A Comprehensive review of a novel tool for drug delivery: Ethosomes

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Abstract- **Ethosomes enable the non-invasive transportation of drugs to the upper layer that is subcutaneous layers of the skin and into the bloodstream. Despite the complicated conceptual foundations of these ethosomal systems, they are simple to create and secure to utilise, significantly expanding their potential applications. To regulate drug distribution and subsequent skin tissue absorption, a number of transdermal therapy methods are there for topical administration to the skin layer. The vesicular approach, which has been used to overcome the obstacle of transdermal drug administration, will be discussed in this review. A number of studies on ethosomes in medicine are also covered.**

The ethosomes are formulated using a variety of techniques that is recently developed for synthesizing ethosomes that is mentioned in the review. Upon composition, ethosomes can be subjected to a range of characterization tests, including as stability, in vitro permeability, pH, particle size, and zeta potential. This part summarizes the most current ethosome modifications based on various pharmacological dose forms, including as patches, gels, and creams. A brief review of updated ethosome patents is also provided. To summarize, ethosome is an excellent delivery mechanism for drugs and cosmetics. The increased transportation of chemical agents through epidermal and cellular membranes via an ethosomal carrier poses a number of further research and development of enhanced medicines present difficulties and opportunities.

Keyword: **Ethosomes, Vesicular Carriers, skin permeation, transdermal drug delivery**

I. INTRODUCTION

Infusion of drug continuously in to the skin is considered as good because it best for liver's first pass metabolism and it keeps the drug in a stable form in the body.[1] Derivatives of liposomes, including Niosomes, and ethosomes etc are the principal lipid dosage forms used in transdermal distribution. Liposomes are primarily transported in hair follicles, whereas Transferosomes and Niosomes travel largely through keratinocyte pores. Ethosomes have demonstrated exceptional efficacy in percutaneous medication delivery when used as a lipid vehicle. In 1997, Touitou developed ethosomes, a distinctive form of UDV in. They are also referred to as elastic nanovesicles due to their exceptional deformability and substantial size (approximately 150–200 nm).[2]

Water, phospholipids, and ethanol are employed to create ethosomal systems. Phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and hydrogenated phosphatidylcholine are among the numerous categories of phospholipids.[3]

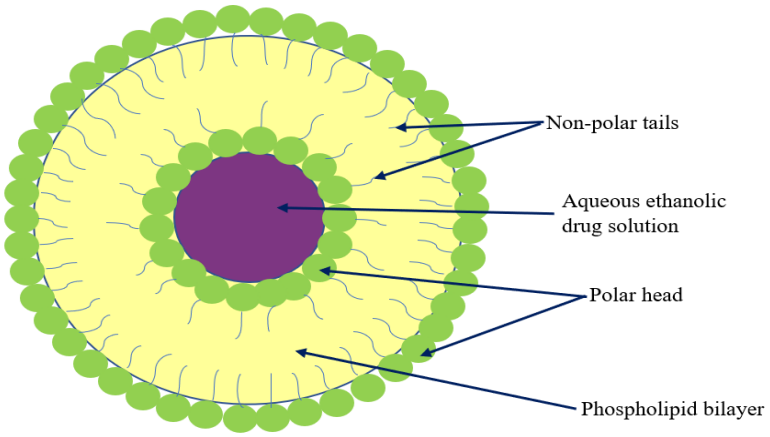

FIG.1 -Structure of ethosome

Types Of Ethosomal Systems

Classical Ethosomes

These are traditionally composed of phospholipids, purified water, and a high concentration of ethanol, reaching up to 44% w/w.

They are an adaptation of traditional liposomes. Traditional ethosomes are preferred over liposomes for TDD due to their smaller size, negative ζ-potential, and improved entrapment efficiency. In addition, when contrasted with traditional liposomes, classical ethosomes shown improved penetration into the skin and durability profiles.[4,5]

Binary Ethosome

Binary ethosomes were produced by incorporating an additional type of alcohol into conventional ethosomes.

