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Review Article

A Technical Note: On Niosomes

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A B S T R A C T

A wide range of substances that serve as carriers can be suspended or captured by the Niosomes Delivery System (MDS), which can then be included into a designed product like a gel cream or powder. The formulation's primary goal is to get the desired medication concentration in the blood. Niosomes are a type of porous medication delivery device for small particles. They are tiny, spherical particles that resemble microscopic and have a broad porous surface. In addition, they may increase stability by altering the drug's release pattern while minimizing negative effects. The serious condition impacting social life is acne vulgaris. Acne can be involved; alternation of follicular keratinization seldom causes significant systemic issues, but maturity, especially for women, which leads to drugs assist to reduce the production of sebum, which is mostly responsible for reducing the formation of acne on the skin. The use of niosomes as carriers for medications that target acne vulgaris is currently receiving more attention in research that focuses on illness detection and a brief to target acne vulgaris. Acne vulgaris is a serious condition that is currently affecting people's social lives. Increased sebum production, bacterial involvement, altered follicular keratinization, and altered follicular barrier are all characteristics of acne. The current review is focused on the niosomes as carriers for the drug targeting the acne vulgaris, brief discussion on the present and future aspects of the niosomes to targetet acne vulgaris.

Keyword: Skin Delivery, Topical Drug Delivery, Acne Vulgaris, Niosomes.

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INTRODUCTION

Skin is the largest organ of the human body and accounts for approximately 15% of an adult's body weight. It has many important functions, such as protecting the body externally, preventing excessive water loss in the body, as well as chemical and biological attacks, and playing a role in maintaining body temperature. The skin irregular and mucous membranes are present throughout the body (Kanitakis, 2002). The integumentary system consists of the skin and its structures (see Fig)

The skin consists of three layers: epidermis, dermis and hypodermis (Kanitakis, 2002). The outer layer, the epidermis, consists of a specialized group of cells called keratinocytes, whose job is toproduce keratin, a long protective protein. The middle layer, the dermis, is mainly a fibrous structure called collagen. The dermis is located on the subcutaneous tissue or lipid membrane and contains small lobes of fat cells called adipocytes. The thickness of the layers is very different and depends on the position of the body. For example, the eyelids have the thinnest epidermal layer, less than 0.1 mm, while the palms and feet have the thickest epidermis, approximately 1.5 mm. The dermis is the thickest part at the back and is 30-40 times thicker than the epidermis.

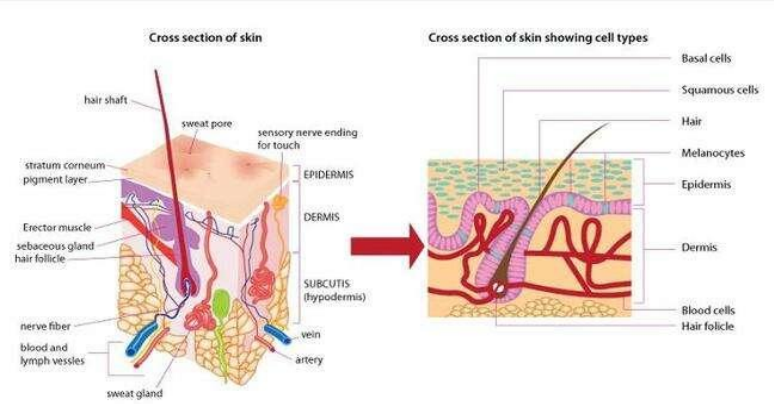

Figure 1: Structure of skin

1. Epidermis:

The epidermis is a stratified layer of squamous epithelium composed of two types of cells: keratinocytes and dendritic cells. Keratinocytes differ from “pure” dendritic cells in having intercellular bridges and more stainable cytoplasm (Murphy, 1997). The epidermis contains many other cells, such as melanocytes, Langerhans cells, and Merkel cells, but the keratinocyte type accounts for the vast majority of cells. The epidermis is generally divided into four layers based on the morphology and location of keratinocytes, which differentiate into keratinocytes: basal cell layer (germinative layer), squamous cell layer (spinous layer), granular cell layer (granular layer), and keratinizing. or the keratinized outer cell layer (stratum corneum) (James et al., 2006 ; Murphy). The lower three layers that make up the nucleated cells of the epidermis are sometimes called the Malpighian layer and the Malpighian network (Murphy). The epidermis is a continuous layer and produces products such as pilosebaceous glands, nails, and sweat glands. The basal cells of the epidermis become a large circle, providing the necessary conditions for skin renewal. The epidermis is a dynamic tissue in which cells constantly move in an asynchronous manner; As individual cells move through theskin, they differentiate not only from each other but also from melanocytes and Langerhans cells.

Cells of the Epidermis

- Keratinocytes
- Melanocytes
- Langerhans’ cells
- Merkel’s cell
- Fibroblasts

Keratinocytes

Keratinocytes are the main cell type of the epidermis, they start from the basal layer, produce keratin and are responsible for epidermal water production by producing and secreting lipids. Keratinocytes also regulate calcium absorption by activating cholesterol precursors to produce vitamin D from UVB light.

Melanocytes

Melanocytes originate from neural crest cells and produce melanin, which mainl determines skin color. They are found between cells in the basal lamina and produce melanin. UVB light stimulates melanin production, protects against UV rays and mimics sunlight. Melanin then moves from cell to cell along a long pathway connecting from melanocytes to neighboring epidermal cells. Melanin granules in melanocytes have undergone a long process of transfer to the cytoplasm of basal keratinocytes. Transfer of melanin to adjacent keratinocyte to the "pigment donor"; It plays a role in the phagocytosis of melanocytes by keratinocyte.

