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TRANSFEROSOMES: EMERGING DELIVERY SYSTEM FOR ENHANCING DRUG PERMEATION THROUGH SKIN

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ABSTRACT

The use of vesicular carriers has lately emerged as a viable technique for reducing the stratum corneum's obstructive effects. Transferosomes, also known as ultradeformable lipids and elastic liposomes, have sparked a lot of interest in cutaneous delivery. They are primarily used to treat a variety of chronic skin conditions, and they are also useful for focused and controlled distribution to ensure patient compliance. These self-assembled nanocarriers are capable of adapting themselves to the stratum corneum's pore size. Edge activators (specific surfactants), phospholipids, buffering agents, and other substances may be found in transferosomes. The impact of edge activators and their concentration gives constructed vesicles the desired flexibility. Elastic liposomes have the capacity to optimize drug solubilization, effective drug loading capabilities, and therapeutic molecule permeability. As nanocarriers, transferosomes have enhanced reflectivity and provide a flexible foundation for effective transdermal applications. These one-of-a-kind nanocarriers also have exceptional elasticity and penetration. These systems are thought to be safe, with effective delivery mechanisms for pharmaceutically and cosmetically active chemical moieties. Recent scientific findings demonstrating the necessity of ultradeformable liposomes have shown consistent and effective drug penetration. This publication includes up-to-date research as well as comprehensive updates on critical difficulties and the use of future transferosomes with improved bioavailability profiles.

KEYWORDS: Transferosomes, Transdermal delivery, Bioavailability, Self-assembled, Skin permeation, Ultradeformable vesicles.

INTRODUCTION

The word 'transferosome' comes from the Latin word 'transferre,' which means 'to carry over,' and the Greek word 'soma,' which means 'body.' A transferosome (Figure 1) is a synthetic vesicle that mimics the features of a cell vesicle or a cell in exocytosis, making it appropriate for regulated and possibly targeted medication delivery. Gregor Cevc developed the basic notion of transferosome in 1991.[1] A transferosome is a complex aggregation that is extremely adaptable and stress-responsive. It is an extremely deformable vesicle with an aqueous core surrounded by a complex lipid bilayer. Because the local composition and form of the bilayer are interdependent, the vesicle is self-regulating and self-optimizing. This allows the transferosome to efficiently traverse different transport obstacles. [2] The transferosomal drug delivery system serves as a drug carrier for non-invasive targeted drug administration and therapeutic agent sustained release, ensuring easy and safe medication delivery. Avoidance of the first-pass metabolism, predictable and extended duration of the activity, the utility of short-half-life drugs, improving physiological and pharmacological response, minimizing undesirable side effects, avoiding drug level fluctuations, inter-patient and intra-patient variations, and mosiac delivery are all potential advantages of the transferosomal drug delivery system over traditional routes. Several ways have been used in medical research to improve the effectiveness of material transfer over intact skin, including penetration enhancers, enhancers, iontophoresis, sonophoresis, and vesicular constructions.[3]

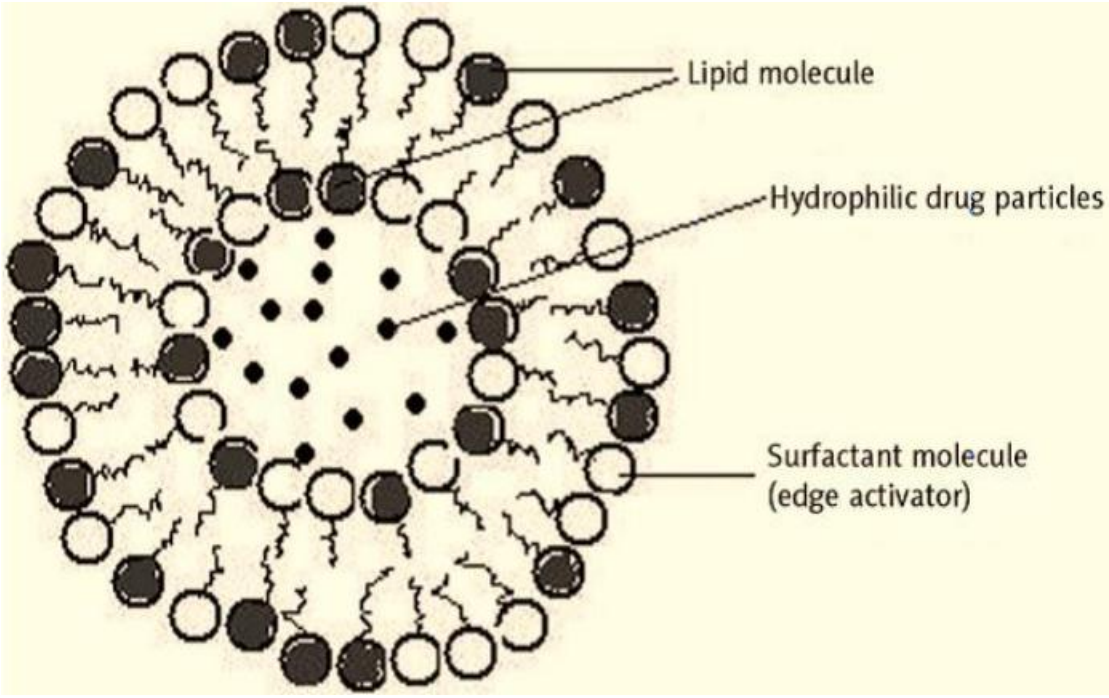

Figure 1: Structural representation of one transferosome unit.

