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Review Article

A Review on Transdermal Drug Delivery System by Ethosomes

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ABSTRACT

Transdermal drug delivery system is one type of more convenient drug delivery system. Skin acts a barrier for transdermal through drug delivery system. Drug across through stratum corneum by low diffusion process. Drug formulation with elastic vesicle or skin enhances vesicles. Etho sources are the ethanolic phospholipids vesicles and which are having higher rate of penetration through the skin. The purpose of writing this Review on ethosome drug focus on the Ethosomes including their mechanism of penetration. Transdermal drug delivery system was came into existence by more than 30 years ago. Ethosomes are the ethanolic phospholipid vesicles. These are used mainly for transdermal delivery of drugs. Ethosomes have higher penetration rate through the skin as compared to liposomes hence these can be used widely in place of liposomes. Ethosomes enhanced skin permeation, improved drug delivery, increased drug entrapment efficiency etc.

Keywords: Transdermal Drug Delivery System, Ethosomes, Drug absorption

INTRODUCTION

The skin covers a total surface area of approximately 1.8m and provides the contact between the human body and the external environment. Dermal drug delivery is the topical application of drugs to the skin in the treatment of skin diseases and other inflammatory conditions. This has the advantage that high concentrations of drugs can be localized at the site of action, reducing the systemic side effects. Transdermal drug delivery uses the skin as an alternative route for the delivery of systemically acting drugs.

Ethosomes are novel carrier system used for delivery of drugs having low penetration through the biological membrane mainly skin. Ethosomes are the slight modification of well-established drug carrier liposome. Ethosomes are lipid vesicles containing phospholipids, alcohol (ethanol and isopropyl alcohol) in relatively high concentration and water. Transdermal drug delivery offers many advantages as compared to traditional drug delivery systems, including oral and parenteral drug delivery system.

Advantages claimed are increased patient acceptability (noninvasiveness), avoidance of gastrointestinal disturbances and first pass metabolism of the drug. The traditional transdermal drug delivery systems involve a patch, in which the drug permeates through various layers of skin, via a passive diffusion pathway.

However, this limits the basic potential of these systems, as stratum corneum is the most formidable barrier to the passage of most of the drugs, except for highly lipophilic, low molecular weight drugs. To overcome the stratum corneum barrier, various mechanisms have been investigated, including use of

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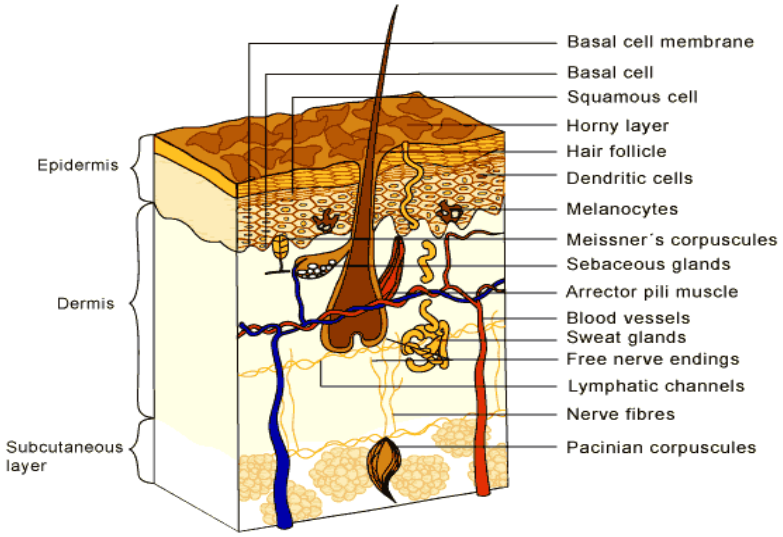
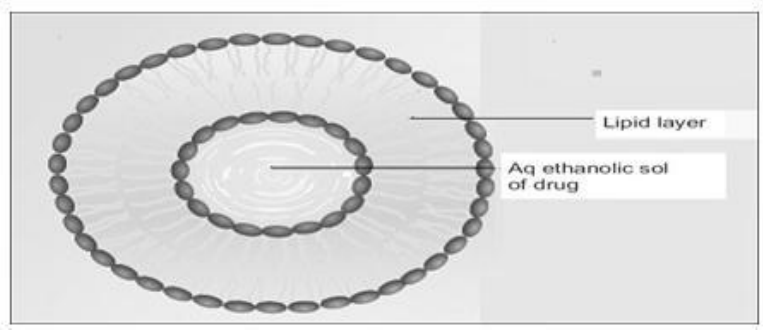
chemical or physical enhancers, such as iontophoresis, sonophoresis, etc. Liposomes, niosomes, transferosomes and ethosomes also have the potential of overcoming the skin barrier and have been reported to enhance permeability of drug through the stratum corneum barrier.



