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A biomimetic approach inspired from resurrection plants to promote skin resilience

Poster 270

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Introduction:

Our skin is frequently exposed to harsh environmental conditions (hot weather, extreme cold, humid climate or air-dried state) that deeply affect its integrity (alteration of dermis structure and skin barrier function) and its resilience (alteration of skin defense capacities). For example, all around the world, in the same day our skin is submitted to strong variation of relative humidity from 40% to 90%.

Resurrection plants can survive over long periods, months and even years, of severe dehydration caused by drought stress (figure 1). To endure these conditions, these plants can reprogram their transcriptome, resulting in a profound alteration of metabolism toward alternative energy supply, hormone signal transduction, antioxidant, prevention of DNA/protein damage (1).

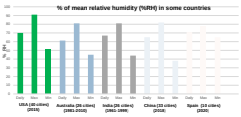

Figure1: Daily variations of relative humidity recorded all around the world.

In addition, they produce also high levels of protective sugars as Raffinose Family Oligosaccharide's (raffinose, galactinol, stachyose, verbascose), trehalose and sucrose. Galactinol is, indeed, a building block molecule for the synthesis of these key oligosaccharides as it was demonstrated in the plant under abiotic and biotic conditions (2, 3, 4). These works evidence the important role of galactinol and pave the rational of our development. Inspired mainly by resurrection plants, and galactinol properties, we developed Galactinol Advanced (GA) through a white biocatalytic method.

In this work we first investigate in human skin cells, the ability of GA to mimic plants resilience strategy to face harsh environmental conditions such as drought, humidity and UV irradiations. Besides, we studied the effect of GA on skin microbiota by using the metaproteomics technology (5,6,7,8), as skin microbiota is a major player in the maintenance of skin health and resilience. In contrast to metagenomics, the widely used technique to study skin microbiota, the metaproteomics provides valuable descriptive and functional insights. Finally, through a clinical investigation we studied the properties of GA to improve skin features known to be altered in photo-exposed skins such as wrinkles and mechanical properties.

Materials & Methods:

Galactinol Advanced synthesis process

GA is synthesized by white biocatalytic method (figure 2) from agricultural-food byproducts i.e. Raffinose from Cotton seeds and Inositol from Rice bran.

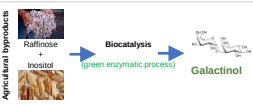

Figure 2: GA biosynthesis from Raffinose and Inositol .

Galactinol Advanced cell protective studies against environmental stresses

Normal human fibroblasts (NHDF) and normal human keratinocytes (NHEK) were exposed to various deleterious stresses mimicking environmental conditions such as UVA, UVB, and heat stress, in presence or not of GA. Then, to observe the damages induced by these stresses, and the protective effects of GA the cells morphologies were studied under a bright field microscope (Zeiss Axiovert 40).

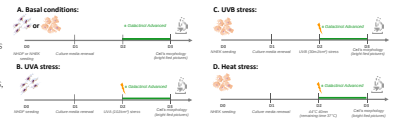

Figure 3: Experimental conditions applied to normal human fibroblasts (NHDF) and normal human Keratinocytes (NHEK). Basal conditions, UVA, UVB and heat.

Clinical investications

Panel description

A double blinded clinical trial was realized on 20 photo-exposed women (from 49 to 65 years old, mean age 54.6 y.o.). A topically application for 28 days on hemi-face, twice a day (morning & evening) of a formula cream containing either Galactinol Advanced at 2% or Placebo.

Evaluation of wrinkles by the fringe projection technique

The analysis of the wrinkles volume of the crow's feet was made at D0, D14 and D28 with AEVA-HE® device (Eotech).

Measurement of the biomechanical properties of the skin

Elasticity and firmness were measured by cutometry (Courage & Khazaka) at D0, D14 and D28 at the level of the maxillary area for each side of the face.

Skin metaproteomics study

Swabs samples were collected from the face area at D0 and D28 and processed as described in figure 4.