Langerhans’ Cells

Langerhans cells (dendritic cells) are the skin's first line of defense and play an important role in antigen presentation. These cells require special stains to be seen and are located in the stratum spinosum. These cells are of mesenchymal origin, are bone marrow-derived CD34-positive stem cells, and are part of the mononuclear phagocytic lineage. They contain Birbeck granules, which are tennis-shaped cytoplasmic organelles. These cells present MHC I and MHC II molecules, carry antigens from the skin, and transport them to the lymph nodes.

Merkel Cells

These cells act as mechanoreceptors for light touch and are found mostly in the fingers, but are also found in the hands, feet, mouth, and genital mucosa. They attach to keratinocytes next to desmosomes and have intermediate keratin filaments whose membrane interacts with white nerve cells in the skin.

Fibroblasts

Procollagen and elastic fibers are produced and secreted by cells. Proteolytic enzymes eventually break down procollagen, forming aggregates and cross-links of collagen. These connections between collagen fibers are highly flexible and resistant to tearing and other mechanical stresses. Collagen makes up 70% of the weight of the dermis, compared to elastic fibers, which make up less than 1% of the weight of the dermis. The moisture barrier, the outer layer of the stratum corneum, has an acidic pH (4.5 to 6.5). The acid mantle refers to the slightly acidic moisture barrier that derives its acidity from the combination of sweat and sebaceous glands. Keratin is held together and remains hard thanks to the acidic crust, which also prevents the formation of dangerous bacteria and fungi. Due to alkaline soaps on the skin surface, keratin fibers become loose, brittle, lose their protective properties and cause more infections, dryness and roughness.

2. **Dermis:**

The dermis is between the sole area and the subcutaneous layer, and its main function is to protect and support the epidermis.

The main functions of the dermis are:

1. Protection
2. Cushioning the deeper structures from mechanical injury;
3. Providing nourishment to the epidermis;
4. Playing an important role in wound healing.

Layers of the Dermis

The two layers of the dermis are the papillary layer and the reticular layer. The upper papillary layer has a thin layer of collagen fibers. The lower reticular layer is thicker and has thick collagen fibers layered parallel to the skin surface. Dermis consists of tissue found all over the body and instead forms a collagen-like layer that gives strength and flexibility to the skin, while elastic tissue gives elasticity to the skin.

Specialized Dermal Cells:

Hair follicles and the arrector pili muscle attached to each hair follicle. Sebaceous (oil) glands and apocrine (scent) glands are associated with hair follicles. This layer also contains eccrine glands, but they are not associated with hair follicles. Blood vessels and nerves pass through this process. Nerves send pain, itch and heat signals. There are also special nerve cells called Meissner corpuscles and Vater-Pacini corpuscles that transmittouch and pressure sensations. [2-3]

Hypodermis:

Subcutaneous tissue is located deep within the dermis and is also known as subcutaneous fascia. It is the deepest part of the skin and contains fat lobules as well as some skin appendages such as hair follicles, nerves, and blood vessels. Subcutaneous tissue consists mainly of fat and acts as an insulator and shock absorber. As we age subcutaneous fat decreases, the skin becomes thinner and less resistant to injury. The decrease in subcutaneous fat means that the role of subcutaneous tissue in limiting fire is not good. The distribution of subcutaneous fat also changes: it decreases on the face and hands, but increases on the thighs and stomach. Fat loss in bones increases the risk of osteoporosis and fractures[5]

Origin of the skin

The future epidermis, formed from the early gastric region, and the visual mesoderm, which comes into contact with the inner part of the epidermis during gastrulation, are collected in the skin. Besides being the dermis, the mesoderm is also important for supporting the differentiation of the epidermal layer, including the mammalian hair follicle. Although dermis treatment is not necessary in this case, the features can still be found in the powdered dermis or tendons, and the strength of the dermis is essential for preserving the old epidermis of humans. Although the pigment cells that make up the neural crest are small, they contribute greatly to the skin.[6]

Functions of the skin

The skin has three main functions:

- Protection
- Thermoregulation;
- Sensation.

Within this, it performs several important and vital physiological functions, as outlined below (Graham-Brown and Bourke, 2006).

Protection

The skin acts as a protective barrier from:

1. Mechanical, thermal and other physical injury;
2. Harmful agents;
3. Excessive loss of moisture and protein;
4. Harmful effects of UV radiation.

Thermoregulation

One of the basic functions of the skin is to protect the body from the effects of cold or heat and to keep the temperature constant. This is done by altering blood flow in the skin vascular bed. In hot weather, blood vessels dilate, the skin turns red, and sweat beads remain suspended on the surface (vasodilation = more blood flow = more direct heat). In cold weather, blood vessels constrict, preventing heat from escaping (vasoconstriction = decreased blood flow = decreased heat). The release and evaporation of sweat from the skin surface also helps cool the body.

Sensation

The skin is a "tactile" organ that responds when we touch or feel something, including things that may cause pain. This is important for people with skin problems because the pain and itching can be very painful and cause great suffering for many people. It is also crucial for many patients who feel their skin is isolated due to touch, color, pain, or how others see them; because many people have experienced the fact that it is considered dirty or spread and should not be touched.

Topical drug delivery systems.[8]

One of the challenges in the delivery of cosmetics is their transport across the skin barrier. Creams contain two types of products: creams are applied, sprayed, or otherwise dispersed on the skin to cover the affected area. Internal ointment used on the mucosa for local mobilization of oral, genital or anorectal tissues. In general, cosmetics penetrate the drug into the skin or mucosal layers, creating local effects at the site of application. Although some unintended drug absorption may occur, it is sub therapeutics quantities and generally of minor concern.

