# Turning back the ageing clock with snow algae active

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## ABSTRACT

Environmental factors and lifestyle choices impact our skin deeply, reaching the cells' DNA and inducing its modification. These so-called 'epigenetic changes' create a signature that contributes to the biological age of the cell, which can significantly differ from the chronological one. Through lifestyle choices and targeted interventions, biological age of the skin can be reversed, and skin appearance can be improved. We developed an extract from snow algae that reduces the skin's biological age by acting on the hallmarks of ageing. These are measurable manifestations of the ageing process inside the cells, revealing the impaired cellular mechanisms that lead to progressive functional decline. *In vitro*, snow algae extract reversed biological age according to the Horvath clock and it modulated protein levels, bringing them back to a younger profile. The extract consistently showed anti-senescence activity, both *in vitro* as well as clinically, and counteracted UV spots appearance despite sun exposure. Furthermore, it promoted TEWL reduction and showed a moisturizing effect


Living conditions, lifestyle, and environmental exposure significantly influence biological age—the body's actual physical condition and functionality, independent of the years a person has lived, which is termed the chronological age (Figure 1). The skin, as the body's primary barrier, is particularly affected by these external and internal factors, which can make one appear much younger or older than their chronological age.

This phenomenon is known as 'epigenetic ageing', and it highlights the need for targeted skin care to maintain health and youthfulness. DNA methylation, the addition of methyl groups to DNA, serves as a key ageing biomarker, accumulating predictably over time.

By analysing DNA methylation patterns in skin cells, scientists can define an ageing clock to estimate epigenetic skin age, which often aligns with visible signs of ageing like wrinkles, reduced elasticity, and pigmentation changes.

The Horvath's clock, for example, measures age across various tissues, thereby not only estimating skin age but also predicting barrier function, UV damage susceptibility, and responsiveness to anti-ageing treatments.[1]

## The hallmarks of ageing

To address the ageing process, it is crucial to understand the biological mechanisms driving it. The hallmarks of ageing are key processes that contribute to the gradual decline in cellular and organismal function, including genomic instability, telomere attrition, epigenetic alterations, and loss of proteostasis, which compromise cellular integrity.[2]

Additionally, deregulated nutrient sensing, mitochondrial dysfunction, and cellular senescence impair energy balance and tissue renewal, while stem cell exhaustion and altered intercellular communication reduce regenerative capacity. Recently identified hallmarks—such as impaired macroautophagy, chronic inflammation, microbiome imbalance (dysbiosis), and extracellular matrix (ECM) changes—further drive age-related decline, with loss of tissue elasticity being a notable effect. Psychosocial isolation can also aggravate these hallmarks (Figure 2).[3]

In skin ageing, these mechanisms impact both the dermis and epidermis. Genomic instability causes DNA damage, and telomere attrition limits cell division. Epigenetic changes and proteostasis loss disrupt collagen and elastin production, leading to wrinkles and reduced elasticity. Mitochondrial dysfunction and deregulated

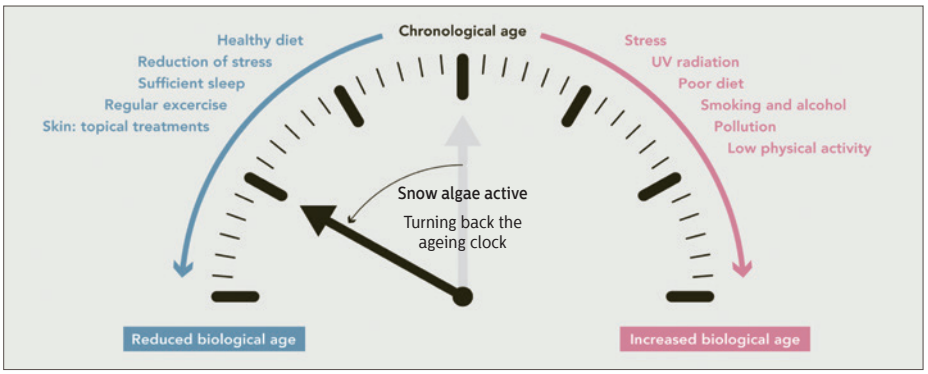


**Figure 1:** Snow algae active turns back the ageing clock


**Figure 2:** Snow algae active targets the hallmarks of ageing

nutrient sensing impair energy production, slowing skin repair.

Senescent fibroblasts accumulate in the dermis, weakening ECM maintenance, while stem cell exhaustion hampers skin regeneration. Chronic inflammation and microbiome dysbiosis increase oxidative stress and barrier dysfunction. Since these processes are interconnected, targeting multiple hallmarks simultaneously is essential for effective intervention.[4]

## Snow algae, thriving in extreme environments

Hidden within the icy alpine and polar landscapes, snow algae thrive in extreme environments like the Swiss mountains. These extremophiles survive freezing temperatures, intense UV radiation, and nutrient scarcity through adaptive strategies.

