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Ethosomal Systems as A Novel Non-Invasive Vesicular Platform Drug Delivery

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ABSTRACT

Objective: Examine how transdermal drug delivery systems can yield advantages over conventional methods, especially in terms of maximizing efficacy while reducing toxicity and by-passing hepatic metabolism. The study also aims to review ethosomal systems as a novel nano carrier for enhanced transdermal drug delivery.

Methods: A comprehensive review of transdermal drug delivery systems with an accent on ethosomes. Three types of ethosomal systems were studied based on their composition, which are transethosomes, binary ethosomes, and classical ethosomes. These methods were explored to determine how the differences in preparation techniques and formulation methods influenced system properties including vesicle size, zeta potential, drug entrapment efficiency, skin penetration and stability.

Results: Ethosomes are emerging as potent transdermal drug carriers. They can encompass drugs with a broad diversity of physicochemical properties, and due to their high ethanol levels, ethanol has been used to increase the penetration of the drug molecules by disrupting the lipid structure of the stratum corneum. (Due to the deeper skin layers may include the subcutaneous layer but the target for transdermal drug delivery that the drug systemically absorbed before reaching to this layer). The variations in composition and preparation techniques impacted key parameters such as particle size, entrapment efficiency, and stability. Transethosomes and binary ethosomes exhibited better flexibility and permeation than conventional ethosomes.

Conclusions: Ethosomal systems have better drug penetration, lower toxicity, and higher therapeutic efficacy. This makes them a promising new way to give drugs through the skin. The performance of formulation ingredients and preparation methods has a big effect on how well they work. More research and improvements to these systems could make them more useful in medicine and pharmacology.

Keywords: Ethosomes, Hot method, Transdermal delivery, Skin permeation.

INTRODUCTION

Continuous intravenous infusion is considered a more effective drug delivery method because it avoids hepatic first pass metabolism and allows for precise control over drug concentrations in the bloodstream. Intravenous administration has many drawbacks, such as the need for hospitalization and ongoing medical care during therapy, even though it has many benefits, such as the fact that it can be done again without risk. These factors have led researchers to explore alternative drug delivery methods, such as transdermal drug delivery ^(1,2). It is now clearer that the skin can be used as a pathway for continuous transdermal medication infusion into the systemic circulation ^(3,4). Antihypertensive, anti-anginal, anti-histamine, anti-inflammatory, analgesic, anti-arthritis steroidal, anti-cancer, and contraceptive drugs are among the several transdermal therapeutic systems that have been created to allow continuous drug infusion via intact skin ⁽⁵⁾. These systems are straightforward to administer and penetrate into the skin tissue because they are made for topical application on the skin's surface ^(6,7).

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Skin

It serves as the initial physical barrier separating us from the outside world and is the biggest organ in our body. It weighs about 4.5–5 kg, or about 12–15% of the average adult's total body weight and covers the entire exterior surface. It can measure up to 2 m².

As illustrated in Figure 1, it is composed of three layers: the outermost layer is the epidermis, followed by the dermis, and the structure beneath the dermis is known as the subcutaneous tissue^(8,9).

Figure 2 depicts the five layers that make up the epidermis. Because it includes keratin protein, which is made from dead keratinocyte cells, the SC is sometimes referred to as a "horny layer." In addition, it contains lipids such as cholesterol, cholesterol esters, ceramides (30–40%), and free fatty acids^(10,11).

Except for the lips, hand palms, and foot soles, appendages (hair follicles) are found across the whole surface of the skin. A percentage of the entire skin surface, roughly 1/1000, is made up of them. The sebaceous gland secretes sebum from each hair follicle. Sebum is composed of triglycerides, waxes and free fatty acids. Skin lubrication and protection are provided by sebum, which also maintains the skin's pH at about 5^(12,13).

Drug Penetration Routes Through the Skin:

The trans-appendageal and trans-epidermal channels are the two potential routes of drug penetration through intact skin, as shown in Figure 3.

Tans-epidermal route includes two pathways: intracellular route in which the drug molecules partition into a keratin-filled corneocyte of stratum corneum and intercellular route, the drug molecules partition into the lipid bilayers between the corneocytes of stratum corneum, lipid pathway. Lipophilic (nonpolar) molecules primarily diffuse intracellularly, whereas hydrophilic (polar) molecules may traverse the intracellular pathway, although with limited permeability^(14,15). The drug molecules diffuse through the lower epidermal layers (viable epidermis) before reaching to the systemic circulation via the capillaries in the dermis.

The trans-appendageal pathway involves chemicals traveling through hair follicles and sweat glands⁽¹⁶⁾. Numerous difficulties with drug distribution through the skin led to the development of various transdermal delivery systems, which are currently on the market but are still only effective for a small number of medications. The capacity to resolve these issues with drug molecule permeation and skin irritation is necessary for further advancements in transdermal delivery. The transdermal market for hydrophilic chemicals, macromolecules, and conventional medications for new therapeutic indications has expanded as a result of the development of novel methods to enhance skin penetration and diminish skin irritation^(17,18).

The Need for Colloidal Drug Delivery Systems

Conventional therapies for topical distribution face numerous challenges, including limited skin barrier permeability, hyperpigmentation, allergic responses, damaged tissues and microphage clearance. To overcome these obstacles and improve drug administration through the topical route, a colloidal drug delivery method is used, Figure 4 summarizes the various types of colloidal drug delivery techniques that are available^(19,20).

