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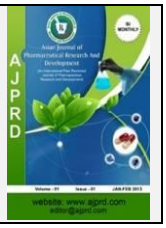

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Review Article

Ethosomal Drug Delivery Systems for Enhanced Topical Delivery of Antiviral and Anti-Inflammatory Drugs

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A B S T R A C T

Ethosomal drug delivery systems have emerged as advanced vesicular carriers designed to enhance the topical and transdermal delivery of therapeutic agents, particularly in the management of dermatological conditions such as herpes simplex and herpes zoster. Conventional topical formulations often face significant limitations due to the barrier function of the stratum corneum, which restricts drug penetration and reduces therapeutic efficacy. To overcome these challenges, vesicular systems have been extensively explored, among which ethosomes have demonstrated notable advantages.

Ethosomes are distinguished by their high ethanol content combined with flexible phospholipid bilayers, which facilitate deeper skin penetration and improved drug permeation. These systems enhance drug entrapment efficiency, increase bioavailability, and enable sustained drug release compared to traditional carriers like liposomes and niosomes. Their unique mechanism involves ethanol-induced fluidization of skin lipids along with vesicle deformability, allowing efficient transport of active compounds across skin layers.

Various aspects of ethosomal systems, including their composition, classification, preparation techniques, and characterization parameters such as vesicle size, zeta potential, morphology, entrapment efficiency, in vitro release, and stability, are critical in determining their performance. Additionally, ethosomes provide a versatile platform for combination therapy by enabling co-delivery of antiviral and anti-inflammatory agents. For instance, simultaneous incorporation of drugs like acyclovir and triamcinolone acetonide offers synergistic benefits by targeting both viral replication and associated inflammation.

Overall, ethosomal systems represent a promising and efficient approach for targeted and controlled topical drug delivery. Their ability to enhance permeability, improve therapeutic outcomes, and support combination therapy highlights their potential as superior alternatives to conventional formulations, paving the way for future advancements in pharmaceutical and clinical applications.

Keywords: Ethosomes, topical delivery, transdermal, antiviral, anti-inflammatory, acyclovir, triamcinolone acetonide.

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INTRODUCTION

Transdermal and topical drug delivery systems have become popular alternatives for administering drugs both locally and systemically because of their non-invasive nature and the many benefits they offer over traditional methods of drug administration (e.g., oral and parenteral). For example, these non-invasive methods avoid first-pass metabolism, improve patient compliance, and allow sustained drug delivery at an active site of action (1,2). However, the effectiveness of topical treatments is limited by the ability of the stratum corneum (the skin's outer layer) to act as a barrier to many pharmacologically active compounds, especially those that are not very lipid-soluble (lipophilic) or have very large molecular weights (2).

The treatment of dermatological disorders such as Herpes Simplex and Herpes Zoster can be done using medications that are capable of treating both viral infections and inflammation. Acyclovir is one medication that has been used successfully as the first choice for treating skin infections caused by the herpes virus (3,34). However, Acyclovir has limited clinical effectiveness when applied directly to the skin because it does not penetrate the skin well and has low bioavailability (5). Corticosteroids, such as Triamcinolone Acetonide, are commonly used to relieve

inflammation, redness, and itching due to skin disorders; however, long-term use of these steroids may lead to adverse reactions and inadequate localized delivery when administered using traditional drug delivery methods (4). Consequently, new and improved methods of drug delivery need to be developed to increase the amount of drug that enters through the skin while minimizing systemic exposure (5).

Nanocarrier-based drug delivery systems are gaining popularity as methods to resolve the limitations of common topical formulations. Vesicular delivery methods (liposomes and niosomes) have been extensively researched; however, their penetration through the skin remains limited (5). Ethosomes are a new class of lipid vesicles that contain elevated concentrations of ethanol and demonstrate improved ability to deliver drugs transdermally and dermally compared to other vesicular methods (6). The flexibility of the vesicular membrane due to the presence of ethanol facilitates drug delivery by disrupting the lipid organization in the stratum corneum, allowing for greater depth of drug delivery using ethosomes (6,7).