To make use of phospholipid vesicles as a transdermal medication carrier, transferosomes were created. These self-optimized aggregates, with their ultra-flexible membranes, can carry the medicine reliably and efficiently into or through the skin, depending on the administration or application method. Transferosomes bypass the barrier to skin penetration by squeezing themselves along the stratum corneum's intracellular sealing lipid.[4] Because of the high vesicle deformability, this is possible owing to the high vesicle deformability, which allows for self-adapting entrance owing to mechanical stress from the environment. When applied under nonocclusive conditions, the ensuing flexibility of the transferosome membrane reduces the danger of full vesicle rupture in the skin and enables transferosomes to follow the natural water gradient across the epidermis. Transferosomes may spontaneously permeate the intact stratum corneum through two intracellular lipid pathways with different bilayer characteristics.[5] When forced against or enticed into a tiny pore, the self-optimizing deformability of conventional composite transferosomes membrane responds to ambient stress, allowing ultra-deformable transferosomes (Figure 2) to alter their membrane composition locally and reversibly. At high-stress locations, the transferosome components that can withstand significant membrane deformation concentrate, while the less adaptable molecules are diluted. This reduces the energy cost of membrane deformation, allowing the resultant extremely flexible particles to enter and subsequently flow through holes quickly and effectively. [6]

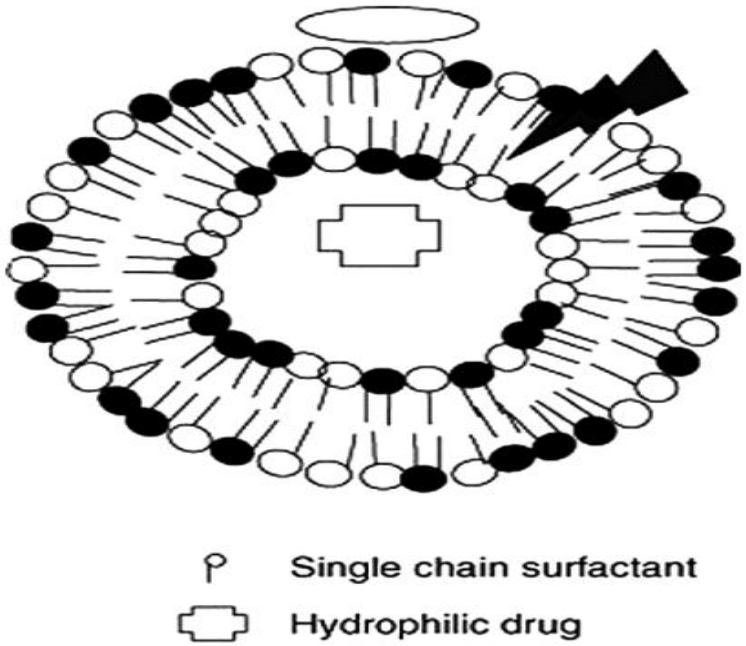

Figure 2: Structure of deformed transferosome.

HUMAN SKIN - ANATOMY AND PHYSIOLOGY

The skin is a vital organ that covers the whole external surface of the human body and acts as a protective barrier between internal organs and the environment. The skin is a dynamic organ that changes constantly throughout one's life as outer layers are removed and interior layers are replaced. Skin thickness varies according to anatomical location, gender, and age of the person.[7] The mucous membranes line the body's surface, and the skin is continuous. The skin of an average adult body covers around 2 m^2 and absorbs roughly a third of the blood moving through the body, as well as serving as a permeability barrier against the transdermal absorption of numerous chemical and biological agents. The skin acts as a barrier between the underlying blood circulation network and the outer world.[8] It protects against physical, chemical, and microbial threats. It maintains body temperature by acting as a thermostat. It aids in the control of blood pressure and protects the human body from UV light penetration. Permeation and absorption of drugs through the dermis are largely determined by the skin.[9]

The structure of the skin is indicated by three distinct layers

- The epidermis is the outermost layer of skin, which provides a waterproof barrier and creates our skin tone.
- The dermis is below the epidermis, which contains tough connective tissue, hair follicles, and sweat glands.
- The deeper subcutaneous tissue (hypodermis) is made of fat and connective tissue.

The epidermis is mostly made up of surface ectoderm, but it also includes neural crest-derived melanocytes, bone marrow-derived antigen-processing Langerhans cells, and neural crest-derived pressure-sensing Merkel cells. Collagen, elastic fibers, blood vessels, sensory structures, and fibroblasts make up the dermis, which is formed mostly from the mesoderm (Figure 3).[10]

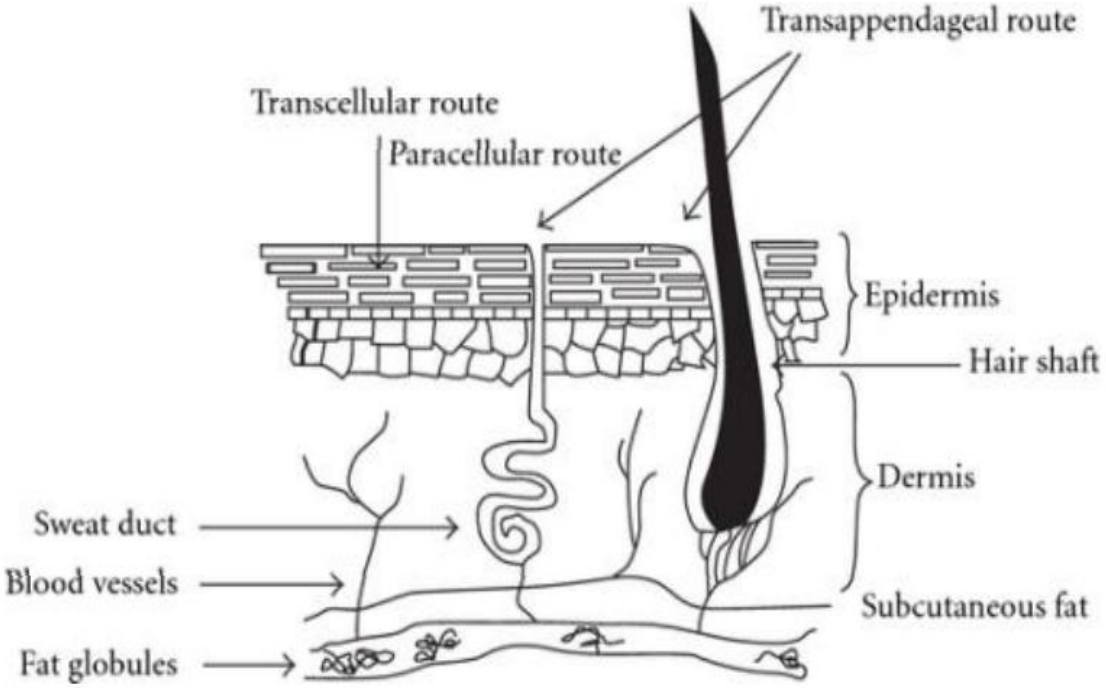

Figure 3: Schematic presentation of human skin.

