α-Tocopherol pro-vitamins: synthesis, hydrolysis and skin accumulation

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AIM OF THE WORK

We synthesized new α-tocopherol pro-vitamins (PV), that could be reconverted in the skin to the active α-tocopherol (VE) and able to release another active moiety in order to obtain a synergic effect. In particular, the attention was dedicated to amino acids such as glycine and alanine and to pyroglutamic acid (PCA), Natural Moisturizing Factor (NMF) components.

Objectives

To set up a new HPLC method to simultaneously analyze PV and VE. To test derivatives sensitivity to enzymatic hydrolysis and to evaluate PV skin permeation and metabolism. The performances were compared with α-tocopherol acetate (VEAc), used as reference.

Enzymatic hydrolysis

- Porcine Liver Esterases concentration: 5 UI/ml.
- Reaction solution: 1:10(v/v) MeOH: DiMethyl-β-Cyclodextrin (DM-β-CD) 5% in PB pH 8 @ 37°C.

METHODOLOGY

Skin extraction

- Heat separation dermis/epidermis
- Extraction: 1h in 2 ml methanol +1000 rpm for 10 min

HPLC analysis

- Column: Nova-pak® C8 (Waters)
- Mobile phase: acetonitrile: water: 2-amino-2-methylpropanol (95: 5: 0.3)
- Flow: 1.5 ml/min
- UV detection: 215 nm

RESULTS

New derivatives synthesis

VE and VEAc skin accumulation

Extent of metabolism (E%)

The stack columns represent the sum of the amount of PV recovered and the amount of VE originated after skin metabolism.

CONCLUSIONS

- The new α-tocopherol derivatives are sensitive to enzymatic hydrolysis.
- They accumulated in a significant extent.
- The new derivatives underwent skin metabolism and originated substantial amount of α-tocopherol.
- They allow the use of more hydrophilic vehicles.
- Their metabolism generates components with synergic and advantageous effects.