WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review on Ethosomes as A Pharmaceuticals Delivery System

[1]Mr. Aniket Ashokrao Bhosale, [2] Mr. Gaikwad T. A.

[1]Student L. N. B. C. Institute of Pharmacy, Satara

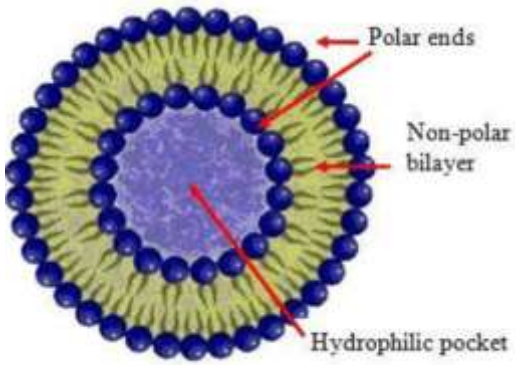
[2] Asst. Professor L.N.B.C. Institute of Pharmaacy, Satara

A B S T R A C T

Drugs are typically administered orally, which has many advantages, including easy administration, but disadvantages, including low bioavailability and a tendency to cause rapid spikes in blood levels, necessitate higher doses or repeated dosing, both of which are challenging for patients and expensive, as well. Given all these drawbacks, novel drug delivery technologies with improved therapeutic efficacy and safety and controlled distribution are required to reduce the size and number of doses. This can be achieved by transdermal delivery which possesses several advantages such as avoids first-pass metabolism, eliminates gastrointestinal irritation reduces frequency of dosing, and rapid termination of drug action. Skin serves as a significant target and a key barrier

Introduction

The body's largest and most accessible organ, the skin, can be used as a potential medication delivery route for systemic effects. The skin is a multilayered, external organ that serves as both a permeability barrier and a protective tissue, keeping outside molecules from entering the body. represents the skin's thickest and most impermeable barrier to drug penetration, limiting transdermal medication bioavailability. Thus, special carriers are needed to get through the skin's natural barrier and transport medication molecules with different physicochemical qualities to the bloodstream. Because they are non-invasive and self-administered, transdermal drug delivery systems have various advantages, including preventing first pass liver absorption, controlled drug delivery, shorter dose duration, and more patient complianceand the main route for the liposomes' transportation is through hair follicles. Ethosomes differ from traditional liposomes, transfersomes, and other lipid dispersions in terms of their structure, method of use, and mode of action. Ethosomes have demonstrated excellent efficacy in percutaneous drug delivery, as a lipid carrier. They also have superior pharmaceutical properties, including room temperature stability, high trap performance, and enhanced compatibility with the SC, thus facilitating the penetration of both hydrophilic and lipophilic drugs through the stratum corneum (SC) into the skin's deep layers more effectively than typical liposoms. It's critical to comprehend how ethanol and lipid concentrations in ethosomes affect the skin. According to evidence, the formulation's use of ethanol facilitated drug solubilization and produced malleable lipid structures that could easily travel through skin corneocytes, improving medication skin retention and permeation. Yet, it is still unclear how ethosomes assist transdermal penetration and what impact they have on the skin. Attenuated total Reflectance, Fourier Transform Infrared Spectroscopy (ATR-FTIR), Confocal Laser Scanning Microscopy, Differential Scanning Calorimeter (DSC), Raman, Scanning Electronic Microscopy (SEM), Transmission Electron Microscopy (TEM), X-ray Photoelectron Spectroscopy (XPS), and Electron Spin Resonance are the main methods used to study the transdermal process at the (ESR). These methods made it easier to research the transdermal system. It has been noted that by maintaining a constant concentration of phospholipids, the size of the ethosomes shrinks as the amount of ethanol increases. The presence of ethanol in ethosome also endows its surface with a negative charge, enhancing colloidal security. However, in contrast to liposomes, ethosomes exhibit higher hydrophilic/ionized drug spillage due to disruption of the phospholipid bilayer's tight seal by the presence of a high ethanol concentration. Extreme arrival of collected material and skin irritation are caused by ethanolosomes with ethanol convergence levels of 30%. Ethosomes are elastic nanovesicles made of phospholipids with a high ethanol concentration (20–45%). As a successful permeation enhancer, ethanol has been planned to be added to the vesicular framework to create the flexible nano-vesicles. There were made ethosomes.



