



ETHOSOMES: A REVIEW

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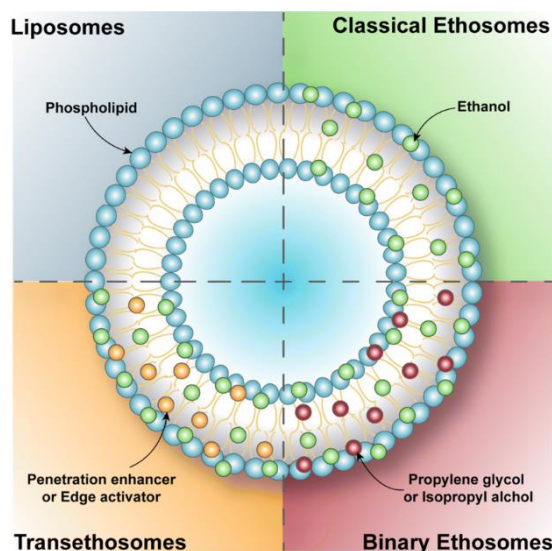
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ABSTRACT :

Ethosomes are a non-invasive delivery technology that allows medications to penetrate deeper epidermal layers and enter the systemic circulation. These flexible and pliable vesicles are specifically designed to improve the delivery of active drugs. Ethosomes' unique shape allows them to encapsulate and transport both highly lipophilic and cationic substances. Ethosomal systems, which are innovative vesicular lipid carriers with a relatively high ethanol content, are intended to carry therapeutic compounds into the deeper layers of the skin and across the skin barrier while taking into account a variety of physicochemical features. This page discusses numerous elements of ethosomes, including their merits, downsides, varieties of ethosomal systems, and uses.

Investigators have made significant progress in delivering medicine effectively into and across the skin over the years. The human body's skin generally covers a surface area of 2m² and receives approximately 33% of the total blood circulation. Clearly, the skin is the largest and most easily accessible organ, which makes it a promising route for administering medications for both localized and systemic effects. The stratum corneum (SC), which is the outer layer of the skin, is situated above the epidermis and dermis, contributing to the skin's layered structure. Interspersed among the various skin layers are fibroblasts, sweat glands, and hair follicles that originate from the dermis and its blood supply. The application of the skin for drug delivery offers numerous advantages, such as the potential to direct the active component for localized effects, avoidance of first-pass metabolism, minimized dose variability, regulated drug release, and enhanced patient adherence, given that it is a non-invasive method. The stratum corneum, which is the outermost layer of the skin, is particularly effective in limiting the penetration of drugs into the epidermis because it comprises insoluble keratin bundles that are stabilized by cross-linked proteins and covalently bonded lipids, thus restricting the drug's transdermal bioavailability.

To enable the transfer of drug molecules with differing physicochemical properties to penetrate the deeper layers of the skin and enter systemic circulation, it is essential to utilize specific carriers that can navigate the natural skin barrier. Recently, innovative lipid vesicles have been developed to tackle the challenge of delivering medications to and through the stratum corneum (SC). Initially, liposomes were designed for topical drug delivery. Since that time, a variety of advanced vesicular systems based on lipids have been introduced. New lipid vesicles, including transferosomes, ethosomes, and binary ethosomes, have been developed to overcome the limitations of traditional liposomes in terms of drug permeability through various layers of the skin.



Advantage of ethosome

1. Ethosomes improve the absorption of drugs through the skin for dermal, transdermal, and intracellular delivery.

2. They can transport a variety of molecules with different physicochemical characteristics, including both hydrophilic and lipophilic substances, peptides, proteins, and other large molecules.
3. The constituents of ethosomes are typically considered safe (GRAS), non-toxic, and authorized for use in pharmaceuticals and cosmetics.
4. With a low-risk profile, the ethosomal structure poses no significant drug development concerns, as the toxicological characteristics of ethosomes are well-documented in scientific research.
5. The ethosomal delivery system is passive and non-invasive, making it ready for immediate market launch.
6. Ethosomal drug delivery systems have broad applications across the Pharmaceutical, Biotechnology, Veterinary, Cosmetic, and Nutraceutical industries.
7. High patient adherence is achieved as the ethosomal formulation is offered in a semi-solid state (gel or cream), leading to enhanced compliance.
9. It is evident that drugs have higher entrapment efficiencies than liposomes.
10. Outstanding stability over extended periods of time is evident.
11. Since alcohol in ethosomes serves as a natural preservative, no additional preservative is needed.
12. Ethosomes are incredibly inexpensive to manufacture.
13. Drugs do not depend on concentration to be transported through the skin.