Propylene glycol (PG) and isopropyl alcohol are the most commonly used alcohols in binary ethosomes (IPA).[6,7,8]

Transethosomes

This ethosomal framework comprises the fundamental elements of conventional ethosomes, along with an additional element that may serve as an extra activation (surfactant) or penetration boost. In order to generate transethosomes, these innovative vesicles combined with the benefits element of liposomes (transfersomes) and ethosomes in one composition.[9,10]

Components of Ethosomes

Mixture of phospholips, hydroalcoholic ethosomes are vesicular carriers that has a high concentration of ethanol content it. Ethosomes typically consist of water, ethanol or isopropyl alcohol, propylene glycol (or alternative glycols), and phospholipids. A mixture like this permits the skin to absorb a large amount of active chemicals. To control medication distribution, the alcohol-to-water or alcohol-to-polyol ratios can be adjusted. Phospholipon 90 (PL-90), a phospholipid derived from soybeans, is one of the most popular. It is often utilized at concentrations come in range from 0.5 to 10% w/w. Another alternative is to add cholesterol to the mixture in levels ranging from 0.1 to 1%. Isopropyl alcohol and ethanol are two forms of alcohol that are beneficial Propylene glycol and transcutol are both of the most frequently utilized glycols. Additionally, PEG-alkyl ethers, which are non-ionic surfactants, can be utilised in conjunction with phospholipids in the formulations that are being discussed. There is also the possibility of including cationic lipids, such as cetrimide, dodecylamine, cocoamide, and POE alkyl amines. This is a realistic option. In the final product, the proportion of alcohol might range anywhere from twenty percent to fifty percent. The non-polar phase is made up of a mixture of alcohol and glycol, with concentrations ranging from 22 percent to 70 percent.

Ethanol- As Penetration Enhancer

Chemicals enhancements for penetration are substances that reversibly diminish the stratum corneum's barrier resistance. Ethanol is one of among the most common permeability enhancers. Several theories have been proposed to explain how ethanol enhances penetration. The drug's solubility can be improved by including ethanol as a solvent into the formulation. This is particularly crucial because less soluble permeants are more likely to be depleted in the contributing vehicle. Ethanol isa little volatile solvent that evaporates rapidly at the temperature of the body. This is intended to establish a pathway through the skin, allowing ethosomes to mix with cells found in the skin's deepest layers.[11,12]

II. METHOD OF PREPARATION

Few are appropriate for the preparation and production of ethosomes. These are straightforward and easy, requiring no complex apparatus or processes.

Methods are:

1. Hot method

When phospholipid is dissolved in water at a temperature of 400 degrees Celsius, the resulting solution is a colloidal one. Using a separate tank, ethanol and propylene glycol are mixed together and then heated to a temperature of 400 degrees Celsius. After the temperature of both combinations has reached 400 degrees Celsius, the organic component is next introduced to the phase that is composed of water. It is possible for the medicine to degrade in either water or ethanol, depending on whether it is hydrophilic or hydrophobic. Sonication of the probe or extrusion operations are two methods that can reduce the size of the vesicles in the ethosomal formulation to the desired degree.[13,14]