Ethosomes exhibit tremendous potential for delivering hydrophilic and lipophilic drugs. The benefits of ethosomes include improved drug entrapment efficiency, enhanced drug permeability, and improved therapeutic outcomes (7). The delivery of antiviral and anti-inflammatory agents via ethosome formulations has generated considerable interest among researchers because of their ability to enable the targeted and prolonged release of drugs to the skin (3,7). The ability to co-deliver multiple therapeutic agents in one ethosome format presents an opportunity for new synergistic treatments for challenging dermatological conditions (5,35).

This review summarizes the available literature on ethosomal drug delivery systems, specifically their role as enhancers of topical delivery of antiviral and anti-inflammatory drugs. This includes discussions on structural characteristics, mechanisms of action, formulation strategies, and comparative advantages of ethosomes over conventional vesicular systems (liposomes and niosomes). Additionally, current advances, contemporary case studies, and future directions associated with ethosomal drug delivery are critically analyzed and used to illustrate how ethosomes can potentially improve therapeutic efficacy and patient clinical outcomes.

Skin Structure and Barrier Function:

The skin, the largest organ in the human body, protects the inside of the body from the outside world and plays an important role in regulating homeostasis (8). The skin consists of three main layers: the epidermis, dermis, and hypodermis. Each of these layers has different anatomical and functional properties (2,8). The outer layer of the skin (epidermis) is considered the "top layer" of the skin. The epidermis is composed of many layers of keratinocytes stacked together (the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum) (2). The stratum corneum is the most important barrier to drug absorption and is composed of dead (flattened) corneocytes in a lipid (fat) matrix organized in a "brick-and-mortar" structure (9). This unique organization provides mechanical strength to the skin and prevents excessive water loss while stopping many different types of substances from being absorbed into the body (including drugs) (9, 10). The dermis, which is the connective tissue layer of the skin, is located underneath the epidermis. The dermis contains abundant collagen and elastin, providing strength and support to the body, as well as blood vessels and nerves to organisms. The dermis also contains appendages, such as sweat glands and hair follicles (8,36).

The dermis plays a significant role in drug absorption once compounds successfully penetrate the epidermal barrier, as it facilitates systemic uptake through its vascular network (2).The hypodermis (subcutaneous tissue) is the innermost layer of the skin and consists primarily of adipose tissue. In addition to providing energy reserves, the hypodermis acts as a thermal insulating layer and a mechanical cushion for underlying structures (8). While the hypodermis is not a substantial barrier to drug permeation, it has an effect on drug distribution and retention in deeper tissues (2). The stratum corneum provides the most important barrier to transdermal and topical drug delivery due to the distinct organization of the lipids in the stratum corneum structure, which restricts the diffusion of both the hydrophilic and lipophilic molecules (9,11). There are generally three main mechanisms of drug permeation through the skin: intercellular (through lipid domains), transcellular (across corneocytes), and appendageal (via hair follicles and sweat glands). Most drugs predominantly permeate via the intercellular pathway because the surface area associated with the appendix pathway is limited (11,37).

Transdermal drug delivery presents several obstacles due to how poorly the stratum corneum absorbs drugs with a high MW, as well as drugs that have low lipophilicity or a high unfavourable partition coefficient (12). The ability of some compounds to be absorbed through the stratum corneum is also affected by the amount of water on the skin, its thickness, its integrity, and the various enzymes found in the skin (2,12). Traditional topical products deliver drugs too rapidly from their application site, do not penetrate deep enough into the dermal tissues, and/or are too unstable to maintain high concentrations of active pharmaceutical ingredients (12,38). These challenges have prompted the development of advanced drug delivery systems (e.g., vesicular carriers and nanocarriers) that can effectively penetrate the skin layers and facilitate drug transfer into the bloodstream (11,13). Therefore, understanding the structure and function of the skin barrier is critical for designing effective topical and transdermal drug delivery systems.

