or Dialkyl polyglycerol
- Alkyl or Dialkyl ethers
- Span (64, 20, 85, 80)
- Tween (20, 40, 60,80)
- Brij (35, 73, 92, 95)

TYPES OF PRONIOSOMES

Dry Granular Proniosomes

1. Sorbitol based proniosomes
2. Maltodextrin 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 are prepared by the fast slurry method. The surface of the proniosome is increased by the use of hollow maltodextrin particles which leads to a thinner surfactant coating that is suitable for rehydration [5].

Liquid crystalline proniosomes: This type of proniosomes are reservoirs for transdermal delivery of the drug. The transdermal patch involves aluminium foil as a baking material along with a plastic sheet. Proniosomal gel is spread evenly on the circular plastic sheet followed by covering with a nylon mesh.

Proniosome as a drug carrier: Proniosomes are very promising carriers for the delivery of numerous pharmacological and diagnostic agents. A number of publications have reported the preparation, characterization, and use of proniosomes as drug carriers. Because of their non-ionic nature, they offer excellent biocompatibility and low toxicity [6]. The unique structure of proniosomes allows the development of effective novel drug delivery systems with the ability to load both hydrophilic and lipophilic drugs. Hydrophilic drugs and lipophilic drugs are entrapped into the aqueous core and membrane bilayer of the proniosome respectively. Proniosomes have also been used as carriers for iobitridol, a diagnostic agent used for X-ray imaging. Topical proniosomes may serve as solubilization matrix, as a local depot for sustained release of dermally active compounds, as penetration enhancers, or as rate-limiting membrane barrier for the modulation of systemic absorption of drugs.

METHODS OF PRONIOSOME

Proniosomes can be Prepared by Following Methods

a. Slurry method
b. Coacervation phase separation method
c. The slow spray coating method

Slurry method: Proniosomes can be prepared by using a solution of cholesterol and surfactants. The non-ionic surfactants used are span and Brij. The coating carrier used is maltodextrin. The drug and stock solution was added to a 100 ml round bottom flask containing 500 mg of maltodextrin carrier. Then chloroform: menthol solution is added to form slurry. The flask is attached to a rotary evaporator for the evaporation of the solvent and it is rotated at 60 rpm-70 rpm, temperature maintained at 45°C and a reduced pressure of 600 mmHg. The process is continuing until the mass in the flask had become a dry free-flowing product. These materials are further dried overnight in a desiccator under a vacuum at room temperature. The dry preparation is referred to as proniosome powder [7].

Coacervation phase separation method: This method is used for the preparation of proniosomal gel. All the required materials, such as surfactants, carriers, cholesterol are taken in a dry and clean wide-mouth glass container and to this, the solvent should be added to it. Then the container is sealed with aluminum foil and placed in a water bath 60°C-70°C until all the materials get dissolved. After that cool the preparation at room temperature until it is converted into proniosomal gel [8].

Slow spray coating method: A 100 ml round bottom flask containing the desired amount of carrier can be attached to a rotary evaporator. The evaporator has to be evacuated and the rotating flask can be rotated in a water bath under vacuum at 65-70°C for 15-20 min. This process is repeated until all of the surfactant

solutions have been applied. The evaporation should be continued until the powder becomes completely dry [9] (Figure 1).

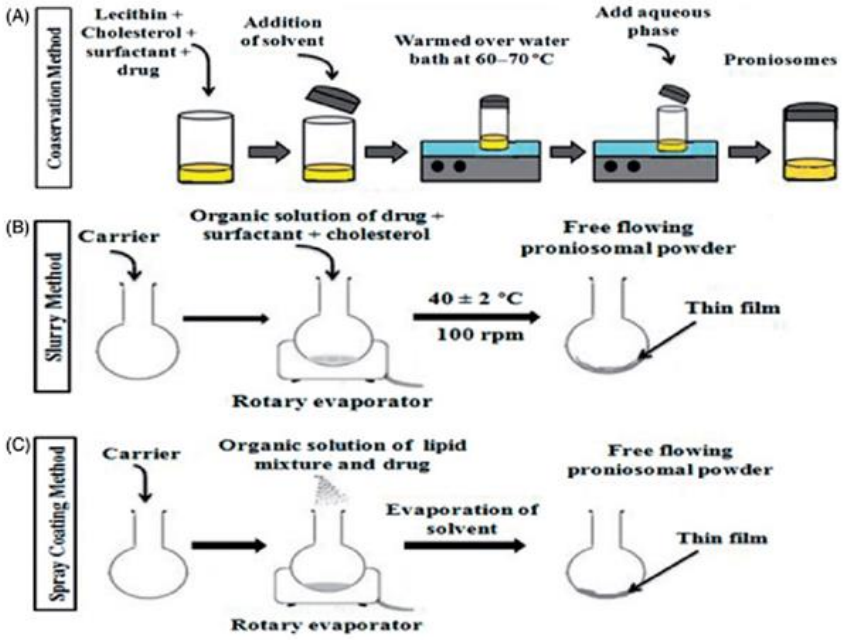

Figure 1: Slow spray coating method

Evaluation Parameters in Proniosome

Particle size and shape analysis: The particle size determination of proniosome powder was carried out using an optical microscope along with a stage micrometer having an accuracy of 0.01 nm. The average of a powder was calculated using the following formula:

