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TRANSDERMAL PENETRATION EFFICACY OF ETHOSOMAL SYSTEMS WITH AND WITHOUT PENETRATION ENHANCER: A COMPARATIVE STUDY

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ABSTRACT

Ethosomal systems are now a days attracting attention of many researchers. This study is designed to observe the effect of penetration enhancers in ethosomal formulations. Ascorbic acid is taken as a model drug; phosphatidylcholine and ethanol are taken for ethosome preparation. Propylene glycol is taken as a penetration enhancer. Ethosomes are prepared by solvent dispersion method with and without penetration enhancer. The drug release profile is compared. Dialysis membrane and human cadaver skin are taken for penetration study. In this study the ethosomes which were prepared by adding penetration enhancers showed better penetration efficiency.

INTRODUCTION: Drug delivery to skin offers many advantages as compared to other route of administration [1]. The stratum corneum provides the greatest resistance to penetration, and it is the rate-limiting step in percutaneous absorption [2]. Various drug delivery technologies have been utilized for drug delivery through the skin. The lipid vesicles are being utilized since last decades. Ethosomes is a novel lipid carrier, recently developed by Touitou *et al.,* showing enhanced skin delivery [3].

Elsayed *et al.,* in 2006 has given the mechanisms by which vesicular systems deliver drugs into intact skin[4]. Ethosomal systems are sophisticated conceptually, but characterized by simplicity in their preparation, safety and efficiency - a rare combination that can expand their applications [5]. In present study ethosomal systems are formulated with the penetration enhancers. The penetration enhancing effect is compared with Ethosomes which were formulated without adding penetration enhancer.

MATERIAL AND METHODS: The sample of Ascorbic Acid was purchased from SD Fine Chemicals; Soy Phosphatidylcholine was a kind gift from Sonic Biochem Extractions Limited Indore (M.P.), propylene glycol was provided by SSIPS Bhilai. Excised human cadaver skin from the abdomen was obtained form CIMS, Bilaspur, India., Dialysis Membrane was purchased form Himedia (Av. Flat width- 29.31mm, Av. Diameter- 17.5 mm, Capacity approx.- 2.41 ml/cm.). Other chemicals and reagents used were of analytical grade.

Preparation of Ethosomes: Ethosomes were prepared by solvent dispersion method: Soya phosphatidyl-choline (Himedia) (3%) is taken and dissolved in 30% of ethanol (90%) with the help of magnetic stirrer (Remi Motors Mumbai), to this solution fine stream of distilled water (100%) was added by a syringe very slowly, then the whole system was stirred for 15- 45 minutes at 700-900 rpm [4] (**Table 1**). Same procedure is repeated by taking penetration enhancers (5% l menthol and 3% oleic acid).

TABLE 1: FORMULATION CODE AND COMPOSITION

Formulation Code	Phosphatidylcholine (%)	Ascorbic Acid (%)	Ethanol (%)	Penetration enhancer (%)
EE	3.0	2.0	30	-
EP	3.0	2.0	30	5

Permeation studies: Selection of receptor solution used for permeation experiments is critical in case of topical/ transdermal application because they mimic the in vitro situation. Aqueous receptor solutions are the most commonly used media for hydrophilic and moderately lipophilic (upto a log P octanol/ water around 2) permeants. Buffered solutions such as phosphate, around Ph 7.4, are often used. In the present study PBS (Ph 7.4) was selected on the basis of partition coefficient.

***In vitro* permeation studies through dialysis membrane:** Dialysis membrane (average flat width- 29.31 mm, average diameter- 17.5mm, capacity factor- 2.41ml/cm) was used as an artificial membrane for preliminary in vitro studies because of simplicity, homogeneity and uniformity. This membrane was hydrated in PBS (pH 7.4) for 24 hours prior to use. The permeation studies were carried out using a modified Franz Diffusion cell. The effective permeation area of the diffusion cell and receptor cell volume was 2.545 cm^2 and 15ml respectively. The temperature of receptor fluid was maintained at 37±1^oC. The receptor compartment contained PBS (pH7.4).

Dialysis membrane was mounted between the donor and receptor compartment. 1 ml formulation of drug was applied to the upper side of membrane in donor compartment. Samples were withdrawn through the sampling port of the diffusion cell at predetermined intervals over 24 hours and analyzed spectrophotometrically. An equal volume of fresh PBS maintained at 37±1^oC was replaced into the receptor compartment after each sampling. Cartesian plots of cumulative amount of drug in receptor compartment versus time were plotted. Flux (Jss, µg/cm^2/hr.) was calculated form the slope of the steady state portion of these graph.

