



ETHOSOMES AND ITS APPLICATION: A REVIEW

Keshav Kumar Gupta

Professor, Buddha Institute of Pharmacy, GIDA, Gorakhpur, UP, India-273209. Email: kesumpharm120185@gmail.com

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Keshav Kumar Gupta

Professor, Buddha Institute of Pharmacy, GIDA, Gorakhpur, UP, India-273209.

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ABSTRACT

Ethosomes have been extensively studied since their first development in 1996; different kinds of ethosomal systems have been produced as a result of the addition of new substances to their original composition. A number of different preparation techniques are used to create these novel carriers. Ethosomal dispersions are used in gels, patches, and creams to provide stability and convenience of use. To evaluate their efficacy in dermal/transdermal dispersion, a variety of in vivo models are used in addition to clinical trials. This paper provides a detailed assessment of the effects of ethosomal system components, preparation methods, and their significant roles in determining the final properties of these nanocarriers. Furthermore, new pharmacological dose formulations for ethosomal gels, patches, and creams are highlighted. The study also provides thorough information on the clinical trials and in vivo studies conducted to evaluate these vesicular systems.

Keywords; Ethosomes, Transdermal, lipid vesicular carriers, Lipid-based vesicles,

INTRODUCTION

Drugs with systemic effects can be administered through the skin, which is the largest and most accessible organ in the body. The strongest barrier to drug penetration via the skin is the stratum corneum, the outermost layer of the skin, which limits the transdermal bioavailability of pharmaceuticals. (1,2) As a result, special carriers are required to penetrate the natural barrier of the skin and deliver drug molecules with different physicochemical properties into the bloodstream. Transdermal drug administration methods have a number of advantages due to their noninvasiveness and self-administerability, such as avoiding the liver's first-pass metabolism, controlled drug distribution, reduced dose intervals, and improved patient compliance. The first transdermal patch containing scopolamine for the treatment of motion sickness was approved in the US in 1979.^(1,2) "Ethanolic liposomes are ethosomes." Ethosomes are noninvasive delivery vehicles that allow medications to enter the systemic circulation or deeply penetrate the skin's layers. These are pliable, squishy vesicles designed to improve the distribution of active ingredients. For many years, the significance of vesicles in particle transportation and cellular communication has been widely acknowledged.⁽³⁾ Vesicles would also make it possible to regulate the drug's release rate over a longer period of time. preventing the medication from being attacked by the immune system or other clearance mechanisms so that it can release the ideal quantity of medication and maintain that level for extended periods of time.⁽⁴⁾ The discovery of an ethosome, a vesicle derivative, was one of the most significant developments in vesicle research. The well-known liposome drug carrier has been slightly modified to create ethosomes. Ethosomes are lipid vesicles that include water, phospholipids, and relatively high concentrations of alcohol (ethanol and isopropyl alcohol). Soft vesicles called ethosomes are composed of phospholipids, water, and ethanol (in larger amounts). Ethosomes range in size from tens of nanometers (nm) to microns (μ). They have a substantially higher transdermal flux and penetrate the skin layers more quickly.^(5,6)

ADVANTAGES OF ETHOSOMAL DRUG DELIVERY^(7,8)

1. Delivery of large molecules (peptides, protein molecules) is possible.
2. It contains non-toxic raw material in formulation.
3. Enhanced permeation of drug through skin for transdermal drug delivery.

4. Ethosomal drug delivery system can be applied widely in Pharmaceutical, Veterinary, Cosmetic fields.
5. High patient compliance: The ethosomal drug is administered in semisolid form (gel or cream) hence producing high patient compliance.
6. Simple method for drug delivery in comparison to Iontophoresis and Phonophoresis and other complicated methods.
7. The Ethosomal system is passive, non-invasive and is available for immediate commercialization.

DISADVANTAGES OF ETHOSOMAL DRUG DELIVERY^(8,9)

They required High blood levels cannot be administered – limited only to potent molecules, those requiring a daily dose of 10mg or less.