Overview of Vesicular Drug Delivery Systems:

The use of vesicular delivery systems has become an important classification of nanocarriers intended to enhance the delivery of therapeutic agents across biological membrane barriers, such as the skin (14). This delivery systems consist of vesicles made from lipids or surfactants that contain and encapsulate hydrophilic and hydrophobic drugs, thus enhancing drug stability and bioavailability and providing targeted delivery of the drug (14,15). Numerous types of vesicular drug carriers, such as liposomes, niosomes, and ethosomes, have been extensively studied to facilitate

topical and transdermal drug delivery, each with unique structural and functional characteristics (15) (Table 1).

Liposomes

Liposomes are spherical vesicles containing phospholipid bilayers that enclose an aqueous core; therefore, they can contain hydrophilic drugs in their core and lipophilic drugs within their bilayer (16). Their structural similarity to biological membranes contributes to the compatibility of liposomes with living tissues and their ability to interact with skin lipids (16,17). Some benefits of liposomes include reduced toxicity of drugs delivered via liposomes compared to non-liposome delivery methods, increased stability of drugs during storage, and greater potential for controlled and sustained release of drugs (17). Furthermore, liposomes enhance the accumulation of the drug in the upper layers of the skin, making them more effective for localized therapy (18). However, conventional liposomes have several limitations, including poor stability, sensitivity to oxidation and hydrolysis, and inability to penetrate the stratum corneum (18,19). In addition, the relatively rigid structures of conventional liposomes limit their ability to perforate the skin barrier and can contribute to less-than-optimal therapeutic outcomes for drugs that need to penetrate deeper into the tissues (19,39).

Niosomes

Niosomes are created through a self-assembly process using surfactants dissolved in water, which are typically stabilized by cholesterol or other agents (20). While liposomes are based on phospholipids, making them less chemically stable and more expensive than traditional liposomes, niosomes can be made using surfactants to create niosomes, which are less expensive than traditional liposome formulations. There has been considerable research on the ability of niosomes as a delivery system for both hydrophilic and hydrophobic drug compounds, especially in terms of improving drug absorption through human skin (21). The advantages of niosomes include improved stability, slow-release properties, better penetration, and reduced side effects compared to drugs delivered via traditional routes. Additionally, niosome vesicles can be tailored to achieve specific sizes, charges, or permeabilities by formulating different surfactant blends. Despite these advantages, niosomes have some limitations (e.g., aggregation, drug release, and comparatively low penetration ability) compared to more evolved vesicular systems (22,40).

Ethosomes

Ethosomes are lipid-based carriers composed of a high percentage (20%–45%) of ethanol, phospholipids, and water (6,41). They are soft and flexible vesicles with greater deformability than traditional liposomes and niosomes, allowing them to penetrate deeper into the skin than other types of vesicles (6,23). The presence of ethanol serves two purposes: it increases the fluidity of the vesicular membrane and alters the organization of lipids in the stratum corneum, facilitating greater drug penetration through the stratum corneum (23). Ethosomes can encapsulate hydrophilic, lipophilic, and amphiphilic drugs, providing various options for topical drug delivery (6). Their unique ability to facilitate drug delivery to both the deeper skin and systemic circulation provides an advantage over traditional vesicular systems (23,24). Ethosomes have also been shown to be very effective in increasing the bioavailability of drugs, improving the therapeutic effect of drugs, and reducing the frequency of dosing for various dermatological therapies (24). These characteristics suggest that ethosomes may be an excellent and novel method for overcoming the limitations of traditional vesicular drug delivery systems.

Table 1: Comparative analysis of Liposomes, Niosomes, and Ethosomes

Parameter	Liposomes	Niosomes	Ethosomes
Composition	Phospholipids + cholesterol	Non-ionic surfactants + cholesterol	Phospholipids + high ethanol (20–45%)
Structure	Rigid bilayer vesicles	Surfactant-based vesicles	Soft, highly flexible vesicles
Skin Penetration	Limited (mainly superficial)	Moderate	High (deep skin penetration)
Mechanism	Fusion with skin lipids	Adsorption and fusion	Ethanol-induced lipid disruption + vesicle deformability
Stability	Low (oxidation prone)	High	Moderate to high
Drug Loading	Good	Good	High
Cost	High	Low	Moderate
Applications	Localized skin delivery	Controlled drug delivery	Deep dermal/transdermal delivery
Limitation	Poor penetration	Aggregation/leakage	Ethanol-related irritation (possible)

Ethosomal Drug Delivery System:

Ethosomes are advanced lipid-based vesicular carriers designed to improve dermal and transdermal drug delivery by increasing drug deposition in the skin and enhancing its permeability (6,42). The defining characteristic of ethosomes is their higher ethanol content than liposomes, which are composed of phospholipids and water (6,13). Ethosomes have a unique composition and flexible structure that allow for the efficient encapsulation and delivery of a vast array of therapeutic agents, including hydrophilic, lipophilic, and amphiphilic drugs (13).

