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USE OF PENETRATION ENHANCERS FOR INCREASING THE *IN VITRO* RELEASE OF FLUCONAZOLE FOR TOPICAL APPLICATION

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ABSTRACT

Fluconazole is an antifungal agent used in the treatment of dermatophytes. The efficiency of the treatment depends on the rate of penetration of the drug into the skin. Topical preparations of fluconazole were prepared as ointment bases containing different penetration enhancers. The topical preparations such as oleaginous base, absorption base, O/W emulsion base, W/O emulsion and water-soluble base were tested for their rheological properties and the in-vitro drug release from the formulation. The penetration enhancers tested were Dimethyl sulfoxide, Propanol and Oleic acid. The results show that water-soluble base containing propanol as the penetration enhancer has the highest release of fluconazole as compared with other formulations.

The tested penetration enhancers could be arranged in the following descending order with respect to the amount of fluconazole released:

Propanol > Dimethyl sulfoxide > Oleic acid

CHAPTER 1

INTRODUCTION

1.1 Research background

Superficial skin infection is the most common disease caused by the dermatophytes (Brennan & Leyden, 1997). This kind of infection can be treated with fluconazole. Fluconazole is an antifungal agent of triazoles class with broad spectra used in the treatment of dermaphytoses (LesherJr, 1999). It acts by inhibiting demethylase, an enzyme involved in the production of ergosterol, which are the important component of the fungal cell membrane (Scully, Ei-Kabir, &Samaranayake, 1994).

Fluconazole is white or almost white crystal-like powder. It is miscible in alcohol and acetone, readily miscible in methanol, slightly miscible in water and very slightly miscible in toluene. In addition, it is a weak base and has high melting point for about 223-224°C (Corrêa& Salgado, 2011). A part of that, fluconazole exhibits polymorphism which appears in two different crystalline form (Gu& Jiang, 1995). The fluconazole-II which is less stable form will transform to fluconazole-I which are more stable due to temperature and pressure (Corrêa& Salgado, 2011; Desai &Dharwadkar, 2009).

Fluconazole topical formulation is one of the effective treatments to skin infection as it able to avoid first pass metabolism by the liver, non-invasiveness and improve patient compliance (Mills, 2013; Singla, Saini, Joshi, &Rana, 2012). Fluconazole can be formulated into different types of topical delivery system including ointment, emulsion, emulgel, lipogel, and micro-emulsion (Güngör, 2013). In this research project, the topical preparation of fluconazole will be formulated into ointment which can be classified into four general bases; oleaginous base, absorption base, emulsion base (which can be