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A REVIEW ON LIPOSOMAL GEL FOR TOPICAL APPLICATION

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ABSTRACT

The novel drug delivery vehicle, liposomes has been established themselves as a promising in the several different basic science and as a viable alternative in several, different applications. Liposomes were the small microscopic spheres with an aqueous core surrounded by one or more outer shells that consisting of lipids were arranged in the bilayers configuration. They will be acceptable superior carriers having ability to encapsulated hydrophilic and lipophilic drugs and protected them from degradation. Liposomes applied on the skin as well as local depot at the same time diminishing the sides effects of these drugs, they act as a solubilizing matrix for poorly soluble drugs and penetration enhancers. They give better absorption from its their has been also affinity to keratin of horny layer of skin and can penetrate deeper into skin. Topical Liposomes formulation could be less toxic and more effective than conventional formulations. The liposomal gel formulations that perform therapeutically better effects than the other conventional formulations, as prolonged and controlled released the topical dosage forms, may also leads to the improved efficiency and better patients compliance.

KEYWORDS: Liposomes, Liposomal gel, Novel Drug Delivery, Topical Application.

INTRODUCTION

Liposomes: It is the small microscopic spheres vesicles, the lipid arranged in a bilayer shells in an aqueous core will be surrounded by one or more outer shells. They are carriers encapsulated both hydrophilic and lipophilic drugs molecules so as considered the liposomes are superior carriers.[1] Liposomes will be also found to have important cosmetics, industrial and medical applications.[2] Liposomes can be substantially improved loading and delivery of drug, and sustained release of medication, thereby offering advantages over traditional dosage formed. Alec D. Bangham in 1961 (England) they produced the first liposomes, who was studied phospholipids and blood clotting. They will be found that phospholipid bonded with water they quickly formed a sphere because one end of each molecules was water soluble, while the opposite end was water insoluble. Water soluble medication added to the water were trapped inside the aggregation of the hydrophobic ends, fat soluble medication were incorporated into the phospholipid layer.[3,4]

Liposomal gel formulation enhanced the drug delivery efficiency through the several routes of administration and have shown to be significantly superior to the other conventional dosage formed especially for the intravenous administration and topical application.[5]

The administered drugs by various routes by liposomal formulation were widely used in pharmaceuticals field as drug delivery system due to their versatility and clinical efficacy. Liposomal formulation were widely used as topical drug delivery system because liposomes will be having the higher diffusivity in the skin compared to most bared drugs.[6]

They may be composed of one or various concentric membranes their size ranges from 20nm to various micrometre. The liposomes useful as the targeted drug delivery system makes by the a sustained released of encapsulated drugs. The adverse or side effects of the drugs can be minimised by controlling the permeability of the liposomes membranes and thus avoiding the released of drugs from its site.

Liposomes will be acceptable and superior carriers and have ability to encapsulated hydrophilic and lipophilic drugs and protect them from degradation. The topical drug delivery system will be an attractive route for local and systemic treatment.[7] There also affinity to keratin of

horny layer of skin and can be penetrated to deeper into skin and hence given the better absorption. Topical dosage forms their formulation, attempts were being made to utilized drug carriers that ensured adequate localisation or penetration of drug within or through the skin in order to enhanced the local and minimised the systemic affect or to ensured adequate percutaneous absorption. Liposomal gel formulation applied on the skin, liposomes act as a solubilizing matrix for the poorly soluble drugs, penetration enhancers and local depot at the same time reducing the side effects of these drugs. So that topical liposomes formulation may be more effective and less toxic than other conventional formulations.

Liposomes were incorporated into gel to enhanced the skin retention of drugs and that provided higher and sustained concentrations of drug in skin at the same time do not enhanced the systemic absorption of drugs. They acted as drug reservoir and that provided localised and controlled drug delivery. By the liposomal gel approach sufficient amount of drug can be delivering into skin so that the adverse effects of drug can be minimised. Carbopol were used as hydrogel which act as a vehicle for liposomes have ability to enhanced the local delivery of drugs. The released of drug were controlled by degradation of hydrogel matrix.[8]

Classification[9]

Liposomes were classified based on different characters

A. Classification based on size of liposomes

1. Large Unilamellar vesicles (LUVs).
2. Medium sized Unilamellar vesicles (MUVs).
3. Small Unilamellar vesicles (SUVs).
4. Giant Unilamellar vesicles.
5. Oligo lamellar vesicles
6. Unilamellar vesicles.
7. Multilamellar vesicles (MLVs).
8. Multivesicular vesicles.

