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Review on a Novel Vesicular Carrier: Ethosome

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Abstract:
Skin is the largest organ of the body, which act as a major target and as well as a principle barrier for topical/transdermal drug delivery. Certain restrictions of transdermal drug delivery system are slow diffusion across the stratum corneum and barrier property of the skin limits the delivery of the drug molecoule through skin. Vesicular formulations are used to overcome these restrictions and there by enhance the administration of drug through skin. Ethosomes are novel non-invasive phospholipid vasicular carrier which contain high concenteration of ethanol. This system offers improved skin permeability and efficient bioavailability due to their structure and composition.

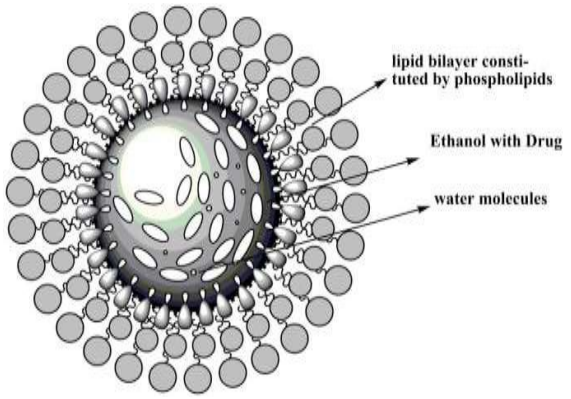
Key words: Ethosome, transdermal drug delivery, lipid vesicular carrier, skin peneteration.

INTRODUCTION:

Topical drug delivery system is considered as one of the most advisable route for treating skin diseases and also an alternative route for delivery of drug into systemic circulation. As compaired to traditional drug delivery, topical drug delivery achieve a constant plasma level for prolonged period of time and also requires less frequent dosing regimen. Although it has some advantages such as self administration, better patient compliance, avoid first pass metabolism, GIT disturbance of drug molecoule and reduction in systemic adverse effect. Ethosomes are advanced form of liposomes having high ethanol content. They encapsulate both hydrophilic & hyodrophobic drug and enhance accumulation of drug. This system have the capacity of prolonging the existence of drug in stratum corneum and also have the capacity to target organ and tissues. Most of the ethosomal drug are administer as semisolid form (gel or cream). Carbapol and HPMC are widely used as a gel forming agents[4[6]][7][8].

ETHOSOME:

Ethosomes were developed by Touitou, 1997. They are mainly used for the delivery of drug molecoule through transdermal route.



Ethosomes are soft, highly flexible vesicle efficiently penetrate through skin and carry this molecoule to the deep layers and systemic circulation. Ethosomal system drug in a matrix of lipids, ethanol and water. Ethanol act as a penetration enhancer by dissolving skin lipid there by enhance the permeation of drug molecoule through skin. Ethosomes overcome the disadvantage of liposomes and proliposomes such as less stability, leakage of drug, fusion of vesicle and breakage of vesicle. The size of the ethosome will be in the range of tens of nanometer to microns(μ)[1][2][3].

COMPOSITION:

Chemical	Example	Use
Phospholipid	Soya phosphotidyl choline Egg phosphotidyl choline Dipalmityl phosphatidyl choline Distearyl phosphatidyl choline	Vesicle forming agent
Polyglycol	Propylene glycol Transcutol	As a skin penetration enhancer
Alcohol	Ethanol Isopropyl alcohol	For providing the softness for vesicle membrane.
Cholesterol	Cholesterol	For providing the stability

ADVANTAGES :

- Ethosomes act as a plat form for the delivery of large and diverse group of drugs such as peptide, protein molecoule.
- As compaired with iontophoresis and phonophoresis ethosomes are simple method of drug delivery.
- High patient compliance – Ethosomal drugs are administered as a semi solid form (gel or cream) which produce better patient compliance.
- Contains non toxic raw material in formulation.
- Relatively simple to manufacture with no complicated technical investments required for the production of ethosome.
- This system is passive, non passive and available for immediate concenteration.
- Widely applied in cosmetics, veterinary herbal drug

technology.

- Permeation enhancer used in the formulation increase the permeability of the skin, so the drug easily cross through skin[4][7][8].

