

Ethosomes serve as a non-invasive drug delivery system capable of penetrating the skin, merging with cell membrane lipids, and releasing pharmaceuticals

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ABSTRACT

The skin is one of the largest and most accessible organs in the human body, and its application as a pathway for drug delivery presents several advantages compared to conventional drug delivery systems. These benefits encompass reduced variability in plasma medication concentrations, prevention of gastrointestinal complications and first-pass metabolism, along with enhanced patient adherence. Transdermal drug delivery systems (TDDS) are characterised as self-contained, discrete dosage forms that, upon application to undamaged skin, administer medications at a controlled rate to the systemic circulation. Ethosomes are innovative lipid carriers consisting of ethanol, phospholipids, and water. These ethosomes are engineered as a non-invasive drug delivery method capable of penetrating the skin, merging with cell membrane lipids, and releasing the drug. Ethosomes can be prepared by either thermal or non-thermal processes. Evaluation criteria for ethosomes encompass dimensions, morphology, drug concentration, and zeta potential. Ethosomes have been effectively assessed for the administration of multiple pharmaceuticals, including cyclosporine, insulin, and salbutamol. Ethosomes possess significant potential as a crucial medication delivery mechanism in the future.

KEYWORDS: Pharmaceutical Delivery, Ethosomes, Dermal Penetration, Transdermal.

INTRODUCTION

The skin is one of the largest and most accessible organs in the human body, and as a pathway for drug delivery, it presents numerous advantages over conventional systems, such as diminished fluctuations in plasma drug concentrations, evasion of gastrointestinal complications and first-pass metabolism, and enhanced patient adherence. The stratum corneum, the outermost layer of skin, serves as a principal barrier against drug penetration, limiting the bioavailability of topically administered drugs. Therefore, it is imperative to investigate and evaluate various delivery carriers capable of penetrating this natural skin barrier for efficient systemic medication administration. Transdermal drug delivery systems (TDDS) are characterised as self-contained, discrete dosage forms that, upon application to undamaged skin, provide the medication(s) through the skin at a regulated pace to systemic circulation. The transdermal route is seen as a potential approach for local and systemic medication administration.

Transdermal drug delivery systems (TDDS) have several advantages over conventional pharmaceutical forms, such as circumventing first-pass metabolism, facilitating sustained drug release, decreasing dosing frequency, mitigating side effects, and improving patient adherence [1]. Transdermal medicine delivery is becoming increasingly important due to its non-invasive mode of administration. It addresses multiple constraints of oral medication administration, including drug breakdown by digestive enzymes, gastrointestinal mucosal irritation, and the first-pass impact. Furthermore, owing to the discomfort linked with the parenteral method, patients favour the transdermal approach. Consequently, transdermal dosage forms are regarded as the most patient-compliant method of drug delivery. Ethosomes were created as innovative lipid carriers consisting of ethanol, phospholipids, and water. Ethosomes are engineered as a non-invasive drug delivery mechanism.

It was revealed that ethosomes are lipid vesicular structures with a relatively high concentration of ethanol. Ethosomes are an innovative carrier system utilised for the

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administration of medications that exhibit low permeability through biological membranes, especially the skin. Ethosomes are a minor modification of the existing liposome drug carrier. Ethosomes are pliable vesicles predominantly made of phospholipids, a significant quantity of ethanol, and water. These vesicles function as an innovative vesicular carrier for improved distribution to and through the skin. The dimensions of ethosomes can be modified from tens of microns to nanometres. Owing to their significant deformability, ethosomes exhibit a remarkable capacity to penetrate unbroken skin. The elevated ethanol concentration in ethosomes distinguishes them, as ethanol destroys the organisation of the lipid bilayer.

