Clinical Insights
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PART 1

RESTORING BARRIER FUNCTION AND SKIN HYDRATION FROM WITHIN BY BOOSTING ENDOGENOUS HYALURONIC ACID PRODUCTION

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"Endogenous HA plays an active role as a dynamic modulator of keratinocyte proliferation and differentiation, barrier formation, inflammation, oxidative stress, skin hydration, cell survival and wound healing. Pre-clinical data show an increase in the deposit of endogenous HA in the epidermis after treatment with HA[5] Rejuvenating Hydrator, which is linked to enhanced HA synthesis and deceased degradation."

Our skin is the natural barrier that protects us from the environment. Some of the most important functions of the skin are blocking external pathogens and other substances from penetrating the body and preventing water loss. These functions are performed primarily by the epidermis by producing a protective, highly impermeable layer (stratum corneum) that permits survival under Earth conditions. Unfortunately, skin barrier dysfunction is one of the hallmarks of aged-skin, placing it in a constant stage of water loss. Externally-induced or disease-related barrier dysfunction sets the stage for premature aging and chronic inflammation. Clinically, the most common signs of barrier dysfunction—with its concomitant increase in water loss—are dry skin, flakiness, itchiness, inflammation and increase in skin sensitivity. Alterations in the epidermal barrier function also facilitate the penetration of irritants or allergens, increasing inflammation and further aggravating barrier dysfunction.

Three approaches with different mechanisms of action can be used to prevent barrier dysfunction-mediated deleterious changes in the skin. These are:

a.) avoid exposure to irritants or stressors,

b.) externally add ingredients that temporarily improve barrier function or

c.) restore endogenous capacity of the skin to form a healthy epidermal barrier from within.

Lifestyle and urban living prevent us from limiting or avoiding the contact with irritants, pollutants and allergens that can damage our skin barrier. Similarly, completely eliminating skin exposure to solar radiation and deleterious environmental conditions such as high heat, dry/cold air and strong winds is very difficult to accomplish. A commonly used approach in the cosmetic industry for the past two decades is to temporarily improve epidermal barrier function by externally replacing lost lipids or water. Although this approach has shown some effectiveness, it does not address the core problem, which is age-related epidermal dysfunction. Additionally, externally added lipids must be protected from lipid peroxidation for them to provide any beneficial effects by either using sunscreen or antioxidants.

SkinMedica's approach to epidermal dysfunction resulted in the creation of HA[5] Rejuvenating Hydrator, a product that restores epi-

