

An Innovative Trio Strategy for Maintaining Skin Hydration Homeostasis

Poster 418

Xu, Yicheng; Maurin, Véronique; Bruguere, Julie; Chevalier, Pascal;
Research and Development Department, Biocosmestic, Bonnelles, France

Introduction:

Various environmental and physiological factors may contribute to the heterogeneity of skin dryness. Bleomycin hydrolase (BLMH) has been identified as critical for the degradation of filaggrin fragments into free amino acids (NMF) in the upper stratum corneum (SC). Recent evidence has demonstrated that the accumulation of the organic osmolyte taurine in keratinocytes is required to maintain cellular water balance under dry skin conditions [1]. Hyaluronic acid (HA), also known as nature's moisturizer, is one of the most hydrophilic molecules in nature [2]. Our previous studies have shown that crosstalk between cutaneous cells from different skin layers is critical for maintaining overall skin homeostasis. Therefore, a multi-layered hydration strategy seems to be particularly important to deal with the skin of different dehydration states under the exosome. The purpose of this study is to investigate a three-in-one strategy of the stratum corneum, epidermis and dermis to maintain skin hydration homeostasis.

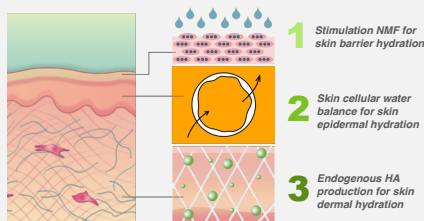


Figure 1: Trio strategy for global skin hydration

Materials & Methods:

Preparation of the natural skin moisturizer

A night blooming flower traditionally used in homeopathy has been identified. A new natural skin moisturizer (NSM) derived from an optimized water extraction of these air-dried flowers picked the morning after blooming. A LC-MS/MS based molecular networking of this natural skin moisturizer has been investigated to confirm that it is a concentrated source of small hydrated carbohydrates.

Primary keratinocyte culture and quantification of target proteins

NHEKs were pre-incubated during 48 hours in absence (control) or in presence the new NSM. BLMH protein levels were quantified in cell lysates. At the end of the 72 hours pre-incubation period, the incubation medium is removed and replaced by hyperosmotic assay medium. 72 hours after medium removal, intracellular taurine levels are measured in cell lysates.

Dermal fibroblast culture and quantification of HA

NHDFs were pre-incubated during 48 hours in absence (control) or in presence of the new NSM. At the end of the pre-incubation period, HA was quantified in cell lysates.

Conclusions:

Each skin layer requires a specific hydration strategy in order to maintain overall skin water balance. The coordinated increase in epidermal BLMH biosynthesis, intracellular taurine accumulation and dermal HA production address multi-layered hydration. This trio strategy may represent a novel approach for maintaining skin hydration homeostasis.

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References:

- [1] Janeke G, Siefken W, et al (2003) Role of taurine accumulation in keratinocyte hydration. *J Invest Dermatol.* 121(2):354–361. [2] Necas J, Bartosicova L, et al (2008) Hyaluronic acid (hyaluronan): a review. *Vet Med.* 8:397–411. [3] Elias PM (2005) Stratum corneum defensive functions: an integrated view. *J Invest Dermatol.* 125(2):183–200. [4] Warskulat U, Reinen A, et al (2004) The osmolyte strategy of normal human keratinocytes in maintaining cell homeostasis. *J Invest Dermatol.* 123:516–521. [5] Schaffer S, Takahashi K, Azuma J (2000) Role of osmoregulation in the actions of taurine. *Amino Acids* 19:527–546. [6] Schaffer S, Azuma J, et al (2003) Why is taurine cytoprotective? *Adv Exp Med Biol.* 526:307–321. [7] Yoshimura T, Inokuchi Y, et al (2021) Age-related decline in the taurine content of the skin in rodents. *Amino Acids* 53: 429–434. [8] Masson F (2010) Skin hydration and hyaluronic acid. *Ann Dermatol Venereol.* 137 Suppl 1:S23–25.

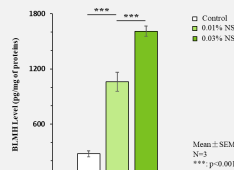
Results & Discussion:

1 SKIN BARRIER HYDRATION

As the outermost layer of the epidermis, SC is thought to perform several important protective cutaneous functions [3]. BLMH as a critical protease required for the complete degradation of filaggrin fragments into free amino acids, can be a key target for hydration homeostasis in the upper skin and barrier protection.

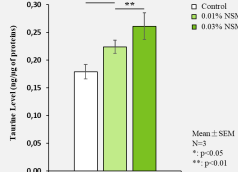
The new NSM at 0.01% and 0.03% significantly increased intracellular level of BLMH in NHEKs in a dose-dependent manner.

Figure 2: Effect of the new NSM on BLMH production in NHEKs



2 SKIN EPIDERMAL HYDRATION

For many dry skin conditions, keratinocytes may be exposed to hyperosmotic stress. Intracellular accumulation of taurine protects keratinocytes from osmotically and UV-induced damages by maintaining cellular water balance and survival [4]. Taurine has also been shown to have antioxidant, anti-inflammatory and membrane stabilizing activities [5, 6]. Therefore, taurine can be a key target of epidermal cell hydration homeostasis in skin dryness. An age-related decline in taurine was recently found in rodent skin [7], whether the same trend occurs in human skin requires further investigation.



Under the hypertonic condition, the novel NSM at 0.01% and 0.03% significantly increased intracellular level of taurine in NHEKs in a dose-dependent manner.

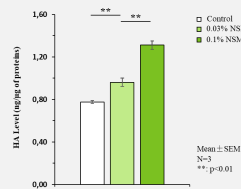
Figure 3: Effect of the new NSM on intracellular accumulation of taurine in NHEKs.

3 SKIN DERMAL HYDRATION

Exogenous HA is widely used in the field of epidermal moisturizing, while endogenous HA plays a central role in deep skin hydration and elasticity [8].

The new NSM at 0.03% and 0.1% significantly increased level of HA in NHDFs in a dose-dependent manner.

Figure 4: Effect of the new NSM on HA production in NHDFs.



The above results reveal that this novel natural skin moisturizer may act on key moisturizing factors in different cutaneous layers to play a triple skin hydration. These have been confirmed in clinical trials (data not shown). Interestingly, in addition to maintaining skin water balance, these factors both have multiple biological activities, especially anti-inflammatory. In the meanwhile, their expression and bioactivities appear to be inversely correlated with age. These seem to confirm the important link between skin moisture loss, immune barrier function and aging.