***Ex vivo* permeation studies through human cadaver skin:** Excised human cadaver skin from the abdomen was obtained form CIMS, Bilaspur, India. The skin was store at 4^oC and the skin was collected not more than 5 days after postmortem. The skin was immersed in purified water at 60^oC for 2 minutes then stratum corneum and viable epithelium was peeled off and immediately used for the permeation experiments. Skin penetration studies were carried out by using Franz- type diffusion cells. The cell had a diffusion surface area of 2.545 cm^2 and a volume of 15ml in the receptor compartment.

Human skin was mounted horizontally with the stratum corneum side up; dividing the cell into two compartments i.e. the donor and the receptor compartments. The dermal side of skin was immersed in PBS (Ph 7.4) and the ethosomal formulation was in contact with outer skin layer. The donor compartment of the Franz diffusion cell was covered with parafilm to avoid any evaporation process. The receptor was filled with Ph 7.4 saline phosphate buffered solution. The receptor fluid was constantly stirred with a magnetic stirring bead in order to ensure its homogeneity. Formulation (1ml) was applied in the donor compartment. Pseudo- sink conditions were maintained throughout the duration of the permeation experiments.

The duration of experiments was 24 hour. At prefixed intervals 1 ml of the receptor phase was withdrawn and analyzed spectrophotometrically to determine the amount of permeated ascorbic acid. The withdrawn volume was replaced with fresh medium and a correction for dilution was carried out. The treatment was carried out at 37^oC, and chamber was kept protected from light. Cartesian plots of cumulative amount of drug present in receptor compartment versus time were plotted. Flux (J_{SS}, mg/cm^2/hr) was calculated from the slope of the steady state portion of these graphs.

TABLE 2: PERMEATION STUDY THROUGH DIALYSIS MEMBRANE AND HUMAN CADAVER SKIN

S. No.	Formulations	Cumulative % drug release (After 24 hr.)	
		Dialysis Membrane	Human Cadaver Skin
01	EE	39.9	43.2
02	EP	41.2	40.7

RESULTS AND DISCUSSION: The extent of drug release from the ethosomal system is of considerable importance because it determines the actual amount of active drug which reaches to the target site.

In present study a modified Franz diffusion cell was employed for release study. In *in vitro* study the dialysis membrane was used as an artificial membrane which acts as a skin barrier, and human cadaver skin was used in ex vivo release studies (Table 2). The release studies depend on the ability of Ethosomal carriers to deliver the drug at the target site. The cumulative % drug release after 24 hr was taken into consideration. In present work, formulation EE and EP shows 39.9 % and 43.2% drug release respectively across dialysis membrane.

And again formulations EE and EP shows 33.55%, and 40.7% drug release respectively across human cadaver skin. Formulation EE is contains drug, phosphatidylcholine and ethanol. And formulation EP contains propylene glycol (PG) as a penetration enhancer. PG increases drug partitioning and drug permeation through the skin. This effect of PG is responsible for higher amount of drug which crosses the skin.

CONCLUSION: By adding some penetration enhancers ethosomal carrier systems can be better utilized for drug delivery. In this study ethosomal systems are prepared and compared with ethosomal systems containing penetration enhancer. Ethosomes containing penetration enhancers showed better results.

REFERENCES:

1. Verma P, Thakur AS, Deshmukh K, Jha AK and Verma S: Routes of Drug Administration. International Journal of Pharmaceutical Studies and Research 2010; 1(1) 54-59.
2. Sinha VR and Kaur MP: Permeation Enhancers for Transdermal Drug Delivery. Drug Development and Industrial Pharmacy. 2000; 26(11): 1131–1140.
3. Dayan N and Touitou E: Carrier for skin delivery of trihexyphenidyl HCl: Ethosomes vs. liposomes. Biomaterials. 2002; 21:1879-1885.
4. Elsayed M.M., Ossama Y. A., Naggar V. F. and Khalafallah N.M., Deformable liposomes and ethosomes: Mechanism of enhanced skin delivery, Int J Pharm. (2006) 322, 60-66.
5. Elsayed M, Abdallah OY, Naggar VF, Khalafallah NM: Lipid vesicles for skin delivery of drugs: Reviewing three decades of research. International Journal of Pharmaceutics 2007; 332(1-2):1-16.

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