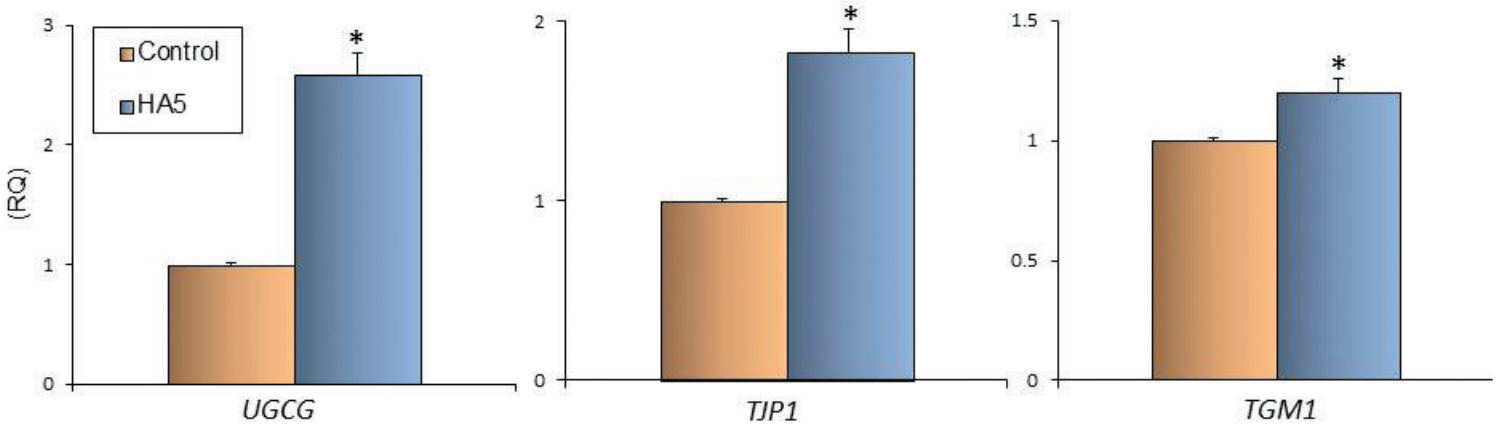

Figure 1: Treatment with HA[5] Rejuvenating Hydrator resulted in signigicantly increased expression of barrier markers in a full thickness tissues (EFT-400) model. UGCG (UDP-Glucose Ceramide Glucosyltransferas) encodes an enzyme that catalyzes the first glycosylation step in the biosynthesis of glycosphingolipids generating glucosylceramides, which are the core structure of many glycosphingolipids of the skin barrier. TJP1 [Tight junction (TJ) protein ZO-1] encodes for a protein that is necessary for the assembling and function of the TJs on the skin. TJs play a crucial role in the formation and maintenance of epithelial barrier. TGM1 (transglutaminase 1) encodes for an enzyme key in the formation of the epidermis by forming the cornified cell envelope.

dermal function and skin hydration by improving the natural ability of the skin to rejuvenate itself. HA[5] Rejuvenating Hydrator triggers epidermal self-rejuvenation through normalization of endogenous epidermal hyaluronic acid (HA) levels. VitisenSCE™ technology, which combines *Vitis vinifera* flower stem cell extract with marine micro-organism polysaccharides and a peptide complex, is the force behind the observed replenishment of endogenous epidermal HA levels as well as the restoration of epidermal homeostasis.

The rationale behind the creation of HA[5] Rejuvenating Hydrator and its mechanism of action were based on the key role of HA on epidermal homeostasis. Endogenous HA plays an active role as a dynamic modulator of keratinocyte proliferation and differentiation, barrier formation, inflammation, oxidative stress, skin hydration, cell survival and wound healing. Pre-clinical data show an increase in the deposit of endogenous HA in the epidermis after treatment with HA[5] Rejuvenating Hydrator, which is linked to enhanced HA synthesis and deceased degradation.[1] Interestingly, interactions of endogenous epidermal HA with its receptor, CD44, are responsible for the regulation of epidermal differentiation with the concomitant stimulation on lamellar bodies formation and secretion and normalization of the lipid barrier composition and therefore its function.[2] As expected, treatment with HA[5] Rejuvenating Hydrator increased expression of markers for keratinocyte proliferation/differentiation (involucrin, loricrin and filaggrin), barrier formation (claudin-1, tight junction protein ZO-1, transglutaminase 1 and UDP-Glucose Ceramide Glucosyltransferase) (Figure 1) and wound healing. Results from an eight weeks clinical study (n= 23) demonstrated that HA[5] Rejuvenating Hydrator used twice daily results in continuous improvements in fine lines/wrinkles (periocular and forehead) and tactile roughness as well as enhanced intrinsic hydration measured by corneometer. These data suggested that HA[5] Rejuvenating Hydrator retrains the skin to enhance endogenous epidermal HA formation restoring epidermal barrier function and homeostasis.

In summary, restoring skin's barrier function is a multifactorial process that involves hydration, lipid composition, and keratinocyte differentiation, all of which can be successfully accomplished by restoring the endogenous levels of epidermal HA. This constitutes a novel approach to address skin disorders characterized by alteration in differentiation, lipid synthesis and barrier formation. The restoration of epidermal health by HA[5] Rejuvenating Hydrator not only impacts skin quality but can also improve the outcome of other cosmetic procedures by controlling susceptibility to inflammation. ■

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