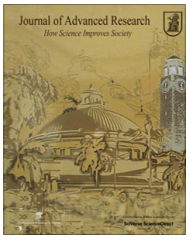
Journal of Advanced Research (2016) 7, 453–461

Cairo University

Journal of Advanced Research



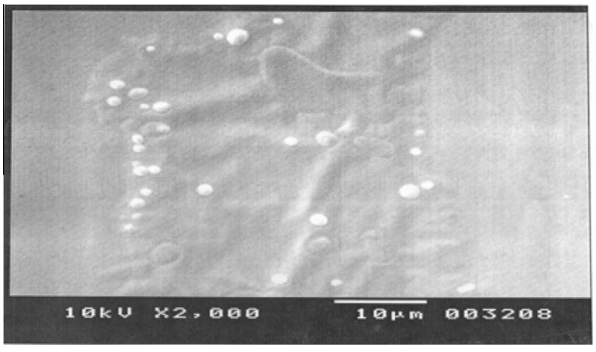
ORIGINAL ARTICLE

In vitro assessment of pharmaceutical potential of ethosomes entrapped with terbinafine hydrochloride

Syed Ahmed Iizhar [a,*], Ismail Ahmed Syed [b], Rukhsana Satar [c], Shakeel Ahmed Ansari [d]

[a] *Department of Pharmaceutical Sciences, Ibn Sina National College of Medical Studies, Jeddah 21418, Saudi Arabia*
[b] *Department of Basic Sciences, Ibn Sina National College of Medical Studies, Jeddah 21418, Saudi Arabia*
[c] *Department of Biochemistry, Ibn Sina National College of Medical Studies, Jeddah 21418, Saudi Arabia*
[d] *Center of Excellence in Genomic Medicine Research, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

GRAPHICAL ABSTRACT



SEM images of F6 ethosomal formulation

Abbreviations: DEE, drug entrapment efficiency; PEG, polyethylene glycol; PI, polydispersity index; TH, Terbinafine Hydrochloride; MR, marketed cream.

* Corresponding author.
E-mail address: iizharahmedsyed@gmail.com (S.A. Iizhar).

Peer review under responsibility of Cairo University.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.jare.2016.03.003

ARTICLE INFO

Article history:
Received 5 January 2016
Received in revised form 8 March 2016
Accepted 9 March 2016
Available online 15 March 2016

Keywords:
Ethosomes
In-vitro drug diffusion
Terbinafine Hydrochloride
Transdermal flux

ABSTRACT

The present study investigates the entrapment of terbinafine hydrochloride (TH) in ethosomal vesicles via unsonicated and sonication method. Carbopol 934P was incorporated in the best formulation, F6, obtained by sonication method. The formulated ethosomal gel obtained as such i.e. F6* was exploited to achieve a zero order release profile of TH. The composition includes phospholipid, ethanol and propylene glycol. Drug entrapment efficiency (DEE), *in-vitro* and *ex-vivo* drug diffusion studies, FT-IR and stability studies of the prepared ethosomes were investigated. The size and shape of F6 ethosomes vesicles were characterized by SEM. *In-vitro* drug release studies were performed using sigma dialysis membrane in phosphate buffer, pH 7.4 for 12 h while drug content was determined by HPLC. DEE was ranked from 55.33 ± 1.32% to 69.11 ± 2.11%. Highest DEE was seen with F6 ethosomal formulation with a vesicle size of 248 ± 1.02 nm. FT-IR studies confirmed that there was no chemical interaction between drug and excipients used in the formulation. *Ex-vivo* result suggested that drug diffusion observed after 12 h from F6* and marketed cream (MR) formulations was 74.01 ± 0.62% and 61.45 ± 0.86%, respectively. The results of similarity factor (f_2 values) for MR and F6* ethosomal gel were 85.14 and 42.63, respectively. It revealed that F6* showed dissimilar dissolution profiles. Transdermal flux value for F6* and MR was found to be 144.61 ± 1.28 μg/cm^2/h and 121.6 ± 1.16 μg/cm^2/h, respectively. This study disclosed that F6* resides at targeted site for a relatively longer period of time thereby signifying the improved patient compliance.

Introduction

Ethosomes are soft malleable vesicles constituting phospholipids, ethanol (relatively high concentration) and water [1]. They act as non-invasive delivery carriers for targeting drugs to deep skin layers. Hence, when integrated into a vesicles membrane, ethosomes promote the vesicle to penetrate the stratum corneum [2]. The utility of ethosomes as a carrier of antiviral drug acyclovir was previously tested by Essa and coworkers for the topical treatment of herpetic infection. They demonstrated significant improvement of ethosomal 5% acyclovir system as compared to a 5% acyclovir cream by performing two-armed, double-blinded, randomized clinical trial [3]. In another study, enhanced drug delivery via ethosomal carrier was observed by an increase in depth and fluorescent activity [4].

A synergistic mechanism was suggested between ethanol, vesicles and skin lipids by Touitou and coworkers for elucidating the role of ethosomes in promoting enhanced drug delivery [5]. It was proposed that "ethanol effect" resulted in an interaction of ethanol with the lipid molecules in the polar head group region and exhibits reduction in the transition temperature of lipids in the stratum corneum, which ultimately increases their fluidity and decreases the density of lipid multilayer. This effect is followed by the "ethosomal effect" which involves the penetration and permeation of lipids due to the malleability and fusion of ethosomes with skin lipids. This step resulted in the release of drug into the deep layers of skin. It should be noted that since ethanol imparted flexible characteristics to vesicles, it allowed the ethosomal vesicles easier and deeper penetration into the deeper layers of the skin. The release of the drug in the deep layers of the skin and its transdermal absorption could then be the result of a fusion of ethosomes with skin lipids, and drug release at various points along the penetration pathway [6].

The pharmaceutical technology in recent years has witnessed the formulation of modified liposomes for skin mediated drug delivery, and in this regard, considerable attention has been paid to vesicular approaches involving transfersomes and ethosomes. These approaches utilize non-toxic and biodegradable chemicals which prolong half-life of a drug in order to provide a sustained drug delivery release effect [7,8]. Ethosomal systems are very efficient in delivering substances in terms of quantity and depth by increasing cell permeability/lipid fluidity [9–11].

In some of the comparative studies, favorable attributes of ethosomes over liposomes, in terms of skin penetration and therapeutic effects as solution and cream have been outlined. These results are encouraging in relation to transdermal delivery of therapeutic agents via ethosomal vesicles [12]. Moreover, terbinafine hydrochloride (TH) is an allyl amine class derivative used for treating local and systemic infections. It is highly effective against dermatophytes and *Aspergillus* species for superficial and systemic fungal infections [13–15].

Hence, the objective of the present study involves the formulation of ethosomes containing Carbopol 934P and phospholipids as vesicle forming agent along with TH to observe its effect at targeted site for a relatively longer period of time with a zero order release profile.

Material and methods

Materials

Terbinafine hydrochloride and propylene glycol were obtained from Orchid Pharmaceuticals, India, and Sandoz Chemicals Ltd., India, respectively. Soya phosphatidylcholine was purchased from Sigma-Aldrich Chem, Germany. Carbopol 934P was procured from Correl Pharma Ltd., Mumbai, India. Cellophane membrane grade 110 was purchased from Hi Media Laboratories, Mumbai, India. Methyl paraben, Propyl paraben, Triethanolamine, methanol and high purity 99.9% Ethanol Omnis Grade were obtained from SD Fine chemicals, Mumbai, India. All other materials were of analytical grade.