When integrated into vesicle membranes, ethanol augments the vesicle's capacity to permeate the stratum corneum. Moreover, the elevated ethanol concentration leads to a lipid membrane that is less densely arranged than in traditional vesicles, yielding a more pliable structure. This enhances medication distribution inside the lipids of the stratum corneum. In contrast to typical liposomes that mainly transport medications to the epidermal surface, ethosomes markedly improve drug penetration through the stratum corneum barrier [3]. Ethosomes are an innovative class of liposome carriers recognised for their superior deformability, trapping efficiency, and improved percutaneous permeability across the stratum corneum. In comparison to traditional liposomes, they provide a more stable architecture, enhancing medication absorption, retention in skin cells, and movement towards target cells. Ethosomes offer extended drug action, are non-virulent, and enhance therapeutic efficacy via sustained release. They circumvent the first-pass effect and gastrointestinal degradation, so ensuring medication stability at the target location while minimising toxicity, adverse reactions, and administration frequency, ultimately improving patient compliance and therapeutic outcomes.

RESEARCH LABORATIONS

The ethosomal system consists of phospholipids, ethanol, and water. The phospholipids utilised in the formulation may possess many chemical structures, including phosphatidyl choline (PC), hydrogenated phosphatidyl choline, phosphatidyl ethanolamine (PE), phosphatidyl glycerol (PPG), and phosphatidyl inositol (PI), among others. The non-aqueous phase typically constitutes between 22% and 70%. Ethanol or isopropyl alcohol may function

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as the alcoholic constituent. Dyes or amphiphilic fluorescent probes, including D-289, Rhodamine 123, Fluorescein Isothiocyanate (FITC), and 6-carboxyfluorescein, are commonly utilised in ethosomes for characterisation reasons [4].

What is the mechanism of action of ethosomes? Vesicles, ethanol, and skin lipids synergistically collaborate to augment the efficacy of ethosomes. In comparison to liposomes, ethosomes have a more robust interaction with skin lipids, resulting in enhanced diffusion of active substances. Ethanol influences the lipid molecules in the stratum corneum by reducing the transition temperature of the lipids in the head group region. This diminishes the density of the lipid multilayer and enhances fluidity, facilitating the drug's deeper penetration into the skin. Moreover, ethanol enhances the smoothness and flexibility of vesicles, facilitating their deeper infiltration into the epidermis. The primary benefit of ethosomes compared to liposomes is their superior drug penetration.

The exact mechanism of medication absorption from ethosomes is still ambiguous. Drug absorption is anticipated to transpire in two separate phases: Effects of Ethanol and Ethosomes Impact of Ethanol: Ethanol functions as a permeation enhancer via the dermal layer. Ethanol infiltrates intracellular lipids, enhancing the fluidity of cell membrane lipids and reducing the density of the lipid bilayer of the cell membrane. Effect of ethosomes: The ethanol in ethosomes enhances cell membrane lipid fluidity, hence augmenting skin permeability. The ethosome readily penetrates the deeper layers of the skin, where it amalgamates with skin lipids and subsequently releases the medication into these layers.

RESULTS AND DISCUSSION

Ethosomal formulation can be made using the hot, cold, and classic mechanical dispersion methods as outlined below. Both approaches are convenient, do not necessitate sophisticated equipment, and are easily scalable at an industrial level. The cold approach involves dissolving phospholipids, drugs, and other lipid molecules in ethanol within a covered vessel at room temperature, utilising vigorous stirring with a mixture [3]. Propylene glycol or another polyol is included during agitation. The solution is subjected to heating at 300°C in a

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water bath. Water heated to 300°C in a separate vessel is incorporated into the mixture, which is thereafter agitated for 5 minutes in a covered container. The particle size of the ethosomal formulation can be reduced to the desired level using probe sonication or the extrusion method. The formulation is ultimately stored under refrigeration.