Their life cycle begins with a green stage in early summer, marked by active growth and reproduction. As summer progresses, they turn red on melting snow, entering dormancy by producing carotenoid pigments that protect against UV rays.[5]

During dormancy, red spores remain visible on the snow, conserving energy until conditions improve. Snow algae also produce secondary metabolites like biopolymers for water retention, antifreeze glycoproteins to prevent ice damage, and stress modifiers to manage environmental challenges. These unique properties make snow algae a valuable resource for skin care and protection.

We therefore investigated the effect of a cosmetic active ingredient (Snow algae active, INCI: Coenochloris Signiensis Extract (and) Maltodextrin (and) Lecithin (and) Aqua/Water) on the ageing clock in skin cells, on seven hallmarks of ageing as well as on the improvement of several skin parameters in placebo-controlled clinical studies.

## Methods

**Epigenetic age clock analysis in human dermal fibroblasts**

Human dermal fibroblasts (HDFs) were cultured over several weeks with culture medium containing or not the snow algae extract, to obtain different passages of aged fibroblasts. At the start of the experiment (passage 7), at an intermediate timepoint (passage 13) and at the end (passage 17), part of the cells was frozen and stored for genomic DNA (gDNA) extraction.

To determine the epigenetic age, and therefore the biological age of the samples, genomic DNA was sequenced using Illumina methylation arrays. The data was then analysed and aligned according to the Horvath Clock, an epigenetic clock based on specific sets of CpG sites, whose altered DNA methylation levels yield the cell's age.

**Beta-galactosidase activity assay**

HDFs were seeded in 96 well plates and incubated with senescence-induction medium. The cells were grown either in presence or absence of snow algae extract for 14 days. Afterwards, nuclei were stained with Hoechst blue reagent for cell number normalization, and fluorescence readings were measured in a multimode plate reader.

After, cells were washed, lysed and spider beta-gal was added. Beta-galactosidase activity was measured with a fluorescence plate reader. Recorded values from the beta-gal assay were normalized to cell number and beta-gal activity was expressed in percentage compared to untreated control. A student t-test was performed for statistical analysis.

**Proteomics**

Primary human keratinocytes were treated either with or without 0.0625% snow algae extract in a pro-ageing medium, which makes the cells age faster, or a control medium. From there, protein expression was analysed by proteomics. Regulated proteins were grouped according to their biological function, and the effect of the pro-ageing medium on their expression levels was quantified and used as the baseline, set to 100%.

**Clinical studies**

With the aim of further substantiating its anti-senescence effect, we tested our snow algae active *in vivo* on a panel of 20 female volunteers aged between 45 and 65 years (mean age: 54.3 years), during summertime in Portugal. A cream containing 2% snow algae active was applied twice daily for 28 days to one-half of the face, while the other half was treated with a placebo formulation.

An analysis of epidermal senescent cell count and morphology was performed using confocal microscopy, both before and after treatment, directly in the volunteers' skin. As well, UV-spots area variation was measured, by capturing images of the volunteer's faces while exposing the patients to a UV lamp.

Additionally, in a double-blind study performed with 21 Caucasian volunteers (19 women and 2 men) of phototype II and aged between 30 and 57 years (mean age: 43.8 years) during wintertime the effect of snow algae active on the skin's barrier function was tested.

Volunteers applied an emulsion with 3% snow algae active on one-half of their faces or the corresponding placebo on the other half of their faces three times per day for a period of 21 days. Transepidermal water loss (TEWL) was measured before and after treatment on the face (cheeks) using a tewameter.

In a third study, an emulsion containing 2% snow algae active or the corresponding placebo were applied twice daily for 14 days to the inner side of the forearm of 20 women aged from 40