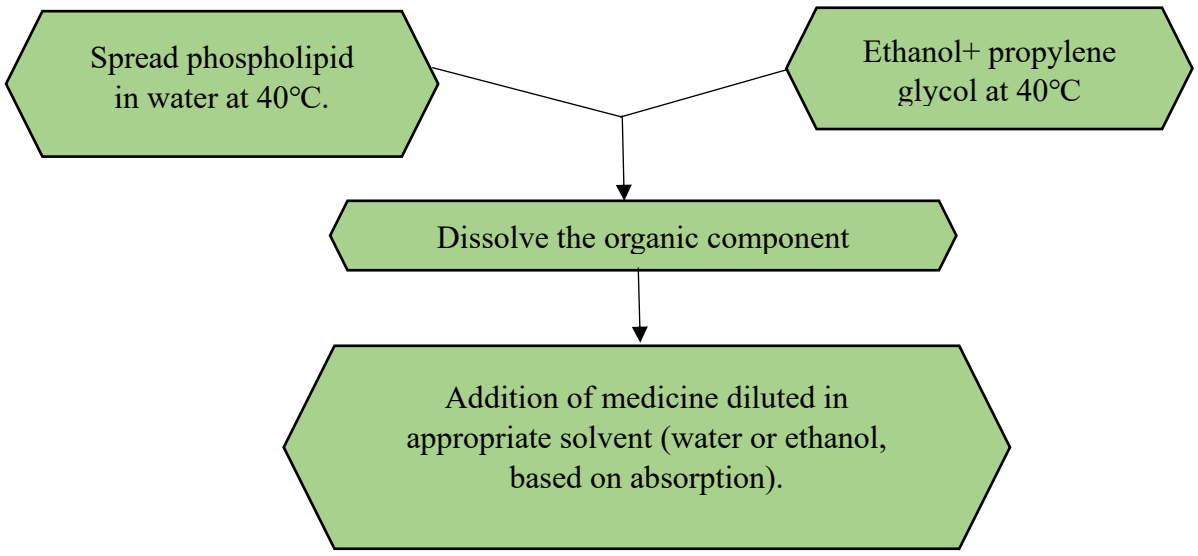

FIG.2- Hot Method

2. Cold method

"The procedure is to dissolve phospholipids, medicines mix other lipid components in ethanol in a closed vessel at ambient temperature while using a mixer to stir continuously. Stir with propylene glycol or another polyol until well combined. This mixture is cooked to 300 degrees Celsius in a water bath. Following adding 300°C water from another pot, the mixture undergoes stirring for five minutes in an enclosed vessel. Penetrating a sonic or extrusion can be used to reduce the size of vesicles of an ethosomal composition to any desirable level. Finally, the mixture is stored in the fridge".[15]