Advantages of topical drug delivery systems.[9]

1. First of all, do not disturb the metabolism.
2. Simple and easy to use.
3. Send more medicine to specific areas.
4. Do not eat conflicting foods.
5. After administration of drugs with short biological half-life and narrow therapeutic window.
6. Suitable for self-medication

Disadvantages of topical drug salivary system. [10]

1. Skin irritation dermatitis may occur as a result of medications or supplements.
2. Possibility of allergic reaction.
3. The main limitations of the remaining microemulsion-based gels are thepoor quality of the microparticles in the skin and the penetration of air bubbles during formation.
4. Some drugs are small in size and are not easily absorbed by the skin.
5. Some drugs have poor skin permeability.

Routes of Administration.[10]

Cosmetic drug delivery generally refers to the direct use of drugs at the site of action on the skin to achieve the desired pharmacological effect, but it has some inherent limitations; This type of medication must pass through many barriers of the skin to reach it. All systemic circulations such as the anus, nose and vagina are examined. Direct application of the drug to the mucosa results in increased absorption of the drug and therefore increased effectiveness. Microemulsion based gels, oral, vaginal, topical, etc. It has been studied for various application routes such as.

Factors affecting topical absorption of drugs:[1]
Physiological and physicochemical considerations are taken into account for drug absorption in topical areas.

Physiological factors:

1. Thickness of skin.
2. Lipid content.
3. Density of hair follicles.
4. Density of sweat glands.
5. pH of skin.
6. Blood flow.
7. Skin hydration.
8. Inflammation of skin.

Physicochemical factors:

1. Partition coefficient.
2. Molecular weight (<400 Dalton)
3. Degree of ionization
4. Effect of vehicles.

Factors to be consideration while choosing a topical preparation:

In general, ointments and creams containing water and oil, which can cause irritation or allergies, are less itchy, while gels are more itchy. If you are allergic to disinfectants or emulsifiers, the cream is not suitable for you. The type of preparation should be appropriate to the type of diseaseAccording to the type of preparation for the location. (For example, for hair, gel or dye)

Niosomes[12]

Vesicles are a new type of medicine that uses hydrophilic drugs in the cavity and hydrophobic drugs in the nonpolar regions of the bilayer, so that hydrophilic and hydrophobic drugs can be released into vesicles. The main reasons for the development of liposomal bacteria are chemical stability, biodegradability, biocompatibility, low cost, easy storage, easy handling and non-toxicity. Niosome, oral route, parenteral route, topical route, ocular route etc. It can be applied by various methods such as. Niosomes are one of the best carriers. In principle, liposomes are similar to liposomes and comparable in drug delivery capacity, but chemical stability and economy make liposomes better than liposomes. Both have a bilayer formed by a non-ionic surfactant in the case of liposomes; In liposomes, the double layer consists of a non-ionic surfactant. Nanobodies are microscopic layers ranging in size from 10 to 1000 nm, made of biodegradable, non-immunogenic and biocompatible surfactants. [8] Vesicles are amphiphilic in nature, allowing hydrophilic substances to enter the cavity, while hydrophobic substances can be trapped in the non-polar regions of the bilayer and hence hydrophilic and hydrophobic substances can be accommodated in vesicles. 12. Vesicles or nonionic surfactant vesicles are microscopic structures formed by mixing alkyl or dialkylpolyglyceryl ether nonionic surfactants with cholesterol and then hydrating them in an aqueous environment. 13Niosomes can capture hydrophilic and lipophilic substances in the aqueous layer and vesicle membrane, respectively. The two layers of the vesicles have a hydrophilic inner and outer structure and a lipophilic region between them. Therefore, many drugs and other devices can be delivered using nanobodies. 14 In nanobodies, the amphiphile-forming vesicles are nonionic surfactants such as Span-60, and small amounts of anionic surfactants such as cholesterol andhexadecyl phosphate are often added.

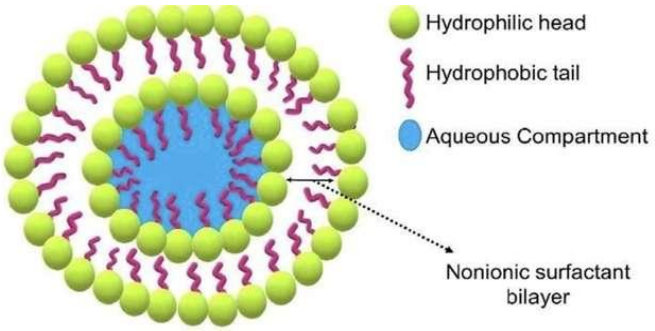

Figure 2: Structure of Niosomes

Composition of Niosomes[16]

Two components use in niosome preparation are

- Cholesterol
- Non-ionicsurfactants .
  - Cholesterol is a steroid derivative, which is used to provide rigidity and proper shape, conformation to niosome form.
  - Non-ionic Surfactants are generally used for the preparation of niosomes. Examples: a. Tweens (20, 40, 60, 80) b. Spans (Span 60, 40, 20, 85, 80) c. Brijs (Brij 30, 35, 52, 58, 72, 76).

Types of Niosomes:[17]

Vesicles can be classified by the number of bilayers (e.g. MLV, SUV) or by size (e.g. LUV, SUV) or by arrangement (e.g. REV, DRV). The different types of niosomes are described below.

1. Multi lamellar vesicles (MLV),
2. Large unilamellar vesicles (LUV),
3. Small unifamellar vesicles (SUV),

1. Multilamellar vesicles (mlv)

The lipid portions of the water body have many bilayers around them. The diameter of these vesicles is approximately 0.5-10 µm. Multilayer vesicles are the most commonly used vesicles. It is easy to make and mechanically stable for a long time. These vesicles are well suited as drug carriers for lipophilic drugs.

2. Large unilamellar vesicles (luv):

This type of vesicle has a balanced water/lipid compartment and therefore allows the capture of large amounts of bioactive substances through the economical use of lipids.

3.Smallunilamellar vesicles (suy):

- Most small monolayer vesicles are prepared from multilayer vesicles by ultrasonic treatment and electrostatic stabilization by French pressure extrusion, hexadecyl phosphate contained in 5(6)-carboxyfluorosazine (CF) charged in Spun 60 as vesicles.