It has been demonstrated that this approach improves drug diffusion and penetration with greater effectiveness and reduced toxicity and allergic reactions (such as burning feelings). Furthermore, because it penetrates quickly through follicular and intercellular channels, it targets particular skin anatomical layers (such as the epidermis and dermis) when applied topically as opposed to through other administration methods^(21,22).

Therapeutic drug permeation across the different layers of the skin and other systemic routes of administration is made possible by ethosomes, colloidal delivery systems, which are made up of sensitive and flexible vesicles that range in size from 1 nm to 1000 nm" (1nm to 1000nm due to ethosomes categorized in the paragraph as colloidal delivery systems moreover, the mentioned ref. (23 and 24) have no microsize range only nanosize range)^(23,24), as illustrated in Figure 5.

Although ethosome and liposomes have a similar composition, ethosome has a higher ethanol content. Ethosomes are mostly composed of phospholipids (such as phosphatidylcholine, phosphatidylserine, and phosphatidic acid) that assemble in a high concentration of water and alcohol (such as ethanol and isopropyl alcohol).

The breaking of the epidermal barrier by ethanol is one of the main reasons that contribute to the success of ethosomes, which are utilized for topical medication administration. Ethosomes include ethanol, which interacts with skin lipids to improve medication penetration and decrease their structural integrity. This disruption, along with the ethosomes' natural flexibility, improves the therapeutic penetration by fusing the formulation's phospholipids with the epidermal layer, as seen in Figure 6: A&B. As a drug's carrier, ethosomes increase the drug's permeability and length of stay while protecting it from the enzymes that break down the skin^(25,26).

Ethosomal System Types

Three different ethosomal system types that are categorized according to their compositions as depicted in Figure 7.

1-Classical ethosomes: phospholipid-based nanocarriers made of water, ethanol, and phospholipids (20–45%). Compared to other ethosome types, they offer superior permeability and ease of formulation. Compared to other types, like binary or trans-ethosomes, which require the addition of surfactants or penetration enhancers that may irritate the skin, classical ethosomes are more stable and compatible with the skin. In terms of production costs, ethosomes based on polymer nanocarriers are more expensive than the classic type⁽²⁷⁻²⁹⁾.

2-Binary ethosomes: Zhou et al. introduced these types of ethosomes. The most common alcohols in binary ethosomes, propylene glycol (PG) and isopropyl alcohol (IPA), were essentially produced by combining classical ethosomes with another kind of alcohol^(30,31).

3-Transethosomes: were the ethosomal systems of the new generation, which Song et al. initially reported in 2012. This system contains the basic components of traditional ethosomes plus an extra material such as an edge activator or penetration enhancer (surfactant). The goal of these novel vesicles was to combine the advantages of traditional ethosomes and flexible liposomes. Transethosomes and binary ethosomes exhibit better flexibility and permeation than classical (conventional) ethosomes — not the other way around. So when comparing within ethosomal systems, classical ethosomes are actually the *least* permeable of the three types^(32,33).

Materials' Effects on The Properties of The Ethosomal System:

Ethanol

Ethanol gives the vesicles unique characteristics such size, stability, ζ -potential, entrapment efficacy, and increased skin permeability, making it a potent penetration enhancer that promotes ethosomal systems. According to reports, ethanol concentrations in ethosomal systems vary between 10% and 50%^(34,35).

Numerous studies found that as ethanol levels rise, ethosome size decreases. Bendas and Tadros discovered that an ethosomal formulation with 40% ethanol had a mean vesicle width that was 44.6% smaller than a conventional liposomal formulation without ethanol^(36,37).

However, the bilayer will become leaky if the ethanol concentration is increased above the optimal threshold, leading to a little increase in vesicular size and a significant reduction in entrapment effectiveness. Furthermore, the vesicles will become soluble if the ethanol concentration is increased further^(38,39). According to certain studies, the ethanol hydrocarbon chain interpenetrates at high ethanol concentrations, decreasing the vesicle's thickness and, as a result, its size. Other researchers claim that ethanol causes steric stabilization, which may lower the average vesicle size, by somewhat changing the net charge of the systems^(40,41).

Vesicular charge is a significant factor that can affect vesicular characteristics, including stability and vesicle-skin interaction. Because ethosomes contain more ethanol, the positively vesicular charge has changed from positive to negative (due to the particles of drug may be positively or negatively charged based on the excipients)⁽⁴²⁾.

Phospholipids

Phospholipids from many sources have been used to construct the ethosomal system. The size, stability, ζ -potential, entrapment efficiency, and penetrating properties of the vesicles are influenced by the kind and concentration of phospholipids used in the formulation. Binary ethosomes for the enhanced topical delivery and antifungal efficacy of ketoconazole^(43,44). In an ethosomal formulation, phospholipid concentrations usually fall between 0.5% and 5%. When phospholipid concentration rises, vesicular size should increase little or considerably due to interconnected physicochemical principles. As more phospholipid becomes available, greater amounts of bilayer material are incorporated into vesicle membranes, leading to the formation of either larger unilamellar vesicles or additional concentric multilamellar bilayers, both of which physically increase overall vesicle diameter. This growth in vesicle size directly contributes to improved EE%, since larger vesicles possess a greater internal aqueous volume that can accommodate more drug molecules, while thicker multilamellar membranes simultaneously provide additional lipophilic compartments for partitioning of hydrophobic drugs, while entrapment efficiency will rise sharply. Nevertheless, this relationship holds true up to a certain concentration, beyond which additional phospholipid concentration increases have no effect on entrapment efficiency^(45,46).