1. Ethosomal administration is not a means to achieve rapid bolus type drug input, rather it usually designed to offer slow, sustained drug delivery.
2. Adequate solubility of the drug in both lipophilic and aqueous environments to reach dermal microcirculation and gain access to the systemic circulation.
3. The molecular size of the drug should be reasonable that it should be absorbed percutaneously
4. Adhesive may not adhere well to all types of skin.
5. May not be economical.
6. Poor yield.
7. Skin irritation or dermatitis due to excipients and enhancers of drug delivery systems.
8. In case if shell locking is ineffective then the ethosomes may coalesce and fall apart on transfer into water.
9. Loss of product during transfer from organic to water media.
10. The main advantage of ethosomes over liposomes is the increased permeation of the drug

METHOD OF PREPARATION

1. Hot method

This process involves dispersing the phospholipid in water by heating it to 400 °C in a water bath until a colloidal arrangement is achieved. Accurately combine the ethanol and propylene glycol in a separate vessel and heat to 400 °C. Next, incorporate the organic phase into the aqueous phase. Now, depending on the drug's solvent, dissolve the active ingredient in either ethanol or water. Either the probe sonication technique or the extrusion approach can be used to shrink the size of the ethosome vesicle to the necessary degree. Depending on whether the medication is hydrophobic or hydrophilic, it is diluted with either ethanol or water. Once the vesicles are prepared, they are either sonicated or extruded to the required size.^(10,11)

2. Cold Method

The cold approach is the most popular and straightforward way to create ethosomes. Dissolve the medication, phospholipid, and remaining lipid components in ethanol in a covered vessel at room temperature while stirring briskly. Next, add another polyol, such as propylene glycol, while the mixture is stirring. In a water bath, the mixture is heated to 300 C. After heating the water to 300 degrees Celsius in a different pot, it is added to the mixture and mixed. The combination should then be covered and left for five minutes. Using the sonication or extrusion methods, the ethosomal formulation's vesicle size might be decreased to the necessary degree. The formulation should ultimately be kept refrigerated.^(12,13)

3. Classic Mechanical Dispersion Method

Soya phosphatidylcholine is dissolved in a 3:1 chloroform:ethanol mixture in a round-bottom flask. Thin lipid coatings occur on the flask wall as a result of the organic solvents being evaporated using a rotating vacuum evaporator at temperatures higher than the lipid transition temperature. Ultimately, remnants of the solvent mixture are extracted from the formed lipid coating by vacuuming the contents for a whole night. The process of hydrating involves turning the flask at the appropriate temperature and adding different amounts of the drug-containing hydroethanolic mixture.⁽¹⁴⁾

CHARACTERIZATION OF ETHOSOMES

Physical Characterization: Ethosomes can be physically described using software called Motic Image Plus. Determining whether or not the ethosomes have been generated is a cost-effective procedure. It is also possible to evaluate the formulation's primary particle size. Malvern Zetasizer ought to be utilised for additional analysis and appropriate sizing.⁽¹⁵⁾

Visualization: Ethosomes can be visualised using scanning electron microscopy (SEM) and transmission electron microscopy (TEM) (SEM). The vesicular form of the ethosome preparation is assessed with a Transmission Electron Microscope (TEM). The samples are dried on a grid covered in carbon before being negatively stained with phosphotungstic

acidic watery mixture. After drying, a 100 Kv accelerating voltage is used to examine the specimen under a microscope at 10-100 k foldenlargements. In order to assess the magnitude and

shape of the vesicles SEM, or scanning electron microscopy, is employed. One drop of ethosomal suspension is affixed to a clear glass stub. After air drying and gold coating with sodium aurothiomalate, it is inspected under a 10,000 magnification scanning electron microscope.⁽¹⁶⁾

Vesicle size and Zeta potential: Photon correlation spectroscopy and the dynamic light scattering system are used to determine the particle size and zeta potential of ethosomes.⁽¹⁷⁾

Entrapment Efficiency: The efficacy of ethosomal vesicles' entrapment can be assessed using the centrifugation method. The vesicles were separated in a high-speed cooling centrifuge set at 4°C for 90 minutes at 20,000 rpm. The amount of medication in the sediment can be determined by lysing the vesicles with methanol and separating the sediment and supernatant liquids.