Subcutaneous fat layer

The hypodermis, or subcutaneous fat layer, connects the overlaying dermis to the underlying body elements. This layer is quite thick in most parts of the body, generally several centimeters thick. The primary function of this layer of adipose tissue is to insulate the body and offer mechanical protection against physical trauma. The main blood vessels and nerves are delivered to the skin through the subcutaneous adipose layer, which may also offer a quickly accessible source of high-energy molecules.[11]

Dermis

Blood and lymphatic vessels, nerve endings, pilosebaceous units like hair follicles and sebaceous glands, and sweat glands like eccrine and apocrine are all entrenched in the dermis. It gives the epidermis physiological support. It is the main component of human skin and is normally 3–5 mm thick. It is made up of a network of connective tissue immersed in a mucopolysaccharide gel, with collagen fibrils providing support and elastic tissue supplying flexibility. This layer is frequently seen as simply gelled water in terms of transdermal drug administration, and so presents a small barrier to most polar medicines, while the dermal barrier may be considered when delivering highly lipophilic compounds.[12]

Epidermis

The epidermis is made up of ten to twenty layers of cells. Melanocytes, which play a role in skin coloring, and Langerhans' cells, which play a role in antigen presentation and immunological responses, are also found in this pluristratified epithelium. The dermal vascular network provides nourishment to the epidermis, as it does to any epithelium. The epidermis is further divided into many layers. The epidermis's basic layer is called the stratum germinativum. The stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum are the layers above the base layer.[13]

Stratum corneum

The stratum corneum is a multilayer stratum of flat, polyhedral-shaped, 2–3 μm thick, non-nucleated cells called corneocytes that is 10–20 μm thick. Corneocytes are predominantly made up of insoluble bundled keratins that are encased in a cell envelope that is held together by cross-linked proteins and covalently attached lipids. Corneodesmosomes are membrane junctions that join corneocytes and help the stratum corneum to stay together.[14] The lipids that make up the intercellular gap between corneocytes come predominantly from the exocytosis of lamellar structures during keratinocyte terminal differentiation. These lipids are needed to maintain a healthy skin barrier. The stratum corneum is the principal barrier to penetration and permeation through the skin. In the most basic sense, the skin can be thought of as a bilaminated membrane, with a penetrating molecule passing through both the lipophilic stratum corneum and the aqueous environment of the underlying viable epidermis and upper dermis to reach the dermal vasculature and rapid systemic distribution.[15]

MATERIALS EMPLOYED

Various phospholipids, surfactants, alcohol, dye, buffering agent, and other materials are often employed in the formulation of transferosomes. Soya phosphatidylcholine, egg phosphatidylcholine, dipalmitoylphosphatidylcholine, and other phospholipids are employed as vesicles-forming agents. Sodium cholate, sodium deoxycholate, Tween-80, Span-80, and other surfactants are utilized to provide flexibility. Ethanol or methanol may be employed as solvents. The hydration media is a saline phosphate buffer (pH 6.4).[16]

FEATURES OF TRANSFEROSOMES

Transferosomes have a structure that includes both hydrophobic and hydrophilic moieties, allowing them to accept pharmacological molecules with a broad range of solubility. Transferosomes may bend and pass through constrictions that are 5 to 10 times smaller than

their own diameter without suffering any noticeable loss. This great deformability allows intact vesicles to penetrate more easily. Low and high molecular weight medications, such as analgesics, anesthetics, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin, may be carried by them.[17] Because they are formed from natural phospholipids, they are biocompatible and biodegradable, comparable to liposomes. They have a high entrapment efficiency, approaching 90% in the case of lipophilic drugs. They prevent the encapsulated medicine from being degraded by the body's metabolism. They serve as a storehouse, gradually releasing their contents. They may be utilized for both systemic and topical medication delivery. Easy to scale up since the technique is straightforward and does not need the use of pharmaceutically undesirable chemicals.[18]

ADVANTAGES OF TRANSFEROSOMES[19]

Transferosomes can deform and pass through narrow constriction without measurable loss.

- They have high entrapment efficiency, up to 90% in the case of lipophilic drugs.
- This great deformability allows intact vesicles to be penetrated more effectively.
- They can transport medications with low and large molecular weights, including analgesics, anesthetics, corticosteroids, sex hormones, anticancer medicines, insulin, gap junction protein, and albumin.
- Transferosomes have a structure that combines hydrophobic and hydrophilic moieties, allowing them to accept medicinal molecules with a broad range of solubility. They serve as a storehouse, gradually releasing their contents.
- Because they are formed from natural phospholipids, they are biocompatible and biodegradable, comparable to liposomes.
- They prevent the encapsulated medicine from being degraded by the body's metabolism.
- Easy to scale up since the technique is straightforward and does not need the use of pharmaceutically undesirable chemicals.

LIMITATIONS OF TRANSFEROSOMES[20]

- Because of their proclivity for oxidative destruction, transferosomes are chemically unstable.
- Another factor that works against the use of transferosomes as drug delivery vehicles is the purity of natural phospholipids.
- The cost of transferosome formulations is high.

PREPARATION OF TRANSFEROSOMES

For the production of transferosome, there are a number of patented and published methods. In general, phosphatidylcholine is mixed with sodium cholate or another appropriate surfactant in ethanol. Among the most popular approaches are:

Suspension homogenization process

Ethanolic soybean phosphatidylcholine is combined with an adequate quantity of edge activators, such as sodium cholate, in this approach. This produced suspension is combined with a Triethanolamine-HCl buffer solution to give a total lipid concentration, then sonicated, frozen, and thawed for 2 to 3-times before being brought to the required size, which is then quantified by photon correlation spectroscopy. Filtration using a 0.2 µm micro porosity filter is used to sterilize the water. The ultimate vesicle size is confirmed using a dynamic light scattering approach.[21]

Reverse phase evaporation method

Lipids dissolved in organic solvents are placed in a round bottom flask in this procedure. Under nitrogen purging, an aqueous medium containing edge activators is introduced. Based on its solubility characteristics, the medication may be introduced to a lipid or aqueous media. After that, the created system is sonicated until it becomes a homogenous dispersion, which should not separate for at least 30 minutes. Under decreased pressure, the organic solvent is then extracted. The system will next transform into a thick gel, followed by the creation of vesicles. Dialysis or centrifugation may be used to remove non-encapsulated material and residual solvents (Figure 4).[22]