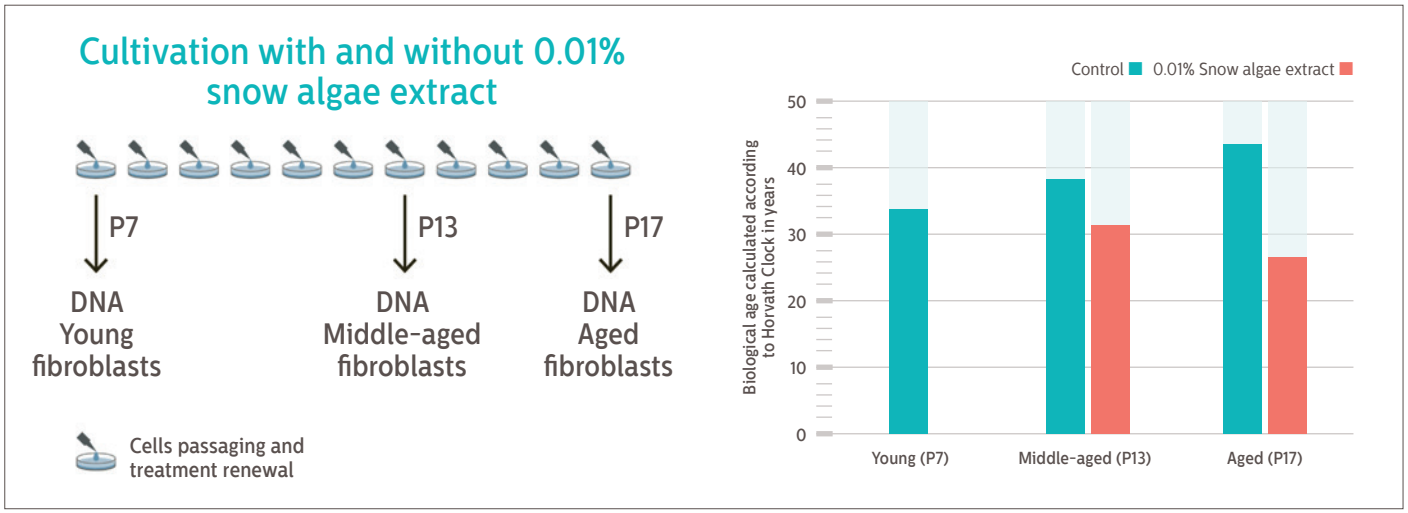


**Figure 3:** Snow algae extract reduces epigenetic age

to 60 years (mean age: 50.4 years). One area remained untreated. The hydration of their skin was determined using a corneometer.

## Results and discussion

The effect of snow algae extract on the ageing clock, or the cells' epigenetic signature, was investigated in human dermal fibroblasts. Quantifying the biological age according to the Horvath clock demonstrated that, with an increasing number of passages, cells' biological age increased.

Treatment with 0.01% snow algae extract was able to reverse this ageing effect, at both of the time points measured (Figure 3). Therefore, snow algae active represents a potent ingredient for slowing biological ageing.

Cellular senescence is a natural process in which ageing or damaged skin cells lose their ability to divide. This contributes to reduced skin