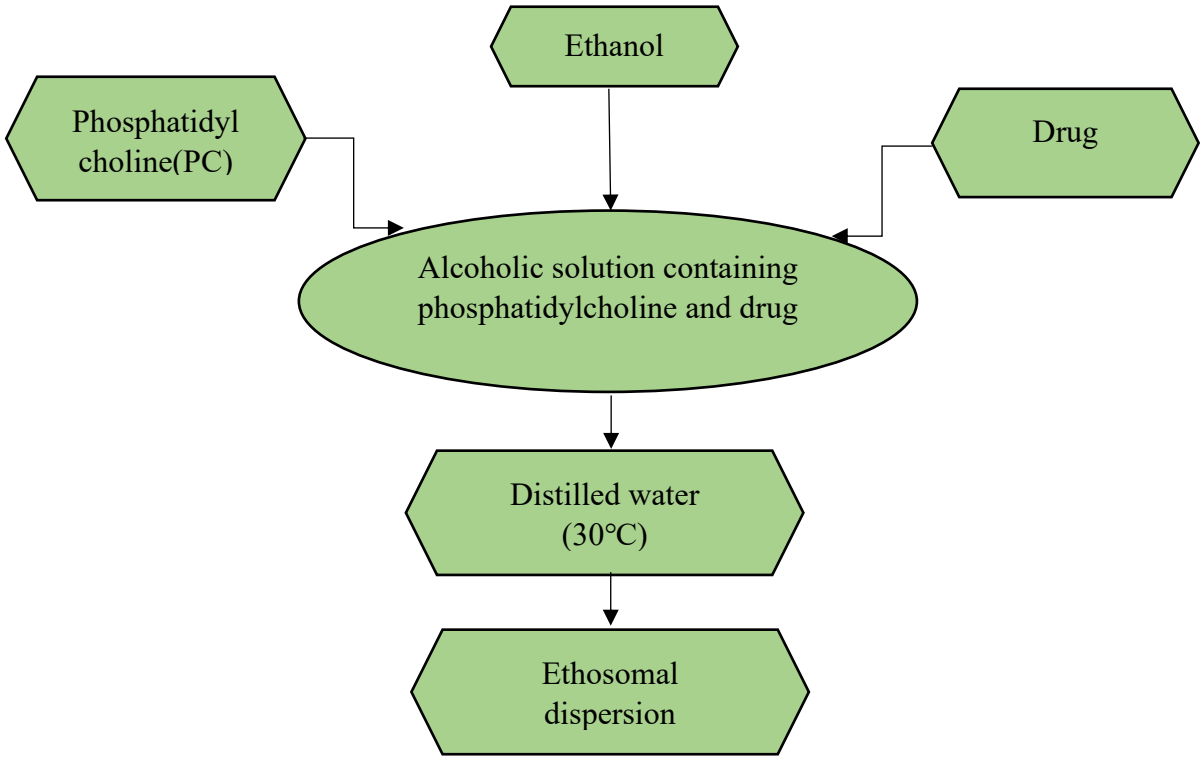

FIG.3- Cold Method[16]

3.Vortex/sonication method edge

This approach makes the ethosome production process simple to understand and productive. To make sure that the components are evenly distributed, phospholipids and edge activators are combined in a phosphate buffer, vigorously stirred, and then vortexed. Next, a sonicator or vortex is used to sonicate the suspension in order to produce vesicles. The sonication duration as well as intensity can be varied to alter the vesicles' size. The suspension is

then extruded through a variety of membrane sizes to produce the required vesicles. The method works effectively for making both hydrophilic and hydrophobic medications because it is scalable and flexible. Moreover, it can be cheaply and rapidly scaled up for large-scale production.

4.Rotary film evaporation

"One effective method for creating ethosomes for drug delivery applications is rotary film evaporation. Phospholipids are dispersed throughout an organic solution in a flask with a spherical bottom. A rotary evaporator is used to evaporate the organic solvent, leaving the inside walls of the flask with a thin lipid coating. Lipid bilayer vesicles carrying the target chemical are produced by hydrating the lipid film with an aqueous solution containing the medication. The size of ethosomes can be adjusted via sonication and extrusion."[17]

5. Traditional mechanical-dispersion technique

Making a lipid solution with phospholipids and ethanol is the first step in the procedure. The drug or its active component is then introduced to the lipids mixture and heated to produce a transparent solution. A high shear is used to physically disperse the cooled clear solution.

Small vesicles with a diameter of 100–300 nm are created by a homogenizer or ultrasonicator. The procedure entails the division of lipid bilayers with the application of intense shear stress, facilitating the development of ethosomes. The ethosome suspension undergoes filtration at the conclusion. The dimensions and morphology of ethosomes are ascertained by techniques such as (DLS) and (TEM) over a membrane to exclude any sizable particles or clumps.

6. Transmembrane pH-gradient method

First, nonmedicated binary ethosomes are prepared, and then active drug loading is carried out. An alcoholic solution made of ethanol and propylene glycol will dissolve the phospholipid (phosphatidylcholine, for instance). Add the citrate buffer solution gradually while stirring constantly at 30 ± 1°C and 700 rpm. The binary ethosomes are prepared when the system has been allowed to cool to ambient temperature. For efficient dispersion and dissolution, the medication is added to the ethosomes and continuously shaken at 700 rpm. Use a 0.5 M NaOH solution to change the outer pH in order to create a pH gradient between the inner (acidic) and outer (alkaline) phases of the ethosomal system.

Drug Permeation In Skin Through Transdermal Drug Delivery System

Skin and Drug Penetration

An understanding of the characteristics of human skin, as well as the attributes that influence barrier function and the permeation of medications into the body via the skin, is necessary to comprehend transdermal drug delivery methods. The skin is composed of numerous histologic layers, which are typically categorised into three primary tissue layers: the epidermis, dermis, and hypodermis. The epidermis is composed of active epithelial basal cells and has a thickness of approximately 150 micrometres. It is the skin's uppermost layer, and differentiation causes cells in the basal layer to migrate to the skin's surface.[18] This process produces a thin, layered, and very durable layer on the skin's surface. The remaining layers of the epidermis are located beneath these other layers form the viable epidermis. The stratum corneum, also referred to as the horny layer, is the obstruction that prevents the free flow of chemical substances compounds inward or outward.[19]

Absorption Through the Skin

The passive diffusion of substances through the skin is referred to as percutaneous absorption. Penetration can occur through shunts, including those supplied by widely dispersed hair follicles and eccrine glands, or through the epidermis itself.