Transition Temperature: Using differential scanning calorimetry (DSC), one may determine the vesicular lipid systems' transition temperature.⁽¹⁸⁾

Surface Tension Activity Measurement: The ring method in a Du Nouy ring tensiometer can be used to determine the surface tension activity of a medication in aqueous solution⁽¹⁹⁾

Vesicle Stability: Vesicles' stability can be evaluated over time by analysing their size and shape. Mean size is measured by DLS, and structural alterations are examined by TEM.⁽²⁰⁾

Drug Content: The amount of medication in ethosomes can be ascertained using a UV spectrophotometer. To quantify this, an altered high-performance liquid chromatographic technique can also be utilised.⁽²¹⁾

Penetration and Permeation Studies: Using confocal laser scanning microscopy (CLSM), one may determine how deeply ethosomes penetrate an object.^(22,23)

APPLICATION OF ETHOSOMES

There are numerous uses for enzymatic phagosomes in medication delivery. Most frequently, ethosomes are used in place of liposomes. The more favoured method of medicine delivery is transdermal. Transdermal delivery of hydrophilic and impermeable medications is possible with the use of ethosomes. Many medications have been used with ethosomal carriers.⁽²⁴⁾

Transcellular delivery

Ethosomes seem to be a feasible substitute for anti-HIV drugs that are marketed commercially. Drug action is thereby prolonged, drug toxicity is decreased, and transdermal flux is enhanced.

Ethosomes are used in pilosebaceous targeting

Targeted medication therapy has been utilised to treat follicle-related diseases such as alopecia and acne with pigoosilinous units. Minoxidil, a lipid-soluble medication used to treat baldness, can be used for piperebaceous targeting for increased clinical efficacy because it accumulates two to seven times greater in the skin of nude mice.^(25,26)

Transdermal delivery of hormones

Issues with oral hormone therapy include poor oral bioavailability, high first-pass metabolism, and a host of other dose-dependent side effects. Every medication is expected to raise the probability of treatment failure.⁽²⁷⁾

Ethosomal system for Menopausal syndromes

The effectiveness of ethosomal compositions in treating menopausal symptoms in women and androgen insufficiency in males has been assessed. A testosterone ethosomalpatch system is used to treat males who are androgen deficient.⁽²⁸⁾

Delivery of anti arthritis drug

For prolonged, targeted drug delivery to the targeted location, topical anti-arthritis medication administration is a preferable option.⁽²⁹⁾

Delivery of problematic drug molecules

Transdermal distribution is a preferable method since large biogenic molecules, such as proteins or peptides, as well as insulin, are completely broken down in the gastrointestinal tract and are therefore difficult to transfer orally. Nevertheless, the penetration of conventional transdermal formulations of biogenic molecules, such as insulin and peptides or proteins, is poor. When these substances are added to ethosomes, permeability and therapeutic efficacy are significantly increased.⁽³⁰⁾

CONCLUSION

For a systemic effect, the transdermal technique is a viable drug delivery method. The permeability of the epidermal barrier makes developing transdermal medication delivery systems extremely challenging. It is possible to get better skin permeability because alcohol is a crucial component of ethosomes. Ethersomexs have ushered in a new age of vesicular research for transdermal drug administration since they have a higher skin permeability than liposomes. Ethersome production is very well known for its ease of use, efficacy, and safety. They can carry a variety of medications, and their composition can be altered to deliver the medication both topically and systemically. Ethosomes have been used to study proteins, peptides, hydrophilic and cationic medicines. Ethosomal formulations therefore have a promising future in transdermal administration of bioactive substances.

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