Cholesterol

When added to ethosomal systems, the solid steroid molecule cholesterol improves the stability and effectiveness of drug entrapment. It reduces vesicular leakage, fusion, and permeability. Although its usual concentration is up to 59%, it has been used in some formulations up to 70% of the total phospholipid content. Several studies have demonstrated that cholesterol led to the expansion of vesicles in ethosomal systems^(47,48).

Dicetyl phosphate

Dicetyl phosphate is frequently used to prevent vesicles from clumping together and to improve formula stability. It is applied in amounts ranging from 8% to 20% of the total phospholipid content. According to Maestrelli et al., vesicles with a significantly negative ζ -potential were produced by all ethosomal formulations

including dicetyl phosphate. Nevertheless, it is still unknown how dicetyl phosphate affects other characteristics of the ethosomal system ^(49,50).

Stearylamine

Positively charged stearylamine has been used in ethosomal formulations. Mycophenolic acid, which is made up of phosphatidylcholine, cholesterol, and stearylamine in a 2:1:1 molar ratio, is one such ethosomal system. Within a week of adding stearylamine to the ethosomal formulation, the vesicles gathered due to a notable increase in vesicular size, a reduction in entrapment efficiency, and a shift in the ζ -potential charge from negative to positive. The reason for all of these effects is that the positive charge of stearylamine is incompatible with the negative charges of soy phosphatidylcholine and mycophenolic acid ^(51,52).

Penetration enhancers or edge activators

Because they drastically change the characteristics of the ethosomal system, selecting the appropriate edge activator or penetration enhancer is one of the most crucial tasks in the creation of transethosomes. a list of the penetration enhancers and edge activators utilized in the transethosome production process, including oleic acid, dimethyl sulfoxide and tween 80, 60 20 in a significant quantity ^(53,54).

Drug/agent effects on ethosomal system properties

The type or physicochemical characteristics of the medicine or substance that will be added are the most crucial elements in ethosomal formulations. This is due to the possibility that the drug or substance will alter the ethosomal systems' characteristics, particularly their ζ -potential and particle size.

Lodzki et al. found that treating an ethosomal system with trihexyphenidyl hydrochloride decreased its vesicular size. After drug loading, the average diameter of the blank ethosomes dropped from 154±15 nm to 109±6 nm. The scientists attributed the effect to the drug's surface-active characteristics. There have also been reports of vesicular size reduction in ethosomal systems loaded with buspirone hydrochloride ^(55,56).

Ethosomes Preparation

Cold method:

The simplest and most popular way to prepare ethosome is the cold technique. The aqueous and organic phases are made separately using this technique. phospholipids, medicinal compounds and other lipid ingredients can be dissolved in 20% to 45% (w/w) ethanol at 25 °C under continuous stirring to obtain a homogeneous solution., after that, the container is heated to 30 °C. In another vessel, water is heated to 30 °C before being added gradually to the original mixture while being constantly stirred. After around five minutes of mixing, vesicle production begins. It's crucial to keep the resultant vesicles at a low temperature. To further decrease the vesicle size and improve homogeneity, the resultant ethosomal dispersion may be sonicated for a predetermined amount of time. as shown in Figure 8-A ^(57,58).

Hot method:

The drug is mixed with propylene glycol and ethanol while it is being heated. Phospholipid dispersion in water is produced at 40 °C. An existing mixture is mixed with this dispersion. Sonication or extrusion may then be applied to reduce vesicle size. The final mixture is then heated to 30 °C. Based on Figure. 8-B

Thin film hydration method:

This ethosome preparation method can be used to encapsulate both hydrophilic and lipophilic medications. It offers better entrapment efficacy and greater control over vesicle size and drug loading than other conventional methods.

Phospholipids are first dissolved in ethanol and an organic solvent like chloroform, methanol, and dichloromethane to create a thin film. A rotary evaporator is then used to extract the solvent. The film inside the flask is continually swirled at the proper temperature while being hydrated with phosphate buffer saline (PBS) or drug-containing water. To increase membrane fluidity and penetration, ethanol is added to the hydrated vesicles, as shown in (Figure. 8-C) ⁽⁵⁹⁻⁶¹⁾.

Characterization of Ethosome :

Visualization of Vesicles by TEM and SEM:

Using a transmission electron microscope (TEM), the vesicular shape of the ethosome preparations is investigated. One milliliter of the sample should be dried on a carbon-covered matrix before being negatively stained using a fluid mixture of phosphotungstic corrosive. Following drying, the sample is seen at 10-100 k-overlay amplifications using a magnifying device with a 100 Kv speeding up voltage. Scanning electron microscopy (SEM) shows the vesicles' size and shape. On an appropriate glass stub, one drop of ethosomal

suspension is placed. After letting it air dry, it is gold-plated with sodium aurothiomalate such that an electron microscope can view it at 10,000 amplifications^(62,63).

Vesicle size and Zeta potential: -

Particle size and zeta potential can be ascertained using dynamic light scattering (DLS), photon correlation spectroscopy (PCS), and an automated inspection system^(64,65).

Entrapment Efficiency (EE%) of ethosomal vesicles:

Lamsal et al. evaluated the entrapment effectiveness of the gliclazide ethosomes using the ultra-centrifugation method. The untrapped drug may be in the supernatant as a result of its size in the molecular range or under sedimentation due to its size higher than 1000nm so the method mentioned just determine the the untrapped drug may be in the supernatant⁽⁶⁶⁾. For two hours, 15 milliliters of ethosomal formulation were spun at 12,000 rpm in a centrifuge tube. The total volume of the supernatant was then calculated. The amount of medication in the supernatant layer was then measured using a UV spectrophotometer. The entrapment efficiency will be calculated using the formula below:

$$\text{Entrapment efficiency} = \left\{ Qt - \frac{Qs}{Qt} \right\} * 100$$

Where, Qt :is the added amount of drug

Qs: is the detected amount of drug in the supernatant.

