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" A Review on Topical Liposomal Gel for the Treatment of Acne"

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Abstract

The pharmacokinetic profile, tissue targeting, and localized medication delivery of synthetic and herbal medicines can all be improved by liposomes, a sophisticated drug delivery method. The structure, classification, preparation techniques, and therapeutic uses of liposomes are examined in this paper, with an emphasis on how they may be used to treat acne vulgaris, a prevalent dermatological ailment. Liposomes are perfect for topical treatments because of their capacity to encapsulate hydrophilic and lipophilic medications, enhance drug absorption through the skin, and reduce systemic adverse effects. Herbal extracts like neem, aloe vera, and green tea can be added to liposomal formulations to provide antioxidant effects and lessen the irritation that synthetic medications cause. Various types of liposomes, including multilamellar and uni lamellar vesicles, are discussed alongside methods for their preparation, such as lipid hydration and solvent injection techniques. Furthermore, the development and evaluation of liposomal gels are addressed through parameters like pH, viscosity, spreadability, skin irritation, and in vitro drug diffusion. Stability studies confirm the potential of liposomal formulations for sustained and targeted dermal drug delivery. This review highlights liposomes as promising carriers for the effective and safer treatment of acne vulgaris.

Keywords : Liposomes, Acne Vulgaris, Liposomal Gel, Herbal Drug Delivery, Skin Penetration, Phospholipid Vesicles, Stability Study

1. INTRODUCTION

1.1. Liposome

The aim to any drug delivery system's goal is to advantageously alter the medication's pharmacokinetics and/or tissue distribution. Particulate carrier systems, such as microspheres, nanoparticles, lipoproteins, micellular systems, and liposomes, are among the many delivery methods that have been developed over time. The liposomic drug delivery technology has generated the most interest among these. Liposomes have been researched for a wide range of therapeutic applications due to its structural diversity, benign constituents, and capacity to transport a broad range of chemicals. Liposomes are drug carriers that contain a wide range of compounds, including proteins, nucleotides, plasmids, and tiny drug molecules. Liposomes' size, composition, charge, and lamellarity can all be altered by formulation and processing. When liposome-containing formulations or cosmetics are applied to the skin, the liposomes are deposited there and start to combine with the membranes of the cells. The liposomes release their active material payload into the cells throughout this process. Because liposomal preparations interact with corneocytes and intercellular lipids to soften and smooth the skin, they lessen skin roughness.Liposomes reduce percutaneous absorption and undesirable side effects while increasing drug concentration in deeper skin layers.

To increase the effectiveness of liposomes, a variety of synthetic and herbal medications are implemented. These are employed as effective plant extract delivery vehicles. Incorporating different extracts, such as green tea, papaya, aloe vera, neem, and turmeric, is possible. By incorporating herbal extract into liposomes, the side effects of synthetic medications are lessened.(1) Topical medication administration is a desirable approach for both systemic and local therapy.Acceptable and effective carriers, liposomes can encapsulate hydrophilic and lipophilic medications and protect them from degradation. Additionally, it has a preference for the keratin of the skin's horny layer and can enter the skin more deeply, improving absorption. To improve local effects and reduce systemic effects, or to assure proper percutaneous absorption, efforts are being made to use drug carriers in the formulation of topical dosage forms that ensure adequate localization or penetration of the drug within or through the skin.When applied topically, liposomes can serve as a local depot, a penetration enhancer, and a solubilizing matrix for poorly soluble

medications all while reducing the side effects of these medications. Compared to traditional formulations, topical liposome formulations may be less harmful and more effective. Because of its accessibility and huge surface area, the skin has been seen as a possible medication delivery system.Transdermal drug delivery systems, which are intended to diffuse different medications over the layers of the skin and into the body, are desirable for a number of reasons, including avoiding the Drug delivery can be continuous, minor intestinal discomfort can be prevented, and oral therapies are associated with varied absorption and metabolic breakdown. Transdermal drug administration systems have utilized liposomes because of its much higher skin diffusivity than that of most bare medications.(2)

