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Review Article

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Development of Ethosomal Gel from Withania Somnifera

Dr A Krishna sailaj* and Shaik Nishad

Associate professor, Department of pharmaceutics, RBVRR Womens College of pharmacy, Barkatpura, Hyderabad.

***Corresponding author**
Dr A Krishna sailaj, Associate professor, Department of pharmaceutics, RBVRR Women's College of pharmacy, Barkatpura, Hyderabad.

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Abstract

Novel drug delivery systems are used to increase administration of drugs through transdermal system. Ethosomes has the ability to permeate through the stratum corneum. Ethosomes are the delivery carriers that enable the drugs to reach the deep skin layers as well as the systemic circulation. These vesicles are well known for their importance in cellular communication and in particle transportation for many years. This article reviews various aspects of ethosomes which includes their preparation, characterization, advantages and their applications in drug delivery. Ethosomes has number of important benefits such as, it improves the drug's efficacy, enhances the patient compliance, comfort and reduces the total cost of treatment.

Introduction

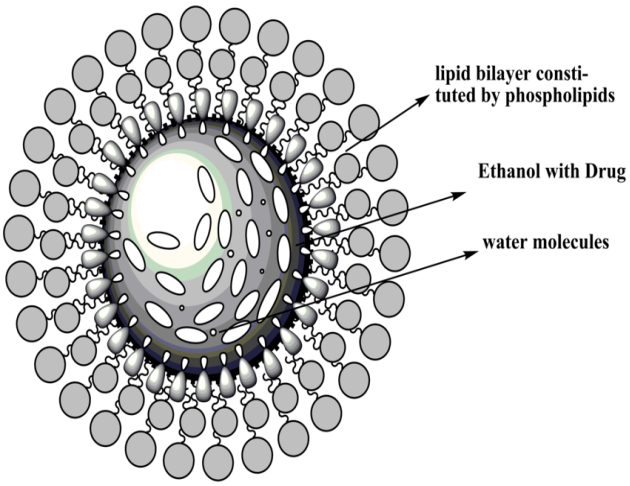
Withania somnifera which is also known as Ashwagandha, winter cherry or Indian ginseng is one of the most important plant in Indian traditional system of medicine which belongs to solanaceae family. It is a small evergreen shrub that grows roughly four to five feet tall. In India it is cultivated in the states of Madhya Pradesh, Rajasthan, Uttar Pradesh and Gujarat. Having wide range of activities, it is used in almost all disorders that affect the human health. Constituents of ashwagandha are withanolides, withaferins a, alkaloids, steroidal lactones and tropine. The plant is exhibiting anti-inflammatory, antipyretic, analgesic, anticancer, neuroprotective and cardio protective [1, 2].

Method of Extraction

The roots of Withania somnifera were collected, dried and powdered. 100 g of coarse powder was extracted using soxhlet extractor with solvent of increasing polarity such as n-hexane, ethyl acetate and ethanol in solid/solvent ratio 0.33, respectively for 10 hrs each. The extract then concentrated in rotary evaporator [3, 4].

Ethosomes

Ethosomes are used mainly for the delivery of drugs through trandermal route. Drug is entrapped in ethosomes which have various physicochemical properties i.e hydrophilic, lipophilic and amphiphilic property. The size of ethosomes may vary from nano meters to microns. Ethosmes are the modified forms of liposomes which contains high ethanol content [5, 6].



Ethosomal Composition

Ethosomes are vesicular carrier that are comprised of hydroalcoholic or phospholipid in which the concentration of alcohols or their combination is relatively high. The various types of additives used in the ethosome preparations are representated in the table [7, 8].

Class	Example	Uses
Phospholipid	Soya phosphotidyl-choline Egg phosphotidyl-choline Di palmityl phospho-tidylcholine Di steryl phosphoti-dylcholine	Vesicle forming com-ponent
Polyglycol	Propylene glycol Transcutol RTM	As a skin penetration enhancer
Alcohol	Ethanol Isopropyl alcohol	For providing the softness for vesicle membrane As a penetration enhancer
Cholesterol	Cholesterol	For providing the stability to vesicle membrane
Dye	Rhodamine-123, Rhodamine Red flurescene iso-thiocyante 6-carboxy flurescence	For characterization study
Vehicle	Carbopol D 934	As a gel former

Table: Different additives employed in the formulation of ethosomes.

Advantages of ethosomes [9].

Ethosmal drug delivery system has much advantage as compared to other transdermal and dermal delivery systems. These advantages include

>Permeation of drug through skin for transdermal drug delivery is enhanced.