Composition

Phospholipids, ethanol, and water provide critical components for the formation of vesicles and the performance of drugs delivered by ethosomal systems (6).

Phospholipids create the basic structure of vesicles through the formation of a bilayer and provide characteristics associated with biocompatibility and the capacity for drug encapsulation. Commonly used phospholipids include phosphatidylcholine, which may originate from natural or synthetic sources and provide stability to the vesicular system (17). Ethanol is another important component of ethosomes, usually at a concentration between 20% and 45%, and significantly contributes to the flexibility and permeability enhancement provided by ethosomal vesicles (6,19). By increasing the solubility of numerous drugs, ethanol also enhances their ability to penetrate the skin layers (19). Water acts as a dispersion medium and allows phospholipid molecules to self-assemble into vesicular structures. Additionally, depending on the chemical composition of the formulation, cholesterol or glycols may be included to help improve the stability of the vesicles and enhance their ability to retain the drug (13).

Mechanism of Formation

Ethanol and phospholipid molecules self-assemble into ethosomes in water (6). The polar head groups of phospholipid molecules interact with ethanol molecules, reducing the intermolecular forces between the phospholipids (19). This interaction increases the fluidity of the lipid bilayer, which is a very important reason for the increased permeability of ethosomes (7,19). Phospholipids are initially dissolved in ethanol, and water is then added slowly while stirring continuously, resulting in spontaneous vesicle formation (6). Ethanol reduces the packing of phospholipids, allowing them to become flexible and malleable. This increased flexibility allows ethosomes to penetrate the narrow intercellular spaces of the stratum corneum and deliver medications to the deeper layers of the skin (7).

Types of Ethosomes

Ethosomes can be broadly classified into different types based on their composition and structural modifications, including classical ethosomes, binary ethosomes, and transethosomes [5] (Fig.1).

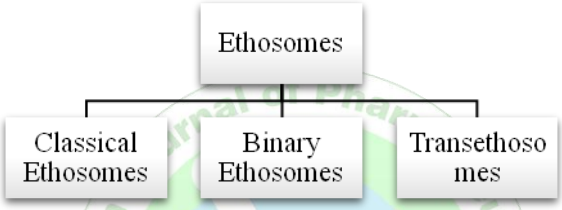

Figure 1: Types of Ethosomes

Classical ethosomes: Phospholipids, ethanol, and water compose classical ethosomes, which are regarded as the most basic type of ethosomal system (6). Owing to its high ethanol content and adjustable vesicular form, classical ethosome use has proliferated in recent years to enhance drug delivery through the skin (6,19).

Binary ethosomes: The addition of a second type of alcohol (such as propylene glycol) to ethanol in binary ethosomes provides extra flexibility to the vesicles and improves skin penetration. The presence of the second alcohol will allow for increases the drug solubility, helping to achieve better passage through the skin and improved stability compared to traditional ethosomes (5).

Transethosomes: Transethosomes, which have edge activators (surfactants) added to an ethosome based system that allows drugs to cross deeper skin layers into the bloodstream and/or systemically, have the ability to deform more easily than either an ethosome or a transferosome by having such additives present in their formulation, and thus allow for much better delivery of the drug through the skin or blood stream than either of these two previous vesicular carrier methods do (25). The combination of these two vesicular carrier methods allows these transethosomal systems to significantly clarify the use of topical and transdermal drug therapy applications (5,25).

Role of Ethanol in Penetration Enhancement:

A major contributing factor to the effectiveness of ethanol in promoting transdermal delivery of medications is its placement within ethosomal systems (6). Ethanol penetrates the lipid components of the stratum corneum, altering the barrier function of the skin, and plays a significant role in its function as a penetration enhancer (26).