Transepidermal Intake

Diffusion over the skin is mostly caused by the trans-epidermal pathway. The stratum corneum provides the majority of the resistance encountered along this channel. Permeation through the trans-epidermal pathway begins with partitioning into the stratum corneum. Diffusion then occurs throughout this tissue.

Absorption via Transfollicular (Shunt Pathway)

Only additional penetration pathways are offered by the skin's structures. Since sebaceous and eccrine glands are found throughout the body, they are the only structures that may be referred to as shunts Eccrine glands possess minute orifices that constitute

only a minute fraction of the body's surface area, despite their extensive distribution. Furthermore, they are either excessively active or evacuated, which prevents molecules from migrating inward despite the gland's discharge.
Due to these factors, they are not regarded as a dependable method of epidermis absorption.
The theorised process of penetration through this pathway entails partitioning into sebum and subsequently diffusing through the sebum to the epidermis's recesses. The dermal vascular system, which serves the hair follicle, is the most likely entry point into the system.

Clearance By Local Circulation
When medications and chemicals reach the systemic circulation, the papillary plexus, which is located in the upper dermis, is the first probable spot where they can do so. Percutaneous absorption is generally assumed to be complete at this point. However, certain molecules avoid the circulatory system and reach deep into the dermis.[20]

Mechanism Of Penetration
The mechanism by which ethosomes penetrate and pass through the skin is not well known. Ethanol has been postulated to have two parallel modes of action: it fluidizes ethosomal lipids as well as stratum corneum lipids.
(Figure 2) Using ethanol to create ethosomes enhances the ability to deform of the resultant vesicles. In addition, the high level of alcohol is likely to harm some stratum corneum lipids. The intercellular and intracellular permeability of ethosomes is improved by the use of these treatments. Before releasing the medicine into deeper layers of the skin, the ultra-deformable vesicles have the ability to build paths through the disordered stratum corneum.[21,22]

In contrast to liposomes, ethosomes have a number of advantages that are among the most noteworthy that the medication is able to penetrate more easily. There is a lack of clarity regarding the method by which ethosomes absorb drugs. As a rule, the process of drug absorption takes place in two stages.[23]
1.Ethanol effect
2.Ethosomes effect

1.Ethanol effect:
Dermatological absorption is improved by ethanol. It is generally thought that the mechanism is responsible for the majority of the penetration-enhancing impact. Ethanol enhances the fluidity of the lipids that constitute the cell membrane by infiltrating intercellular lipids, while concurrently decreasing the density of the lipid bilayer.

2.Ethosomes effect:
The ethosomes' ethanol-induced increase in the fluidity of the cell membrane molecules results in an increase in the skin's permeability, which in turn impacts the skin's capacity to absorb and release substances. As a result, the ethosomes are capable of easily entering the deeper layers of the skin, where they collaborate with the skin's lipids to facilitate the release of the drugs into the deeper layers of the skin, thereby accomplishing the desired effect.

Suggested Method of Skin Penetration of Ethosomes
The entry of the ethosomes into the skin process was schematically depicted in the stratum corneum. Lipid multilayers in the stratum corneum are densely packed and conformationally organized under physiological conditions. Ethanol, a component of ethosomal preparations, increases the fluidity of SC lipids by reacting with lipid molecules in polar headgroup areas. It is anticipated that the high alcohol content will partially extract SC lipids. These techniques improve ethosomes' permeability both inside and between cells. Ethanol also makes the ethosomal membrane more pliable, which raises the permeability of the skin.