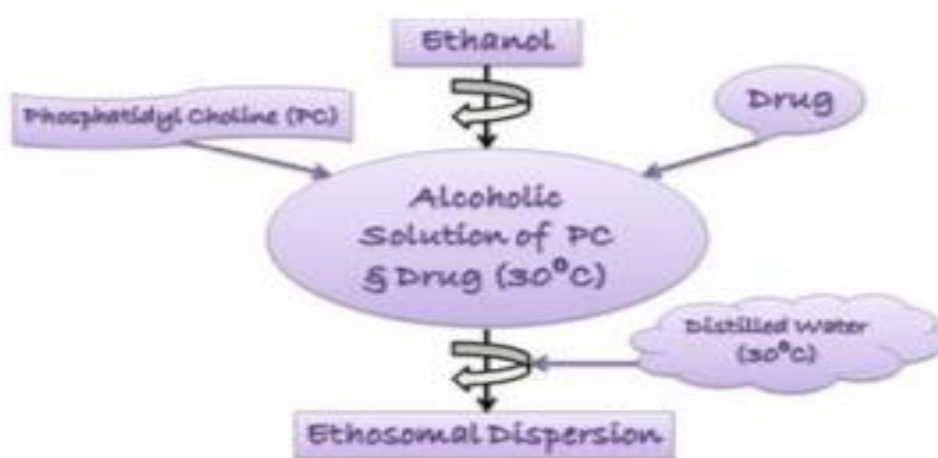


Fig.1: Preparation of Ethosomes by Cold Method

This approach involves dispersing phospholipid in water by heating it in a water bath at 400°C until a colloidal solution is achieved. Ethanol and propylene glycol are combined in a separate vessel and heated to 400°C. Upon reaching 400°C, the organic phase is incorporated into the aqueous phase. The medication is dissolved in water or ethanol based on its hydrophilic or hydrophobic characteristics. The vesicle size of the ethosomal formulation can be reduced to the desired extent utilising probe sonication or the extrusion approach.

