

Management of irritant dermatitis by promoting a rapid and effective epidermal healing

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Introduction

Skin is often exposed to aggressors that could alter epidermis and give rise to local irritation such as irritant contact dermatitis. When the skin barrier is disrupted by an injury, the wound healing process is triggered for a fast and complete skin recovery: after the vascular and inflammatory stage, the epidermis repair or re-epithelialization starts, and is then followed by the dermal-epidermal junction rearrangement and finally the remodelling of the dermal extracellular matrix.

During re-epithelialization, keratinocytes undergo morphological and functional changes in three main steps: 1/ migration in order to close the gap; 2/ proliferation to fill the gap and 3/ maturation in order to restore a stratified, organized and functional epidermis able to cover the injury and to insure its role of protective barrier.

An emulsion for irritant contact dermatitis containing emollient, anti-irritant, anti-microbial and healing (Cu-Zn-Mn complex) products has been evaluated for its epidermal repair efficacy.

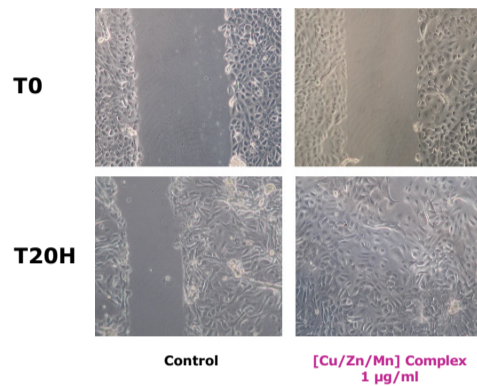
Results

The [CU-ZN-MN] triad as a key actor of re-epithelialization at cellular level

The migration ability of normal human epidermal keratinocytes (NHEK) has been evaluated in presence of a [Cu-Zn-Mn] complex by using the Scratch Assay (Fig. 1).

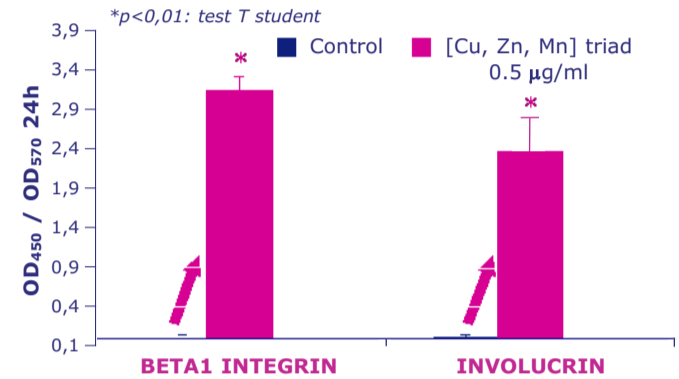
Moreover, [Cu-Zn-Mn] triad effect on the production of proliferation and differentiation markers (beta1 integrin and involucrin respectively) has been measured in NHEK by ELISA dosage (Fig. 2).

Figure 1: Migration capacity of keratinocytes (Scratch Assay)



► The [Cu, Zn, Mn] triad recovered rapidly the gap by enhancing cell migration and thus was able to promote initiation of wound healing process

Figure 2: Beta1 Integrin and Involucrin production in NHEK



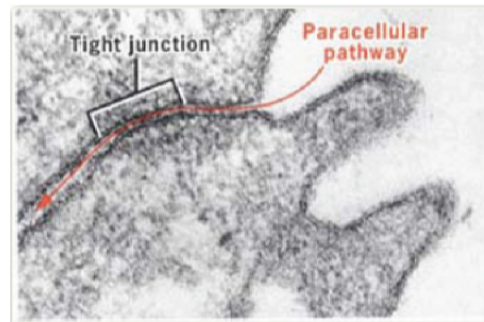
► The [Cu, Zn, Mn] triad stimulated proliferation and differentiation markers at epidermal level

By enhancing the main steps of cellular re-epithelialization process, the [Cu-Zn-Mn] triad promotes the regeneration and repair of the epidermis

Epidermal repair efficacy of an emulsion: *in vitro* demonstration

Figure 3: Trans Epithelial Electrical Resistance TEER measurement is an indirect assessment of tight junction stability (*stratum granulosum*) and consequently is a direct measure of the functionality of barrier function in epithelial tissue: it reflects the global resistance and quality of the barrier: **Barrier disruption = ↓ TEER**