“Before delivering the medication into deeper skin layers, the interdigitated, elastic ethosome vesicles can construct passageways through the disordered SC. Ethosomes and skin lipids may then combine to cause drug transdermal absorption. It is anticipated that this will result in drug releases at different locations along the penetration path”.[24]

Advantages
1. The transfer of substantial molecules (peptides and protein molecules) is plausible.
The formulation comprises innocuous basic materials.
3. Enhanced transdermal medicine administration through improved skin medicament penetration.
4. Ethosomal drug delivery methods possess diverse applications in pharmaceuticals, veterinary medicine, and cosmetics.
5. A higher level of patient adherence is achieved as a result of the fact that the ethosomal drug is provided

in a semisolid formulation (gel or cream), which helps patients adhere consistently.
6. A straightforward approach for drug distribution, as contrast to iontophoresis, phonophoresis, and other complex methods.
7.In addition to being non-invasive and passive, the Ethosomal system is also readily available for quick manufacture.[25]

Limitations of Ethosomal Drug Delivery
1. In terms of cost, it is not feasible.
2. Low rate of production.
3. Itching of the skin or dermatitis are induced by excipients and enhancers in medicine administration systems.
4. If the outermost layer locking is insufficient, the ethosomes may aggregate and break apart when transported into water.
5. During the process of transitioning from organically based to aqueous media, material is lost.[26]

Ethosomes Incorporated in Suitable Dosage Form

Since its first restriction, the vast majority of published research has focused on ethosomal systems. Considering the high alcohol content of ethosomal suspension, there are advantages to using it in conjunction with a suitable vehicle for transdermal or cutaneous distribution. These advantages include increasing patient compliance, extending the amount of time that the medication is in touch with the skin, reducing the amount of ethanol that evaporates, enhancing the therapeutic efficacy of the drug, improving the stability and shelf life of the ultimate form of administration, and boosting the drug's therapeutic efficacy.[27] Ethosomal systems have been employed to develop innovative drug formulations in a number of delivery systems, including gels, transdermal patches, and creams.

Ethosomes in Gel Form
Ethosomal gels differ in their pH, viscosity, spreadability, and extrudability. Carbopol and hydroxypropyl methylcellulose are the two most often utilized gel-forming agents for integrating ethosomal systems throughout all of their associated categories. Due to the fact that these polymers contain the necessary viscosity and bioadhesion qualities, they are suitable for use in ethosomal systems. Researchers compared the transdermal penetration and release mechanisms of medications derived from ethosomal gels to those of conventional gels and creams that are available for purchase in the market. This study aims to demonstrate that the ethosomes nanocarrier system possesses enhanced clinical potential and offers a favourable design for ethosomal gels, facilitating the transdermal administration of complex molecular protein medications. that can be employed with various transdermal delivery drugs, including those used in Chinese medicine, vaccines, and interleukins. This is one of the goals of this research.[28,29]

Ethosomes in patch form
Although ethosomal patches must be made with moulds, their production and evaluation are more challenging than those of ethosomal gels. The transdermal distribution properties of non-ethosomal testosterone patches and Testoderm’s ethosomal patches have been investigated both in vitro and in vivo.[30] The two patches had the same size and pharmacologic content. The ethosomal patch deposited seven times the amount of medication on the skin than the testodermal patch. In terms of predicted permeation, since ethosomal patches enable the application of ethosomes in occlusive settings, they offer a number of benefits over ethosomal gels and creams.

Ethosomes in Cream Form
Prior research has shown that if the drug or substance delivered by the ethosomal systems is paired with suitable administration techniques like gels, patches, and lotions, penetration through the skin improves.[31] While creams may be favoured for cosmetic formulations, ethosomal systems are optimally designed for the suggested carriers (gels). The production and examination of ethosomes with naringin have facilitated the investigation of naringin's antioxidant potential to neutralise free radicals. The ethosomes were then utilised in sunscreen formulations including titanium dioxide (TiO2) and zinc oxide (ZnO) to achieve requisite skin penetration and longevity.[32]

Application
Therapy for Microbial and Viral Skin Infection
Ethosomal systems are very much useful in topical infection because its capacity to penetrate the drug in the upper layer of the skin effectively.

