

## **Tocopherol, Retinol, and Coenzyme Q<sub>10</sub> Penetration Study**

### **- Final Report-**

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We have been commissioned by AQUANOVA German Solubilisate Technologies (AGT) GmbH to study the stratum corneum penetration of tocopherol, retinol, and coenzyme Q<sub>10</sub>. The objective of this study was to characterize the penetration of these three substances into the human stratum corneum *in vivo*.

### **Materials and Methods**

#### **Study Products**

Five test formulations were studied:

- (1) Water-soluble 20% Tocopherol Solubilisate
- (2) Water-soluble 10% Retinol Solubilisate
- (3) Water-soluble 5% Coenzyme Q<sub>10</sub> Solubilisate
- (4) Cream Containing 2.5% Vitamin E Solubilisate (equivalent to 0.5% vit. E)
- (5) Cream Containing 0.5% Vitamin E

#### **Test Formulation Application**

Twenty-five healthy volunteers had the study products applied to defined test areas on their volar forearms in standardized fashion three times daily for 7 days. Each treatment consisted of the application of 200 µL of study product to a 5x5 cm test area.

#### **Detection of Test Substance Penetration into the Stratum Corneum**

After the treatment period, multistep lipid extraction with acetone, ethanol, and n-hexane/isopropanol was performed concurrently with 15 tape strippings.

Acetone achieves superficial extraction from the stratum corneum. Ethanol extracts lipids from the deeper layers, and extraction with n-hexane/isopropanol reaches the basal layers of the stratum corneum, including the epidermal barrier lipids.

A series of 15 tape strippings reaches the entire stratum corneum including the basal layers of the epidermal barrier.

Tocopherol, retinol, and coenzyme Q<sub>10</sub> were quantitated in the extraction solutions and in strips 1, 3, 5, 8, 10, 12, and 15 by high-performance liquid chromatography. The HPLC assays were performed by Dr. Nissen, DermaConsult GmbH.

## **Results**

### **Water-soluble 20% Tocopherol Solubilisate – Tape Stripping**

Tocopherol showed excellent penetration throughout the entire stratum corneum: Larger concentrations (29.4 µL/mL) were even found in the basal layers of the stratum corneum.

### **Water-soluble 20% Tocopherol Solubilisate – Multilayer Lipid Extraction**

Tocopherol was detected in all layers of the stratum corneum. Of note, the concentration in the basal layers of the stratum corneum was as high as 95.4 µg/mL.

### **Water-soluble 10% Retinol Solubilisate – Tape Stripping**

Retinol showed linear penetration and was found in larger concentrations (5.7 µL/mL) even in the basal layers of the stratum corneum.

### **Water-soluble 10% Retinol Solubilisate – Multilayer Lipid Extraction**

Retinol was quantitated in all layers of the stratum corneum. Particularly high was the retinol concentration in the basal layers of the stratum corneum (27.9 µg/mL).

### **Water-soluble 5% Coenzyme Q<sub>10</sub> Solubilisate – Tape Stripping**

Coenzyme Q<sub>10</sub>, like retinol, showed linear penetration and was also detectable in the basal layers of the stratum corneum.

### **Water-soluble 5% Coenzyme Q<sub>10</sub> Solubilisate – Multilayer Lipid Extraction**

Coenzyme Q<sub>10</sub> was quantitated in all layers of the stratum corneum. Particularly high was the coenzyme Q<sub>10</sub> concentration in the basal layers of the stratum corneum (15.7 µg/mL).

## **Cream – Tape Stripping**

After application of both vitamin E solubilisate and the commercially available vitamin E formulation, vitamin E was found in all layers of the stratum corneum, including the basal layers. Only in the middle layers (tapes 8 and 10) was the concentration statistically significantly lower with the commercial vitamin E formulation. After application of the vitamin E solubilisate formulation in particular, vitamin E appears to accumulate in the middle layers of the stratum corneum.

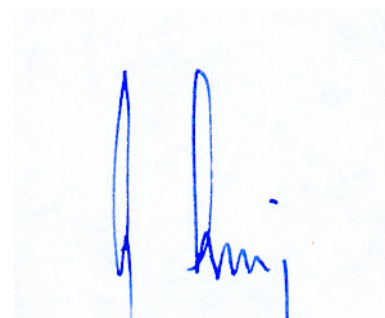
## **Cream – Lipid Extraction**

With both formulations, vitamin E was detectable in all layers of the stratum corneum, and no statistically significant difference was found.

## **Conclusion**

The solubilisates are equally suitable for the penetration of tocopherol, retinol, and coenzyme Q<sub>10</sub>. A particularly important finding is the detection of high concentrations in the basal layers of the stratum corneum where a positive interaction with the epidermal barrier is likely. Tocopherol, retinol, and coenzyme Q<sub>10</sub> can all be expected to have a moisturizing effect and to stabilize the epidermal barrier function.

The cream is a suitable vehicle for tocopherol penetration. Accumulation of vitamin E in the basal layers of the stratum corneum was obtained with both the vitamin E solubilisate and the commercial vitamin E formulation, suggesting a favorable effect on the epidermal barrier function. The vitamin E solubilisate appears to accumulate in the middle layers of the stratum corneum, suggesting a potential depot function.

A handwritten signature in blue ink, appearing to read 'W. Gehring', is centered on the page. The signature is written in a cursive style with a small dot above the 'i'.

Bietigheim, Germany, July 14, 2003

Prof. Dr. Wolfgang Gehring