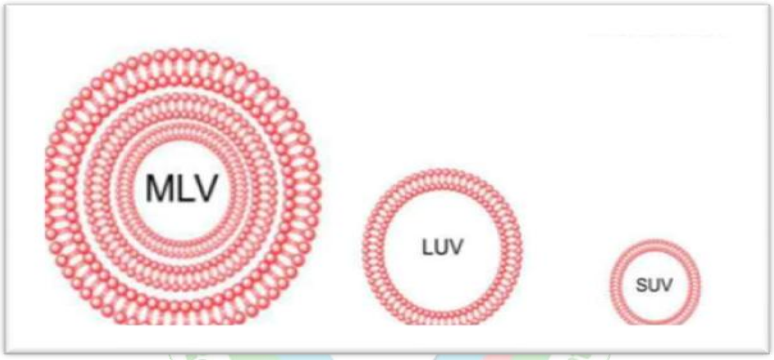

Figure 3: Types of Niosomes

Method of preparation of Niosomes:[18,19,20,21]

The method of preparation influences the size, size distribution and number of bilayers, entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.

a)Thin film hydration method
b) Reverse evaporation technique
c) Ether injection method
d) Sonication
e) The bubble method
f) Micro fluidization
g) Membrane extrusion method

a) Thin film hydration method (TFH):

The TFH method is currently one of the most widely used and convenient methods for the preparation of nanoliposomes. In the TFH method, the drug is dissolved in an organic solvent such as chloroform or a mixture of organic solvents in a round-bottom flask; surfactant and cholesterol are added in different proportions. The organic solvent was removed using a rotary evaporator under vacuum at 60°C until a thin film was formed. The membrane was dried under vacuum for 5 min to remove remaining solvent. Additionally, the dried film was hydrated in phosphate buffer with pH 7.4 at 60º C. Hydration of the lipid membrane leads to the formation of lipoid bodies. The resulting vesicle suspension is mixed by vortexing and ultrasonicated with a probe sonicator.

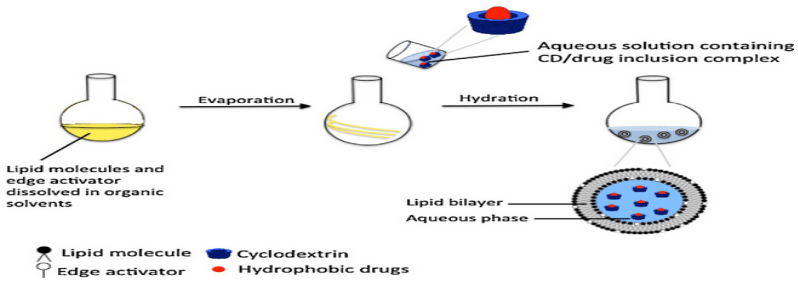

Figure 4: Thin film hydration method (TFH)

b) Reverse evaporation technique:

In this way, the correct weight (1:1) of cholesterol and surfactant is dissolved in a mixture of diethyl ether and chloroform. The aqueous phase containing the drug is then added thereto and the resulting two phases are sonicated at 4-5°C. The resulting clear gel is sonicated again by adding a small amount of phosphate buffered saline (PBS). The organic phase was then removed under reduced pressure at 40°C. The resulting vesicle suspension was diluted in PBS and heated in a water bath at 60 °C for 10 min to form vesicles. Store the liposome suspension in an airtight container in the refrigerator.

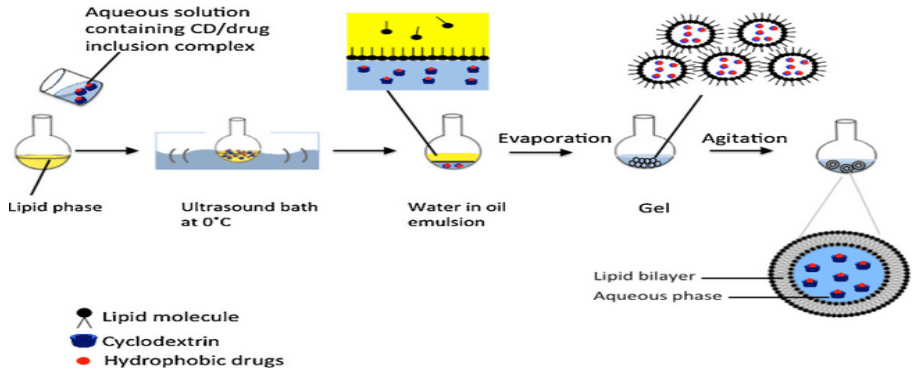

Figure 5: Reverse evaporation technique

c) Ether injection method:

In this method, nonionic surfactants and cholesterol are dissolved in diethyl ether and then the drug is dissolved in the above lipid solution to prepare liposomes. Then put this solution into a syringe and slowly inject it into the aqueous phase (phosphate buffer pH 7.4) in the beaker through the needle and mix gently. Evaporation of the solvent leads to the formation of liposomes, which are separated by ultracentrifugation.

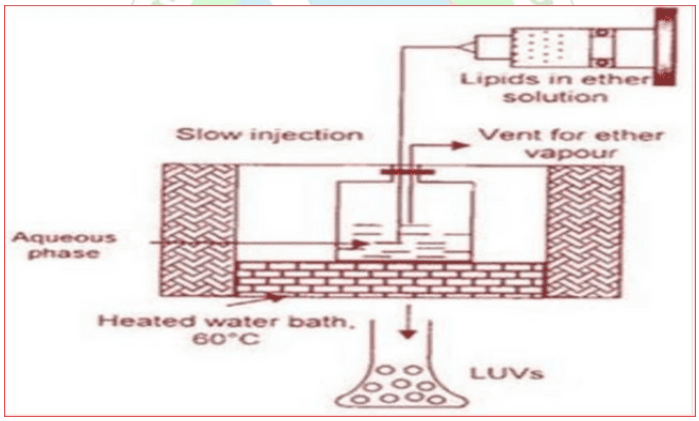

Figure 6: Ether injection method

d) Sonication:

In this model, the aqueous phase containing the drug is added to the mixture of surfactant and cholesterol in 10 ml glass bottles. The mixture is then sonicated for 3 minutes at 60º C using an ultrasonic generator with a titanium probe to form nanobodies.