DISADVANTAGES:

- Loss of product during transfer from organic to water media.
- For rapid treatment ethosomal delivery is not effective as it deliver the medicament at sustained rate.
- This system results poor yield.
- For ethosomal delivery the medicament should have adequate molecoular size[4][7][8].

TYPES OF ETHOSOME:

1. Classical ethosome
2. Binary ethosome
3. Trans ethosome

MECHANISM OF DRUG PENETRATION:

The main advantage of ethosome over liposome is the increased permeation of the drug. The drug absorption probably occurs in following two phases:

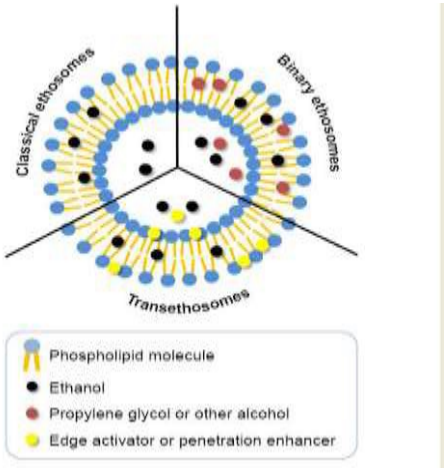
- Ethanol effect
- Ethosome effect

Ethanol effect:

Ethosomes act as penetration enhancer through the skin. The mechanism of its penetration enhancing effect is well known. Etanol penetrates into intercellular lipids and increase the fluidity of cell membrane lipids and decrease the density of lipid multilayer of cell membrane.

Ethosome effect:

Increased cell membrane lipid fluidity caused by the ethanol of ethosome results increased skin permeability. So the ethosomes permeates very easily inside the deep skin layers, where it get fused with skin lipids and release the drug into deep layer of skin[4][5][8].



Comparison of classical, binary and trans ethosome:

Parameter	Classical ethosome	Binary ethosome	Trans ethosome
Composition	Phospholipid Ethanol Stabilizer Charge inducer Water Drug	Phospholipid Ethanol Propylene glycol/other Charge inducer Water Drug	Phospholipid Ethanol Edge activator (surfactant)/ Penetration enhancer Water Drug
Morphology	Spherical	Spherical	Regular/irregular shape
Size	Smaller than classical liposome	Equal to, smaller than classical ethosome	Size based on type and & concenteration of penetration enhancer and edge activator used
Entrapment efficiency	Higher than classical liposome	Higher than classical ethosome	Typicaly higher than classical ethosome
Skin permeation	Typicaly higher than classical liposome	Typicaly equal to or higher than classical ethosome	Typicaly higher than classical ethosome
Stability	Stable than classical liposome	Stable than classical ethosome	No particular trenddetermine
Zeta potential	Negatively charged	Negatively charged	Negatively/positively charged

MECHANISM OF DRUG ACTION:

