W4209

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

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AIM OF THE WORK

We syntesized 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.

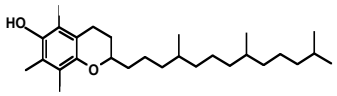
Objectives

To set up a new HPLC method to simoultaneously 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–tocopheryl acetate (VEAc), used as reference.

METHODOLOGY

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.



Skin accumulation

- Franz type diffusion cell (area 0.6 cm^2)
- Donor solution
  - a) PV in 1:1 EtOH:PG 20%
  - b) VE and VEAc 1% in Isopropyl myristate
- Barrier: Rabbit ear skin
- Receptor solution: DM-β-CD 5% in a 0.9% NaCl solution.
- Duration: 2, 4, 6 hs @ 37°C

Skin extraction

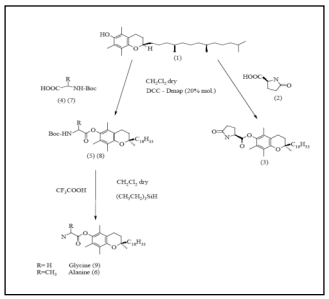
- Heat separation dermis/epidermis
- Extraction: 1h in 2 ml methanol
- 11000 rpm for 10 min

HPLC analysis

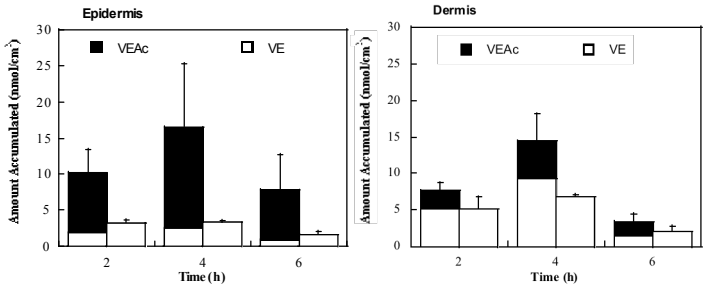
- Column: Nova-pak® C8 (Waters)
- Mobile phase: acetonitrile: water: 2-aminoeptane (95: 5: 0.3)
- Flow: 1.5 ml/min
- UV detection: 215 nm

RESULTS

New derivatives synthesis



VE and VEAc skin accumulation

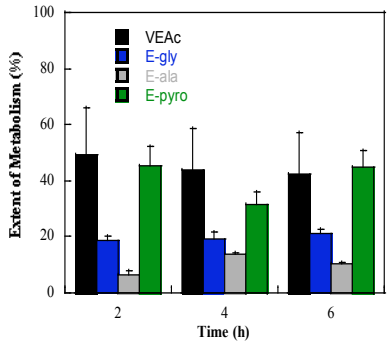


Extent of metabolism (E%)

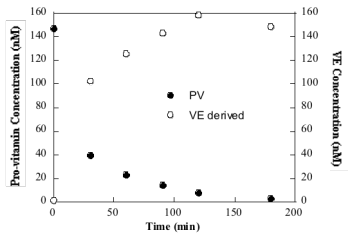
Extent of metabolism (E%) calculated according to:

$$E = \frac{VE}{VE + PV}\%$$

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



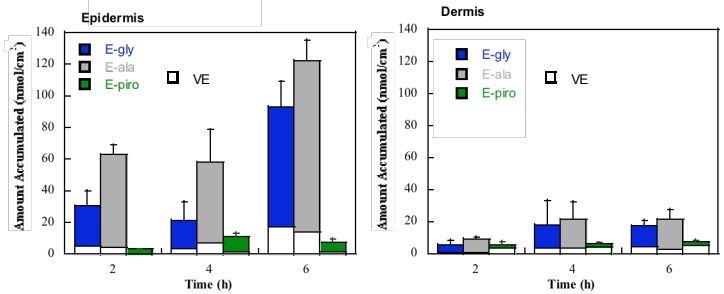
Enzymatic hydrolysis kinetics



Half-life calculated according to first order reaction

	VEAc	E-gly	E-ala	E-pyro
Half-life (min)	47.5 ± 7. 9	49.5 ± 7. 2	142 ± 1	2360 ± 747

New derivatives skin accumulation



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 synergistic and advantageous effects.