Structure of skin Fig No.1 [1]

· External environmental and prevent dehydration from transdermal layer tissue[1,2,3].
· Hydrophilic drugs and water molecules are not able to cross the skin layers.
· Stratum corneum having highly keratinized, enveloped and stabilized by protein and lipids due to covalent bonds.
· TTDS avoids 1st pass metabolism lower fluctuation in place drug concentration and good patient compliance.
· Active drug is to penetrate through the stratum corneum slow diffusion through dead horney layer of skin i.e. stratum corneum
· Various mechanisms have been invented to improve the penetration of drug through the skin [2,4].
· Including chemical or physical enhance such as iontophoresis, sonophoresis etc.
· Liposome transforms ions and electrons which are enhance permeable through the stratum corneum [5].



Structure of Ethosome Fig No.2 [6]

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The non-invasive approaches the prodrug.

Drug and vehicle interaction[7,8]:

· Selection of correct drug or prodrug.
· Chemical potential adjustment.
· Ion pairs and complex coacervatives
· Eutectic system.

Stratum corneum modification:

· Hydrates
· Chemical penetration enhancers

a) Stratum corneum bypassed or removed

· Micro needles array.
· Stratum corneum ablated
· Follicular delivery.

b) Electrically assisted methods[9,10]:

· Ultrasound (phonophoresis, sonophoresis).
· Iontophoresis.
· Electroporation.
· Magnetophoresis.
· Photo mechanical wave.

c) Vesicles and particles

· Liposomes and other vesicles
· Transferosomes
· Niosomes
· Ethosomes

Advantages of ethosomes drug delivery:

· Large molecules such as peptides, proteins easy to delivery.
· In formulations contains non-toxic raw materials.
· Increases penetration of drug through the skin to systemic circulation[8,11,12].
· Better patient compliance
· The ethosomal system is passive non-invasive and is available for immediate commercialization.

Method of preparation:

Two conventional method used for the preparation of ethosome as followed by

· Cold method
· Hot method

Cold method:

This method is most commonly used for the preparation of ethosomal formulation.

· In this method drug phospholipids materials are dissolved in external in a covered vessel at room temperature by vigorous stirring.
· Propylene glycol or polyol is added during stirring.
· This mixture is heated to 30°c centigrade in a water bath.
· The water heated to 30°c centigrade in separate vessel added to mixture then stirred in covered vessel.
· The vesicle size of decreased to using sonication [13] or extrusion [14] method. Finally formulation stored in refrigeration [15].

Hot method:

· In this method phospholipid is dispersed in water by heated in a water bath at 40 °c until colloidal solution obtained.
· In a separate vessel ethanol and propylene glycol are mixed and heated to 40 °
· The organic phase added to aqueous phase.
· The drug dissolved in water / ethanol depends upon the hydrophilic / properties
· the vesicle are on decreased to using probe sonication or extraction method [16,17]

MECHANISM OF DRUG PENETRATION[18,19,20,21]

The mechanism of drug absorption from ethosomes followed by two phases.

1. Ethanol effect
2. Ethosomes effect

1. Ethanol effect:

· Ethanol act as a enhance penetration through the skin.
· Ethanol penetrates in the intercellular lipids and increased fluidity of cell means due to decreased the density of lipid multilayer cell membrane[22,16]

2. Ethosome Effect:

· Ethanol increased lipid fluidity of ethosomes result increased skin permeability.
· Ethosomes easy to permeate inside deep layer which fused with skin lipids and release the drug layer of skin.

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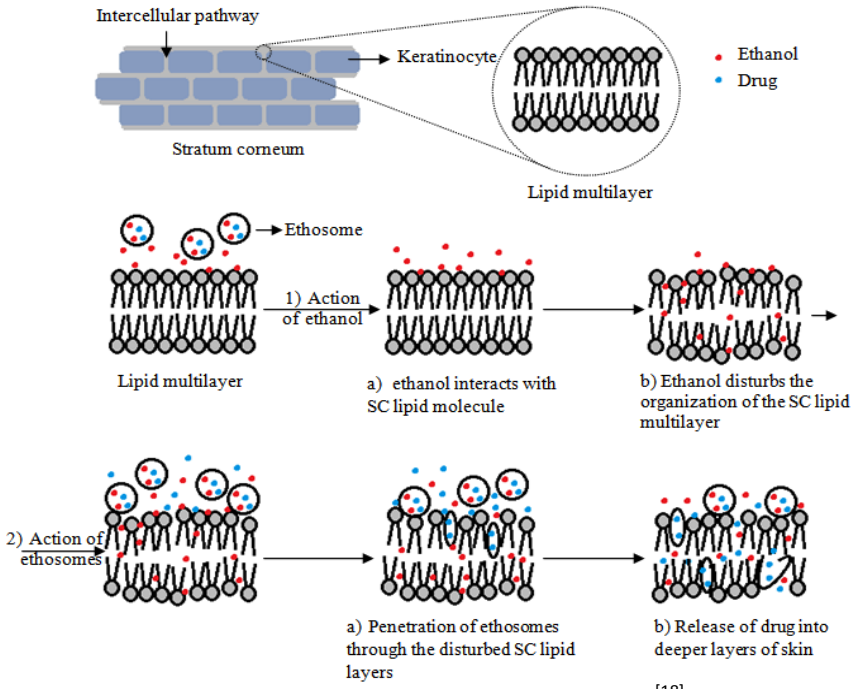