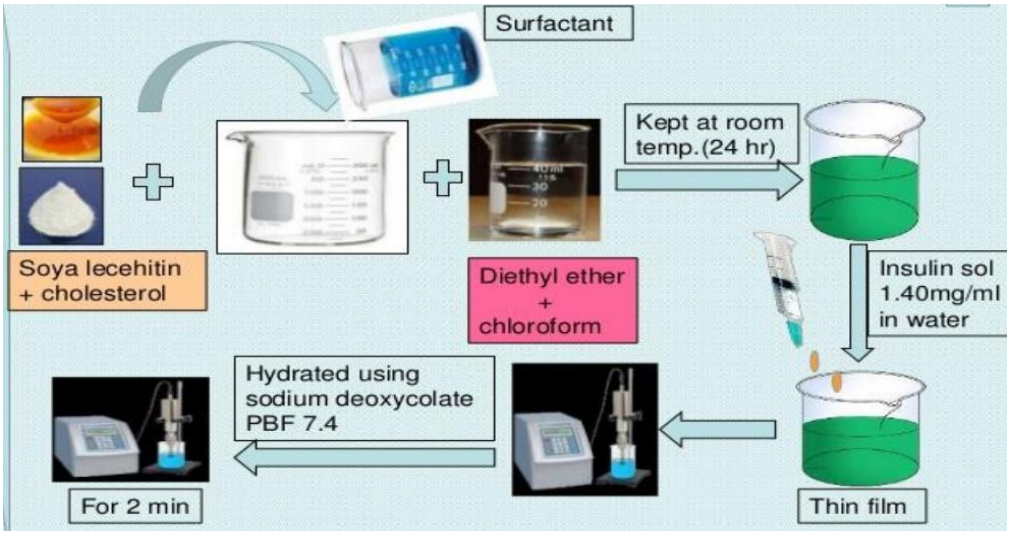

Figure 4: Reverse phase evaporation method.

Rotary film evaporation method

Bangham was the first to create the handshaking technique, commonly known as the rotating film evaporator technique. Phospholipids and surfactants are required in this process to arrange a thin layer. A mixture of crude solvents like chloroform and methanol in which a phospholipid and ethanol solution is structured. This approach is often employed in the study of multilamellar vesicles. The produced solution is transferred to a round-bottomed flask and rotated at a constant temperature and pressure (higher than the glass transition temperature of lipids). A layer of lipids and edge activators forms on the flask's walls. The twisted film is hydrated with an aqueous medium containing medication, which causes the lipids to expand and form bilayer vesicles. The superior vesicles may be sonicated or extruded to generate vesicles of the appropriate size.[23]

Modified handshaking process

The lipid film hydration technique is another name for this technology. Ethanol and chloroform are combined in a 1:1 ratio. Lipid and edge activators are dissolved in this pharmacological combination. The solvent is eliminated by evaporation. Handshaking is possible at temperatures above the liquid transition point (43°C). A thin lipid coating forms within the flask wall as a result of continual rotation. The preparation is left overnight to allow the solvent to completely evaporate. The film is hydrated with phosphate buffer for 15 minutes and gentle shaking is performed at the appropriate temperature (Figure 5).[24]

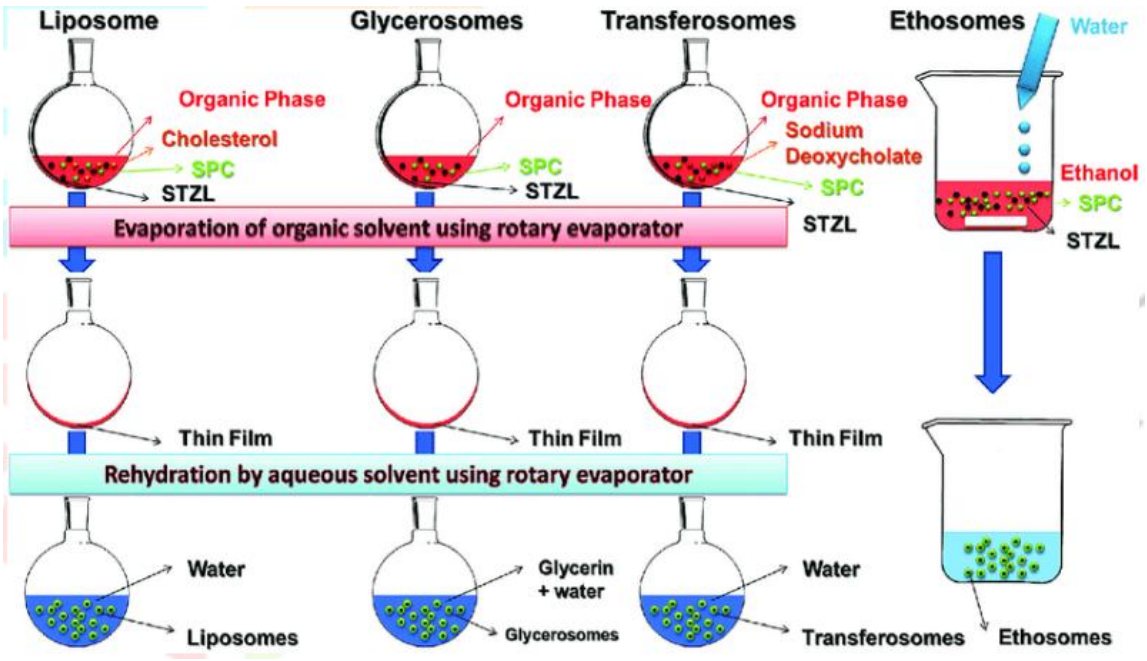

Figure 5: Rotary film evaporation Method/ Modified hand shaking method.