By using the supernatant layer to calculate the untrapped drug, the entrapment efficiency can be indirectly determined. Once the sediment layer of the ethosomes is removed by centrifugation, the liquids of the sediment and supernatant are separated using the direct technique. The amount of drug in the sediment was ascertained by lysing the vesicles with one milliliter of 0.1% Triton X 100 and then diluting it with one hundred milliliters of methanol. After the vesicles were ruptured to release the medication, the drug content was measured using a UV spectrophotometer. The following formula was used to determine the percentage of entrapment:

$$EE\% = \text{amount of drug in sediment/amount of drug added} \times 100$$

Transition Temperature:

Differential scanning calorimetry (DSC) can be used to determine the transition temperature (T) of vesicular lipids in an aluminum container that is heated at a rate of 10 °C per minute while being exposed to a constant nitrogen stream⁽⁶⁷⁻⁶⁹⁾.

Skin Permeation Studies

Confocal laser scanning microscopy (CLSM) makes it possible to quantify how well the ethosomal preparation penetrates the epidermis.

Drug Content

The drug content of ethosomes can be detected using UV spectrophotometer light. This can also be assessed using a modified fluid chromatographic method for elite execution^(70,71).

Surface Tension Measurement

The ring method in a Du Nouy ring tensiometer can be used to assess the drug's surface tension activity in an aqueous solution.

Phospholipid-ethanol interaction

To concentrate on the phospholipid-ethanol relationship, we used 31P-NMR with proton decoupling calorimetry and differential scanning calorimetry.

Degree of deformability and Turbidity

The degree of deformability of the ethosomal preparation can be measured using an extruder, and the turbidity of the preparation can be measured using a nephelometer⁽⁷²⁾.

In vivo irritation test:

In vivo irritation test is conducted on healthy New Zealand White rabbits, which are preferred due to the thinness and relative permeability of their skin compared to other animal models. Prior to the study, the dorsal skin of each rabbit is shaved 24 hours before application to remove hair without abrading the skin surface. The ethosomal formulation is applied to a defined area (typically 2.5 cm × 2.5 cm) of intact and, in some protocols, abraded skin under a semi-occlusive patch for a fixed duration, most commonly 4 hours. After patch removal, the

sites are evaluated at 1, 24, 48, and 72 hours for the presence and severity of erythema (redness) and edema (swelling), as outlined in the Draize scoring system ⁽⁷³⁾.

Application of Ethosome:

1. Antiviral drug delivery
2. Topical DNA Delivery
3. Hormone Transdermal Administration
4. Anti-parkinsonian drug delivery
5. Delivery through Transcellular
6. Anti-Arthritis Drug Delivery
7. Antibiotic Delivery.

Advantages of Ethosome delivery

There are a number of benefits to using ethosomes as a way to deliver medicine. They can be used to give medicines through the skin and on the skin ^(74,75). Because they are not toxic, biocompatible, or biodegradable, they are a safe and effective way to give drugs ⁽⁷⁶⁾. They are a versatile drug delivery system that can transport both hydrophilic and hydrophobic medications ⁽⁷⁷⁻⁷⁹⁾. Each vesicle can hold a lot of medicine because it can hold a lot of drugs. This makes the overall treatment more effective and cuts down on the number of times the medicine needs to be given ⁽⁸⁰⁾. Additionally, the ethanol in ethosomes can help stabilize and protect the vesicles from degradation. This prolongs the medication's shelf life and reduces the need for frequent reapplication ^(81,82). Additionally, ethosomes improved the drug's ability to penetrate the skin by making the cell membrane more fluid and permeable. This increased the amount of medication that could reach the underlying tissues and improved the overall efficacy of the treatment ⁽⁸³⁾. Ultimately, ethosomes can be altered to target specific cells or tissues, improving the overall specificity of the treatment ⁽⁸⁴⁾.

Limitations of Ethosome delivery

As a medication delivery system, ethosomes have several advantages, but they also have certain disadvantages. The time-consuming and complex preparation, which can lower production efficiency, and the restricted stability caused by the vesicles' sensitivity to temperature and humidity, which can make storage and shipping difficult, are some of the key disadvantages ^(85,86). Additionally, the lack of in vivo studies makes it difficult to fully understand the potential benefits and drawbacks of using ethosomes as a drug delivery method ^(87,88). Additionally, they might cause erythema and skin irritation if not optimized and show some conflict with some drugs ^(89,90).

Pharmacological, medicinal, or physical repercussions could result from the interference. This could change the drug's stability, bioavailability, or solubility. A hydrophilic drug, for instance, may become less soluble and delivery-accessible if it is encapsulated in a lipid bilayer; it may also become incompatible with the lipid-based structure of ethosomes and show decreased efficacy; or it may become unstable and produce toxic byproducts or inactive metabolites. Additionally, they can interact with other excipients and medications in the formulation and are sensitive to pH and temperature fluctuations ^(91,92). By employing the right formulas and enhancing the production and composition of the ethosomes, many of these restrictions can be removed ^(93,94). It is crucial to remember that more investigation is required to completely comprehend the advantages and disadvantages of ethosomes as a medicine delivery method ⁽⁹⁵⁾.

Future of Ethosome

These are only a few instances of how skin care products could be delivered via ethosomes. They have also been investigated for the delivery of other cosmetic agents, including hyaluronic acid, collagen, and peptides. These compounds have shown great promise in improving skin hydration, firmness, and elasticity; ethosomes may further their efficacy ^(96,97).