B. Classification based on method of preparation

1. Vesicles prepared by reverse phase evaporation.
2. Vesicles prepared by French press.
3. Vesicles prepared by extrusion method.
4. Vesicles prepared by Fusion.
5. Stable plurilamellar vesicles.
6. Dehydration and rehydration vesicles.
7. Frozen and thawed MLV.

C. Classification based on composition and in- vivo application

1. pH sensitive liposomes
2. Temperature sensitive liposomes
3. Cationic liposomes
4. Long circulating liposomes.
5. Targeted liposomes.

Advantages of liposome

1. Liposomes increased the efficacy and therapeutic index of drugs.
2. Liposomes increased the stabilities of drug via encapsulation.
3. They increases solubility of the drugs.
4. Targeted and controlled drugs delivery will be possible.
5. Site avoidance effects.

PREPARATION OF LIPOSOMES

Materials and Excipients:- Liposomes have the composition included the natural or synthetic phospholipid, phosphatidylcholine (also known as lecithin) and phosphatidylethanolamine constituted the two major structural components of the most biological membranes. Liposomes bilayers may also contain other constituents such as cholesterol, hydrophilic polymer conjugated lipids and water. Cholesterol has been largely used to improved the bilayer characteristics of the liposomes. Through the membrane that is improved the membrane fluidity, stability of bilayers and reduced the permeability of water soluble molecules.[10]

Preparation Method

Classical Methods Technique – There are four classical methods of liposome preparation. Mozafari, M.R., Johnson, C., Hatziantoniou, S. & Demetzos, C. "Nano liposomes and The different between the various methods were the way in which lipids have been drying down from organic solvents and then redispersed in aqueous media.[11]

1. Hydration of a Thin Lipid Film: Bangham Method: The preparation of liposomes production that methods technique was original methods was initially used for formulation of liposomes.[12] In the organic solvent a mixture of phospholipid and cholesterol were dispersed. Then, organic solvents was removed by means of evaporation (using a Rotary Evaporator at reduced pressure). Finally, the dried lipidic film deposited on the flask wall was hydrated by adding an aqueous buffer solution under agitation at temperature above the lipid transition temperature. The preparation yields a population of multilamellar liposomes (MLVs), heterogeneous both in size and shape (1-5 um diameter). Thus, liposome size reduction techniques, such as sonication for SUVs formation or extrusion through polycarbonate filters forming LUVs.[12]

2. Reverse- Phase Evaporation Technique: In this method technique, the lipidic film were prepared by evaporating organic solvents under reduced pressure. The system was purged with nitrogen and the lipids were re-dissolved in a second organic phase which will be usually constituted by diethyl ether or isopropyl ether. Large unilamellar and oligo lamellar vesicles were formed when an aqueous buffer was introduced into the mixture. The organic solvent will be subsequently removed and the system were maintained under continuous nitrogen. These vesicles have aqueous volume to lipid ratios that will be 30 times higher than multilamellar vesicles.[13]

3. Solvent (Ether or Ethanol) Injection Technique: In this technique, the solvent injection methods involved the dissolution of the lipid into an organic phase (ethanol or ether), followed by the injection of the lipid solution into aqueous media, producing liposomes.[14]

In 1973, first described the ethanol injection method.[15] The ethanol injection methods the main relevance their resides in the observation that a narrow distribution of small liposomes (under 100 nm) can be obtained by simply injecting an ethanolic lipid solution in water, in one step, without extrusion or sonication.[16]

The ether injection method differs from the ethanol injection methods since the ether were immiscible with the aqueous phase, which is also heated so that the solvent is also heated so that the solvent will be removed from the liposomal product. The method involved injection of ether- lipid solutions into warmed aqueous phase above the boiling point of the ether. The ether vaporized upon contacting the aqueous phase, and the dispersed lipids forms primarily unilamellar liposomes.[17]

4. Detergent Dialysis:- In this method the production of liposomes their size range of 40-180 nm, will be formed when the lipids were solubilizing with detergents, the defined mixed micelles yielded.[18] In controlled dialysis removed by the subsequently detergent, phospholipid from homogeneous unilamellar vesicles with to the usefully large encapsulated volume.