>Ethosmal system is passive, non invasive and is used for immediate commercialization

>Ethosmes delivers large and diverse groups of drugs across skin.

>Ethosomes does not contains toxic materials in formulation, ethosomal drug is administered in semisolid form that produces high patient compliance.

>Ethosomal drug delivery is simple when compared to other complicated methods.

Mechanism of Penetration [10].

The mechanism of drug absorption from ethsosmes occurs in two phases

1) Ethanol effect

2) Ethosomes effect

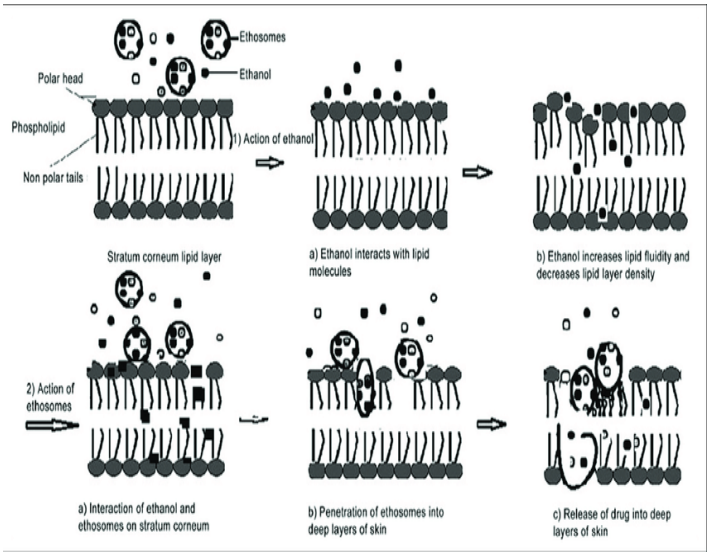
Ethanol Effect

Ethanol acts as penetration enhancer through the skin which penetrates into intercellular lipids and increases the fluidity of cell membrane lipids and also decreases the density of lipid multilayer of cell membrane.

Ethosomal Effect

The ethanol of ethosomes causes increase in cell membrane lipid fluidity which results in increased skin permeability. Ethosomes penetrates easily inside the deep skin layers, where it gets fused with skin lipids and releases the drug into deeper layer of skin.

Mechanism of Penetration



Method of Preparation [11].

Cold Method

This is the most common method used for the preparation of ethosomal formulation. In this method, phospho lipid, drug and other lipid materials are mixed. The water is heated to 300c in a water bath.The water heated to 30oc in a separate vessel is added to the mixture, which is then stirred for five minute in a covered vessel. The vesicle size can be reduced to desired extent using sonication method or extrusion method and then finally the formulation is stored in refrigerator.

Hot Method

This method involves dissolving of phospholipids in water in a water bath at 400c until a colloidal solution is obtained. In a separate vessel propylene glycol and ethanol are mixed and is heated to 40oc.Once both the solutions reach to 400c, the organic phase is added to aqueous phase. The drug is dissolved in water or ethanol depending upon its hydrophilic/hydrophobic properties. The vesicle size can be decreased to desired size using sonication method or extrusion method and the formulation is stored in refrigerator.

Characterisation of Ethosomes [12].

Visualisation of vesicles: Vesicles are visualized by Transmission electron microscopy and scanning electron microscopy.

Entrapment efficiency: Ultra centrifugation technique is used to determine entrapment efficiency.

Vesicle size and zeta potential: Vesicle size is measured by Dynamic light scattering (DLS) and photon correlation spectroscopy (PCS). Zeta potential is an important parameter that affects aggregation of vesicles and depicts the physical stability of vesicular systems and it can be measured by zeta meter.

Surface tension activity measurement: It is measured by ring method by Dunoy ring tensiometer.

Penetration and permeation methods: Depth of penetration can be visualized by confocal laser scanning microscopy.

Stability of ethosomes: The ability to retain the drug by ethosomal formulations was checked by subjecting the preparations to different temperatures i.e 25±20c, 37±20c and 45 ±2oc for different periods of time. The stability of ethosomes also can be determined by monitoring size and morphology of vesicles using DLS and TEM.

Therapeutic Applications of Ethosomes [13, 14].

>It is used in the transdermal delivery of hormones.
>It is used in the treatment of herpetic infection.
>It is used for transdermal delivery of hydrophilic and impermeable drugs through skin.
>It is used in pilosabeceous targeting.