Thin film hydration technique

This approach is classified into three steps

1. A thin coating of vesicle phospholipids and surfactants is dissolved in an organic solvent (such as chloroform or methanol). Heating takes place above the lipid's transition temperature. The procedure is carried out in a rotary evaporator to liberate the mixture of organic solvent. Any residues of solvent are eliminated by vacuuming it overnight.
2. The created film is hydrated for one hour at 60 RPM using an appropriate buffer. The generated vesicles are allowed to expand for 2 hours at room temperature.
3. Prepare tiny vesicles by sonicating prepared vesicles in a bath sonicator for 30 minutes at 50°C or at room temperature. When using a probe sonicator, sonication is done for 30 minutes at 40°C. By manually extruding the sonicated vesicles 10-times through a polycarbonate membrane, a sandwich layer of 200 nm – 100 nm is obtained.[25]

Ethanol injection method

The aqueous solution containing the medication is heated by continual stirring at a steady temperature. Edge activators are injected dropwise into the aqueous solution, coupled with an ethanolic solution of phospholipids. As the aqueous medium comes into contact with the solution, the lipid molecules precipitate and form bilayered structures. When compared to other approaches, the technique is straightforward to scale up, simple, and highly reproducible, providing a number of advantages (Figure 6).[26]

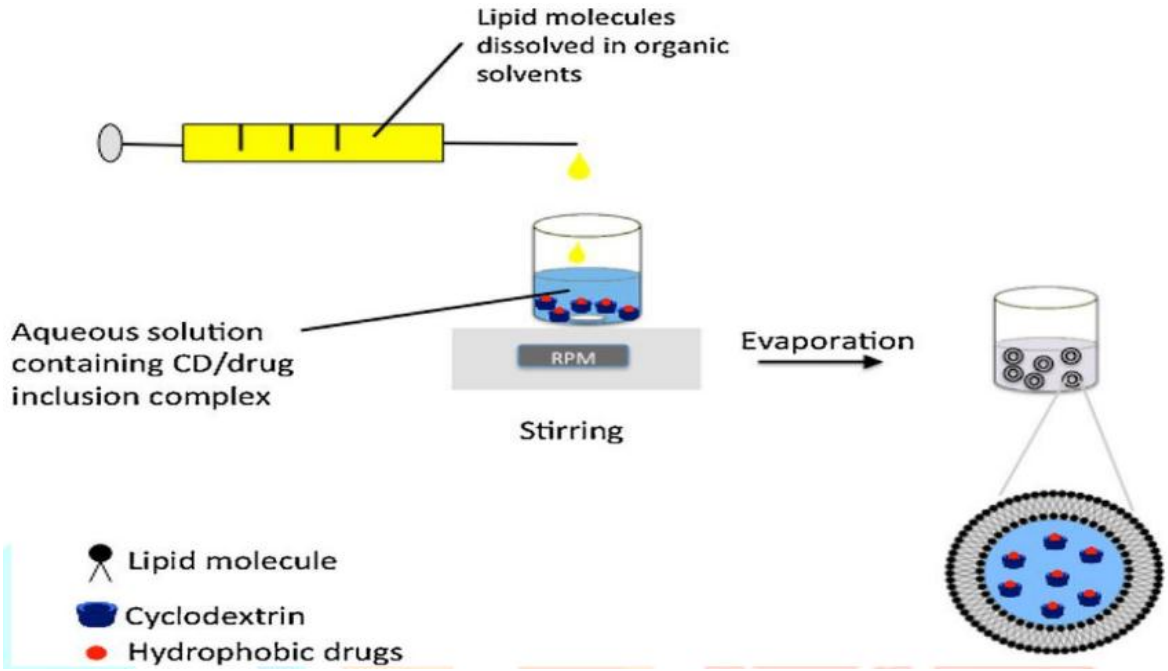

Figure 6: Ethanol Injection Method.

Freeze-Thaw method

This strategy comprises both low and high-temperature exposure. The multilamellar vesicles are frozen at very low temperatures and then heated to very high temperatures. After transferring the prepared suspension to a tube at 30°C for 30 seconds, it is immersed in a nitrogen bath. After freezing, they are subjected to high temperatures in a water bath. This operation is carried out eight-times to nine-times (Figure 7).[27]

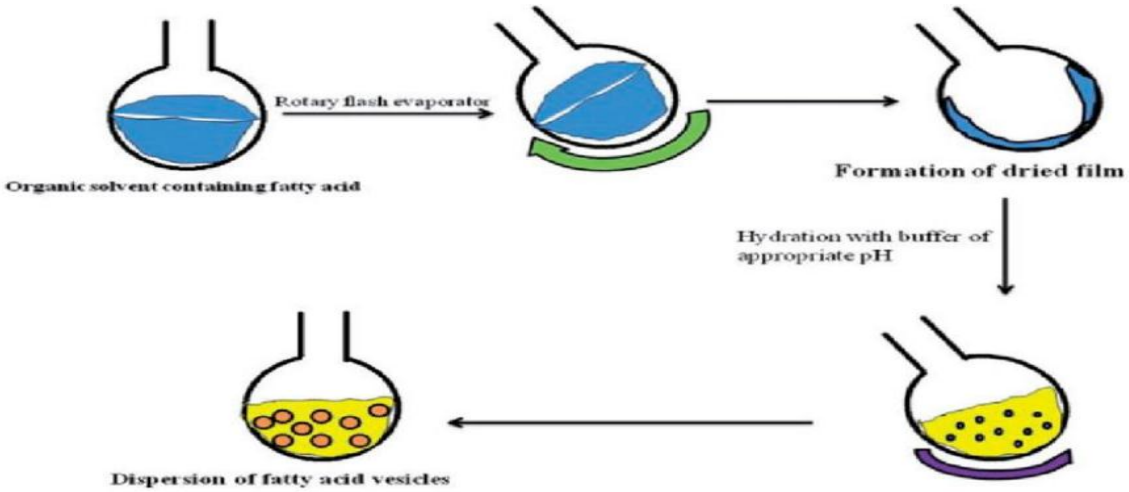

Figure 7: Freeze-Thaw method.