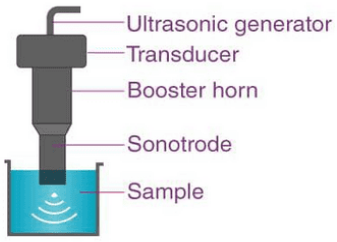

Figure 7: Sonication

e)Bubble method:

It is a new machine for the preparation of vesicles, three neck round bottom flask placed in the bath to control the temperature, the first and second neck are placed in cold water reflux and temperature, nitrogen is entered from the third neck. . Cholesterol and surfactant are dissolved in buffer (pH 7.4) at 70°C and nitrogen gas is bubbled at 70°C to form liposomes.

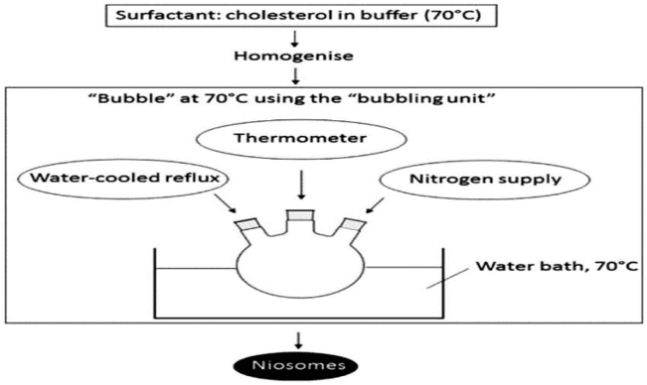

Figure 8: Bubble method

f) Micro fluidization:

The principle involved in this technology is the submerged jet principle, in which two fluidizing streams interact at ultra-high velocities in microchannels in an interface chamber. The collision of the thin liquid with the front is a process that causes energy to enter the body while still in the area of vesicle formation. It leads to the production of liposomes with greater uniformity, smaller size and better reproducibility.

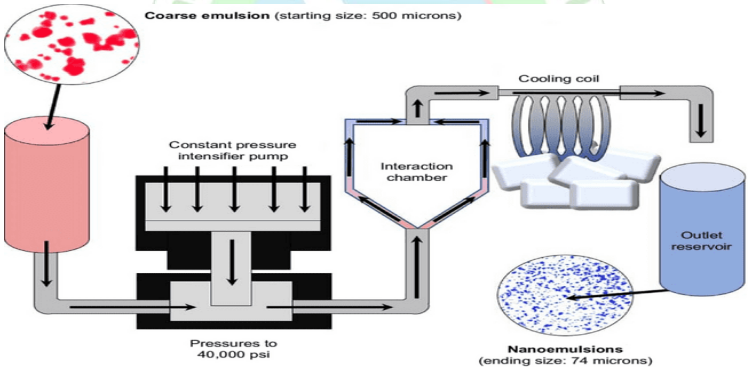

Figure 9: Micro fluidization

g) Membrane extrusion method:

With this method, sachets of the desired sizecan be prepared. The mixture of surfactant, cholesterol, and diethyl phosphate in chloroform forms a thin-film rotary evaporator. The film is then hydrated with an aqueous chemical polycarbonate film and the resulting suspension is extruded and placed in a series of 8 channels.

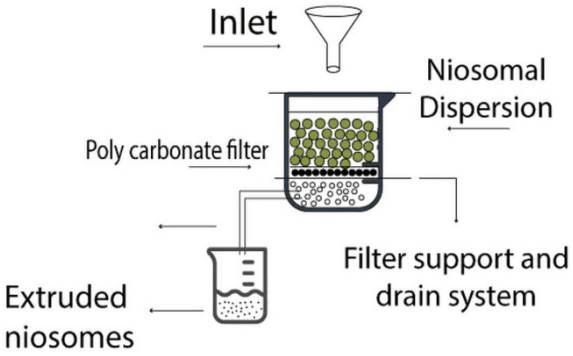

Figure 10: Membrane extrusion method

Application of Niosomes:[22,23]

Transdermal delivery of drugs by niosomes

Slow penetration of drug through skin is the major drawback of transdermal route of delivery. An increase in the penetration rate has been achieved by transdermal delivery of drug incorporated in niosomes.

Niosomes as drug carriers

Niosomes have also been used as carriers for Iobitridol, a diagnostic agent used for Xray imaging. Topical niosomes 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.

Leishmaniasis

Leishmaniasis infection is caused by the parasite namely as genus Leishmania which infiltrates the cells of the spleen and liver. Test study conducted by the use of niosomes showcased that it was possible to give higher levels of the drug without triggering the side effects of it, and thus provides greater effectiveness of the treatment.

Anti-neoplastic treatment

Most antineoplastic drugs cause severe side effects. Niosomes can alter the metabolism; prolong circulation and half life of the drug, thus decreasing the side effects of the drugs.Niosomes decrease rate of proliferation of tumor with higher plasma levels accompanied by slower elimination. Tumoricidal activity of niosomally formulated methotrexate is higher as compared to plain drug solution.

Peptide drug delivery

Application of niosomes has also shown that peptides can be protected from the peptide breakdown in gastrointestinal track by few enzymes. Forexample in an in vitro study conducted for delivering vasopressin drug through oral delivery system by entrapment in niosomes significantly provides protection from breakdown thus increasing the integrity of the peptides.

