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Niosomal gel drug delivery system: A review

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Abstract
Noisome have a important role in drug delivery because they can reduce toxicity and modify pharmacokinetic and bio-availability. Topically applied noisome can enhance the residence time of drugs in the stratum corneum and epidermis, while reducing the systemic absorption of the drug. Niosomal gel dermal drug delivery act as drug containing reservoirs and the modification of the vesicular compositions or surface properties can adjust the drug release rate and the affinity for the target site. Niosomal gel drug delivery beneficial in the treatment of superficial and systemic fungal infections. niosomal gel can be applied by ocular route.

Keywords: niosomal gel drug delivery system, antifungal, topical, ocular

Introduction

Novel drug delivery carriers have great importance for dermal delivery. The lipidic and nonlipidic vesicular systems like liposome, transfersome, ethosome, and niosome are used to reduce the problem related with topical conventional formulation.

Drug delivery system using novel vesicular carrier, such as liposome or niosome, have more advantages compared to microspheres, nanoparticles, and other systems in terms of better entrapment of drugs target site specificity, and handling premature drug release (burst effect). In 1985, niosomes were studied as an alternative to liposome because niosomes have more benefits over liposome such as they are more stable, nontoxic, and economic due to low cost of nonionic surfactant as compared to phospholipids which are prone to oxidation. Incorporation of surfactants within niosomes may increase the efficacy of the drug, possibly by facilitating its uptake by the target cells. Niosomes are biodegradable, biocompatible, relatively nontoxic, and an alternative of liposome. They can be utilized in the delivery of wide variety of drugs as it has capability to entrap hydrophilic, lipophilic, and amphiphilic drugs [1]. Niosomes proved to be a promising drug carrier and has potential to reduce the side effects of drugs and increased therapeutic effectiveness in various diseases. Incorporation of surfactants within niosomes may increase the efficacy of the drug, possibly by facilitating its uptake by the target cells. 1 Novel drug carriers intended for use in skin diseases are often designed to increase the load ability of APIs and reduce side effect [10].

ocular delivery can be attained through different strategies that include the use of bio adhesive polymers, penetration enhancers and the advanced design of micro- and nanoparticulate delivery systems [9]. This article presents an overview of the properties of niosomal gel, techniques of preparation of niosomal gel, evaluation parameters.

Characteristics of Niosomes

1. Niosomes can entrap solutes as like a analogous to liposomes.
2. Niosomes are osmotically active and stable.
3. Niosomes possess an infra structure consist of hydrophobic and hydrophilic mostly combine and so also accommodate the drug molecules with a wide range of solubility.
4. Niosomes have a flexibility in their structural characteristics (composition, fluidity and size) and can be designed as per required condition.
5. Niosomes can also improve the performance of the drug molecules.
6. More availability to the site of administration by protecting the drug from biological environment.
7. Niosomes surfactants are biodegradable, biocompatible, and non-immunogenic [2].

Advantages

1. Niosomes are osmotically active and stable.
2. They enhance the stability of the entrapped drug
3. While Handling and storage of surfactants do not require any special conditions.
4. Niosomes carrier may also increase the oral bioavailability of drugs.
5. Niosomal gel enhance the skin penetration of drugs.
6. niosomal gel can be used as ocular, topical route.
7. The surfactants are biodegradable, biocompatible, and non-immunogenic.
8. Improve the therapeutic activity of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug.
9. The niosomal dispersions in an aqueous phase can be emulsified in a non-aqueous phase to control the release rate of the drug and administer normal vesicles in external non-aqueous phase [3].
10. Niosomal gel drug delivery useful in the treatment of superficial and systemic fungal infections

Method of Preparation of Niosomes

1. Thin film hydration method

Film hydration method is use for drug-loaded niosomes with slight modifications. Weigh accurate quantities of the surfactant and cholesterol in 7:3 molar ratio then dissolve in a chloroform: methanol mixture (2:1 v/v) in a round-bottom

flask. Remove the organic solvent by using a rotary flash evaporator under reduced pressure. Then hydrate dried film with 5 ml phosphate buffered saline (PBS, pH 7.4) with a gentle rotation in a water bath. Maintain the water bath temp at 55 ° C for 30 minutes then subsequently left at room temperature for 6 hr for complete hydration. Then sonicate niosomes to reduce vesicles size using a probe sonicator under an ice bath for 3 minutes. Store the final niosomal suspension at refrigerator temperature for further studies [4]. Formulations of niosomeal suspension equivalent to 2 % w/w incorporate into the gel base composed of Carbopol 934), glycerol, Triethanolamine and distilled water 5)

2. Niosome preparation using polyoxymethylene alkyl ether

The size and number of bilayer of vesicles consisting of polyoxymethylene alkyl ether and cholesterol can be change using an alternative method. Increase the Temperature above 60°C transforms small unilamellar vesicles into large multilamellar vesicles (>1 μm), while vigorous shake at room temperature shows the opposite effect, i.e., transformation of multilamellar vesicles into unilamellar ones. The transformation from unilamellar to multilamellar vesicles at higher temperature may be the characteristic for polyoxyethylene alkyl ether (ester) surfactant, since it is known that polyethylene glycol (PEG) and water remix at higher temperature due to breakdown of hydrogen bonds between water and PEG moieties. Generally, free drug is removed from the encapsulated drug by gel permeation chromatography dialysis method or centrifugation method. Often, density differences between niosomes and the external phase are smaller than that of liposomes, which make separation by centrifugation very difficult. Addition of protamine to the vesicle suspension facilitates separation during centrifugation (5) Formulations of niosomeal suspension equivalent to 2 % w/w incorporate into the gel base composed of Carbopol 934, glycerol, Triethanolamine and distilled water.