ETHOSOMAL SYSTEM TYPES

1. Classical ethosomes

Traditional ethosomes, which differ from traditional liposomes in that they include water, phospholipids, and high ethanol concentrations of up to 45% w/w. It was claimed that traditional ethosomes were superior to traditional liposomes for transdermal medication distribution since they were smaller and had a negative potential for increased efficiency without clogging. Furthermore, classical ethosomes showed superior skin penetration and stability profiles compared to classical liposomes. Drugs collected in conventional ethosomes had molecular weights ranging from 130.077 Da to 24 kda.

2. Binary ethosomes

Zhou et al. introduced binary ethosomes. We were basically made by combining a novel type of alcohol with the traditional ethosomes. The two ethosomes that are most frequently utilised in binary alcohols are propylene glycol (PG) and isopropyl alcohol (IPA).

3. Transethosomes

The most recent ethosomal systems are known as transethosomes, and Song et al. first identified them in 2012. This ethosomal system combines the fundamental elements of conventional ethosomes with an extra substance, such as a surfactant or penetration enhancer, in its composition. These new vesicles were created in an effort to construct transethosomes by combining the benefits of traditional ethosomes with deformable liposomes (transfersomes). Many studies have found that transethosomes have better qualities than conventional ethosomes. In order to develop more distinctive ethosomal systems, several edge activators and penetration enhancers were researched. There have been reports of pharmaceuticals being captured by transethosomes with molecular weights ranging from 200-325 kda to 130.077 Da.

COMPOSITION OF ETHOSOMES

1. Ethanol

An effective penetration booster is ethanol. By delivering the vesicles unique dimensional features, including size, potential, stability, clog avoidance, and improved skin permeability, it plays a significant role in ethosomal systems. There have been reports of ethanol concentrations in ethosomal systems ranging from 10% to 50%. Several studies came to the conclusion that the size of the ethosomes would shrink when the ethanol concentration was raised. The bilayer would become leaky if the ethanol concentration was raised over the optimal level, which would result in a slight increase in vesicular size and a large loss in the effectiveness of trapping. It would also solubilize the vesicles by increasing the ethanol concentration. Vesicular load is a significant factor that can have an impact on vesicular characteristics including stability and skin vesicle contact.

2. Phospholipids

The ethosomal scheme was created using phospholipids from several sources. While creating an ethosomal system, choosing the right phospholipid type and concentration is crucial since it will affect the scale, the efficiency of the trapping, potential vesicular properties, stability, and penetration. DPPG (1,2-dipalmitoyl sn-glycero-3-phosphatidylglycerol) was added to the ethosomal formulation to create highly negatively charged vesicles, whereas DOTAP or another cationic lipid was used to create cationic ethosomal vesicles (1,2- dioleoyl-3- trimethylammonium-propane [chloride salt]). Phospholipid concentrations in an ethosomal formulation typically vary from 0.5% to 5%. A rise in phospholipid concentration may cause a slight to moderate increase in vesicular size, but it will significantly enhance the efficacy of trapping. Yet, the partnership is only lasting till a specific.

3. Cholesterol

As cholesterol is a steroid molecule that is stable, its incorporation into ethosomal structures improves the stability and clogging efficiency of medications. This prevents leaking, lowers the vesicle's permeability, and prevents fusing of the vesicles. In most formulations, it is employed at a concentration of 3%, although in some, it has been utilised up to 70% of the formulation's total phospholipid concentration. According to numerous studies, cholesterol causes ethosomal systems' vesicular size to expand

4. Dicetyl phosphate

To prevent vesicle aggregation and to increase formulation stability, dicetyl phosphate is frequently utilised. In the ethosomal formulation, it is employed in quantities ranging from 8% to 20% of the total phospholipid concentration. The effects of dicetyl phosphate on other ethosomal system characteristics, however, are still unknown.