Mechanism Of drug Penetration Fig No.3[18]

CHARACTERIZATION OF ETHOSOMES [6,23]

1. Vesicle shape:

Ethosomes visualized by using transmission electron microscopy (TEM) and electron microscope (SEM).

2. Size and zeta potential:

Ethosome particle size can determined by dynamic light scattering (DCS) and photon correlates zeta potential of formulation measured by zeta met spectroscopy.

3. Entrapment efficiency:

The entrapment efficiency of drug increased by ultra-centrifugal technique [24].

4. Transmission temperature:

The vesicular lipid system by transition temperature can determined by differential scanning calorimetery.

5. Surface tension activity measurement:

The surface tension of drug measured by Dunouy tension meter.

6. Drug content:

Drug content can be determined by using spectrophotometer. This can quantify by high performance liquid chromatographic method. [10]

7. Vesicle stability:

The stability of vesicles can be determined by size and structure of the vesicles measured by DLS and structure changes are observed by TEM.

8. Skin permeation studies:

Preparation of ethosomal to penetrate in the skin layer can be determined by CLSM conaofocal laser scanning microscopy (CLSH) [25].

Ethosome composition:

· Which consists of phospholipids, ethanol and water [26]

· Ethosome contain phospholipids such as phosphatidyl choline (PC) phosphatic acid(PA), phosphatidyl series (SE)phosphatidyl ethanosome (PS), phosphatidyl linostril [27].

· The concentration of non-aqueous phase range between 22-70 % (alcohol and glycol

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· Polyglycol such as propylene glycol, and alcoholic like ethanol, isopropyl alcohol as penetration enhancers
· Dyes rhodamin- 123, rhodamine red [3,11].
· Vesicle used as carbopol as a gel forms.

MECHANISM OF ACTION OF LIPOSOMES [28]

In the free drug mechanism the drug permeates through skin after exiting from the vesicles25. In the penetration enhancing mechanism after application of vesicles, changes in the ultra-structures of the intercellular lipids were seen suggesting a penetration enhancing effect.26 In vesicle adsorption to and/or fusion with the stratum corneum the vesicles may adsorb to the stratum corneum surface with subsequent transfer of drug directly from vesicles to skin or vesicles may fuse and mix with the stratum corneum lipid matrix, increasing drug portioning into the skin[24,28,29].

The interaction of liposomes with human skin has been reviewed and it was concluded that they can be taken into the skin but cannot penetrate through intact healthy stratum corneum, instead they dissolve and form a unit membrane structure.[14, 30] In intact vesicular skin penetration mechanism, (Fig.2 at D) traditional liposomes with intact vesicles cannot penetrate the human skin but ultra-deformable liposomes have been reported to invade the skin intact and go deep enough to be absorbed by the systemic circulation. The trans appendage penetration route plays a minor role in transdermal delivery from liposomes. Electron microscopy indicated that liposomes up to 600nm of diameter can penetrate through skin but those of 1000nm or more remain interiorized in the stratum corneum.[30]

Deposition was higher in hairy guinea pigs but with regard to penetration through skin, no Difference could be found between hairless and hairy guinea pigs. Also, vesicular delivery through shunts was excluded on the basis that there were no significant variations between Different animals or humans with diverse densities of hair follicles, with regard to the Trans-ferosomal input of insulin.[15] The trans-follicular delivery from liposomes was enhanced only after it was combined with iontophoresis technique.

DISCUSSION AND CONCLUSION

The ethosomes more advantages when compared to transdermal delivery. It delivers large molecules such as peptides protein molecules. Non-invasive drug delivery carriers of ethosomes that enable to drug delivery systemic circulation. High patient compliance as administered in semisolid form (gel cream) and various applications in pharmaceutical, veterinary and cosmetic field.

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