UNIVERSITI TEKNOLOGI MARA

STUDY ON SKIN DELIVERY OF TOCOTRIENOLS AND UBIQUINONE LOADED IN NANOEMULSIONS: EFFECT OF NATURAL OILS AND FATTY ACIDS AS VEHICLE AND PENETRATION ENHANCER

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ABSTRACT

The increasing demand for skincare products has led to the rapid rise of the global cosmetics business over the past few decades. Many cosmetics and dermatological products have used vitamin E and ubiquinone as antioxidants. However, the skin delivery of these compounds has not been satisfactory. This implies that benefits from these antioxidants are not optimised, while wastage incurs costs. It is postulated that the solutions to this conundrum (of attempting to boost antioxidant delivery while keeping the product price low) are, one, to substitute a substance that is high in tocotrienols (a subfamily of vitamin E), two, adopting a novel delivery system in the form of nanoemulsions (NEs), and the inclusion of permeation enhancers. It has been shown that tocotrienols have greater antioxidant efficacy than tocopherols. The (NEs) formation technique with low mechanical energy allows this approach to be more affordable and advantageous to the industry. The objective of this research was to enhance the skin absorption of vitamin E isomers in combination with ubiquinone loaded in the oil phase of a NE produced from nanophase gel (NPG). On research methodology, first, was the validation by high-performance liquid chromatography (HPLC) assay method for the simultaneous determination of vitamin E isomers (α-, δ-, γ-tocotrienols), and ubiquinone in diverse samples from the various stages of this study. The preparation of NEs was by using the D-phase emulsification technique. Initially pre-concentrated NEs known as NPG was formulated. Then the NPG was self-emulsified in water to produce NEs. NPG consists of sucrose monoester as a surfactant, glycerine as the aqueous phase, and natural oils (palm kernel oil and olive oil) in combination with fatty acids (lauric acid and oleic acid) as penetration enhancers. Franz diffusion cell method was used to test the permeation profiles of vitamin E isomers and ubiquinone through a polycarbonate membrane for the *in vitro* study. For *ex vivo* skin penetration of vitamin E isomers and ubiquinone, loaded in the NPG NE, the formulation was applied topically to the hairless rat abdomen skin and examined. The HPLC assay was sensitive and selective with good linearity in the range. The total run time of chromatographic analysis was 8 minutes, allowing for high throughput. The preparation of NEs in palm kernel oil resulted in formulations with an average size of 161nm±1.62, PDI value of 0.173±0.03, and -23±1.07, zeta potential. As for the NE in olive oil, the average size reported was 161nm±1.60, PDI value of 0.191±0.02, and zeta potential of -28.6±3.56. From the prepared NEs with a mean droplet size of 400 nm, it was found that the α- and δ-tocotrienol more readily permeated through the rat full-thickness skin than γ-tocotrienol and ubiquinone. The optimum absorption of tocotrienols into the epidermal layer of rat skin is provided by NEs produced from NPG concentrations in the order of 40%>50% >30%. While for ubiquinone absorption, NPG concentrations in NEs were determined to be in the range of 50%>40%>30%. In both the dermal layer and the receptor phase, a low concentration of both actives was detected. This was probably due to the NPG NEs being negatively charged, and causing the electrostatic repulsion exerted by the negatively charged cell membrane and preventing the actives from entering the membrane. In conclusion, by adopting the three approaches in this study, namely using tocotrienols as antioxidants, loading actives in NEs and inclusion of permeation enhancers, the absorption of actives at the epidermis increased. Therefore, this strategy may be beneficial for the cosmetic industry.

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