5. Stearylamine

An agent with a positive charge is stearylamine. Stearylamine was added to the ethosomal formulation, which significantly increased vesicular size and reduced entrapment. As stearylamine has a lower molecular weight than skin, it can easily enter skin (296.5 Da).

various alcohols In addition to ethanol, other alcohols including PG and IPA are also employed to create binary ethosomes. efficiency and a switch from a negative to a positive -potential charge that caused the vesicles to aggregate in a week.

6. Propylene glycol

A common penetration enhancer is PG. It has been discovered that this affects the ethosomal features of size, trapping capacity, permeability, and stability when utilised at concentrations between 5% and 20% in the creation of binary ethosomes. Particle size will be reduced more in ethosomal systems with PG integration than in systems without PG. Particle size was significantly reduced from 103.70.9 nm to 76.30.5 nm when the PG concentration was increased from 0% to 20% v/v. It is hypothesised that PG increases viscosity and antihydrolysis property to improve ethosome stability.

7. Isopropyl alcohol

The effect of IPA on the effectiveness of entrapment and skin permeation of an ethosomal system loaded with diclofenac was investigated by Dave et al. Three different formulations have been created: binary ethosomes, which include roughly 20% IPA and 20% ethanol, and a vesicular system, which contains 40% IPA. Classical ethosomes have 40% ethanol. The trapping efficiency of the vesicular device containing 40% IPA was found to be higher (95%) than that of the binary ethosomes (83.8%).

MECHANISM OF PENETRATION

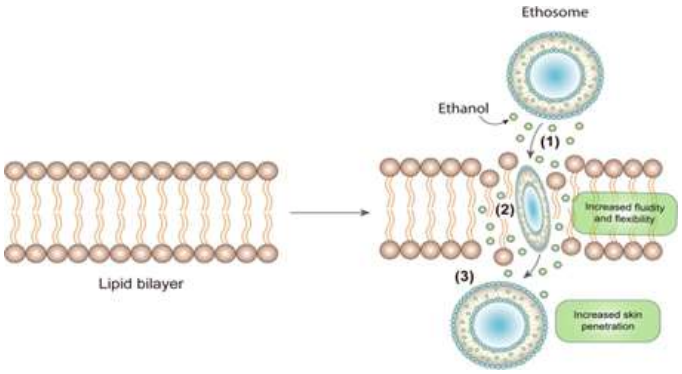
Although the precise method of ethosomal drug administration is still up for question, a number of processes most likely work together to produce the desired effect. The stratum corneum lipid multilayer is densely packed and firmly conformationally organised at physiological temperature. Ethosomes are unique due to the high ethanol concentration because ethanol causes the skin's lipid bilayers to become disorganised. As a result, when ethanol is absorbed into a vesicle membrane, vesicles can pass through the stratum corneum. Due to the high ethanol concentration, the lipid membrane is also less compactly packed than conventional vesicles but is still stable, allowing for a more malicious form that allows it to fit through narrow passages like those made to rupture the corneum lipid stratum. Interactions between ethanol

1. **Ethanol Effect:**

Alcohol acts as a penetration booster via the skin. Its increasing effect on penetration has a well-known mechanism. Ethanol permeates intercellular lipids, increasing their fluidity and decreasing the density of the cell membrane's multilayer of lipids.

2. **Ethosomes Effect:**

The ethosomal ethanol increases the lipid fluidity in the cell membrane, which increases the skin's permeability. Hence, the ethosomes rapidly enter the deep layers of the skin where they have merged with skin lipids and release the medications into the blood's deep layer. The ethosomes' penetration mechanism is described.



CHARACTERIZATION EVALUATION OF ETHOSOMES

Skin-vesicle interaction research various imaging techniques, for instance, to evaluate how ethosomal formulations better penetrate the skin. Fluorescence microscopy, laser microscopy (CSLM) confocal scanning, eosin hematoxyl staining, and transmission electron microscopy were employed. When combined, these imaging techniques also improved comprehension of how the structure and vesicle penetration paths are modulated. Traditional liposomes could only penetrate to the stratum corneum, the top layer of skin. Liposomes free of alcohol had almost no deep penetration. Comparatively, the ethosomal carrier was used to spot deeper and more of 6-CF and Rhodamine 123's dispersion (dermis-layer).