New Large- Scale Liposomes Technique Method

1. Freeze Drying
2. Spray- Drying
3. Modified Ethanol Injection Method
4. Super Critical Reverse Phase Evaporation
5. Heating Method.

Preparation of Liposomal Gel[19]: The liposomal gel were prepared by using Carbopol 934 NF. The required amount of carbopol 934 powder were dispersed in distilled water under constant stirring with the glass rod, and to avoid the formation of dispersible lumps and allowed to the hydration for 24 hours at the room temperature for swelling the prepared products. The incorporation of liposomes containing drug were mixed in to the carbopol gel with a mechanical stirrer (25 rpm and 2 minute), then triethanolamine dispersed in to formulation to maintain the pH of skin and to formed the liposomal gel formulations.

Evaluation of Liposome

1. Structural characterization[20]

Photon correlation spectroscopy, field flow fractionation, gel permeation, gel extrusion, and vesicle size, shape, and size distribution are assessed physically. The size of the liposomal vesicles can be precisely determined using electron microscopy techniques such as transmission electron microscopy (TEM) and scanning electron microscopy (SEM). One of the easiest ways to figure out the size and size distribution of the vesicles is to use laser light scattering. The inability to identify the liposome's average bulk property is the only downside.

2. Entrapment efficiency[21]

Centrifugation was used to separate the drug linked with the liposome from the substance that was not entrapped. Liposome were centrifuged for one hour at 20,000 rpm at a 4°C regulated temperature. After the supernatant containing the unentrapped medication was removed, its pH was determined using UV spectrophotometer in comparison to phosphate buffer (pH 7.4). Calculate the amount of medication entrapped in a liposo me was determined as EE (%) = [(Cd-Cf)/Cd] 100.

Where Cf is the concentration of free drug and Cd is the t otal drug concentration.

The experiment was repeated three times to determine th e entrapment efficiency, and the results were reported as mean standard deviation.

3. Optical microscopy

This technique is helpful for determining the size of big vesicles and involves the use of bright field, phase contrast, and fluorescent microscopes.

4. Zeta potential[22]

This helpful evaluation technique can be used to ascertai n the liposomal vesicle's charge.

The charge at the vesicle movable surface, or zeta potenti al, is measured in liposomes to determine how much floc culation or de-flocculation has occurred.

5. In- vitro skin permeation studies

The lipid content and permeability of a biological membranes are similar to those of human skin. It was utilized as a model membrane for the skin permeation study. The temperature was regulated by mounting the skin sample between the two half- cells of a side-by- side diffusion chamber using a water jacket set to 37° C. The donor chamber containing the liposomes formulation was in contact with the skin’s dorsal surface. Dissolution medium was poured in to the receptor chamber, and a synchronous motor- driven sta- shaped Teflon magnetic bar was used to agitated the mixture. The receptor sample solution was removed at predetermined intervals and the same volume of new medium was then introduced back into the chamber. The sample analysed from concentration of materials and the cumulative amount of permeation was plotted against time by suitable analytic techniques.

6. Content Uniformity and Drug Content[23]

UV spectrometry was used to evaluate the drug content after the gel sample (100 mg) was removed. Analysing the drug concentration in gel obtained from three to four separate sites within the container allowed for the

determination of content homogeneity. In the instance of the liposomal gel, it was agitated with enough methanol to extract the medication, and a UV Spectrophotometer was used for analysis.

7. Stability studies[24]

The ability of vesicles to retain the drug (i.e., drug retentive behaviour) was assessed by keeping the liposomal suspensions and liposomal gel at two different temperature conditions, I.e., 4-8 °C (Refrigerator, RF), 25±2°C (Room temperature; RT), for a period of 60 days. Sample were withdrawn periodically and analysed for the drug content and particle size for liposomal suspension and drug deposition for liposomal gel in the manner described under entrapment efficiency and particle size distribution studies.

8. CONCLUSION

Both hydrophilic and lipophilic medicines can be easily encapsulated in liposomal formulations. Carbopol gel dispensing is a reliable method for achieving stable liposomal formulations. Liposomal dispersion and gels were found to have higher skin penetration and deposition than other traditional forms. Liposomal gel technique allows for component entrapment, which reduces negative effects while also improving stability, elegance, and formulation flexibility.

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