3. Transmembrane pH Gradient

In this method, surfactant and cholesterol are dissolve in chloroform and evaporate to form a thin lipid film on the wall of a round bottomed flask. Then occurring film is hydrate with a solution of citric acid by vortex mixing and the resulting product is freeze-thawed for niosome formation. Add the aqueous solution of drug is into niosomal suspension, after that add phosphate buffer to maintain pH between 7.0 and 7.2. According to this method, the interior of niosome has a more acidic pH value than the outer medium. The added unionized drug passes through the niosome membrane and enters the niosome. The drug ionizes in an acidic medium and cannot escape from the niosomal bilayer [6].

4. Reverse phase evaporation method

For Preparation of Niosomes use the reverse-phase evaporation technique. Weigh accurate quantity of surfactant (span 20, 60, 80) and cholesterol equivalent to drug then mixed in 250 ml long-necked quick fit round bottom flask and dissolved in 10 ml chloroform. The organic solvent slowly evaporates under reduced pressure, using a rotary evaporator, at 40°C produce a thin lipid film. Redissolve the lipid film in 10 ml diethyl ether, and the drug dissolve in 5 ml acetone mix with 5 ml distilled water. The mixture sonicates for one minute, swirl by hand, and resonicate for another minute. The organic solvents evaporate on the rotary evaporator under reduced pressure for two hours. Allow the niosomes to equilibrate at room temperature. Keep the niosomal dispersion in the refrigerator to mature overnight (4°C). Select the drug-loaded niosomes and incorporate into different gel bases. Gels containing 0.5% w/w drug dissolve in polyethylene glycol 600 (20% w/w) also prepare for comparison. The polymers can use Carbopol 934, pluronic F-127 and HPMC, sodium carboxy methyl cellulose and sodium alginate. The require quantity of carbopol 934 weigh accurately and dispersed in a small amount of distilled water to prepare an aqueous dispersion. Allow the aqueous dispersion to hydrate for 4-5hours. Add drug into dispersion and properly disperse it. Adjust the pH to 6 by addition of 1% (w/v) triethanolamine solution. Adjust the final weight of the gel to 10g with distilled water. 16

Evaluation parameters of niosomal gel

Particle size

The particle size of the niosomal suspension determine by optical microscopy. A drop of niosomal suspension place on a glass slide. A cover slip place over the niosomes suspension and evaluate the average vesicle size by an ordinary optical microscope using a precalibrated ocular eye piece micrometer [7]

pH Measurements

The pH of the gel formulations delivers by using digital pH meter. Calibrate the pH meter before measurement and take the readings by dipping the glass rod into the gel formulations [11].

Stability Studies

Select the niosomal formulation based on entrapment efficiency and *in vitro* release studies. Keep niosomal suspension and niosomal gel in sealed glass vials for to assess the stability studies and store them in two different storage conditions, that is, refrigeration temperature and room temperature for a period of 30 days. Withdraw samples at different time intervals over a period of one month and the residual content determine spectrophotometrically [11].

***In vitro* drug release study of niosomal gel**

An *in vitro* drug release study performs using modified Franz diffusion cell of capacity 60 ml. Dialysis membrane place between receptor and donor compartments. Niosomal gel (NG) equivalent to 1 g is place in the donor compartment and because of the very low solubility in water, methanolic phosphate buffer (pH 5.6) IS use as receptor compartment. The diffusion cells are maintained at 37.2 C with magnetic stirring at 100 rpm throughout the experiment. One milliliter of aliquots is withdrawn at different time intervals up to 24 h from receiver compartment and replace with the same amount of fresh methanolic phosphate buffer solution (PBS) to maintain the sink conditions. The sample are analyze using UV spectrophotometry at wavelength 236.5 nm [12].

Spreadability and viscosity

The spreadability of formulation depends on its viscosity, Observations of spreadibility are indicate that the gel easily

spreadable in response to the when little force will apply. These assure that the formulation can maintain a good wet contact time when applied at the target site. The viscosity of all the gel formulations can find to be in desirable range [13].

Drug content

The content of all the niosomal are determine at 306.20 nm against blank by using the UV visible spectrophotometer. The results will in the official limits [13]

Entrapment efficiency of niosomes

The entrapment efficiency of niosomes prepare by each of the methods determine by ultracentrifuging the niosomal dispersions at 40,000 × g for 30 min. The clear supernatant is analyzed spectrophotometrically and give the amount of unentrapped drug. Amount of entrapped drug are obtained by subtracting amount of unentrapped drug from the total drug incorporated [15]

Percentage entrapment = entrapped drug (mg)/ total drug added (mg) × 100

Conclusion

Delivery of antifungal drugs to target region of the skin is a great challenge in terms of therapeutic aspect. In this context, formulation of topical product Niosomal gel plays a key role for penetration of the drugs across skin. Besides, the physicochemical properties of drug molecules such as lipophilicity are also effective parameter. Generally, antifungal drugs are highly lipophilic compounds, which can affect the penetration of drugs across stratum corneum. Niosomal gel drug delivery is very useful in the treatment of superficial and systemic fungal infections. niosomal gel can be applied by ocular and topical route. niosomal gel be apply by ocular, topical route niosomal gel have prolonged retention and enhanced penetration and that will automatically improve therapeutic properties. Niosomal gel will be used for treatment of eye diseases and fungal infections. Various formulation strategies have emerged over recent years to optimize new drug delivery carriers of antifungal drugs [14].

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