Skin irritation, stability, and shelf life are only a few of the problems with ethosome delivery of skin cosmetics, which is still in its early stages. However, there are many potential benefits to employing ethosomes as a cosmetic delivery system, and further research is needed to fully explore their potential in this field ⁽⁹⁸⁻¹⁰¹⁾.

Layers of Human Skin

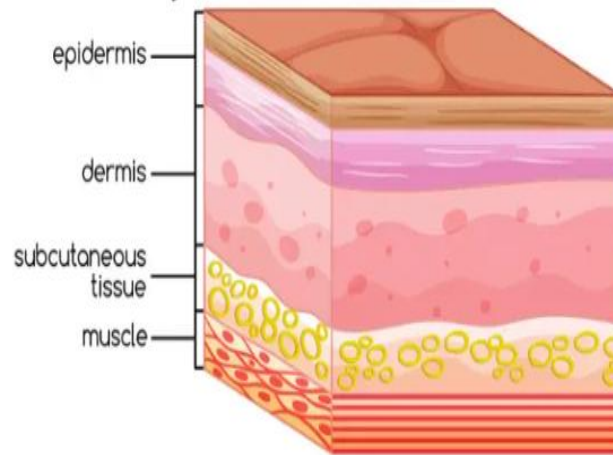


Figure 1: Schematic representative the anatomy of the skin ⁽⁸⁾