1. **Filter membrane-vesicle interaction study by scanning Electron microscopy**

In order to do this, filter membranes with 50 nm pore sizes must be placed in diffusion cells along with 0.2 ml of vesicle solution. The filter's lower side came into contact with phosphate buffer saline solution, while the upper side was exposed to the air (having pH6.5). The filters were taken out after an hour, fixed in Karnovsky's fixative overnight at 4°C, and then dehydrated using ethanol solutions with varying concentrations (30%, 50%, 70%, 90%, 95%, and 100% v/v in water). The filters were then ready for SEM examinations.

2. Skin permeation studies

With a pair of scissors and a knife, the abdominal skin of test animals (rats) was meticulously peeled from the underlying connective tissue. The excised skin was placed on aluminium foil, and the dermal side of the skin was gently peeled off to remove any clinging fat and/or subcutaneous tissue. The volume permeation areas of the effective difusion cell and receptor cell were 1.0 cm2 and 10 ml, respectively. It was maintained at 32 °C, plus or minus 1 °C. The receptor compartment contained a phosphate buffered saline solution (10 ml pH 6.5). Between the donor and the receptor compartment, it sandwiched removed skin. Ethosomal formulation was applied to the skin's epidermal layer (1.0 ml). 0.5 ml of samples were collected at 1, Using the diffusion cell's sampling port, samples were taken at 2, 4, 8, 12, 16, 20 and 24 hour intervals and subjected to a high performance liquid chromatography test for analysis.

3. Stability study

The vesicles were maintained at 4 °C 0.5 °C in order to gauge their stability. After 180 days, the vesicle size, zeta potential, and trapping effectiveness were calculated using the aforementioned method.

4. Drug uptake studies

In 24-well plates (Corning Inc.) with 100 l RPMI medium applied, drug absorption into MT-2 cells (1,1106 cells / ml) occurred. Cells were treated with 100 l of the drug solution in phosphate buffer saline solution (pH 7.4), ethosomal formulation, or marketed formulation. Following this, drug absorption was measured using HPLC test analysis of the drug material..

5. HPLC assay

During in vitro skin permeation experiments and in MT-2 cell, the amount of drug permeated in the receptor compartment was determined by HPLC assay using methanol: distilled water: acetonitrile mixture (70:20:10 v / v) as a mobile step.

6. Statistical analysis

The statistical significance of all the produced data was evaluated using ANOVA followed by studenized range testing. Using the PRISM program, a confidence limit of P.

APPLICATIONS OF ETHOSOMES

Ethosomes, the high ethanol derived vesicles are capable of penetrating deeper layers of the skin and thus tend to be vesicles of choice for transdermal drug delivery via the skin of hydrophilic and impermeable drugs.

Hormone delivery

Many problems with oral hormone distribution include high first-pass metabolism, limited oral bioavailability, and a wide range of dose-dependent adverse effects. Moreover, oral hormonal preparations that strongly rely on patient adherence to these adverse effects. Every medication missed is known to increase the probability of treatment failure. By comparing the transdermal delivery of testosterone-loaded ethosomes (Testosome) to the transdermal delivery of testosterone patch (Testoderm patch, Alza) through rabbit pinna skin, Touitou et al. revealed the ability of ethosomes in hormonal delivery. They found that the ethosomal formulation showed approximately 30-times higher skin permeation of testosterone. The volume of medicine deposited for the ethosomal formulation was significantly (p50.05) greater (130.76 18.14 and 18.32 4.05 mg at the end of 7 hours for Testosome and Testoderm, respectively). Respectively. After applying Test some instead of Testoderm, the area under the curve (AUC) and Cmax of testosterone considerably increased. As a result, research conducted both in vitro and in vivo have revealed improved testosterone bioavailability and skin permeability from ethosomal formulation..

