Correlation of *In Vitro* Gene Expression Analysis with *In Vivo* Efficacy

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Abstract

The objective of this research was to conduct in vitro gene expression testing of hydrolyzed jojoba esters and correlate these results with randomized, double-blind, vehicle-controlled in vivo efficacy studies. Gene expression testing of 1% hydrolyzed jojoba esters in glycerin produced the following statistically significant gene expression changes over the vehicle: up regulation in AQP3, AQP5, KLK5, KLK6, KLK7, TXN, TXNRD, and CAT; and down regulation in TNF, MKI67, and EDN1. Current literature shows associations between AQP3 and APQ5 and skin hydration, as well as associations between TNF and an inflammatory response. Three small IRB approved studies were carried out to obtain efficacy data. Study 1: An oil in water emulsion containing 1% hydrolyzed jojoba esters produced statistically significant (p<0.05) increases in skin hydration compared to the vehicle, one and two hours post application (43% and 67%, respectively, n=17). Study 2: A water-based toner containing 0.2% hydrolyzed jojoba esters produced statistically significant (p<0.05) increases in skin hydration compared to the vehicle toner, one and two hours post application (22% and 16%, respectively, n=15). Study 3: Inflammation was studied in vivo by evaluating erythema and barrier function of insulted (i.e. dry shaved) skin. The addition of 0.2% hydrolyzed jojoba esters to a baby wipe formulation produced statistically significant decreases in erythema (p<0.05) and increases in barrier function (p<0.05) as compared to the vehicle baby wipe (n=14). These studies demonstrate the correlation between in vitro gene expression data and in vivo efficacy. Additional in vivo studies will be performed to evaluate desquamation, antioxidant responses, proliferation, and pigmentation as indicated by the remaining genes that were impacted by hydrolyzed jojoba esters.

Introduction / Background

Hydrolyzed jojoba esters are multifunctional ingredients that have been utilized and/or tested in a variety of cosmetic and personal care formulations such as creams/lotions, hand sanitizers, nonwoven wipes, sunscreens, sunless tanners, shampoos / conditioners, toners / astringents, face washes, face (sheet) masks, and oil-free formulations. Its film-forming properties make it ideal for rinse-off products and products that require water resistance or to extend the period of residence time on the skin.

Hydrolyzed jojoba esters are made by the hydrolysis of jojoba oil, and are available in two forms: high concentration (HC HJE) [INCI: Hydrolyzed Jojoba Esters (and) Jojoba Esters (and) Water (Aqua)] and low concentration (LC HJE) [INCI: Hydrolyzed Jojoba Esters (and) Water (Aqua)].
**Objective:** To determine the effect of LC HJE on gene expression in vitro using full thickness skin.

**Method:** Gene-expression testing of hydrolyzed jojoba esters (LC HJE) was conducted by Genemarkers, LLC (Kalamazoo, MI) using quantitative PCR to measure changes in gene expression using the MatTek full thickness skin system (EpiDerm FT).

**Results:** The data indicates statistically significant change over the vehicle in gene expression for genes related to the following biological functions.

- **Up regulation of AQP3 and AQP5** suggests an increase in skin hydration.
- **Down regulation of TNF** suggests a reduction in the inflammatory response.
- **Up regulation of KLK5, KLK6, and KLK7** suggests an increase in stratum corneum shedding and keratinocyte turnover (desquamation).
- **Up regulation of TXN, TXNRD1, and CAT** suggests an increase in antioxidant response.
- **Down regulation of MKI67** is in agreement with anti-aging literature (proliferation).
- **Down regulation of EDN1** suggests a reduction in pigmentation / brightening effect.

1. AQP (aquaporin), TNF (Tumor Necrosis Factor), KLK (kallikrein), TXN (Thioredoxin), TXNRD (Thioredoxin Reductase), CAT (Catalase), MKI (Marker of proliferation Ki-67), and END (Endothelin 1).
2. Corneometer® CM 825, Tewameter™ 300, and Mexameter MX 18 are products of Courage + Khazaka Electronic GmbH, (Köln, Germany).

**Conclusions**

- Hydrolyzed jojoba esters increased skin hydration in vivo, and produced up regulation of biomarkers associated with skin hydration (AQP3 and AQP5) in vitro.
- Hydrolyzed jojoba esters reduced erythema and increased barrier recovery in vivo, and produced down regulation of biomarkers associated with an inflammatory response (TNF) in vitro.

**References**

1. AQP (aquaporin), TNF (Tumor Necrosis Factor), KLK (kallikrein), TXN (Thioredoxin), TXNRD (Thioredoxin Reductase), CAT (Catalase), MKI (Marker of proliferation Ki-67), and END (Endothelin 1).
2. Corneometer® CM 825, Tewameter™ 300, and Mexameter MX 18 are products of Courage + Khazaka Electronic GmbH, (Köln, Germany).
3. Study was conducted on a 1% hydrolyzed jojoba esters (i.e. 5% LC HJE solution in glycerin. Final Report available upon request.
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