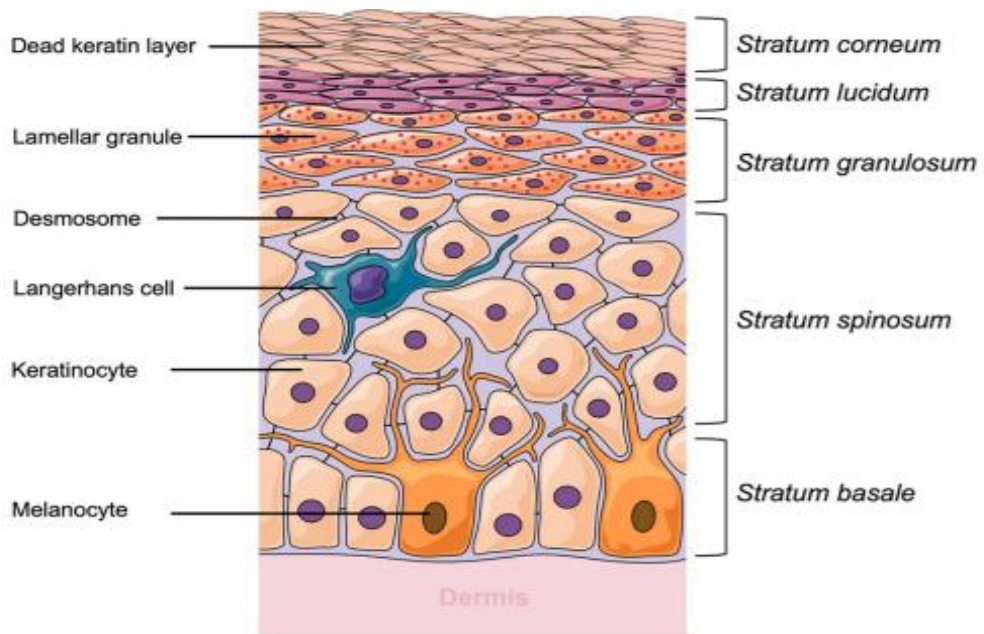


Figure 2: Schematic representation of epidermis layer of human skin ⁽¹⁰⁾

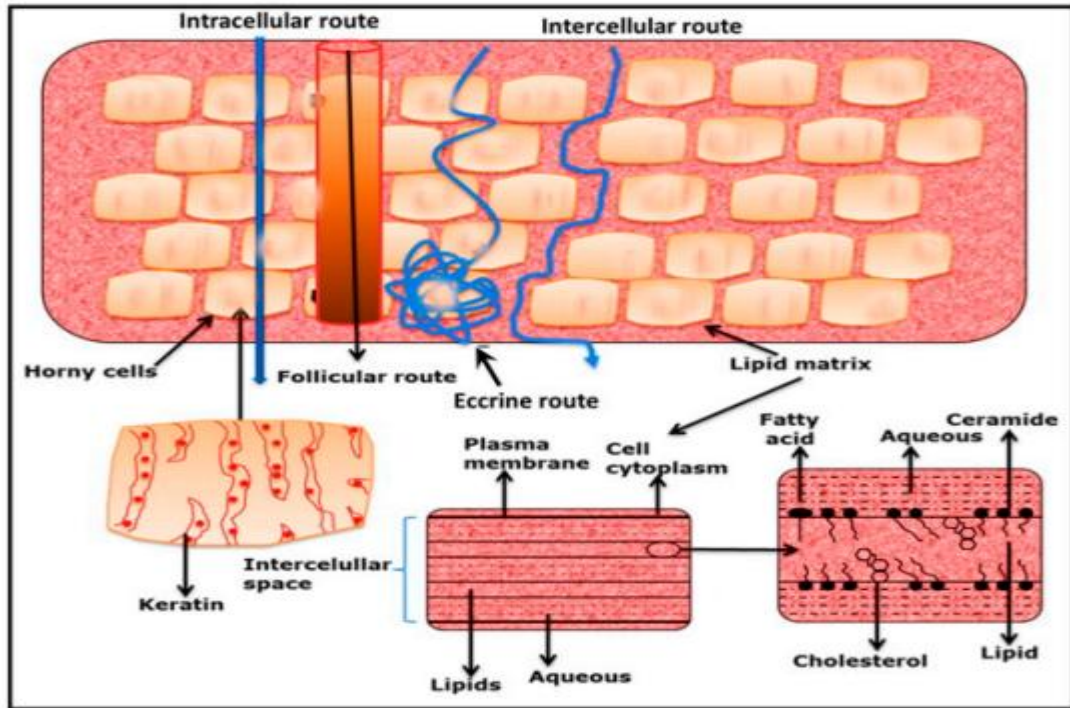


Figure 3: Potential pathways for drug penetration through human skin ⁽¹⁴⁾

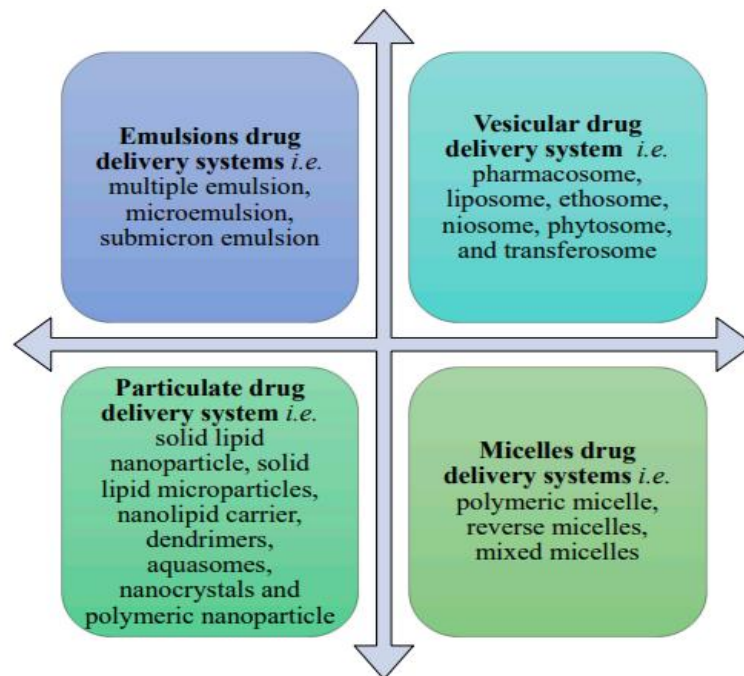


Figure 4: Classifications of colloidal drug delivery systems ⁽²³⁾

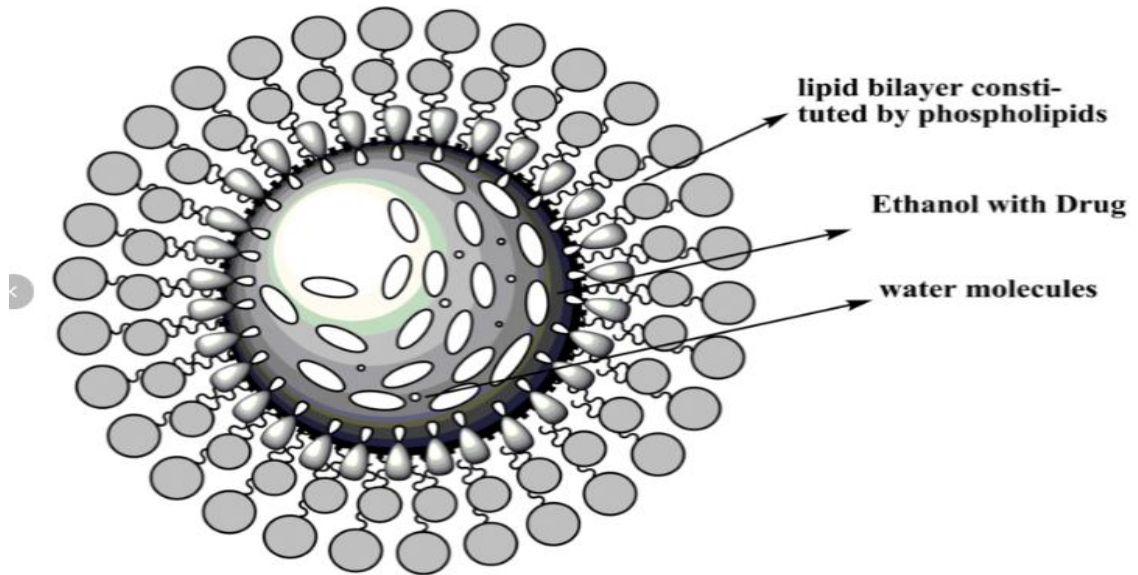