Vortexing/Sonication method

The mixed lipids (edge activators, phosphatidylcholine, medicinal drugs) are all combined in phosphate buffer. It is then vortexed to create a milky suspension. After sonication, the suspension passes through a process of extrusion via polycarbonate membranes (Figure 8). [28]

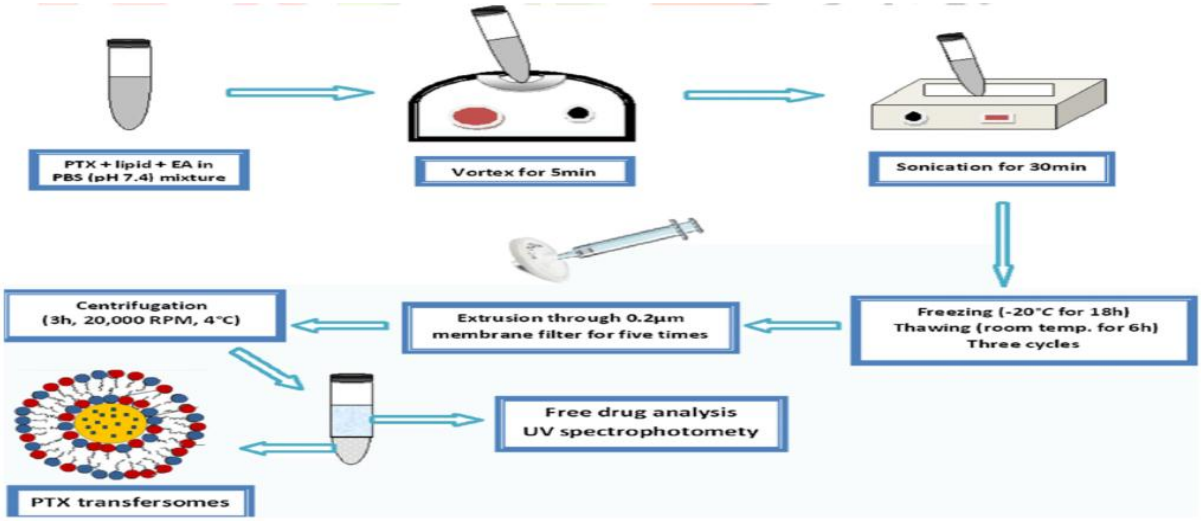

Figure 8: Vortexing/Sonication method.

OPTIMIZATION OF FORMULATION CONTAINING TRANSFEROSOMES

The preparation and qualities of the transferosomes may be affected by a number of process factors. As a result, the preparation technique was improved and confirmed. The process variables are determined by the manufacturing technique for the formulation.[29] The imperative process factors involved in the creation of transferosomes include:

1. The ratio of lecithin to surfactant
2. The impact of different solvents
3. The impact of different surfactants
4. Medium for hydration

The entrapment efficiency of the medication was chosen for optimization. The other variables were maintained constant through the development of a specific system.

MECHANISM OF ACTION OF TRANSFEROSOMES

The carrier aggregate is made up of a single amphipathic polymer, such as phosphatidylcholine, that self-assembles into a lipid bilayer in aqueous solvents and closes into a simple lipid vesicle. Lipid bilayer flexibility and permeability are enhanced when a bilayer softening component, such as a biocompatible surfactant or an amphiphile medication, is added. By matching the local concentration of each bilayer component to the local stress encountered by the bilayer, the resultant transferosome vesicle can readily and quickly modify its shape to the environment.[30] Transferosome is distinguished from other vesicles by its artificial membrane, which is softer, more flexible, and more changeable. The higher propensity to bind and hold water is a favorable consequence of high bilayer deformability in transferosomes. A highly deformable and hydrophilic vesicle will constantly try to prevent dehydration; this may include a transport mechanism that is similar to but not identical to forward osmosis.[31] To provide proper hydration, a transferosome vesicle placed to an open biological surface, such as non-occluded skin, penetrates its barrier and migrates into the water-rich deeper layers. Barrier penetration necessitates reversible bilayer deformation, but the vesicle integrity or barrier characteristics must not be jeopardized in order for the underlying hydration affinity and gradient to stay in place. The transferosome must discover and impose its own path into the organ since it is too big to disperse through the skin. [32] The carrier's capacity to broaden and overcome the hydrophilic pores in the epidermis or another barrier (e.g. the plant cuticle) is aided by the transferosome vesicles. The drug molecules may then disperse and attach to their target thanks to the progressive

release of the agent from the drug carrier. Unless the vesicle is actively taken up by the cell in a process termed endocytosis, drug transport to an intracellular action site may also include the carrier's lipid bilayer fusion with the cell membrane (Figure 9).[33]

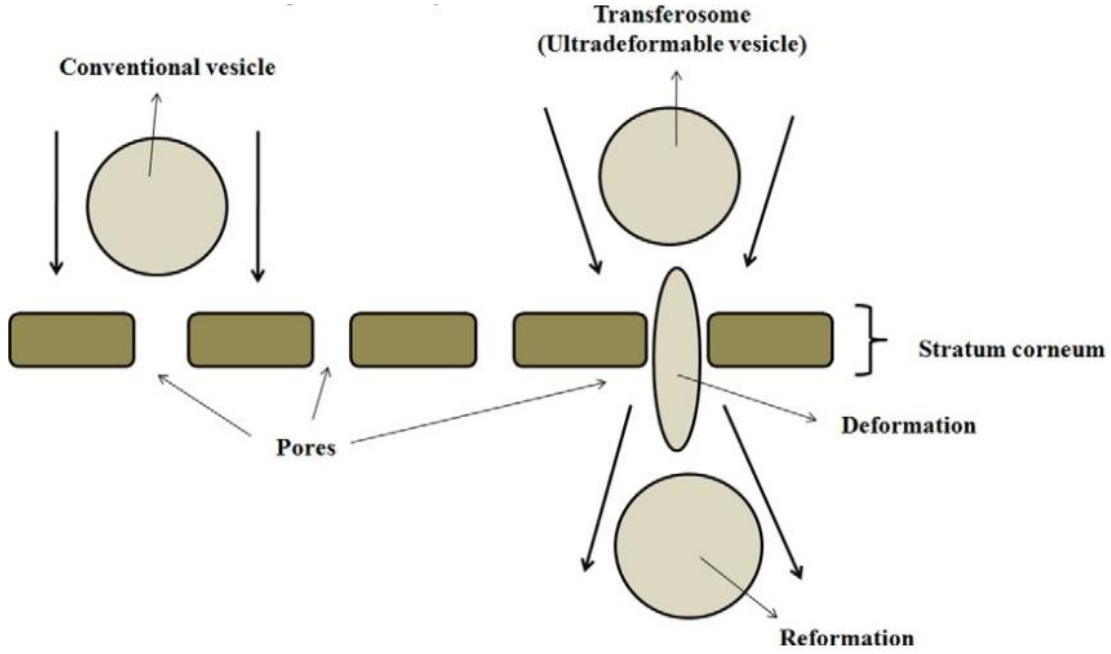

Figure 9: Interaction of transferosomes with skin tissue.