Disadvantage of ethosome

1. If patients are allergic to ethanol or any of the components found in ethosomes, an allergic reaction can be identified.
2. Ethosomal carriers are specifically intended for transdermal applications, as opposed to other carriers like solid lipid nanoparticles and polymeric nanoparticles, which can be used for a variety of delivery routes.
3. Because ethanol is flammable, it is critical to use caution during the planning, application, transportation, and storage operations.
4. The yield is particularly low, which may make it economically untenable.
5. There is a risk of product loss when moving from organic solvents to aqueous media.
6. This approach is limited to powerful chemicals requiring a daily dosage, whether long or short.
7. Ethosomal administration is not meant for quick drug delivery in bolus form; rather, it is designed to enhance the medication's gradual and continuous release.
8. The medicine must be sufficiently soluble in both lipophilic and aqueous conditions to ensure dermal microcirculation and access to systemic circulation.
9. The drug's molecular size must allow for adequate percutaneous absorption.
10. Adhesives may not provide appropriate adhesion for all skin types.
11. The use of excipients and penetration enhancers in medication delivery systems might cause skin irritation or dermatitis.

Methods of Preparation

The creation of ethosomes is based on simple and efficient scaling approaches that do not require the use of sophisticated pilot or industrial equipment. The procedure of manufacturing ethosomes incorporates two simple methods: the "cold" and the "hot" method.

Cold Method

This approach is one of the most used for preparing ethosomes, with two basic and simple setups. In the first setup, phospholipids and other lipid components are dissolved by vigorous stirring in ethanol at room temperature with a mixer such as the Heidolph mixer, while polyols such as propylene glycol are added continually. This operation is carried out with steady stirring, followed by heating to 30 °C in a water bath. In the following setting, water is heated to 30°C in a separate container, and the mixes from the previous setups are combined, followed by five minutes of stirring in a covered vessel. The vesicle size of the ethosomal formulation can then be decreased to the required extent via sonication or extrusion procedures.

Hot method

The hot approach includes dispersing phospholipids in water by heating it in a water bath at 40 degrees Celsius until a colloidal solution is created.

In a separate container, a mixture of ethanol and propylene glycol is made and heated to the same 40 °C.

When the temperature of both combinations exceeds 40 °C, the aqueous and organic phases merge. Depending on whether the medicine is hydrophilic or hydrophobic, it is dissolved in water or ethanol.

The size of the ethosomal formulation vesicles can be decreased to the desired level via probing sonication or an extrusion procedure

Classical Mechanical Dispersion Technique

Phospholipid is dissolved in an organic solvent or a combination of organic solvents in a round bottom flask (RBF). Above the lipid transition temperature, a rotary vacuum evaporator is used to remove the organic solvent, leaving a thin lipid film on the RBF's walls. To guarantee that any remaining solvent is removed from the lipid coating, place the flask under vacuum overnight. The lipid layer is then hydrated with the drug's hydroethanol solution, with

the flask spun and optionally exposed to periodic sonication at the suitable temperature. The resulting ethosomal suspension is then cooled to room temperature and stored in a refrigerator.

Ethanol Injection and Sonication Technique

This approach involves injecting the phospholipid dissolved in ethanol into the aqueous phase using a syringe device at a flow rate of 38 µl/min. Following injection, the mixture is homogenized for five minutes with an ultrasonic probe.

Types of ethosomes

Ethosomal systems include ,

classical ethosomes.

Classical ethosomes are an alternative to regular liposomes, including phospholipids, water, and a significant amount of ethanol, up to 45% w/w. In terms of transdermal drug administration, classical ethosomes outperform typical liposomes due to their smaller size, negative charge, and improved entrapment efficiency.

Binary ethosomes

Zhou et al. first suggested the concept of binary ethosomes in 2010. These systems are generated by combining a new type of alcohol and standard ethosomes. Propylene glycol (PG) and isopropyl alcohol (IPA) are the most frequent alcohols employed in the production of binary ethosomes

Transethosomes

Song et al. initially described transethosomes, a unique category of ethosomal systems, in 2012. This technique adds a surfactant or penetration enhancer to the fundamental ingredients of traditional ethosomes. Transethosomes were developed with the goal of combining the benefits of regular ethosomes and deformable liposomes (transferosomes) into a single formulation. Numerous investigations have shown that transethosomes have better qualities than standard ethosomes

Application

1. Several studies have shown that ethosomes can effectively heal viral and microbial skin illnesses. Animal models were used to investigate the efficacy of the bacitracin and erythromycin ethosomal systems in treating deep skin infections.
2. Ammonium glycyrrhizinate ethosomes have been shown to reduce inflammation in human skin.
3. In vivo studies on rabbits demonstrated that ethosomal patches effectively address androgen deficiency in males and alleviate menopausal symptoms in females, resulting in positive outcomes.
4. Research suggests that ethosomes have analgesic and antipyretic characteristics and can treat erectile dysfunction.
5. Recent research suggests that ethosomes can carry DNA molecules to skin cells, allowing for expression.

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