Figure 5: Illustration of ethosomal structure ⁽²⁴⁾

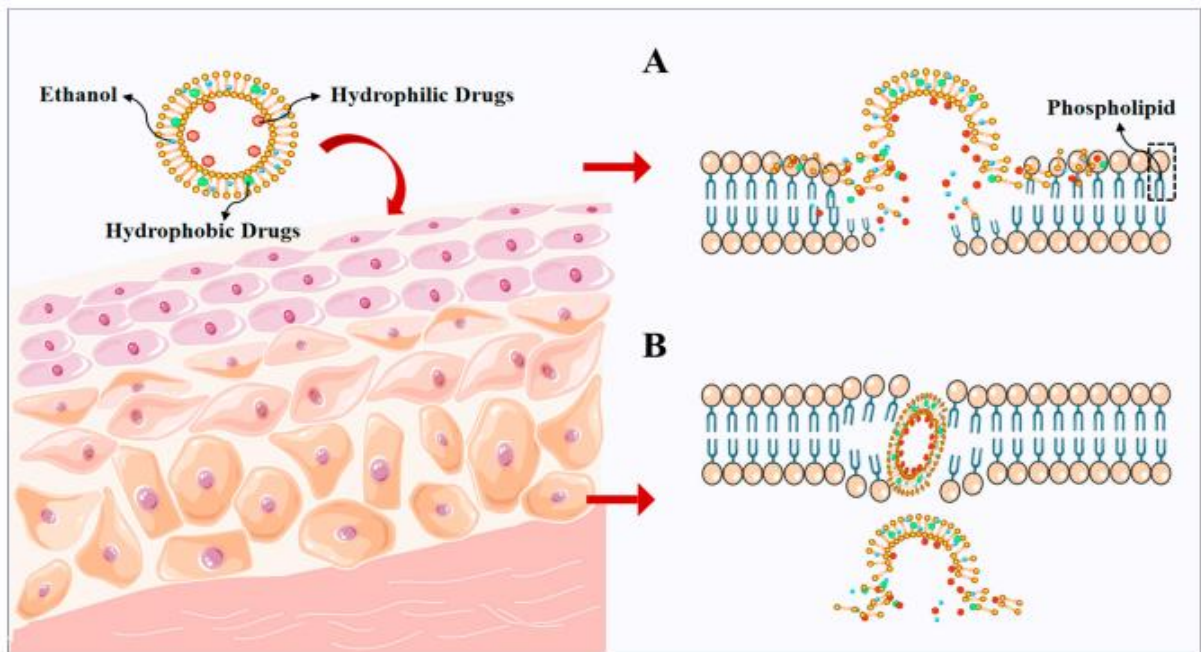


Figure 6: The main mechanisms of ethosome penetration. (A) Ethanol effect, (B) Ethosomes effect⁽²⁶⁾

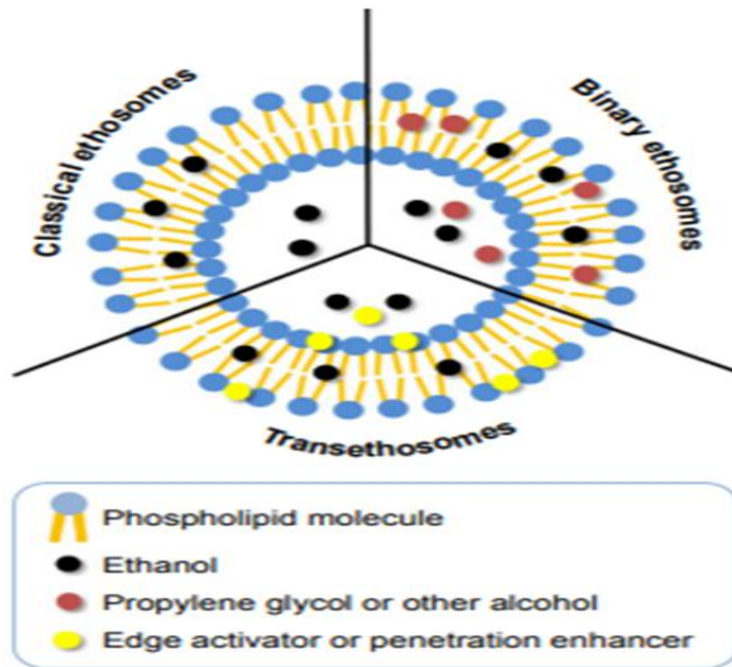


Figure 7: An illustration of the various ethosomal system types ⁽¹⁰²⁾

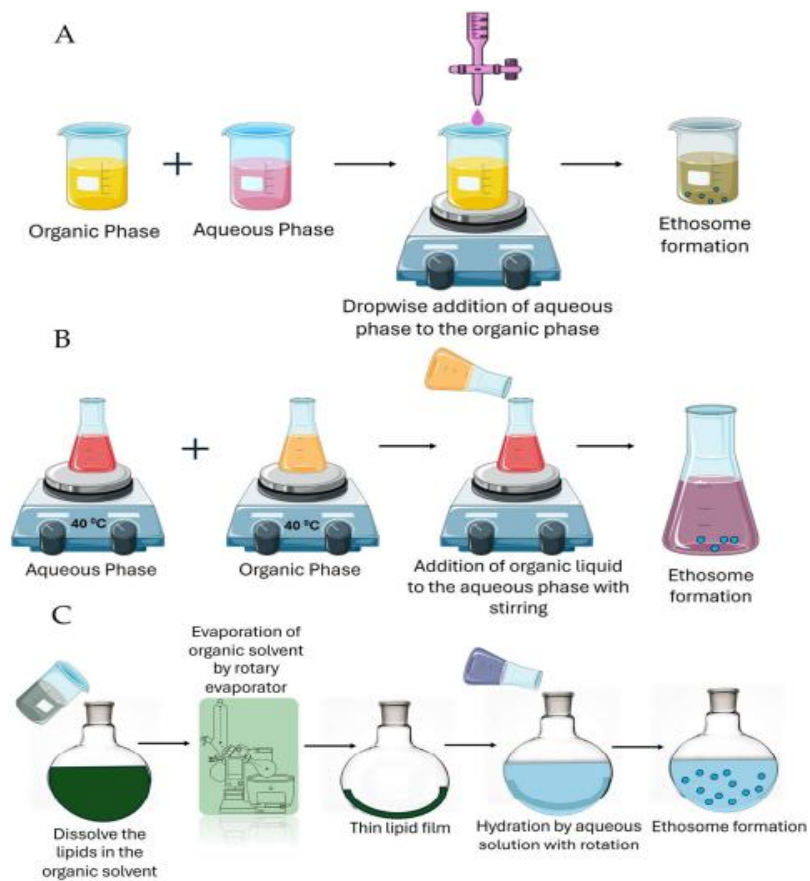


Figure 8: Methods of ethosomes preparation A: cold method B: hot method C: thin film hydration method ⁽⁶¹⁾