Disruption of Stratum Corneum Lipids

Ethanol is a highly effective enhancer of drug permeability, primarily because it disrupts the highly ordered structure of lipids in the stratum corneum (26,27). Ethanol disrupts the lipid structure by interacting with the polar head groups of the lipids in the skin, which increases the fluidity of the lipids and decreases their packing density in the intercellular matrix (27). This disruption of the lipid structure is the primary mechanism by which the stratum corneum loses its barrier properties, allowing drug molecules to diffuse across the skin (27,28). Ethanol may also enhance permeability by extracting certain lipid components from the stratum corneum (28).

Increased Drug Solubility

Ethanol also aids drug delivery by improving the solubility of hydrophilic and hydrophobic drugs in the formulation (6). As an additional solvent, ethanol increases the thermodynamic activity of drugs, helping them pass through the skin layers. The increase in solubility and partition coefficient produces larger drug concentration gradients, which encourage the passive diffusion of the drug through the skin barrier (12).

Synergistic Effect with Phospholipids

Ethanol has a synergistic effect on phospholipids within ethosomal systems, increasing vesicle fluidity and permeability (6,19). Ethanol intercalates into the phospholipid bilayer, reducing the intermolecular

interactions between the phospholipids and creating a vesicular structure that is more fluid and deformable (19). The increased deformability of ethosomes allows them to penetrate the small intercellular spaces of the stratum corneum faster than typical vesicles (7,19). Additionally, the combined effects of lipid disruption caused by ethanol and the increased flexibility of the vesicles increase the overall efficacy of drug delivery with ethosomal systems (7).

Comparison with Other Penetration Enhancers

Compared to other chemical enhancers, such as dimethyl sulfoxide (DMSO), ethanol is regarded as a safe and reliable enhancer for penetration enhancement. While DMSO provides a very strong penetration-enhancing ability, it can cause skin irritation, toxicity, and damage to skin proteins over time at high concentrations (29,30). In comparison, ethanol is generally accepted in both pharmaceutical and cosmetic products, is well tolerated, has reversible effects on skin lipids, and has a good safety/efficacy profile (29). Therefore, ethanol is an appropriate choice for use in vesicular drug delivery systems (e.g., ethosome systems) because of its balance of safety and efficacy (6). Finally, the various ways in which ethanol exerts its many functions, such as disrupting lipids, solubilizing, and synergistically interacting with phospholipids, demonstrate that ethanol is essential for enhancing transdermal drug delivery.

Formulation and Preparation Methods:

The formulation and preparation of ethosomal systems are critical determinants of their physicochemical characteristics, stability, and drug delivery performance (6).A wide variety of methodology has been developed to make ethosomes of any size, containing desired amounts of drug, and with adequate permeation abilities (5,6). The two techniques most commonly used in the preparation of an ethosomes is the cold method and hot method (5).

Cold Method

The most popular methods for formulation of ethosomes. This method involves two different setups. First setup deals with dissolving ethanol at room temperature with phospholipid and other lipid molecules. Continuous addition of polyols like propylene glycol (PEG) where Heidolph mixer is used for vigorous stirring then heating at 30◦C in water bath. The second setup is followed by heating water at 30◦C in a different vessel. Blending of both the mixtures (from first and second setup) together and stirred for 5 mins using a covered vessel. The vesicle size of ethosomal formulation can be decreased to desirable size with the help of extrusion or sonication method. The formulation is finally refrigerated for storage.(31) Refer Fig. 2.