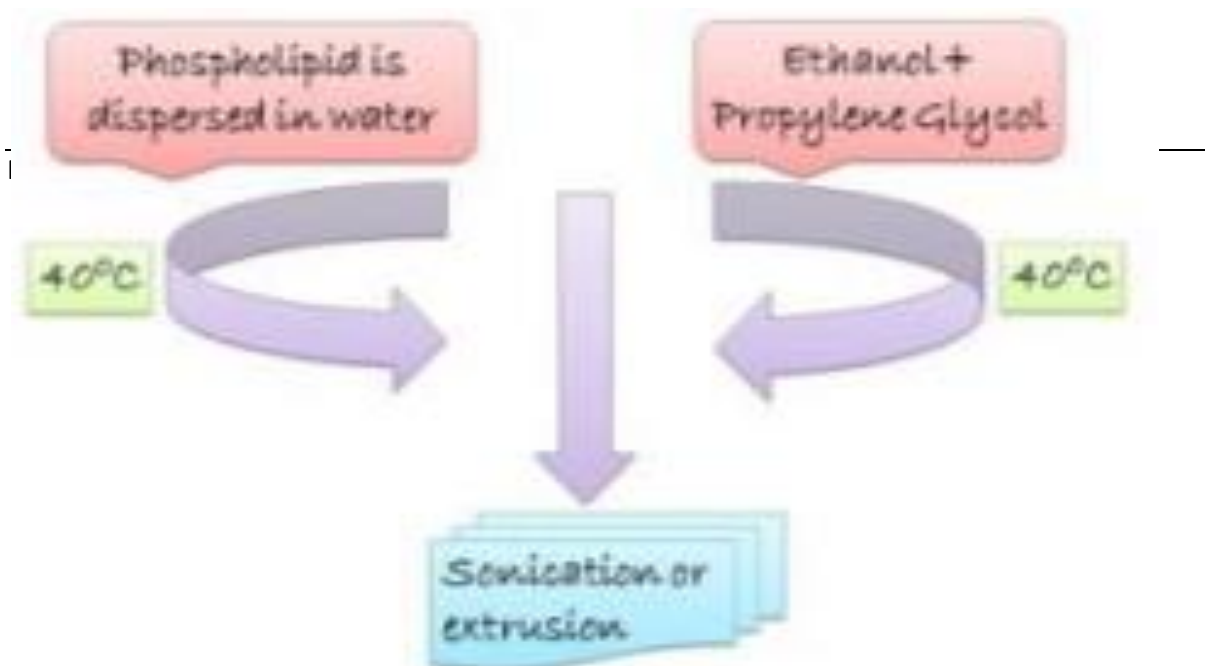


Fig.2: Preparation of Ethosomes by Hot Method

The classic mechanical dispersion method involves dissolving soya phosphatidylcholine in a chloroform:methanol combination (3:1) within a round-bottom flask. The organic solvents are eliminated using a rotary vacuum evaporator above the lipid transition temperature to create a thin lipid coating on the flask's wall. The solvent combination residues are eliminated from the deposited lipid film by maintaining the contents under vacuum overnight. Hydration is performed using varying concentrations of a hydroethanolic mixture containing the medication, with the flask being rotated at an appropriate temperature. Benefits: Ethosomes are non-invasive, passive delivery devices composed of safe, non-toxic components in their formulation. Its composition is harmless and is utilised in cosmetic and pharmaceutical applications. Facilitate the transport of many molecules with distinct physicochemical properties, including peptides, other macromolecules, and both hydrophilic and lipophilic substances [2]. They are provided in a semi-solid dose form and exhibit high patient compliance. Ethosomes provide a platform for the administration of diverse pharmaceuticals across multiple therapeutic categories.

Ethosomes may aggregate and precipitate due to inadequate shells, rendering them uneconomical. Adhesive will not adhere to all types of skin. Dermatitis and skin irritation have arisen due to the enhancers and excipients utilised in the medication delivery method. Product loss transpires when ethosomes are moved from the organic phase to the aqueous phase. The administration of ethosomes did not result in a rapid bolus-type drug delivery. They were engineered for prolonged and gradual medication administration. Multiple studies have

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demonstrated that ethosomes are an efficacious treatment for viral and microbial dermal infections. Animal models of deep skin infections were employed to design and evaluate the efficacy of the bacitracin and erythromycin ethosomal system. Ammonium glycyrrhizinate ethosomes exhibited an anti-inflammatory impact on the skin of human volunteer participants when generated. In vivo testing on rabbits revealed that ethosomal patches for addressing androgen deficiency in males and menopausal symptoms in females exhibited markedly superior outcomes. Research suggests that ethosomes may demonstrate analgesic, antipyretic, and efficacious effects in the treatment of erectile dysfunction. Research has indicated that ethosomes may facilitate the topical transport of DNA molecules, allowing skin cells to express certain genes.

Vesicular Configuration Ethosomes can be readily observed with transmission electron microscopy (TEM) and scanning electron microscopy (SEM). **Vesicle Dimensions and Zeta Potential** The particle size of ethosomes can be ascertained by dynamic light scattering (DLS) and photon correlation spectroscopy (PCS). The zeta potential of the formulation can be quantified using a zeta meter. **Transition Temperature** The transition temperature of the vesicular lipid system can be ascertained by differential scanning calorimetry (DSC). **Pharmaceutical Entrapment** The entrapment effectiveness of ethosomes can be assessed using the ultracentrifugation method. **Pharmaceutical Composition** The drug concentration in ethosomes can be quantified using a UV spectrophotometer. This can also be quantified using a modified high-performance liquid chromatography approach. **Measurement of Surface Tension** The surface tension of a medication in aqueous solution can be quantified using the ring method with a Du Nouy ring tensiometer [1]. **Stability Investigations** The stability of vesicles can be evaluated by analysing their size and structure over time. The mean size is assessed using dynamic light scattering (DLS), while structural alterations are examined by transmission electron microscopy (TEM). **Cutaneous Permeation Investigations** The penetration capability of the ethosomal formulation into epidermal layers can be assessed using confocal laser scanning microscopy (CLSM).

CONCLUSIONS

Ethosomes constitute a sophisticated and promising drug delivery technology, offering numerous advantages, including higher drug stability, improved skin penetration, and increased therapeutic efficacy. Their capacity to transport both hydrophilic and lipophilic pharmaceuticals creates novel prospects in the transdermal administration of many treatments. Nonetheless, additional research and development are necessary to comprehensively ascertain their long-term stability, safety, and efficacy in clinical applications.

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