UNIVERSITI TEKNOLOGI MARA

NANOEMULSION LOADED WITH PALM VITAMIN E FOR COSMECEUTICAL APPLICATIONS

TOMMY JULIANTO BIN BUSTAMI EFFENDI

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the result of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

Name of Student	:	Tommy Julianto bin Bustami Effendi
Student I.D. No.	:	2005767742
Programme	:	PH990
Faculty	:	Faculty of Pharmacy
Title	:	Nanoemulsion Loaded with Palm Vitamin E for Cosmeceutical Applications
Signature of Student	:	.....
Date	:	August 2014

ABSTRACT

Nanoemulsion is one of the alternative nano-lipid delivery systems of lipophilic active ingredients into the human skin in pharmaceutical and cosmetic applications. Palm vitamin E extract is a natural lipophilic active that contains α-, β-, δ-, γ-tocotrienols and α-tocopherol. Palm vitamin E has the potency as an antioxidant for delaying the skin ageing process in cosmetic application, although the skin absorption of palm vitamin E in conventional formulations is considered low. The high lipophilicity of palm vitamin E isomers causes the limitation in the skin permeation. The skin penetration can be enhanced by the loading of palm vitamin E extract in an oil phase of a nanolipid-delivery system such as nanoemulsion. Therefore, the potency of nanoemulsion loaded with palm vitamin E extract was studied. Palm vitamin E extract was loaded in two nanoemulsions prepared by two different techniques and then incorporated into polymeric hydrogels. The skin absorption and pharmacokinetics of vitamin E isomers loaded in nanoemulsion hydrogels were investigated. Liquid chromatography assay method of α-, δ-, γ-tocotrienols and α-tocopherol in various samples of the different stages of this study was successfully validated and re-validated. Nanoemulsion formulations were developed firstly by the formation of lyotropic phase system as a pro-nanoemulsion (nanophase gel) by heat mixing, and secondly by using self nano-emulsifying technique by cold mixing. Two oils were used in the nanoemulsion formulation development; palm oil was formulated as a nanoemulsion by using hot mixing technique and, *Nigella sativa* oil nanoemulsion was prepared by using cold mixing of self emulsifying system. Palm oil nanoemulsion was formulated with the aid of design experiment as semisolid hydrogel by loading carbomers (Carbopol 934 and 940) and then characterized by the droplet size distribution to determine the best formulation for loading with palm vitamin E extract. The effect of carbomers incorporated in nanoemulsion formulations on the droplet size distribution, semisolid rheology and texture was determined by using expert design experiment to select a stable formulation for permeation studies. The *in vitro* vitamin E isomers permeation through the polycarbonate membrane was investigated using Franz diffusion cells. The vitamin E isomers permeation through polycarbonate membrane depended on the pore size of membrane and the concentration of Carbopol 940 in nanoemulsion hydrogel formulations. The different formulation of nanoemulsion formulation has not shown any affect on the permeation profiles of vitamin E isomers. Finally, the *in vivo* skin penetration of α-, δ-, γ-tocotrienols and α-tocopherol loaded in nanoemulsion hydrogel by topical application on the hairless rat abdominal skin was investigated. The accumulative amount of vitamin E isomers in rat skin epidermis and the bioavailability of vitamin E isomers measured in the rat plasma showed that nanoemulsion hydrogels with small droplets size provided high skin absorption. δ-tocotrienol in the form of nanoemulsion hydrogel with mean droplet size of 100nm was preferably absorbed through the rat skin compared to γ-, α-tocotrienols and α-tocopherol.

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