CHARACTERIZATION OF TRANSFEROSOMES[34-36]

Transferosomes are characterized in a similar way as liposomes, niosomes, and micelles. For transferosomes, the following characterization criteria must be examined.

1. Vesicle size Distribution and Zeta potential

Malvern Zetasizer's Dynamic Light Scattering device was used to evaluate vesicle size, size distribution, and zeta potential.

2. Vesicle morphology

Photon correlation spectroscopy or the dynamic light scattering (DLS) approach may be used to estimate vesicle diameter. Using photon correlation spectroscopy or dynamic light scattering (DLS) studies, samples were produced in distilled water, filtered through a 0.2 mm membrane filter, and diluted with filtered saline. TEM, phase contrast microscopy, and other techniques may be used to view transferosome vesicles. The size and shape of vesicles over time may be used to estimate vesicle stability. DLS measures mean size, whereas TEM looks for structural changes.

3. Number of vesicles per cubic mm

This is a crucial element for improving process composition and other factors. Transferosome formulations that have not been sonicated are diluted five times in a 0.9 % sodium chloride solution. For additional investigation, a hemocytometer and an optical microscope may be employed. The Transferosomes in 80 small squares are counted and calculated using the following formula:

Total number of Transferosomes per cubic mm = (Total number of Transferosomes counted × dilution factor × 4000) / Total number of squares counted

4. Entrapment efficiency

The percentage entrapment of the medication added is used to calculate entrapment efficiency. The entrapment efficiency was measured by using a mini-column centrifugation technique to separate the unentrapped medication. The vesicles were ruptured with 0.1 percent Triton X-100 or 50 % n-propanol after centrifugation. The entrapment efficiency is expressed as:

Entrapment efficiency = (Amount entrapped / Total amount added) × 100

5. Drug content

Depending on the analytical method of the pharmacopeia drug, the drug content can be determined using one of the instrumental analytical methods such as modified high-performance liquid chromatography method (HPLC) using a UV detector, column oven, auto sample, pump, and computerized analysis program.

6. Turbidity measurement

A nephelometer may be used to determine the turbidity of medication in an aqueous solution.

7. Degree of deformability or permeability measurement

The permeability research is one of the most essential and unique parameters for the characterization of transferosomes. The deformability test is carried out using pure water as a control. The preparation of transferosomes is filtered through a large number of holes of defined size. Dynamic light scattering (DLS) measurements are used to record particle size and size distributions after each pass.

8. Penetration ability

Fluorescence microscopy may be used to assess the capacity of Transferosomes to penetrate.

9. Occlusion effect

In the case of classic topical medicines, occlusion of the skin is thought to aid drug penetration. Elastic vesicles, on the other hand, suffer from the same problem. The fundamental driving factor for vesicle penetration through the skin, from its comparatively dry surface to its water-rich deeper layers, is the hydrotaxis of water. Occlusion has an effect on hydration forces because it stops water from evaporating from the skin.

10. Surface charge and charge density

Zetasizer may be used to determine the surface charge and charge density of Transferosomes.

11. *In vitro* drug release

The penetration rate is determined using *in vitro* drug release research. Before more costly *in vivo* investigations, the time required to achieve steady-state permeation and the permeation flux at a steady-state, as well as information from *in vitro* tests, are utilized to improve the formulation. Transferosomes suspension is incubated at 37 ± 1°C for assessing drug release, and samples are obtained at various periods, with the free drug separated by microcolumn centrifugation. The quantity of drug released is then determined indirectly using the original quantity of drug entrapped as a starting point.

12. *In vitro* skin permeation studies

This research employed a modified Franz diffusion cell with a receiver compartment capacity of 50 ml and an effective diffusion area of 2.50 cm^2. Using goat-skin in a phosphate buffer solution, *in vitro* drug research was conducted (pH 7.4). Fresh goat abdominal skin was obtained from the abattoir and utilized in the penetration tests. The skin was moistened in a regular saline solution after the hairs on the abdomen were removed. By rubbing the skin's adipose tissue layer with a cotton swab, the adipose tissue layer was eliminated. The skin was maintained in an isopropyl alcohol solution and maintained at 0-40°C. The treated skin was placed horizontally on the receptor compartment with the stratum corneum side facing upwards towards the donor compartment of the Franz diffusion cell to conduct the skin permeation investigation. The donor compartment's effective permeation area exposed to the receptor compartment was 2.50 cm^2, and the receptor compartment's capacity was 50 ml. The receptor compartment was filled with 50 ml of phosphate-buffered saline (pH 7.4) and swirled at 100 RPM with a magnetic bar. The formulation (equal to 10 mg of medication) was applied to the skin, and the diffusion cell's top was covered. To maintain sink conditions, 1 ml aliquots of the receptor medium were removed at regular intervals and replaced with an

equivalent amount of new phosphate buffers (pH 7.4). The release profile was calculated using correction factors for each aliquot. Any instrumental analytical method was used to examine the materials.

13. Physical stability

The initial proportion of medicine entrapped in the formulation was established, and sealed glass ampoules were used to preserve it. For at least three months, the ampoules were kept at 4 ± 2°C, 25 ± 2°C, and 37 ± 2°C. After 30 days, samples from each ampoule were tested to see whether there was any medication leakage. The % drug loss was estimated by retaining the initial drug entrapment at 100%.

APPLICATIONS OF TRANSFEROSOMES[37-38]

1. Delivery of insulin

Transferosomes have shown to be a viable method of administering big molecular weight medications to the skin in a non-invasive manner. Insulin is usually given by a subcutaneous injection, which is cumbersome. Insulin encapsulation in transferosomes (transfersulin) solves all of these issues. The earliest symptom of systemic hypoglare appears 90 to 180 minutes after Transfersulin injection on undamaged skin, depending on the carrier composition.

2. Delivery of corticosteroids

Corticosteroids have also been delivered via transferosomes. By adjusting the epicutaneously delivered medication dosage, transferosomes increase the site-specificity and overall drug safety of corticosteroid administration into the skin. Corticosteroids based on transferosomes are physiologically active at doses many times lower than those now used to treat skin disorders.