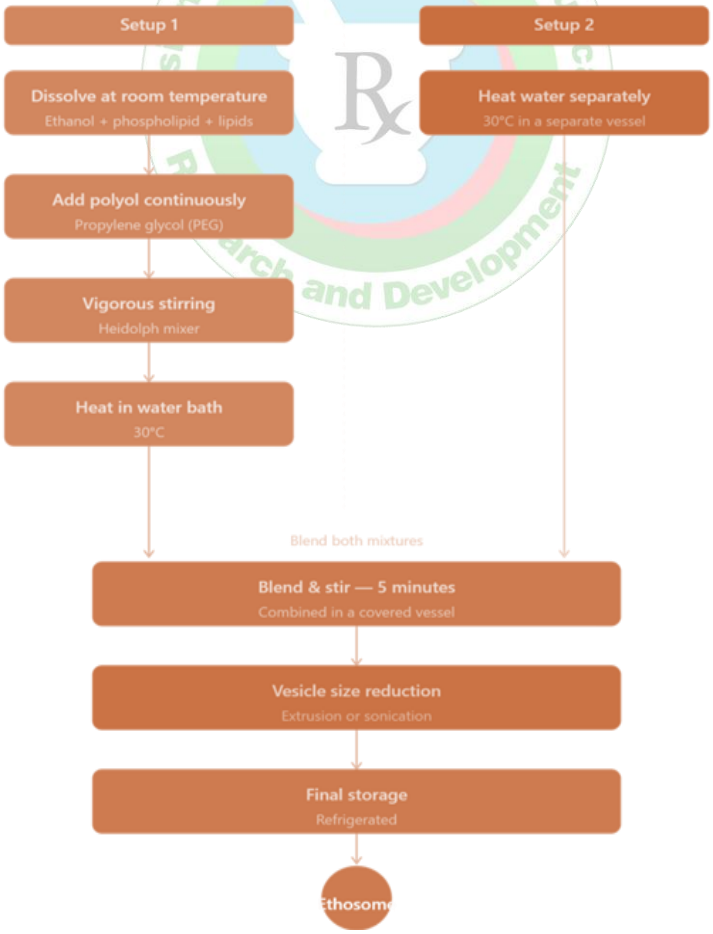

Figure 2: Ethosomes by Cold Method

Hot Method-

Phospholipid dispersed in an aqueous solution by heating at 40°C in a water bath until a colloidal dispersion was formed. Ethanol, propylene glycol and drugs were combined in another container and heated upto 40°C. Organic phase added to aqueous phase and stirred for 5 minutes. Size of ethosomal formulation was reduced to desired size after sonication (32).

Characterization of Ethosomes:

Comprehensive characterization of ethosomal systems is essential to evaluate their physicochemical properties, stability, and performance in topical and transdermal drug delivery [6]. The key characterization parameters include vesicle size, zeta potential, entrapment efficiency, morphology, in vitro drug release, and stability studies [5,6]

Vesicle Size and Zeta Potential

Vesicle size is a critical parameter that influences the penetration, distribution, and overall efficacy of ethosomal formulations [5].It is commonly measured using dynamic light scattering (DLS), which provides information on particle size distribution and polydispersity index [7].Smaller vesicles generally exhibit enhanced skin permeation due to their ability to traverse intercellular pathways in the stratum corneum [4,5].Zeta potential is an important indicator of the surface charge and stability of vesicular systems [7].A higher absolute value of zeta potential (positive or negative) indicates better stability due to electrostatic repulsion between vesicles, which reduces aggregation [5,7].

Entrapment Efficiency

Entrapment efficiency represents the percentage of drug encapsulated within the ethosomal vesicles relative to the total amount of drug used in the formulation [5].It is typically determined using techniques such as ultracentrifugation, dialysis, or filtration to separate free drug from entrapped drug [7].Higher entrapment efficiency is desirable as it enhances drug loading capacity and contributes to sustained drug release [12].Factors such as lipid concentration, ethanol content, and drug solubility significantly influence the entrapment efficiency of ethosomes [5,19].

Morphology (TEM/SEM)

The morphology and structural characteristics of ethosomal vesicles are commonly evaluated using microscopic techniques such as transmission electron microscopy (TEM) and scanning electron microscopy (SEM) [7].TEM provides detailed information about vesicle shape, size, and internal structure, often revealing spherical or slightly elongated vesicles with a bilayer configuration [7,25].SEM, on the other hand, is useful for analyzing surface morphology and vesicle aggregation behaviour [25].These techniques confirm the formation of vesicular systems and help in assessing uniformity and structural integrity [7].