Marketed Products of Ethosomes

Sr no	Name of product	Uses	Manufacturer
	Decroin cream	Antiaging cream,delaying the visibe signs of aging	Genome cosmetics
	Nanominox	First minoxidil containing product, which uses ethosmes. It contains 4% minoxidil, which is a well known hair growth promoter that should be metabolized by sulfation to the active compound	Germany
	Skin genuity	Powerful cellulite buster which reduces orange pee	Nottingham, UK
		Used for thetreatment of Herpes virus	Trima,Israel

Ethsomal Gel Preparation [15].

The ethsomal gel preparation involves preparation of gel base, carbopol 934 is commonly used gel and at low concentration it forms good consistency transparent gel. It will be prepared by dispersing carbopol934 in distilled water in which glycerol is previously added. To this accurately weighed quantity of methy paraben and propyl paraben were added and the mixture was neutralized by adding triethanolamine. Then the ethosomal formulation was slowly added to carbopol 934 gel base with stirring to get the ethosomal gel.

Evaluation of Ethosomal Gel

PH Measurement: The pH of gel was measured by using pH meter.
Viscosity: Viscosity was determined by Brookfield viscometer, spindle s64.
Drug content of formulated gels: Drug content was estimated by dissolving 100 mg of formulation in methanol and filtered. The volume was made up to 100 ml and the absorbance was measured at 212 nm.
In vitro diffusion study: In vitro diffusion study was carried out by using Franz diffusion cell with cellophane dialysis membrane of grade 110.

References

1. Barry BW (2001) Novel mechanisms and devices to enable successful transdermal drug delivery. Eur J Pharm Sci 14: 101-114.
2. Patel S (2007) Ethosomes: A promising tool for transdermal delivery of drug, Pharmainfo.net 5.
3. Touitou E, Dayan N, Bergelson L, Eliaz M (1999) Ethosomes-novel vesicular carriers for enhanced delivery: Characterization and skin penetration properties. J control release 65: 403-418.
4. Yuefeng Rao, Feiyue Zheng, Xingguo Zhang, Jianqing Gao, Wenquan Liang (2008) In vitropercutaneous permeation and skin accumulation of finasteride using vesicular ethosomal carriers. AAPS Pharmsci Tech 9: 860-865.
5. Zhou Y, Wei Y, Liu H, Zhang G, Wu X (2010) Preparation and evaluation of ethosomal total alkaloids of Sophora alopecuroides loaded by a transmembrane pH-gradient method. AAPS PharmSciTech 11: 1350-1358.
6. Jain S, Umamaheswari RB, Bhadra D, Jain NK (2004) Ethosomes: A novel vesicular carriers for enhanced transdermal delivery of an anti HIV agent. Indian J. Pharm Sci 66: 72-81.
7. Gangwar S, Singh S, Garg G, Ethosomes (2010) A novel tool for drug delivery through the skin, Journal of Pharmacy Research 3: 688-691.
8. Kumar KP, Radhika PR, Sivakumar T (2010) Ethosomes-A Priority in Transdermal Drug Delivery, International Journal of Advances in Pharmaceutical Sciences 1: 111-121.
9. Ainbinder D, Touitou E (2005) Testosterone Ethosome for enhanced transdermal delivery, Drug delivery 12: 297303.
10. Elsayed MM, Abdallah OY, Naggar VF, Khalafallah NM (2006) Deformable liposomes and Ethosomes: Mechanism of enhanced skin delivery. Int J Pharm 322: 60-66.
11. Bhalaria MK, Naik S, Mishra AN (2009) Ethosomes: A novel system for antifungal drugs in the treatment of topical fungal diseases. Indian J Exp Biol 47: 368-375.
12. Sheer a, Chauhan M (2011) Ethosomes as vesicular carrier for enhanced transdermal delivery of Ketoconazole Formulation

and Evaluation. IJPIs J Pharm Cosmetol 1: 1-14.
13. Verma D D, Fahr A (2004) Synergistic penetrations effect of ethanol and phospholipids on the topical delivery of Cyclosporine. A J Control Release 97: 55-66.
14. Nandy BC, Gupta RN, Rai VK, Tyagi LK, Roy S (2009) Transdermal Iontophoresis delivery of Atenolol in combination with penetration enhancers: optimization and evaluation on solution and gels. Int. J. Pharm. Sci. Drug Res 1: 91-99.
15. Dayan N, Touitou E (2002) Carrier for skin delivery of triexphenidyl HCl: Ethosomes vs. liposomes. Biomaterials 21: 187985.