Advantages ofNiosomes24

- Being water-based vehicle niosomes offer better patient compliance as compared to other oily dosage forms.
- Drugs of different solubilities can be accommodated as niosomes consisting of amphiphilic, hydrophilic and lipophilic moieties together.
- Alternating the composition of vesicles provides control over different varying characteristics of niosomes such as concentration, tapped volume, lamellarity, size and surface charge
- Different routes can be opted to deliver niosomes at targeted site of action, such as oral, parenteral and topical.
- Surfactants do not need any special or essential conditions for handeling and storage.
- Niosomes can enhance the bioavailability and penetration of drugs which are poorly absorbed form skin.
- Niosomes entrap the drugs with greater efficiency.
- By using niosomes systemic clearance of the drug is delayed thus increasing the therapeutic effect.
- Niosomes are stable, osmotically active and increase the stability of entrapped drug.
- Niosomes can act as depot and discharge the drug in a controlled mode.
- Niosomes can protect the drug from biological environmental conditions and restrict the effect only at the specific targeted site.

Disadvantages of Niosomes:25

- Poor drug loading capacity.
- Unpredictable gelation tendency.
- High water content.
- Low hydrophilic drugs loading capacity due to partitioning effects.

Evalution of Niosomal Gel:

Physical appearance NJ

The prepared gel was examined for clarity, color, homogeneity and the presence of foreign particles.

pH

2.5 g of gel were accurately weighed and dispersed in 25 ml of distilled water. The pH of the dispersion was measured by using a digital pH meter.

Viscosity measurement:

Viscosity was determined by Brookfield programmable DV III ultra viscometer. In the present study, spindle no. CP 52 with an optimum speed of 0.01 rpm was used to measure the viscosity of the preparation.

Content uniformity

The drug content of the prepared gel was carried out by dissolving accurately weighed quantity of gel equivalent to 10 mg of the drug in 100 ml volumetric flask and volume was made up to 100 ml with methanol. The content was filtered through Whatman filter paper No. 41. 5 ml of above solution was taken into a 25 ml volumetric flask and volume was made up to mark with methanol. The content of Ketoconazole was determined at 243 nm against blank by using the Shimadzu UV/visible spectrophotometer. The drug content was determined from the calibration curve of Ketoconazole. The tests were carried out in triplicate results are given in Table 2.

In vitro drug diffusion study

The apparatus consists of a glass cylinder open at both ends. A dialysis membrane soaked in distilled water (24 h before use) is fixed to the one end of the cylinder with the aid of an adhesive. Gels equivalent to 10 mg of Ketoconazole is taken inside the cell (donor compartment) and the cell is immersed in a beaker containing 100 ml of PBS pH 7.4 containing 10% v/v methanol (to maintain sink condition), act as receptor compartment. The whole assembly is fixed in such a way that the lower end of the cell containing gel is just above the surface of the diffusion medium (1-2 mm deep) and the medium was agitated using a magnetic stirrer at the temperature 37 ± 0.5°C. Aliquots (5 ml) are withdrawn from the receptor compartment periodically and replaced with same volume with fresh buffer. The samples were analyzed

by using UV-visible spectrophotometer at 225 nm.[16,17] The tests were carried out in triplicate.

Natural polymer used in formulation of Niosomes

- Tamarind seed polysaccharides
- Turmeric
- Guar gum
- Chitosan
- Fenugreek polysaccharides

Natural polymer:[26]

Natural polymers, on the other hand, are abundant and similar to those found in biological extracellular matrices. Therefore, natural polymers are easily accepted by the human body and have high bioactivity and biocompatibility. Natural polymers can be divided into three main groups according to their chemical structure: (i) polysaccharides, (ii) proteins and (iii) polyesters. This chapter provides an overview of polysaccharide-based biomaterials, their properties, and applications in drug delivery and tissue engineering. Special attention is paid to polysaccharides such as (i) hyaluronic acid (HA), (ii) chondroitin sulfate, (iii) chitin and chitosan, (iv) alginate and (v) cellulose. Chemical and biological properties of polymers and their popular derivatives are also discussed. Natural forms of polysaccharides may not provide all the properties required for a particular biomedical application. Therefore, this chapter also focuses on polysaccharide derivatives and their combinations with other polymers for various biomedical applications.

Physiochemical properties of natural polymer:[27]

Homogenecity\Polydispersits :

Natural polymers, such as proteins, are uniform in size and invariant. Such polymers are considered homogeneous or monodisperse. Most natural polymers are made by condensation polymerization. Natural polymers tend to biodegrade easily and do not harm the environment or humans.

Classification of natural polymer

Natural polymers are classified in three main categories such as:

- Plant origin
- Animal origin
- Microbes origin

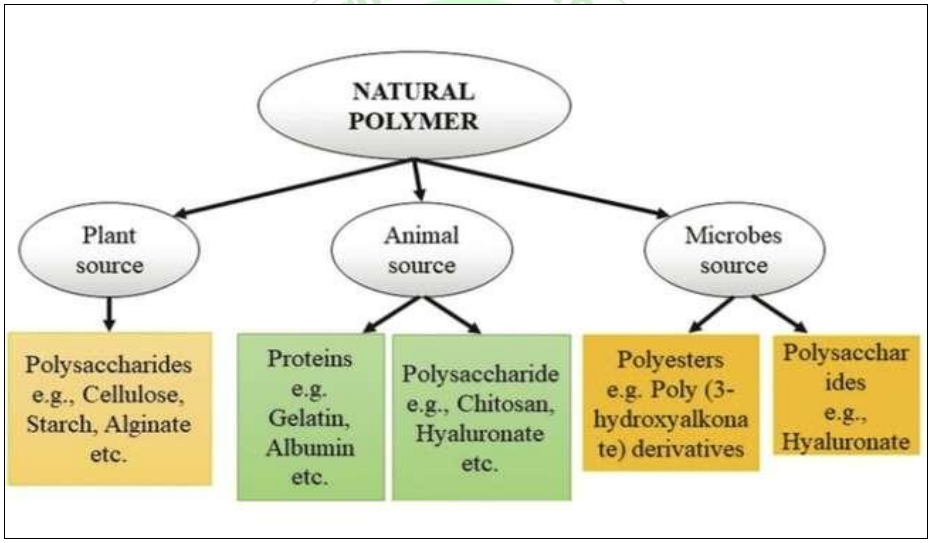

Figure 11: structure of Natural polymers

Disadvantages Of Natural Polymers:27

1) Microbial contamination During production, they are exposed to external environment and hence, there are chances of microbial contamination.