3. Delivery of Proteins and Peptides

Transferosomes have long been employed as a transport vehicle for proteins and peptides. Proteins and peptides are big biogenic molecules that are difficult to transfer into the body and are totally destroyed in the gastrointestinal system when taken orally. These are the reasons why these peptides and proteins must still be injected into the body. To ameliorate these circumstances, a variety of ways have been created. The bioavailability of transferosomes is comparable to the bioavailability of the identical protein solution injected

subcutaneously. After repeated epicutaneous injection of transferosomal preparations of this protein, a robust immune response was produced.

4. Delivery of interferons

Interferons, such as leukocytic generated interferon-α (INF-α), have been carried by transferosomes. INF-α is a naturally occurring protein with antiviral, antiproliferative, and immunomodulatory properties. Transferosomes offer the potential to provide regulated drug release and increase the stability of labile pharmaceuticals when used as drug delivery vehicles. Researchers investigated the formulation of transferosmes comprising interleukin-2 and interferon-α for possible transdermal use. They found that transferosome-trapped IL-2 and INF-α were delivered in adequate concentrations for immunotherapy.

5. Delivery of anticancer

Medications using transferosome technology, anti-cancer medications like methotrexate were attempted for transdermal administration. The outcomes were positive. This provides a novel therapy option, particularly for skin cancer.

6. Delivery of anesthetics

The use of anesthetics in the suspension of highly deformable vesicles, transferosomes, provides topical anesthesia in less than 10 minutes under the right circumstances. The maximum pain insensitivity is similar to that of a subcutaneous bolus injection (80 %), but the action of transferosomal anesthetics lasts longer.

7. Delivery of Non-Steroidal Anti-Inflammatory drugs (NSAIDs)

NSAIDs are linked to a variety of gastrointestinal adverse effects. Transdermal delivery of ultra-deformable vesicles may solve these issues. Diclofenac and Ketoprofen have both been the subject of research. In 2007, the Swiss regulatory authorities approved the commercialization of ketoprofen in a Transferosome formulation; the medication is planned to be commercialized under the brand name Diractin.

8. Delivery of herbal drugs

Transferosomes may enter the stratum corneum and provide nutrients locally, allowing the skin to continue its functions. In this regard, Capsaicin Transferosomes have been developed, which demonstrate superior topical absorption as compared to pure capsaicin.

9. Applications in cosmetics

Cosmetics demand is steadily increasing over the globe in order to enhance the attractiveness and prevent skin damage. Cosmeceutical goods improve one's appearance while simultaneously providing therapeutic advantages (Figure 10).

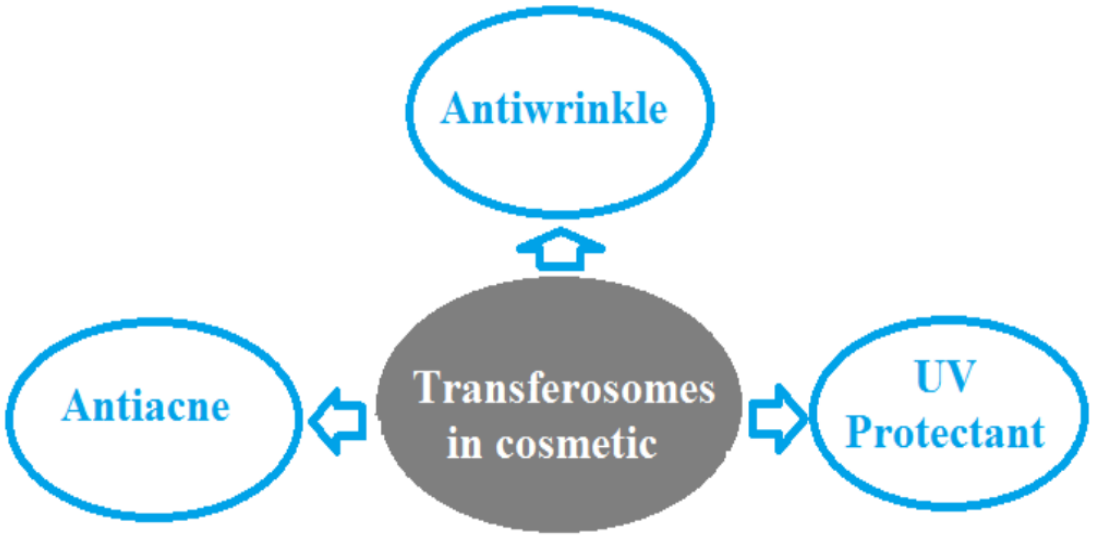

Figure 10: Transferosomes' applications in cosmetic technology.

CONCLUSION

Because of its unique and varied qualities, the transdermal route has long been the preferred method of medication delivery. However, the stratum corneum's impermeability is a serious challenge for transdermal distribution, since it presents a total barrier to drug penetration. As a result, the transferosomal system stresses the successful delivery of hydrophilic and hydrophobic medicines, as well as amphiphilic substances. Because of their reduced dosage frequency, greater effectiveness, greater loading capacity, and greater topical applications, as well as greater stability characteristics, transferosomes are a suitable and outstanding technique. Transferosomes have a promising future as a means of transporting active pharmaceuticals with site-specificity, as well as being used in a variety of aesthetic methods. There are still a few issues to work out in terms of oxidative degradation, purity, and retention property. As a result, prospective process improvements need unique considerations and technology developments. Furthermore, advances in the synergistic potential of components and active compounds must be researched globally in order to support the future possibilities of these gifted nanocarriers. It's also worth noting that extensive research based on convincing preclinical and clinical investigations is necessary to acquire the data needed to determine the safety of difficult pharmaceuticals prior to industrial scale-up. Improvements

in scientific views are still required for the creation of novel transferosomes, which will most likely concentrate on better treatment regimens employing more sophisticated, promising, and well-organized new techniques. It is also crucial to look into novel pharmaceutical excipients with extra properties in order to reduce the present downsides of transferosomes. In the future, industrial pharmaceutical businesses may look at new possibilities for major developmental properties of transferosomes that are correctly customized.

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CONFLICT OF INTEREST

The authors declare no Conflict of Interest regarding the publication of the article.

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