In-Vitro Drug Release

In-vitro drug release studies are conducted to evaluate the release profile of the drug from ethosomal formulations over time [5].These studies are typically performed using diffusion cells, such as Franz diffusion cells, with suitable membranes to simulate skin conditions [12].Ethosomal formulations often exhibit controlled and sustained drug release compared to conventional formulations due to encapsulation within vesicles [19].The release kinetics can be analyzed using various mathematical models to understand the mechanism of drug release [12].

Stability Studies

Stability studies are essential to assess the physical and chemical stability of ethosomal formulations during storage [6].Parameters such as vesicle size, zeta potential, drug content, and entrapment efficiency are monitored over time under different storage conditions [5,19].Factors such as temperature, light, and ethanol evaporation can significantly influence the stability of ethosomes [19].Proper formulation optimization and storage conditions are required to maintain the integrity and efficacy of ethosomal systems throughout their shelf life [6].

Combination Drug Delivery Using Ethosomes:

Combination drug delivery using vesicular systems has emerged as a promising strategy to enhance therapeutic efficacy by simultaneously targeting multiple pathological pathways (33). Ethosomes, owing to their unique composition and high skin permeation capability, provide an efficient platform for the co-delivery of multiple drugs within a single carrier system (13).

Co-loading of Antiviral and Anti-inflammatory Drugs

Co-loading of antiviral and anti-inflammatory agents in ethosomal systems has gained significant attention for the treatment of dermatological conditions associated with infection and inflammation (3,13).Antiviral drugs such as Acyclovir are effective in inhibiting viral replication, while anti-inflammatory agents like Triamcinolone Acetonide help reduce inflammation, erythema, and associated symptoms (3,4).The incorporation of both drugs into a single ethosomal carrier enables synchronized delivery and improved localization at the target site (13).Ethosomal vesicles facilitate enhanced penetration of both agents into deeper skin layers, overcoming the limitations associated with conventional topical formulations (7,13).

Synergistic Therapeutic Effects

The combined delivery of antiviral and anti-inflammatory drugs offers synergistic therapeutic effects by addressing both the causative agent and the associated inflammatory response (3).Antiviral agents act by inhibiting viral DNA replication, thereby reducing viral load, while corticosteroids suppress inflammatory mediators and immune responses (4).This dual mechanism leads to faster symptom relief, reduced lesion severity, and improved patient outcomes compared to monotherapy (3,7).Furthermore, co-delivery systems can reduce the required dose of individual drugs, thereby minimizing potential side effects and improving treatment safety (7).Ethosomes enhance this synergistic effect by ensuring efficient drug penetration and sustained release at the site of action (6).

Relevance in Viral Skin Diseases

Combination ethosomal drug delivery systems are particularly relevant in the management of viral skin

infections such as Herpes Simplex and Herpes Zoster (3).These conditions are characterized by viral replication along with significant inflammation, pain, and skin lesions, necessitating a dual therapeutic approach (3,7).Topical co-delivery of antiviral and anti-inflammatory agents using ethosomes can improve drug bioavailability at the infection site and enhance therapeutic effectiveness (6).Additionally, targeted delivery to affected skin layers reduces systemic exposure and associated adverse effects (6,7).The use of ethosomal systems for combination therapy thus represents a promising approach for improving the management of complex dermatological conditions involving both infection and inflammation.

CONCLUSION:

Ethosomal drug delivery systems offer a promising advancement in topical and transdermal therapies, especially for antiviral and anti-inflammatory drugs. Their unique composition, with high ethanol content and flexible phospholipid vesicles, enhances penetration through the stratum corneum, overcoming the limitations of traditional vesicular carriers like liposomes and niosomes. This leads to improved drug entrapment efficiency, permeability, and controlled release, resulting in enhanced therapeutic efficacy and patient compliance. The ability to co-deliver antiviral and anti-inflammatory agents synergistically addresses both infection and inflammation, making ethosomes particularly effective in treating complex dermatological conditions such as Herpes Simplex and Herpes Zoster. Continued optimization in formulation and characterization techniques supports the potential of ethosomal systems as targeted, efficient, and safer alternatives to conventional topical drug delivery methods, with promising prospects for future clinical applications.

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