1.2. Advantages of liposome

A. It is possible to avoid precipitation in the bloodstream and at the injection site.
B. One of the few intravenous solubilizers that is well tolerated is phospholipid.
C. Give tumor tissues specific passive targeting.
D. Raise the therapeutic index and safety.
E. Use encapsulation to increase stability
F. The effect of site avoidance. (3)

Liposomes can be classified using a variety of methods, the most widely utilized of which are size and structure. "Liposomes and Their Uses in Biology and Medicine" was the title of the classification. The various classes in the classification are named using three-letter acronyms. Additional categories that are employed include those based on the liposomes' composition and production processes.

1.3.1 Classification of liposome based on structure of parameters

1. Multilamellar Large vesicles > 0.5µm
2. Oligolamellar vesicles 0.1-1µm
3. Unilamellar vesicles (All size range)
   a) Small unilamellar vesicles 20-100nm
   b) Medium sized unilamellar vesicles
   c) Large unilamellar vesicles >100nm
   d) Giant unilamellar vesicles >1µm
4. Multivesicular vesicles >1µm (4)

2. Acne : Acne vulgaris is a common skin condition, causing changes in pilosebaceous units (PSU) and skin structure consisting of a hair follicle and its associated sebaceous gland, via androgen stimulation. It is characterized by non-inflammatory follicular papules or comedones and by inflammatory

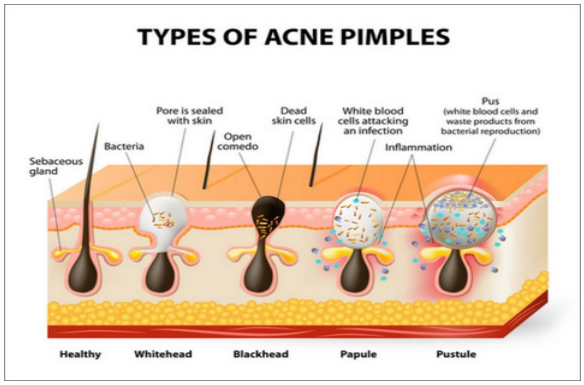

Figure 1(8)

2.2. Causes of acne 1. Hormone levels in women change during the menstrual cycle. 2. Although greasy or fried foods, pizza, and junk food are generally bad for you, they don't cause or worsen acne. 3. Hormonal changes brought on by pregnancy or adolescence. 4. Particular medications, such birth control pills or corticosteroids. 5. Excessive washing to get rid of impurities from acne might dry up and irritate the skin. Therefore, it is actually preferable to wash gently. 6. Prednisone, deltasone, orasone, prednisone-M, liquid red, and steroids containing iodides, bromides, or injectable or oral steroids can cause or worsen acne. 7. Stress. 8. As a result of cosmetic use (9) 9. Hyperactivity of the sebaceous glands (excessive lipid release) Hyperkeratosis,(or rapid keratinization), takes place at the hair infundibulum.Bacterial activity (Propionibacterium acnes) promotes comedogenesis.Follicular obstruction combined with sebum, keratinocytes, and inflammation Occupational hazards include things like prolonged exposure to chemicals, air pollutants, and high humidity levels.

Hormones, environmental factors, or inherited susceptibility can all contribute to acne.(10)

2.3. Factor Affecting of Acne

1. Propionibacterium acnes, or P. acnes.
2. Alterations in follicle keratinization
3. Inflammation
4. Increased androgen-induced sebum production
5. Due to Cosmetics
6. Hormonal Changes and Menstruation
7. Diet
8. Genetic (11)

3. Methods of preparation of liposomes

A) Multilamellar Liposomes (MLV)

1. Lipid hydration method : The most popular technique for creating MLV is this one. A lipid solution is dried until a thin film forms at the bottom of a round-bottom flask. The film is then hydrated by adding aqueous buffer

and vortexing the mixture for a while. The hydration process is carried out at a temperature higher than either the lipid's gel-liquidcrystalline transition temperature (Tc) or the Tc of the lipid mixture's highest melting component. Depending on their solubilities, the chemicals to be encapsulated are added to either an organic solvent containing lipids or an aqueous buffer.This approach makes it easy to create MLV, and these liposomes can include a wide range of chemicals.The method's shortcomings include a heterogeneous size distribution, low internal volume, and low encapsulation efficiency.