Anti-Inflammatory Ethosomal Systems
Paolino et al. explored ammonium glycyrrhizinate (AG) ethosome on human subjects that had

chemically induced erythema from methyl-nicotinate for the treatment of inflammatory skin conditions. A reflectance visible spectrophotometer was utilized to evaluate the erythema index and compare the anti-inflammatory efficacy of the ethosomal AG system to aqueous or hydroethanolic pharmaceutical solutions after skin erythema was either already treated or treated.

According to the findings, AG ethosomes reduced the degree and duration of erythema much more than the other formulations. Within three hours following topical therapy, areas treated with AG ethosomes showed no erythema; however, sites treated with the drug's aqueous or hydroethanolic solutions showed chemically generated erythema. It's worth noting that no anti-inflammatory impact was discovered when empty ethosomes were tested for any possible consequences. The ethosomal AG system already treated the skin for 1, 3, and 5 hours, and the erythema index decreased. This suggests that the system was effective at reducing the appearance of erythema. The system's pre-treatment for five hours generated the most significant outcome.[33]

Menopausal Syndrome Ethosomal Systems

The success rate of ethosomal compositions in treating menopausal symptoms in women and a lack of androgen associated with menopause in men has been assessed. "To address men's androgen deficiency, Testosome, a testosterone ethosomal patch technology, was created. In vivo studies comparing testosterone levels in rabbits following any number of doses (at least once daily for five days) of Testoderm patch (Alza) or Testosome were carried out."

The results of applying a single patch showed that there were not any substantial variations between the groups that were being tested to observe. However, after applying the patches to the skin of the rabbit pinna on a daily basis for a period of five days, the AUC and Cmax values for Testosome were found to be 2.1 and 2.3 times greater than those for Testoderm 22, respectively.[34]

Treatment of Erectile Dysfunction

PGE1 ethosomal system was employed in the pilot clinical study to see whether the ethosomal system could be helpful in treating erectile dysfunction. Additionally, 16 guys have had this treatment of the PGE1 ethosomal system to determine whether or not it could result in a favorable outcome. Additionally, it was shown that 12 out of 15 males who were studied saw an increase in penile stiffness and peak systolic velocity following a single usage of the ethosomal system.

Additionally, it was seen that there were no adverse effects, not even erythema, and that this could be a viable therapy strategy for the ethosomal system.

Pain relieving And Antipyretic Ethosomal Systems

Transdermal ethosomal ibuprofen has been shown to have antipyretic and pain-relieving pharmacological effects in two animal models: tail flick nociception mice and rats with fever generated by Brewer's yeast. When ibuprofen gel was applied topically to the skin of fevered rats, their body temperature gradually decreased and returned to normal in three hours. For at least 12 hours, the human body temperature stayed low (370 ± 02 C). On the other hand, the rat's body temperature dropped to baseline after an hour of oral therapy, although it only stayed low for seven hours before rising to 380 ± 04 C.

"The pain-relieving benefits of oral therapy and ethosomal ibuprofen gel were compared in mice using the tail flick test. The ethosomal ibuprofen approach demonstrated a statistically significant increase in impact between 120 and 360 minutes after treatment. For at least six hours, the effect persisted. The information acquired for this investigation indicates that humans can test the ethosomal ibuprofen gel's analgesic and antipyretic properties."[35]

Cosmetic Usage of Ethosomes.

The incorporation of ethosomes into cosmeceuticals not only has the advantage of enhancing the durability of cosmetic substances while simultaneously reducing the skin irritation caused by irritating cosmetic chemicals, but it also has the potential to enhance transdermal penetration, particularly in forms that are flexible.[36] Yet, the substance and shape of the vesicles are among the most crucial factors to think about when reaping the benefits of elastic vesicles for cosmeceutical applications. [37] When it comes to the delivery of medications, ethosomes have a wide range of potential applications. In most cases, ethosomes are used as a replacement for liposomes. The transdermal method of administering medication is frequently chosen as the preferred method. Through the use of ethosomes, it is possible to transdermally administer

drugs that are both hydrophilic and impermeable through the skin. The ethosomal carrier has been utilized in the administration of a variety of drugs.[38]

