A unique gel matrix moisturizer delivers better skin barrier through increase of long chain acyl ceramide species

Apostolos Pappas¹, Allison Rush¹, Anna Nicolaou², Julie Bianchini¹, Luke Brownbridge², Manpreet Randhawa¹

¹Johnson & Johnson Consumer Inc., Skillman, NJ, USA;
²Laboratory for Lipidomics and Lipid Biology, School of Health Sciences, University of Manchester, Manchester, UK

Disclosure: This work was supported by Johnson & Johnson Consumer Inc.
• AP, AR, JB, and MR are employees of Johnson & Johnson Consumer Inc.
• AN and LB received research support from Johnson & Johnson Consumer Inc.
Role of very long chain ceramides in stratum corneum barrier function

- Skin maintains a dynamic barrier by ceaselessly adapting to its inner and outer environments.
- Stratum corneum lipids are important components of the epidermal barrier, playing a critical role in maintaining its ability to provide diffusive resistance to internal water loss and external xenobiotics while maintaining adequate skin hydration.
- Ceramides are the key components that maintain the lipid barrier.

Molecular structure and nomenclature of ceramide classes; each class contains numerous species that vary in chain lengths:
- Ceramide nomenclature based on polar head group joining the fatty acid chain and sphingoid base by amide bond
- 12 identified ceramide classes in human stratum corneum = 4 sphingoid bases x 3 fatty acid moieties

- Changes in the ceramide composition, in particular reduced levels of very long chain (VLC) acyl ceramide species containing esterified omega (EO) linkages, have been associated with a disrupted lipid configuration (less long and more short periodicity phase) and consequently disrupted skin barrier function (increased TEWL), as is the case with atopic dermatitis.
- Previous work has shown that topically administered ceramides do not penetrate the stratum corneum barrier; therefore, an essential approach to repair or fortify the skin barrier is treatment with a moisturizer that builds critical VLC-ceramide species from within for an intact lipid configuration.

Objectives & methods

Objectives

- Measure the in vivo effect of a gel matrix moisturizer on the stratum corneum ceramide profile, in particular VLC acyl ceramide species, to substantiate previous in vitro data demonstrating increased expression of ceramide synthesis genes
- Demonstrate the impact of ceramide profile on clinical benefits including barrier integrity and skin hydration

Methods

In vitro gene expression of ceramide synthesis genes

- Genes isolated from human skin equivalents 48 hours post-treatment using Qiagen RNeasy kit with DNase I digestion
- Reverse transcription was performed using High Capacity cDNA kit
- All gene expression data (Taqman assays) were normalized by POLR2A or/and GAPDH reference genes
- Relative gene expression was calculated by comparative CT

Clinical study to collect tape strips for ceramide analysis

- Female subjects, 35-55 years old with self-perceived dry and dull facial skin
- Luekoflex® tape strips collected at baseline and Week 12 for ceramide analysis
- Instrumental measures to assess clinical benefit: skin barrier (TEWL) assessments and hydration (capacitance) measurements

Quantitation and profiling of ceramide composition

- Ceramide and protein content extracted from tape strips
- Quantitation of ceramide composition by ultraperformance liquid chromatography with electrospray ionization and tandem mass spectrometry (UPLC/ESI-MS/MS) vs. CER[N(25)S(18)] internal standard
- Raw amounts (pmole/tape) converted to relative amounts (% of total ceramides)
- Profiled according to ceramide class or chain length distribution

Gel matrix treatment significantly improved the ceramide profile

After 12 weeks of product use on the face, the following improvements in the ceramide profile were observed:

- Significant increases in the levels of all three VLC ceramide classes containing the esterified omega linkage (EOH, EOP, EOS)
- Significant increases in the levels of the ceramide chain lengths containing 67, 68, and 69 carbons
- Increased the sum of VLC ceramides containing 66-70 carbons
- Substantial increase in the mean ceramide chain length

Conclusions

Gel matrix moisturizer demonstrated the improvement of dynamic skin barrier at the molecular level, which manifested in clinical-level improvements in skin barrier and hydration after 12 weeks of use.

Gel matrix moisturizer induced the in vitro gene expression of ceramide synthesis genes.

Gel matrix moisturizer increased the levels of very long chain acyl ceramides that are critical to skin barrier.

Gel matrix moisturizer significantly improved the skin barrier and skin hydration.

As opposed to topically applied ceramides which are too large to penetrate the stratum corneum barrier, components of the gel matrix moisturizer were delivered deep into skin to increase the levels of VLC ceramides from within.

- VLC ceramides are required to achieve an optimal lipid configuration (long periodicity phase) for an intact and hydrated skin barrier.

- Taken together, these results demonstrate the notion that therapeutic hydration with a gel matrix formula can significantly improve dynamic skin barrier by induction of VLC ceramide species, hence leading to better barrier and hydrated skin.

- Furthermore, subjective assessments demonstrated that the gel matrix moisturizer provided appealing aesthetics, as was the intent during formula development, to avoid occlusive, heavy, and greasy emollients.