2. Solvent Spherule Method : A technique for creating MLVs with a uniform size distribution.The procedure comprised dispersing the tiny spherules of volatile hydrophobic solvent, in which lipids had been dissolved, in aqueous solution. MLVs were created when an organic solvent was carefully evaporated in a water bath.(2)

B) Small Unilamellar Liposomes

1) Sonication Method: Here, MLVs are sonicated in an inert atmosphere using either a probe sonicator or a bath type sonicator. The primary disadvantages of this approach include extremely low internal volume/encapsulation efficiency, potential phospholipid and chemical degradation, exclusion of large molecules, metal contamination from the probe tip, and the existence of MLV in addition to SUV.

2) French Pressure Cell Method: MLV is extruded through a tiny hole at 20,000 pressure and 4°C. Compared to the sonication process, this approach provides a number of advantages. The process is straightforward, quick, repeatable, and requires handling unstable materials gently. Compared to sonicated SUVs, the resultant liposomes are a little bigger. The method's limitations include its inability to reach a certain temperature and its comparatively small working volumes (maximum of 50 mL).

C) Large Unilamellar Liposomes (LUV): These days, medicines and macromolecules are encapsulated using them because to their high internal volume and encapsulation efficiency.

1) Solvent Injection Methods:

a) Ether Infusion Method : In an aqueous solution of the material to be capsulated, a solution of lipids dissolved in diethyl ether or an ether/methanol mixture is gradually injected at 55-65 °C or under low pressure. Liposomal production results from the subsequent vacuum-assisted elimination of ether. The population is heterogeneous (70-190 nm), and substances to be encapsulated are exposed to high temperatures or organic solvents. These are the method's primary disadvantages.

b) Ethanol Injection Method : A large amount of buffer is quickly injected with an ethanol lipid solution. The MLVs are created instantly. The method's disadvantages include the population's heterogeneity (30–110 nm), the liposomes' extreme dilution, the difficulty of completely eliminating ethanol due to its azeotrope formation with water, and the potential for several physiologically active macromolecules to become inactive even in the presence of trace amounts of ethanol.

c) Calcium-Induced Fusion Method : LUV is made from acidic phospholipids using this process. The process is founded on the finding that adding calcium to SUV causes fusion, which forms multilamellar structures in a spiral pattern (Cochleate cylinders). The creation of LUVs occurs when EDTA is added to these preparations. The primary benefit of this approach is the ability to gently encapsulate macromolecules. Although they vary in size, the resultant liposomes are primarily unilamellar. The main drawback of this approach is that only acidic phospholipids can provide LUVs. (3)

d) Freeze-thawed liposome preparation method : SUVs are rapidly frozen and then gradually thawed. Collective elements are scattered to LUV by the brief sonication. When SUV is produced using the freezing and defrosting process, unilamellar vesicles are created. This kind of synthesis significantly reduces the concentration of growing phospholipids while increasing the medium's ionic power. The efficiency of encapsulation is raised from 20% to 30%. (4)

4.Preparation of Liposomal gel

After weighing the appropriate quantity of Carbopol 940, it was gradually added to 90 milliliters of distilled water while being continuously stirred with a magnetic stirrer to avoid the unavoidable creation of aggregates. The gel swelled under normal stirring conditions for approximately 12 hours, or until it was completely enlarged and translucent, following the addition of a solid material. Other additives including 15% w/v polyethylene glycol-400 (PEG-400), 0.5% w/v triethanolamine, methylparaben, and propylparaben were added to create a homogenous gel dispersion. By combining the gel with the 10 ml liposomal dispersion formulation, liposomal gel formulations were created. Sterile bottles containing the finished liposomal gel compositions were used for storage.(12)

5. Evaluation parameters for liposomal gel

Physical evaluation

The formulations Liposomal gel's organoleptic properties, occlusiveness, and washability were assessed.