Table 1: Ethosomes as a drug delivery system

Sr. No.	Drug	Ethosomal Delivery's Objective	Uses
1.	Minoxidil	• Pilocebaceous focusing on • The amount of skin buildup has greatly risen.	Treatment of baldness
2	Testosterone	• Elevated metabolism of the first pass • Poor oral bioavailability • Numerous adverse effects that depend on dosage	Steroidal hormone
3	Zidovudine and lamivudine	• Good uptake by cells	Anti-HIV
4	Bacitracin	• Good uptake by cells	Antibacterial
5	Erythromycin	• Good cellular uptake	Antimicrobial
6	DNA	• Transduction into skin cells	Management of Genetic Conditions

Reliability of Ethosomal Systems

The components of ethersomes are generally safe (GRAS). Numerous studies have been conducted regarding whether or not ethosomal systems that are administered topically to the skin are safe, both in vitro and in vivo. Ethosomal systems are safe for skin cells, according to in vitro studies on cell cultures.
Histological reports of the skin at the exact location that was treated following both single as well as chronic usage of ethosomal systems that included multiple molecules (e.g., BH, ibuprofen, testosterone, CBD, etc.) exhibited no alterations in the general structureor thickness of the horny layer, as well as no infiltration of inflammatory cells into the skin.[39]

Health and safety Tests with Ethosomes
1. Human investigations reveal that there are no indications of erythema after 12-24 and 48-hour treatments.
2. Additionally, there has been no reported adverse effects to marketed ethosomal preparations.

Patented

Professor Elka Touitou led a team of students from the Hebrew University School of Pharmacy Department of Pharmaceutics to create the insignia. The ethosome delivery method has been successfully implemented in an array of products that have been successfully introduced to the market by Novel Therapeutic Technologies Inc. (NTT), which is affiliated with Hebrew University.[40,41]

A. Nanominox© Minoxidil-based hair tonics enhance hair growth. Marketed by Sinere.
B. Noicellex TM: In Japan, ethosome's anti-cellulite composition is available for purchase.
C. Lipoduction TM: Mostly made up of pure grape seed extracts (antioxidants), this anti-cellulite product is sold in the US.
D. Physonics: It is London's Skin Genuity anti-cellulite gel.

Approaches for Characterizing Ethosomes
In general, ethosomes can be recognized by a range of methods, including vesicle shape, size distribution, zeta potential, dynamic light scattering, confocal laser scanning microscopy, and in vitro drug release investigations. This page describes the factors and description processes used for ethosomes.[42,43,44]

Table 2: EVALUATION TESTS

	EVALUATION OF ETHOSOME		
Sr. No.	PARAMETERS	ESSENTIAL	METHOD
1	Size and shape	Assess the penetration of the skin	SEM, TEM, DLS

2	Drug content	Helpful for calculating vesicle preparation quantity.	UV, HOLC
3	Stability studies	To determine vesicle development's self-life.	SEM, TEM, HPLC
4	Zeta potential	Consistency of vesicles	Zeta meter
5	Entrappement efficiency	Suitability of method	Ultracentrifugation
6	Skin permeation	Establishes the pace of drug transportation through the skin.	CLSM
7	In-vitro dissolution	"Compute the medication release rate from the vesicle."[45]	"Farzan diffusion cell"[46]

III. CONCLUSION

Ethosomes are a non-invasive carrier for administering distinctive pharmaceuticals that have different physicochemical properties to the skin. They are ideal for both local as well as systemic uses and exhibit controlled/sustained drug release, good biocompatibility, low toxicity, and other benefits in the pharmaceutical industry. Research have shown that ethosomes can improve transdermal medication delivery for different drugs.

To improve skin permeability and medicinal effectiveness, ethosomal systems should be included into gels, patches, or creams. To improve business applications and boost the ethosomal system's stability, more research is necessary.

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