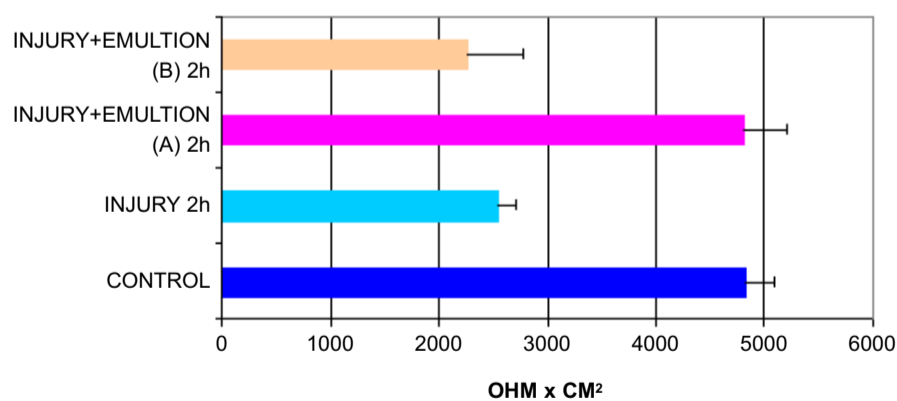
A mechanical injury has been performed with a special device on the surface of reconstructed human epidermis (SkinEthic® RHE). A cosmetic emulsion (A) containing the [Cu-Zn-Mn] triad compared to a cosmetic emulsion (B) were topically applied immediately after injury. Analysis were defined at 2h and 2h followed by 24h recovery.



The TEER, a functional parameter of barrier quality, was measured on epidermis before the injury and 2h after injury in presence or not of the emulsions (Fig. 4).

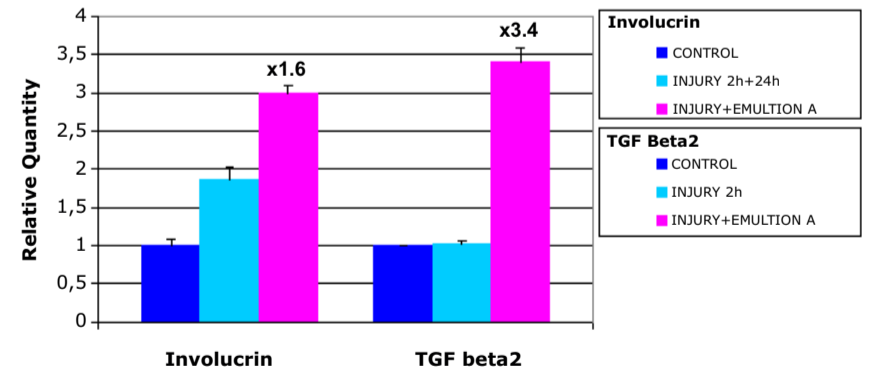
Then in order to understand the molecular mechanism involved in emulsion (A) activity, specific genes expression has been analyzed by QRT-PCR (TaqMan technology, GAPDH housekeeping gene): TGF beta2, a growth factor playing a key and early role in keratinocytes migration, the first step of healing process; Involucrin, terminal differentiation marker involved in the epidermis maturation final step during re-epithelialization (Fig. 5).

Figure 4: TEER evolution 2h after epidermal injury



► Only the topical application of the emulsion (A) containing the [Cu-Zn-Mn] triad induced a significant increase of TEER 2h after injury promoting an early barrier recovery for regenerating a functional epidermis

Figure 5: Gene expression of Involucrin and TGF beta2 in RHE



► The emulsion (A) induced a significant over-expression of migration and differentiation key markers promoting an early, fast and long-term epidermal repair

The emulsion (A) containing the [Cu-Zn-Mn] triad accompanies the skin for a proactive, lasting and optimized epidermal repair

Conclusion

The [Cu-Zn-Mn] triad clearly shows re-epithelialization activities at cellular level. These results are confirmed and expanded by the rapid, lasting and optimized healing properties of the emulsion (A) observed on injured-reconstructed epidermis.

The association of the [Cu-Zn-Mn] healing complex with emollient, anti-microbial and anti-irritant ingredients supports the cosmetic relevance of this emulsion for the management of irritant contact dermatitis.