

ExpoZen[®]: an active ingredient modulating reactive and sensitive skin microbiota

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Introduction

The skin is colonized to hundred of diverse bacterial species from the four phyla Actinobacteria, Proteobacteria, Firmicutes and Bacteroidetes, which act as a part of the body's first line of defence against the external environment (Natsuga, 2014). These microorganisms are generally classified into two groups, resident and transient microbes (Grice et al., 2008), resident microbes being not harmful under most conditions and may provide some benefits to the host. The diversity of these transient and resident microbes is determined by different characteristics of local surface areas such as moisture, pH value, internal (age, sex and genotype) and external factors such as nutrition, lifestyle, climate pattern, and cosmetics (Baldwin et al., 2017). The disequilibrium of the skin microbiome, named dysbiosis, and the decreased microbial biodiversity have been linked with many diseases, including acne, eczema, rosacea, and psoriasis. More recently, Seite et al. (2018) hypothesized that bacteria could affect the pathophysiology of the sensitive skin syndrome. However, the data concerning this relationship are scarce. The term sensitive skin has been used to describe phenomenon of hyperreactivity, which develops ex-

aggerated reactions when exposed to the stressful factors. It is also defined by the self-reported presence of different sensory perceptions, including tightness, stinging, burning, tingling, pain and pruritus in response to stimuli that normally should not provoke such sensations. Its diagnosis, pathophysiology and treatment are still under discussion, but it has become evident that all environmental factors (such as sun radiations, i.e. ultraviolet, visible light and infrared wavelengths, air pollution) contributing to skin alterations, recently regrouped in the so-called "skin aging exposome", need to be considered in relation with sensitive skin (Krutman et al., 2017). Potential mechanisms of sensitive skin involve skin neurosensory dysfunction, neurogenic inflammation, epidermal barrier disruption, immune cells activity (transient receptor potential channels-TRP), and hyperreaction of the skin blood vessels. In fact, after enhanced activation of TRP sensory proteins by triggering factors, neurotransmitters, such as vasoactive intestinal polypeptide (VIP), substance P (SP) and calcitonin gene-related polypeptide (CGRP), initiate neurogenic inflammation, inducing vasodilatation and cell degranulation. It also appears that non-specific inflammation is linked to the release of cytokines (IL-8) and tumor necrosis factor (TNF).

Considering the high prevalence of sensitive skin (Misery et al., 2007), its treatment represents an excellent target for active ingredients in cosmetics. Various naturally derived complex mixtures such as botanical extracts have been used for long time. The application of algae in cosmetic products have recently received more attention in the treatment of skin problems. Algae are rich-sources of structurally novel and biologically active metabolites,

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with great industrial potential and accessibility. Among them, *Halymenia durvillei* is a red alga belonging to the Rhodophyceae family, abundant in a vast area of the Indian Ocean. Red algae are often small and can live in the deepest known as depths for organisms containing chlorophyll. *Halymenia durvillei* contains phycocolloids, which are the constituent polysaccharides of cell membranes. The current interest in these polysaccharides is due to their known bioactivities, conferred by their anti-allergic, neuroprotective, cytotoxic, anti-nociceptive, and immunomodulatory properties, making them promising bioactive products and biomaterials.

Based on these data, the first aim of this study was to study the effect of ExpoZen® versus placebo on the bacterial skin microflora after 15 days and 28 days of treatment by using next-generation sequencing experiments (16S RNA sequencing) on samples collected from 30 volunteers suffered from reactive and sensitive skin. The second objective was to evaluate the effect of ExpoZen® on neuroinflammation (TNF- α) using an *ex vivo* model. Finally, an *in vivo* study was performed in a panel of 25 volunteers using clinical and instrumental evaluations.

Results and Discussion

At the species level, *Corynebacterium kroppenstedtii*, a specie particularly observed in the case of redness (Rainer et al., 2017) is noted before ExpoZen® treatment. 28 days of ExpoZen® treatment decreased the proportion of this specie (Figure 1) and increased the level of *Staphylococcus epidermidis*, known to be a beneficial bacteria for skin. At the same time, ExpoZen® treatment limits the decrease in microbial diversity (evaluated with the Shannon index).

ExpoZen® also induces a non significant decrease of TNF- α (-21%) compared to control after 6 days of treatment. A significant

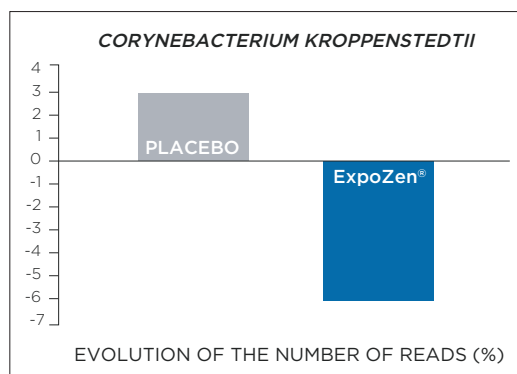


Figure 1. Evolution of *Corynebacterium kroppenstedtii* after the use of ExpoZen®

decrease of the expression of NK1-R (-43%, $p < 0.01$), TRPV-1 (-67%, $p < 0.001$) and a decrease of VEGF (-16%) were also reported when compared to control.

In vivo study shows that ExpoZen® decreases significantly skin sensitivity, irritability, heat sensations, pain, flushes, and redness after 28 days of applications (Table 1). A significant decrease (-15%, $p < 0.05$) of the surface of erythrosis was also observed with our extract (Figure 2). Finally, 90% of the women declared that the product had a soothing effect when applied after the stinging test.

	D28 vs D0
Skin sensivity	-19% *
Skin irritability	-34% *
Heating sensations	-40% *
Pain	-33% *
Flushes	-37% *
Redness	-24% ***

Table 1. evolution of the skin irritability, sensitivity, heating, pain, flushes and redness state from D0 to D28 using the SS-10 scale (3) (* $p < 0.05$, *** $p < 0.001$ vs D0)

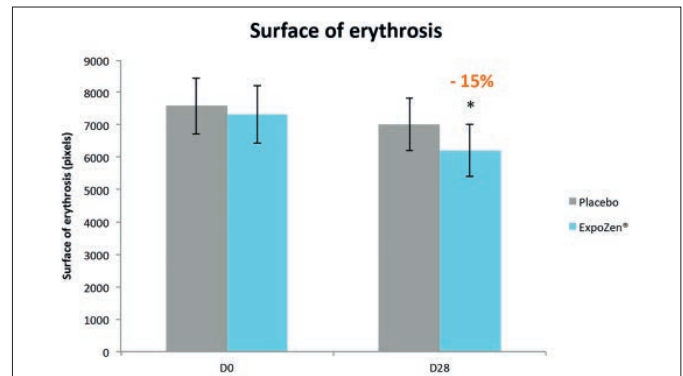


Figure 2. Effect of ExpoZen® on erythrosis (* $p < 0.05$ vs D0)

Conclusion

ExpoZen® provides a protection for sensitive and reactive skin aggressed by daily environmental insults, named exposome. It reduces and soothes the feelings of discomfort. It is able to modulate skin microbiota and promotes specific beneficial bacteria development while limiting the growth of strains involved in redness and inflammation. The skin is soothed and healthier, contributing to wellbeing enhancement.

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