Transcellular delivery

Ethosomes have been shown to be an effective penetration enhancer and carrier device for the transcellular delivery of various therapeutic agents in active clinical trials. In contrast, almost no fluorescence was observed when integrated in a hydroethanolic solution or classic liposomes. After 3 min of incubation, the intracellular existence of each of the three tested probes was evident.

Pilosebaceous targeting

There is growing awareness of the potential importance of sebaceous glands and hair follicles for percutaneous medication delivery. The utilisation of pilosebaceous units as depots for targeted therapy, notably for the treatment of follicle-related diseases like acne or alopecia, has attracted interest. The use of the follicles as transportation shunts for systemic drug administration has also received a lot of attention.

ADVANTAGES OF ETHOSOMES:

1. Ethosomes improve medication transport for dermal, transdermal, and intracellular use through skin.
2. Provide a variety of molecules, including peptides, proteins, and other macromolecules, as well as hydrophilic and lipophilic compounds.

3. The ethosomes' constituent parts have received approval for usage in pharmaceutical and cosmetic products, are non-toxic, and are generally recognised as safe (GRAS).
4. Low risk profile: Because the toxicological profiles of ethosome features are well documented in the scientific literature, there is no danger associated with the large-scale drug development of ethosome structures.
5. The ethosomal system may be immediately marketed because it is passive and non-intrusive.
6. The pharmaceutical, biotechnology, veterinary, cosmetic, and nutraceutical industries can all benefit from ethosomal drug delivery systems.
7. Good patient compliance: The semi-solid gel or cream form in which the ethosomal medication is administered results in high patient compliance.
8. A straightforward drug delivery approach as opposed to sonophoresis, iontophoresis, and other complex procedures.
9. Simplicity of industrial scale-up: Ethosome production is quite straightforward and doesn't require expensive technical inputs. It is simple to prepare multiliter quantities for ethosomal formulation.
10. Ethosomes improve the efficient passage of medications across or through the skin, allowing the drug to reach the targeted area of the skin or the blood.

DISADVANTAGES OF ETHOSOMES:

1. 1.If a patient is allergic to ethanol or any of the ethosomal components, an allergic reaction can be detected.
2. Ethosomal carriers are relevant solely for transdermal application, in contrast to other carriers (solid lipid nanoparticles, polymeric nanoparticles, etc.) that can be employed for numerous routes.
3. Because ethanol is flammable, proper precautions should be used when applying, transporting, and storing it.
4. Extremely low yield, possibly not economically viable.
5. Product loss when switching from organic to water media.
6. It is only allowed for powerful compounds that need a lengthy or short daily dose.
7. Ethosomal administration is normally designed to give constant, sustained drug delivery, not fast drug input in the form of a bolus.

CONCLUSION

In contrast to the skin permeability demonstrated by liposomes, vesicular research for topical distribution has gained new insight thanks to ethosomes. Drugs used to treat androgenic alopecia and male pattern hair loss may be transported over the scalp via ethosomes. Even though the mechanism of action is mostly unclear, drugs like finasteride and minoxidil can be investigated for topical administrations using ethosome to avoid the negative effects of the standard dosage form. Even though the US FDA has not approved dutasteride, the 5 alpha-reductase enzyme inhibitor, the androgen receptor antagonists spironolactone and cyproterone acetate, and the prostaglandin analogue latanoprost for treating male pattern baldness, these compounds can still be investigated using ethosomes as carriers at the institutional level. By blocking the enzyme 5'-reductase, Phyllanthus niruri extracts (petroleum ether) have shown encouraging outcomes in an animal model for the treatment of testosterone-induced alopecia. The ethanolic extracts of the rhizomes of Zingiber officianalis and the seed extracts of Croton tiglum, both purified by the sodhana process using milk, were used in an equal ratio for topical administration as a paste to treat alopecia areata. For the creation of topical formulations to treat male pattern baldness, ethosomes containing pharmaceuticals or herbal substances might be thoroughly researched. Proteins, cationic medicines, peptides, and hydrophilic pharmaceuticals can also be enclosed in ethosomes.