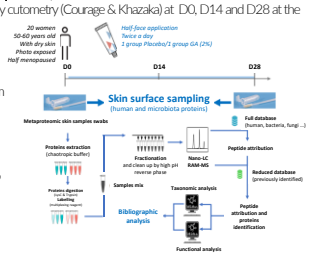

Figure 4: Flow chart from swabs sampling to metaproteomics study.

Results & Discussion:

Impacts of environmental stresses on normal human skin cells

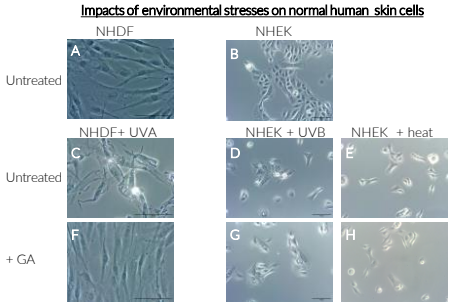

Figure 5.: Bright field pictures of fibroblasts (NHDF), keratinocytes (NHEK) after UVA (C & F), UVB (D & G) or heat (E & H) stresses. A, B, C, D, & E without treatment, F, G & H after GA addition.

In comparison to unstressed condition (figures 5 A & B), an altered morphology in all stress conditions (figures 5 C, D & E) is observed. The cells appear thicker, elongated and less numerous. GA treatment attenuates the deleterious effects induced by all stresses studied (figures 5 F, G & H). These results show the strong cells protective effects of GA.

Clinical datas

Biometrological skin results

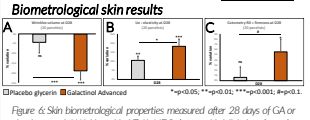

Figure 6: Skin biometrological properties measured after 28 days of GA or placebo use. A. Wrinkles with AEVA-HE® (t test with Minitab software). B & C. Elasticity & firmness (Cutometer).

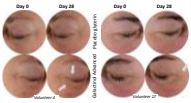

Figure 7: Illustrative pictures of crow's feet Area (ColorFace®).

GA improves skin quality when used topically (2%). The following skin benefits demonstrated: Visible reduction of wrinkles by -18.9%, Improvement of skin elasticity (+18.2%) , improvement of skin firmness (+5.5%).

Metaproteomics results

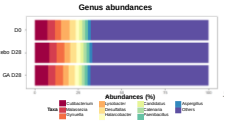

Figure 8: Major microbiota taxa abundances proportions at genus level for each group (Placebo or GA).

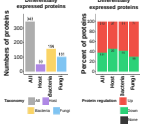

Figure 9: Number or percent of proteins significantly regulated by GA after 28 days of use..

The taxonomic analysis (figure 8) reveals no major difference in microbiome composition between sampling at D0 (before treatment) and after 28 days of GA treatment highlighting that GA respects skin microbiota balance. This result demonstrates that GA is safe toward skin microbiota.

Figure 10: WordCloud representation of main enriched functional pathways identified through HoiXplore.

The functional analysis of all significantly regulated proteins (figure 9) reveals that GA stimulates (figure10) :
- the proteostasis mechanisms in human cells and in bacterial cells by stimulating the expression levels of proteins belonging to HSPs (HSP70 binding protein),
- the expression of UDP-glucuronic acid decarboxylase1,
- the expression of Late cornified envelope proteins 1 B and 3B,
- the expression of detoxication enzymes produced by skin microbiota (superoxide dismutase).

Results from biometrological and metaproteomics studies are in accordance and confirm the skin protective effects of GA.

Conclusions:

Thanks to a biomimetic approach, we developed a biotech based active ingredient efficient to promote skin resilience and healthiness. The *in vivo* investigations highlight the strong biological activities of GA to healthiness when used topically at 2% for 28 days. The skin metaproteomics results demonstrate that GA helps to maintain essential and various skin defense capacities beneficial against environmental stresses. These regulated proteins at keratinocytes and microbiome levels lead to visible outcomes noticed on the biometrological results: improvement of skin wrinkles, mechanical properties and skin healthiness.

Acknowledgements:

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