Ethosomes

↓

Skin disruption occur due to the presence of ethanol

↓

Lipid fluidity of the skin increase

↓

More permeation through the skin

↓

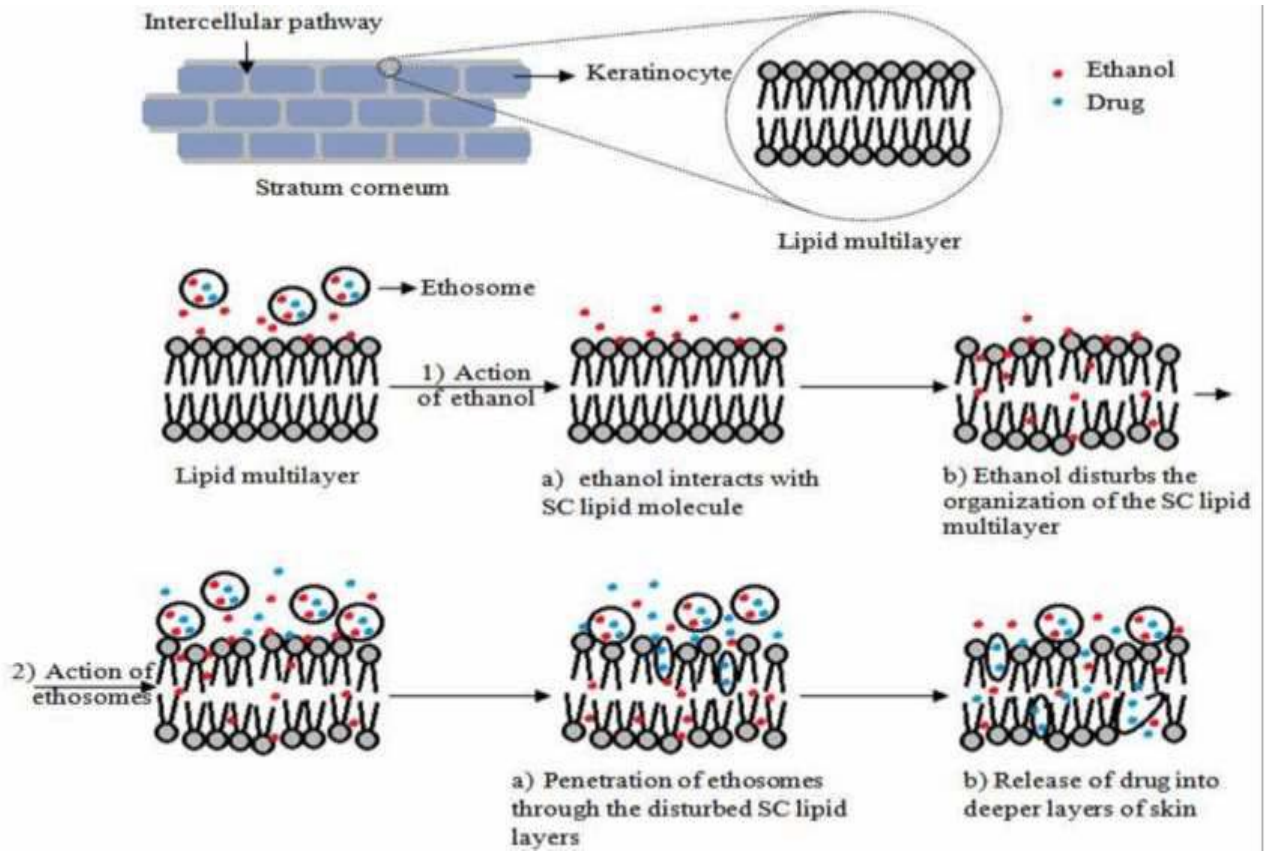
Ethosomes pervade inside

↓

Combine with skin lipids

↓

Imprison the drug into deep skin layers



METHODS OF PREPARATION:

- Cold method
- Hot method

Cold method:

In this method phospholipid, drug and other lipid material is mixed. Add propylene glycol or polyol during stirring. This mixture is heated to 30℃ in water bath. In a separate vessel water is heated upto 30℃ and add to the initialy formed organic phase under continuous stirring. The vesicular size range of ethosome reduced by using probe sonicator or extrusion method and after that this preparation is kept under cold temperature.

Hot method:

In this method phospholipid is disperse in a water by heating in a water bath at 400℃ until a colloidal solution is obtained. In a separate vessel ethanol and propylene glycol are mix and heat upto 400℃. Once both these mixtures reach to 400℃. The organic phase is add to the aqueous phase. Drug is dissolve in ethanol or water depending on its hydrophilic or hydrophobic properties. The size of the vesicle is reduced by using probe sonicator or extrusion method[1][4][5][8].

CHARACTERIZATIONS:

1. Visualization of vesicle:

Vesicles can be visualised by using transmission electron microscopy (TEM), scanning electron microscopy (SEM).

2. Vesicle size and zeta potential:

The size of the vesicle can be measured by using dynamic light scattering (DLC) and photon correlation spectroscopy (PCS). While zeta potential is used to determine the physical stability of the vesicle. Aggregation of the vesicle affect its physical stability of the vesicular system. This can be measured by using zeta meter.

3. Entrapment efficiency:

The drug entrapment efficiency of the ethosome measured by using ultra centrifugation technique.

4. Penetration and permeation studies:

Penetration depth of the ethosome can be visualized by confocal laser scanning microscopy (CLSM).

5. Stability study:

Determine by keeping the preparation at different temperature ie. 25±2℃, 37±2℃ & 45±2℃ for different period of time and after that stability samples are evaluate for size and morphology of the vesicle using DLS and TEM.