2) Batch to batch variation Synthetic manufacturing is controlled procedure with fixed quantities of ingredients while production of natural polymers is dependent on environment and various physical factors.

3) The uncontrolled rate of hydration Due to differences in the collection of natural materials at different times, as well as differences in region, species, and climate conditions the percentage of chemical constituents present in a given material may vary.

ACNE: [28,29,30]

Acne vulgaris is a skin disease primarily of the pilosebaceous glands and affects the area where the largest sebaceous glands are located, including the face, back, and groin. It is a universal disease, occurring in all cultures and affecting 95% of boys and 83% of adults. girls. Derived from the Greek word "akme" meaning peak or apex, acne is a benefit or benefit of the pilosebaceous unit. The correct name for acne is acne vulgaris. Acne is the most common skin disease between the ages of 18-25. Acne vulgaris is a pilosebaceous skin disease caused by the formation of seborrhea, comedones, inflammatory lesions and the presence of Propionibacterium acnes, Staphylococcus epidermidis and Staphylococcus aureus in the follicular channels and almost universal sebum production. 95% of boys and 83% of girls of all races.

Figure 12: structure of Acne

Creams are the first line of treatment for all types of acne. Human skin acts as a strong barrier to prevent exposure to cosmetics. Epidermis, dermis and subcutaneous tissue are the three layers of skin; The stratum corneum is the outer layer of the epidermis and acts as a strong anti-permeability barrier. The main purpose of drug therapy is to ensure local penetration and retention of drugs into the skin system. When treating medications, the human skin model is limited by the material and medication used by the body; Drugs must have sufficient lipophilicity and a molecular weight of <500 Da. Therefore, many ways to promote and increase access to medicines have been investigated. Active substances such as alcohol, polyols, surfactants, fatty acids, esters, pyrrolidone, amines, amides, sulfoxides, terpenes, alkanes and phospholipids that enter the body or enable the skin meat to enter the body can be used.

Epidemiology 31,32

In 2010, approximately 9.4% of the population suffered from acne. 90% of people had acne during adolescence and sometimes into adulthood. Moderate to severe pain affects approximately 20% of people. While acne rates are lower in rural areas, acne may not occur in non-Western groups such as Papua New Guinea and Paraguay. 9.8% of women have this condition, compared to 9.0% of men. About 1% of men and 5% of women over the age of 40 have this problem. It affects people of all races, but it is not clear whether race plays a role in this condition. In the United States, acne affects 40 to 50 million people, approximately 16% of the population, and approximately 3 to 5 million people.

Etiology Of Acne33

Increased sebum production by SG, hyperkeratinization of sebaceous ducts, colonization of pilosebaceous sebum ducts by Propionibacterium acnes, and inflammation are all factors that can cause acne. The severity of acne is related to seborrhea, which in turn is related to the infundibulum of the hair follicle. In mild cases of acne, hyperkeratosis, hyperkeratosis, and exfoliation of infundibular keratinocytes occur, leading to comedone formation. In severe acne, the infundibulum ruptures, releasing sebum into the dermis, causing an inflammatory response.

Pathogenesis of acne Vulgaris [34]

Acne affects the pilosebaceous unit of the skin; There are many diseases that occur at different levels of inflammation, including acne scars and pigmentation. Acne is usually seen on the face, chest, back and arms where the sebaceous glands are high. The four main pathological features of acne are increased sebum secretion, irregular shedding of hair follicles, proliferation of Propionibacterium acnes, and local inflammation.

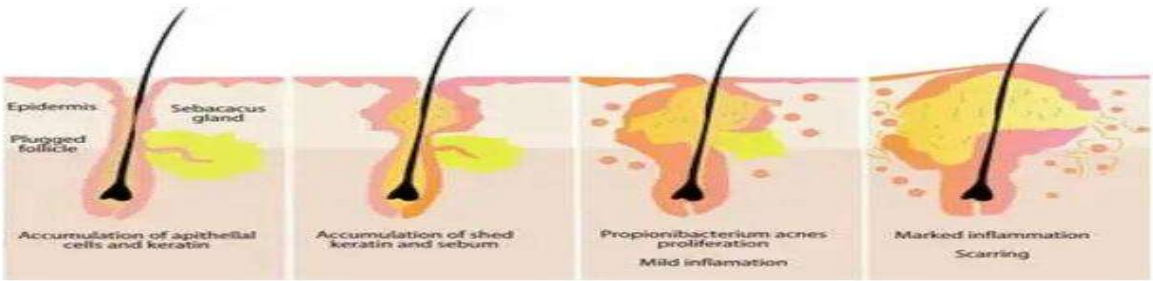

Figure13: Pathogenesis of Acne Vulgaris

Treatment of Acne: [35]

The treatment of acne depends on its severity and persistance

Treating mild acne:

Acne can usually be treated with OTC (over-the-counter) medications. Most acne OTC5 products may contain the following active ingredients:

1. **Resorcinol**:
   It is a crystalline phenol derived from various resins. It helps in the break down of blackheads and whiteheads.