Washability

Liposomal gel formulations were tested for washability by first putting the gel to the skin, then determining how simple and thorough it was to wash it

off with distilled water while physically monitoring the results.

Measurement of pH

A digital pH meter was utilized to ascertain the pH of the prepared gels. Readings from the pH meter were taken while the electrode was submerged in the gel.

Viscosity study

The Brookfield viscometer was used to measure viscosity by choosing an appropriate spindle number and rpm. After five minutes, the spindle groove was dipped, the rpm was set, and a reading was taken using 30 grams of gel preparation that had been stored in a 50 milliliter beaker. Viscosity was determined using a factor. The process was carried out three times, and the mean of the observations was noted.

Spreadability

After pressing 0.1 g of each formula between two slides, the gel sample was left for roughly 5 minutes. There is no more spreading than anticipated. Cm were used to measure the spread circles' diameters. The values were interpreted as spreadability comparisons. S = ML/T. where S stands for spreadability, M for weight attached to the top slide, L for glass slide length, and T for time taken in the slide's separation. Extrudability study

In order to determine the gel compositions, gel was filled into the collapsible tubes. A 0.8 cm gel ribbon's extrusion weight in grams was used to calculate the gel formulation.

Skin irritation test

Human participants were used in this experiment. After obtaining their informed agreement, three volunteers were selected for a single formulation and the trial was conducted. It was putting gel on a 4-square-inch patch of the hand. After that, the irritation's outcome was completed.

Extract content

1 ml of each liposomal gel formulation was precisely measured and then transferred to 100 ml of dry, clean volumetric flasks in order to quantify the extracted content. A homogenous mixture of distilled water and ethanol in a 1:1 ratio was poured to the volumetric flasks, the volume was adjusted to 100 ml using the same mixture, and it was sonicated for five minutes. UV-visible spectrophotometer was used to test the solutions' absorbance at 250 nm.

In vitro diffusion studies

The equipment, which consists of a cylindrical glass tube that was opened at both ends, was used to measure the drug release from the formulations. After the cellophane membrane had been soaked in the medium for 24 hours, 1 gm of gel (10 mg) was evenly applied to its surface and secured to one end of the tube.The entire structure was fastened so that the gel-

containing tube's lower end barely touched (1-2 mm deep) the surface of the diffusion medium, which is 100 ml of pH 5.8 phosphate buffer in a 100 ml beaker. The assembly was kept at 37 °±2 °C on a thermostatic hot plate with a magnetic stirrer. The contents were agitated for five hours at 100 rpm using a magnetic bar. Five milliliters of samples were taken out at various points in time and replaced with five milliliters of fresh buffer. Following the appropriate dilution, the sample was examined at 269 nm.

Stability study

Under the necessary circumstances, stability tests of liposomal suspension and gel were conducted for a month. Stability tests were conducted more quickly by maintaining the temperature between 4°C and 38°C. By contrasting the physical inspection, pH reading, drug content, and in vitro diffusion investigations, the stability was assessed.(13)

6. Conclusion : Liposomes are a promising and adaptable drug delivery technology, especially for the treatment of acne vulgaris and other dermatological disorders. In topical formulations, they are very useful because they can encapsulate hydrophilic and lipophilic medicines, improve skin penetration, and lessen systemic side effects. The use of herbal extracts such as aloe vera, green tea, neem, and turmeric enhances therapeutic effectiveness by offering anti-inflammatory and antioxidant properties with little side effects. Better drug stability, regulated release, and increased patient compliance are all provided by liposomal gels. It is possible to improve the safety and effectiveness of liposomal systems by adjusting their preparation techniques and assessment criteria. For the treatment of acne and more general dermatological conditions, liposome-based formulations therefore have a great deal of promise as safe, effective, and targeted substitutes.

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