$$X = \frac{E(Xi)}{N}$$

The angle of repose: The angle of repose is the angle formed by the horizontal base of the bench surface and the edge of a cone-like pile of granules. It can be calculated as:

$$\Theta = [\tan^{-1}(h/r)]$$

Drug entrapment efficiency: The entrapped drug proniosome was determined by exhaustive dialysis method or by centrifugation method. The entrapment efficiency of the drug was calculated by using the following equation:

$$\% \text{ Entrapment Efficiency} = \frac{\text{Amount of drug entrapped}}{\text{The total amount of drug}} \times 100$$

In-Vitro Drug Release

In-vitro release pattern of proniosomes suspension was carried out by dialysis bag method. A dialysis sac was washed and soaked in distilled water. The vesicle suspension was pipette into a bag made up of tubing and sealed followed by placing the dialysis bag into a beaker containing 200 mL of PBS pH 7.4 [10-13]. The vessel was placed over a magnetic stirrer (50 rpm) and the temperature was maintained at 37°C ± 0.5°C. Samples were withdrawn at predetermined time intervals and immediately replaced with the fresh medium to maintain the sink condition throughout the experiment. Samples were diluted and analyzed for drug content by using a UV/visible spectrophotometer at 265 nm [14-16].

Stability Study

Stability study is a routine method performed on drug substances and products and employed at various stages of product development. To study the diffusion of the drug from Proniosome, a drug release study was carried out. Stability of proniosomal dispersion was carried out for 30 days at 2°C-80°C and Room temperature. The response obtained for different parameters proniosomal dispersion during the stability period [17-19].

DISCUSSION

Application of Proniosome

Proniosome in gene delivery: Some non-viral vectors found as an alternative to viral gene delivery systems. Among non-viral vectors, proniosomes could also potentially serve as gene delivery systems because it has shown favorable properties for gene delivery such as low cost, easy to formulate, good stability, easy production, and less toxic due to presence of non-ionic surfactant [20-23].

Drug targeting: One of the most useful aspects of proniosome is its ability to target drugs. The efficiency and specificity of cellular targeting of niosomal drug delivery systems can be further improved by active targeting for tumor therapy, by using a ligand coupled to the surface of niosomes, which could be actively taken up. Proniosomes can be used to target drugs to the reticuloendothelial system. The reticuloendothelial system (RES) preferentially takes up proniosome vesicles. Proniosomes can also be utilized for targeting drugs to organs other than the RES. A carrier system (such as antibodies) can be attached to proniosomes (as immunoglobulin's bind readily to the lipid surface of the proniosome) to target them to specific organs [24-26].

Anticancer drug delivery: The therapeutic efficacy of many anticancer drugs is limited by their poor penetration into tumor tissue and by their severe side effects on healthy cells. Various attempts have been made to overcome these drawbacks, including the use of proniosomes as a novel drug delivery system. Proniosomes can alter the metabolism; prolong circulation and half-life of the drug, thus decreasing the side effects of the drugs. Proniosomes are decreased rate of proliferation of tumours and higher plasma levels accompanied by slower elimination [27].

Delivery of antibiotics and anti-inflammatory agents: Proniosomal carriers are also suitable for the delivery of antibiotics and anti-inflammatory agents. These carriers have been used extensively to improve poor skin penetration and as well as enhance skin retention of the drugs [28]. A goal of topical delivery is that the drug is transported through the stratum corneum, thereby effectively reaching the target tissue. The proniosomal gel developed by Jacob, et al. demonstrated successful delivery of acyclovir through topical administration.

CONCLUSION

Recent advancements in the field of scientific research have resulted that proniosomes are used as a drug carrier for better targeting of the drug at a specific tissue destination because they are made up of non-ionic surfactant, so less toxic and have an opportunity of loading hydrophilic, lipophilic drugs or both drugs together. The relevant studies demonstrated that proniosomes improve the stability of the entrapped drug, reduce the dose, and enable targeted delivery to a specific type of tissue.

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