6. Degree of deformality and turbidity

Degree of deformality of the preparation can be performed by extrusion method and the turbidity of the preparation can be performed by using nephelometer.

7. Drug content:

Content of drug in the ethosome determine by using modified high performance liquid chromatographic method[1][7][9][10].

APPLICATIONS:

1. In the treatment of herpetic infection:

As compaired with 5% acyclovir cream, 5% acyclovir ethosomal preparation shows significant improvement in the treatment of herpetic infections and also results improved pharmacodynamics profile, increase the skin permeation.

2. Transcellular delivery:

As compaired to the marketed formulation, ethosomes to be an alternative for anti HIV therapy. This results prolonging drug action, reduce drug toxicity, improve transdermal flux.

3. Ethosomes are used in pilosabeceous targeting:

Ethosomal vesicle shows high ethanol content which efficiently penetrate to the deep layer of skin. This vesicle appear as a effective choice for transdermal drug delivery of hydrophilic and impermeable drug through the skin and also results improved dermal deposition, improve intercellular delivery, increase bioavailability.

4. Transdermal delivery of hormones:

First pass metabolism, low oral bioavailability and several dose dependent side effects are common problems that associated with oral administration of hormones. To avoid this transdermal delivery is used. The risk of failure of treatment is increase with each pill missed.

5. Ethosomal system for Menopausal syndromes:

Ethosomal compositions have been tested for their efficiency in the treatment of androgen deficiency associated with menopause in men and menopausal syndromes in women. A testosterone ethosomal patch system, testosome, was designed for the treatment of androgen deficiency in men.

6. Delivery of anti arthritis drug:

Topical delivery of anti arthritis drug shows better option for selective delivery of drug to the desired site for prolong period of time[5][7][8].

CONCLUSION:

The main disadvantage of transdermal drug delivery is the poor penetration of most drug molecoules across skin. As mentioned above it can conclude that ethosomes can provide better skin permeation than other vesicular carrier like liposome. Ethosomes offers safety, efficacy, long term stability, simplified industrial manufacture as well as better patient compliance. Hence ethosomes can become a promising drug carrier in future not only for topical treatment of local and systemic disorder but also for cosmetics and pharmaceutical field.

REFERENCE:

1. Agarwal S, Gautam G, Rajpoot N. A review on ethosomes: an advanced approach to transdermal drug dekivery system. International Research Journal of Pharmacy. 2019;10(4):14-20.
2. Shelke O, Kulkarni A. Formulation development and evaluation of nano ethosomal gel of tramadol hydrochloride. Journal of Nanomedicine and Nanotechnology. 2018;9(5):2-6.
3. Grace X F, Suganya K, Shanmuganathan S. Development of terminalia chebula loaded ethosomal gel for trans dermal delivery. Asian Journal of Pharmaceutical and Clinical Research. 2018;2(12):380-3.
4. Nimmy J K, Krishnakumar, Dineshkumar B, Smitha K N.

Ethosomal gel: a review. European Journal of Pharmaceutical and Medical Research. 2017;4(4):301-5.
5. Eswar K A. A review on novel trends in vesicular carrier for enhanced transdermal delivery: ethosomes. International Journal of Scientific Research. 2017;6(4):268-270.
6. Sundari B T, Navya S. Formulation and in vitro evaluation of topical ethosomal gel of miconazole nitrate. World Journal of Pharmacy and Pharmaceutical Sciences. 2017;6(8):1882-98.
7. Sultana S S, Krishna S A. Ethosomes: a novel approach in the design of transdermal drug delivery system. International Journal of MediPharm Research. 2016;2(1):17-22.
8. Tiwari A, Mishra K, Nayak K, Yadav S K. IOSR Journal of Pharmacy. Ethosomes: a novel vesicular carrier system for therapeutic applications. 2016;6(9):25-33.
9. Rathore A R, Khambete H, Jain S. Preparation and characterization of repaglinide loaded ethosomal gel. International Journal of Pharmaceutical and Biological Archives. 2013;4(2):385-90.
10. Maurya S D, Prajapati S K, Gupta A K. Formulation development and evaluation of ethosome of stavudine. Indian Journal of Pharmaceutical Education and Research. 2010;44(1):102-8.