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Nanostructured vitamin E phosphate: Characterizing its cutaneous permeation and interaction with skin lipids

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Background: Vitamin E (alpha tocopherol, α-T) can provide protection from ultra violet radiation (UVR) induced skin damage and photo-ageing. However, α-T is easily oxidized and, due to its oily form, it is not easily delivered into the epidermis where it elicits its photo protective effects. The aim of this study was to investigate the cutaneous permeation and human stratum corneum (SC) lipid interactions of α-tocopherol phosphate (α-TP), a new, chemically stable, water-soluble powder derivative of vitamin E, to in order to evaluate if it displayed the potential to be used as a photo-protective agent.

Methods: The solubility and critical aggregate concentration (CAC) of α-TP was determined at different pHs. The aggregate size at pH7.4 was determined using dynamic light scattering (DLS) and atomic force microscopy (AFM). The α-TP diffusion from a 90% saturated solution through three cellulose ester membranes of different molecular weight cut-offs (MWCO) was compared at pH7.4 and 9 using Franz diffusion cells. A topical dose of 7.5mg/cm2 was used to test the α-TP and α-T porcine skin deposition using a tape stripping protocol. A SC lipid model composed of ceramide, cholesterol, and palmitic acid, which mimicked the SC intercellular lipids, was employed to test the interactions of α-TP and α-T with the SC lipids in a series of Langmuir trough experiments.

Results: The solubility of α-TP increased with an increase in pH (20.72±0.99 and 36.45±2.27mg/ml at pH7.4 and 9, respectively) ($p<0.05$). Aggregates were formed only at pH7.4, CAC – 4.2mM. The aggregate size at pH7.4 was 9.36±1.59nm using DLS and 26.80±1.79nm using AFM. The diffusion of α-TP through the cellulose membranes at pH9 was better compared to pH7.4. Skin deposition studies demonstrated that α-TP, when administered in a pH7.4 vehicle, showed significantly higher deposition in SC and epidermis compared to α-T (531.65±311.75 vs. 75.66±7.24 and 280.69±47.30 vs 51.81±5.95μg, respectively) ($p<0.05$). The injection of α-TP in the sub phase of the Langmuir constant area assays induced a surface pressure change of ~10 mN/m whereas, α-T induced a surface pressure change of <3 mN/m.

Conclusion: Adding a phosphate to α-T generated an amphiphilic molecule that aggregated in solution, but the aggregates were small enough to pass into the skin, perhaps via follicular route. Once in the skin the enhanced intercellular lipid interactions allowed α-TP to pass through the SC into the epidermis more effectively than α-T.

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