Table 1: Differences between ethosomal types according to formulation, preparation, and characterization⁽³³⁾

SYSTEM	COMPOSITION	MECHANISM OF ACTION	KEY ADVANTAGES	LIMITATIONS	TYPICAL APPLICATIONS
Classical ethosomes	Phospholipid (soy lecithin or PC) + high ethanol (20–45%) + water	Ethanol fluidizes both vesicle membrane and skin lipids; soft, deformable vesicles penetrate intercellular spaces of stratum corneum	Deep skin penetration; enhanced transdermal flux; prolonged drug release; simple formulation	Ethanol can cause skin irritation; vesicle stability concerns; limited for very hydrophilic drugs	Testosterone, ketoprofen, cyclosporin A, acyclovir
Binary ethosomes	Phospholipid + ethanol + isopropyl alcohol (IPA) + water (dual alcohol system)	Synergistic action of two alcohols further disrupts skin lipid bilayers; IPA acts as co-penetration enhancer and additional fluidizer	Superior skin penetration vs. classical ethosomes; better entrapment of lipophilic drugs; improved flux rates	Higher alcohol content may irritate sensitive skin; formulation optimization more complex	Highly lipophilic drugs, hormones, anti-fungals (e.g., clotrimazole, miconazole)
Transethosomes	Phospholipid + ethanol + edge activator (Tween 80, Span 80, sodium deoxycholate) ± water	Edge activators destabilize vesicle membrane, creating ultra-deformable, elastic vesicles; can squeeze through pores smaller than their own diameter under hydration gradient	Highest deformability index; excellent skin permeation; can carry both hydrophilic and lipophilic drugs; reduced ethanol content possible	Edge activator selection critical; complex optimization; potential surfactant-related skin reactions	Proteins, peptides, macromolecules, anti-inflammatory drugs (diclofenac, curcumin)

CONCLUSION

In conclusion, ethosomes have a promising future. The critical role that structural components such as water, ethanol, and phospholipids play in controlling the physical properties of ethosomal cells and in ethosomal activity has been made clear by this review. Ethosomes are preferable to transdermal and dermal administration systems due to their exceptional qualities as a non-invasive drug delivery technique and their ability to enhance skin penetration. The size, zeta potential, and entrapment efficiency of each form of ethosomes were distinct, and as Nano carriers, ethosomes had a major influence on transdermal delivery methods.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

FUNDING

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ETHICS STATEMENTS

This study doesn't need ethical approval from an ethics committee according to the research integrity rules in your country

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الأنظمة الإيثوسومية كمنصة حويصلية مبتكرة لتوصيل الأدوية

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الهدف: يهدف هذا البحث إلى دراسة كيفية تحقيق أنظمة توصيل الدواء عبر الجلد مزايا مقارنة بالطرق التقليدية، خاصة من حيث زيادة الفعالية العلاجية وتقليل السمية، إضافة إلى تجاوز الاستقلاب الكبدي. كما يهدف إلى استعراض الأنظمة الإيثوسومية كناقلات نانوية مبتكرة لتعزيز توصيل الأدوية عبر الجلد.

المنهجية: تم إجراء مراجعة شاملة لأنظمة توصيل الدواء عبر الجلد مع التركيز على الإيثوسومات. وتمت دراسة ثلاثة أنواع من الأنظمة الإيثوسومية بناءً على تركيبها، وهي: الترانسايثوسومات، والإيثوسومات الثنائية، والإيثوسومات التقليدية. كما تم تحليل تأثير اختلاف تقنيات التحضير وطرق الصياغة على خصائص النظام، بما في ذلك حجم الحويصلات، وجهد زيتا، وكفاءة احتجاز الدواء، ونفاذية الجلد، والاستقرار.

النتائج: تُعد الإيثوسومات من النواقل الواعدة لتوصيل الأدوية عبر الجلد، إذ يمكنها احتواء أدوية ذات خصائص فيزيائية-كيميائية متنوعة. ويفضل احتوائها على نسب عالية من الإيثانول، فإنها تعزز انتشار الدواء إلى الطبقات العميقة من الجلد. كما تبين أن التغيرات في التركيب وطرق التحضير تؤثر بشكل ملحوظ على المعايير الأساسية مثل حجم الجسيمات، وكفاءة الاحتجاز، والاستقرار. وقد أظهرت كل من الترانسايثوسومات والإيثوسومات النتائج مرونة أعلى ونفاذية أفضل مقارنة بالإيثوسومات التقليدية.

الاستنتاجات: تتميز الأنظمة الإيثوسومية بقدرتها على تحسين نفاذية الدواء وتقليل السمية وزيادة الفعالية العلاجية، مما يجعلها وسيلة واعدة لتوصيل الأدوية عبر الجلد. كما أن مكونات الصياغة وطرق التحضير تلعب دوراً مهماً في تحديد كفاءتها. ومن المتوقع أن تسهم المزيد من الدراسات والتطويرات في تعزيز استخدامها في المجالات الطبية والدوائية.

الكلمات المفتاحية: الإيثوسومات، الطريقة الساخنة، التوصيل عبر الجلد، اختراق الجلد.