Development and Antimicrobial Evaluation of Binary Ethosomal Topical Gel of Terbinafine Hydrochloride for the Treatment of Onychomycosis

K. Shruthi, D. Narendar, N. Arjun and Veerabrahma Kishan*

Laboratory of Nanotechnology, Department of Pharmaceut ics, University College of Pharmaceutical Sciences, Kakatiya University, Warangal, Telangana State- 506009, India.

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ABSTRACT

The objective of this investigation was to prepare and evaluate the binary ethosomal gel containing terbinafine HCl (TH) to treat onychomycosis. It was reported that binary ethosomes possessed good permeation and stability characteristics than ethosomes. Binary ethosomes of TH were prepared by film hydration method. Prepared binary ethosomes were evaluated for optimized system. Further, ex-vivo skin permeation studies were conducted with rat skin. The formulation of binary ethosomes was converted to gel by using carbopol 934 and evaluated for rheological properties. Antifungal testing of gel was done by cup plate method, using Candida albicans and zones of inhibition of growth were measured. The size, ZP and EE of the prepared binary ethosomes ranged from 200-320nm, -20 to -30mV and 70-92% respectively. In-vitro and ex-vivo diffusion studies indicated that formulation BE4 with greater amount of binary alcoholic phase, showed faster release and increased flux over others. SEM studies revealed that binary ethosomes were in spherical shape. Based on size, EE, drug release profile and antifungal studies, the BE4 formulation was selected for gel preparation. The prepared 0.5% binary ethosomal BE4 gel showed good content uniformity, pH 5.5, no skin irritation, good consistency and better rheological behaviour. Further, antifungal studies of BE4 gel indicated that gel had lower antifungal activity than plain BE4 formulation, probably due to gelling effect in agar diffusion studies. In conclusion, we developed a pharmaceutical gel containing binary ethosomes of BE4 having TH to provide anti-fungal effects useful for the treatment of onychomycosis.

KEYWORDS: Terbinafine HCl; Onychomycosis; Binary ethosomes; Topical gel; Cup plate method.

Introduction

Onychomycosis is a fungal infection of the toenails or fingernails. It mainly causes fingernails or toenails to thicken, discolour, disfigure and split. Half of all nail disorders are caused by onychomycosis, and it is the most common nail disease in adults. It is caused by three main classes of organisms: dermatophytes, including Epidermophyton, Microsporum, and Trichophyton species (fungi that infect hair, skin and nails and feed on nail tissue), yeasts, and non-dermatophyte molds (Boni, 1998).

Most of the medicines used to treat onychomycosis were not very effective because, they cannot penetrate the nail deep enough (Archan and Deepshikha, 2011). Hence, there is a need to develop an effective topical treatment that can increase the permeation of drug through stratum corneum, allow site-specific administration and minimize the systemic exposure of the therapeutic agent (Gyati et al., 2013). Therefore, colloidal drug carrier systems such as micellar solutions, vesicle and liquid crystal dispersions, as well as nanoparticle dispersions, liposomes, and other micelles like niosomes, transfersomes and ethosomes consisting of small particles of 10-400 nm diameter show great promise as drug delivery systems (Bhalaria et al., 2009; Patel and Bhargava, 2012).

Ethosomes are novel lipid carrier systems, and are the modified forms of liposomes containing high ethanol content, being developed by Touitou et al., 2000. Ethosomal drug delivery is non-invasive and delivers the drug to the deep skin layers or the systemic circulation (Vivek et al., 2012). They are reported to have better permeation (Jain et al., 2007).

Ehab and Mina, 2007 reported that the in vitro skin permeation studies of ethosomal gel showed much more efficiency in delivering salbutamol sulphate than liposomes. Zhang et al., 2012 compared the skin permeation of ethosomes, binary ethosomes, and transfersomes against liposomes under non-occlusive condition. The binary ethosomes showed most effective drug penetration through skin. Sarath et al., 2012 reported that the percentage drug released from ethosomes was nearly 26% greater than plain drug incorporated cream across cellulose membrane.