2. **Benzoyl Peroxide:**
   Benzoyl peroxide is a white crystalline powder and acts as a peeling agent, helpful in clearing pores, reducing the bacterial count in the affected area. Benzoyl peroxide kills bacteria and slows down oil production from glands.
3. **Salicylic Acid:**
   Salicylic Acid helps to break down the blackheads and whiteheads, reduces shedding of cells which line the follicles of the oil glands and is effective in treatment of inflammation and swelling. It helps the epidermis to shed skin more easily, prevents pores from becoming blocked and at the same time allows new cells to grow.
4. **Sulfur:**
   Sulfur, in its native form, is a yellow crystalline solid. It helps to break down blackheads and whiteheads.
5. **Retin-A:** It helps to unplug blocked pores. Retin-A contains Tretinoin, an acid from of vitamin A, also known as all-trans retinoic acid (ATRA). It acts as a chemical peel and checks skin aging
6. **Azelaic Acid**:
   It is a saturated dicarboxylic acid found naturally in wheat, rye, and barley. Azelaic acid strengthens the cells that line the follicles, stops oil eruptions and reduces bacterial growth and inflammation. It is useful for patients with dark skin, dark patches on face (melasma) and persistent brown marks from acne.
7. **Topical antimicrobials –**
   Topical antimicrobials (clindamycin, erythromycin, and sodium sulfacetamide) are used in patients with moderate to severe acne.

Cause of Acne:[36]

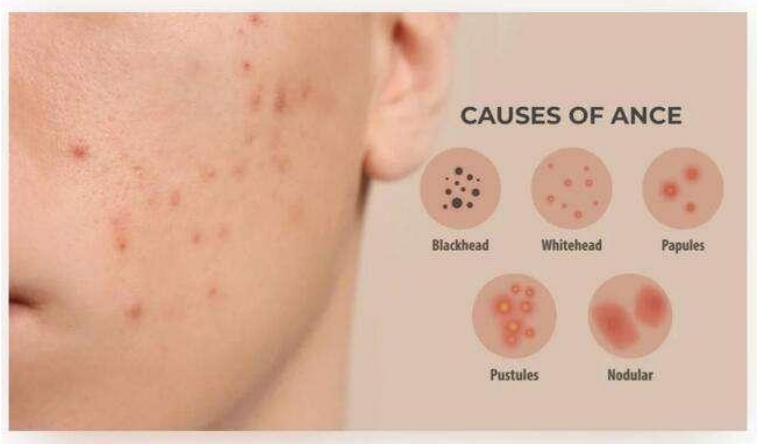

Figure 14: Types of Acne

- Hormonal changes due to aging or pregnancy.
- Certain medications, such as antibiotics or corticosteroids.
- Foods that contain more sugar or carbohydrates, such as bread and chips.
- Most young people experience acne problems in their youth. During this period, hormonal changes occur in the body. These hormones increase oil production, increasing the risk of acne. Hormonal acne associated with puberty usually resolves from adolescence to adulthood.

Characteries of Oily Skin:35

Oily skin is caused by excessive secretion of sebum. Bacteria that kill sebum can cause acne and pimples, which can lead to acne. When acne occurs, erythema (redness), tumor (swelling), heat (increased heat), soreness (pain), and failure (failure) are all signs of inflammation.

Types of Acne/Pimples:[35]

A. **Whiteheads:**
   These remain under the skin and are very small.
B. **Blackheads:**
   These are clearly visible, are black in colour and appear on the surface of the skin. It is not caused by dirt. So scrubbing face vigorously will not help.
C. **Papules:**
   These are visible on the surface of the skin. These are small bumps, usually pink.
D. **Pustules**:
   They are clearly visible on the surface of the skin. They are red at their base and have pus at the top.
E. **Nobules:**
   These are large solid pimples clearly visible on the surface of the skin. They are painful and are embedded deep in the skin.
F. **Cysts:**

These are painful, filled with pus and are clearly visible on the surface of the skin. It causes scars on the skin. All these types of acne in general are termed as acne or pimples. Nobules and cysts are generally found in person with very oily skin and are severe in nature and takes time to heal

- Acne symptoms include whiteheads, blackheads, small bumps, nodules and cysts.
- Although acne is a normal result of the body, the following important conditions can worsen the condition.
- Changes in female hormones during pregnancy.
- Make it effective by picking pimples, scratching them or pressing hard.
- Cover the entire forehead and face with clothing, hats and sports helmets to prevent acne from getting worse.

- It is best to avoid eating pizza, greasy and fried foods, and junk food that have nothing to do with your health, even if they do not cause acne or cause more severe pain.
- Excessive cleaning of acne can cause dryness and irritation of the skin. Therefore, gentle cleaning methods should be preferred.
- Never apply pressure on the acne.
- Acne may be genetically predisposed or worsened in some patients.

CONCULSION

Dermatologists and cosmetic chemists aim to develop new technologies and specialized commodities. New cosmetic and dermatological formulations can be created with a greater understanding of skin physiology and knowledge of its structure and function. The pharmaceutical formulator has to have a thorough grasp of the physicochemical characteristics of the drugs and polymers used in order to perform this unique approach of drug administration effectively. The medicine's topical active period is extended by niosomes capacity to extend the drug's stay in the skin and allow prolonged drug release for up to 12 hours. These traits support the idea that MDS might serve as a platform for a new generation of dermatological and cosmetic procedures. To completely comprehend the extent of drug distribution in the stratum corneum, epidermis, and dermis layers of skin as well as the mechanism of drug penetration, all of which are still in their infancy, further study is, however, necessary. Due to the unique characteristics of the niosomes drug delivery system, including greater product functionality and elegance, longer release, improved drug release profile, and decreased toxicity, a variety of pharmaceutical applications in the near future might provide a possible possibility

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