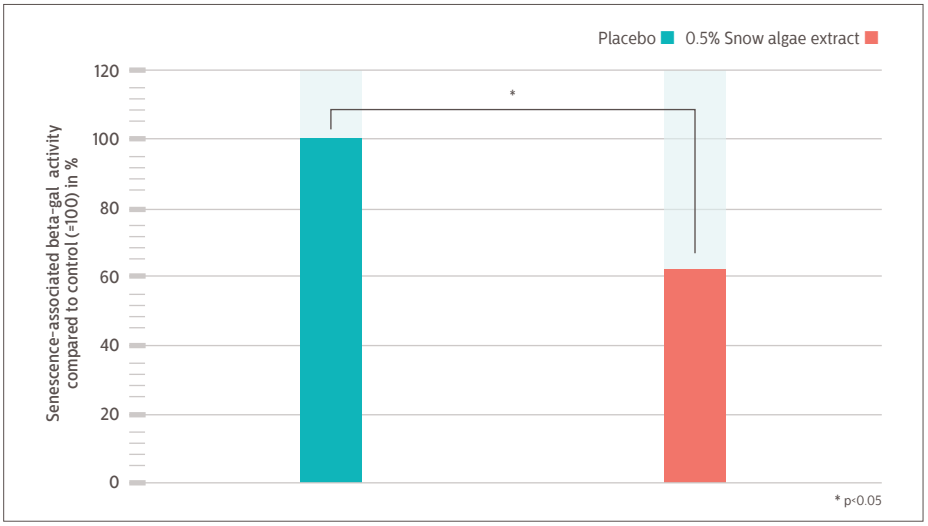


**Figure 4:** Snow algae extract prevents cellular senescence

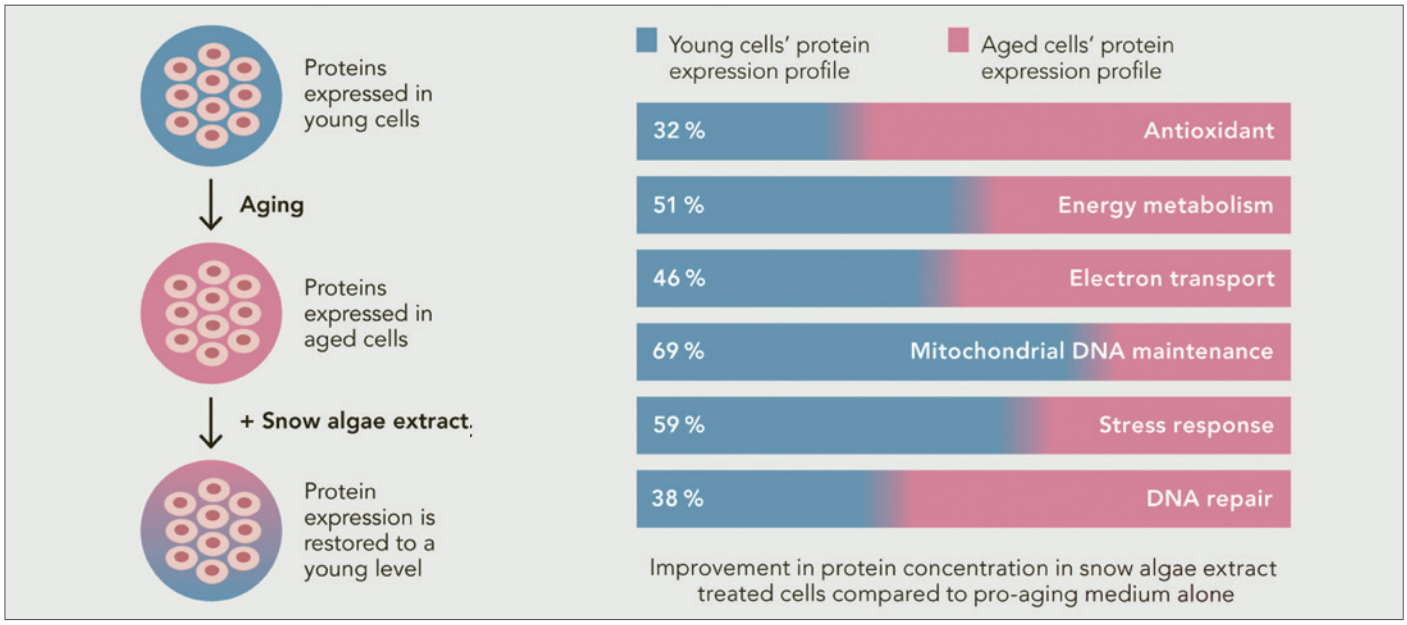


**Figure 5:** Snow algae extract preserves mitochondrial activity and genomic stability

regeneration and latent inflammation in the skin and, therefore, the appearance of wrinkles over time.

The effect of snow algae extract in preventing senescence was investigated by measuring beta-galactosidase activity. Beta-galactosidase is widely used in molecular biology as a reporter enzyme due to its activity having been shown to correlate with cellular senescence.

In this instance, the effect of 0.1% snow algae extract on beta-galactosidase activity was evaluated on human dermal fibroblasts. Treatment with snow algae extract resulted in a reduction of beta-galactosidase activity by 37%, which demonstrates anti-senescence activity (Figure 4). This shows that snow algae active can delay cellular ageing by preventing senescence, an important hallmark of ageing.

The effect of snow algae extract on two other hallmarks of ageing, mitochondrial dysfunction and genomic instability, was evaluated in another study, where primary human keratinocytes were treated either with or without 0.0625% snow algae extract in a pro-ageing medium and protein expression was analysed through proteomics.

Snow algae extract had a corrective effect on the protein expression changes that were induced by the ageing medium. More specifically, snow algae extract preserved mitochondrial activity by reducing the alterations in the expression of proteins involved in energy metabolism, electron transport, mitochondrial DNA maintenance, and antioxidant and stress responses (Figure 5).

Moreover, snow algae extract likely preserved genomic stability, as observed by the DNA repair protein levels being closer to young cells. Therefore, snow algae active has the potential to restore the skin to a more youthful proteomic profile

The hallmarks of ageing manifest themselves as measurable phenotypes that can be clinically observed on the skin. For example, it has recently become possible to detect and quantify senescent cells *in vivo*, directly in the patients' skin.

These cells can be distinguished from normal cells by their altered morphology, which becomes larger and flatter. Treatment with 2% snow algae active had a positive effect on the number of senescent cells in the volunteers' skin. In fact, given that the study took place in Portugal during summertime, the number of senescent cells increased on the volunteers' skin, which was likely due to sun damage.

However, the ratio of senescent versus normal cells decreased by 1.5% compared to initial conditions in areas treated by the snow algae active, while it increased by 19.3% in areas treated by the placebo (Figure 6).

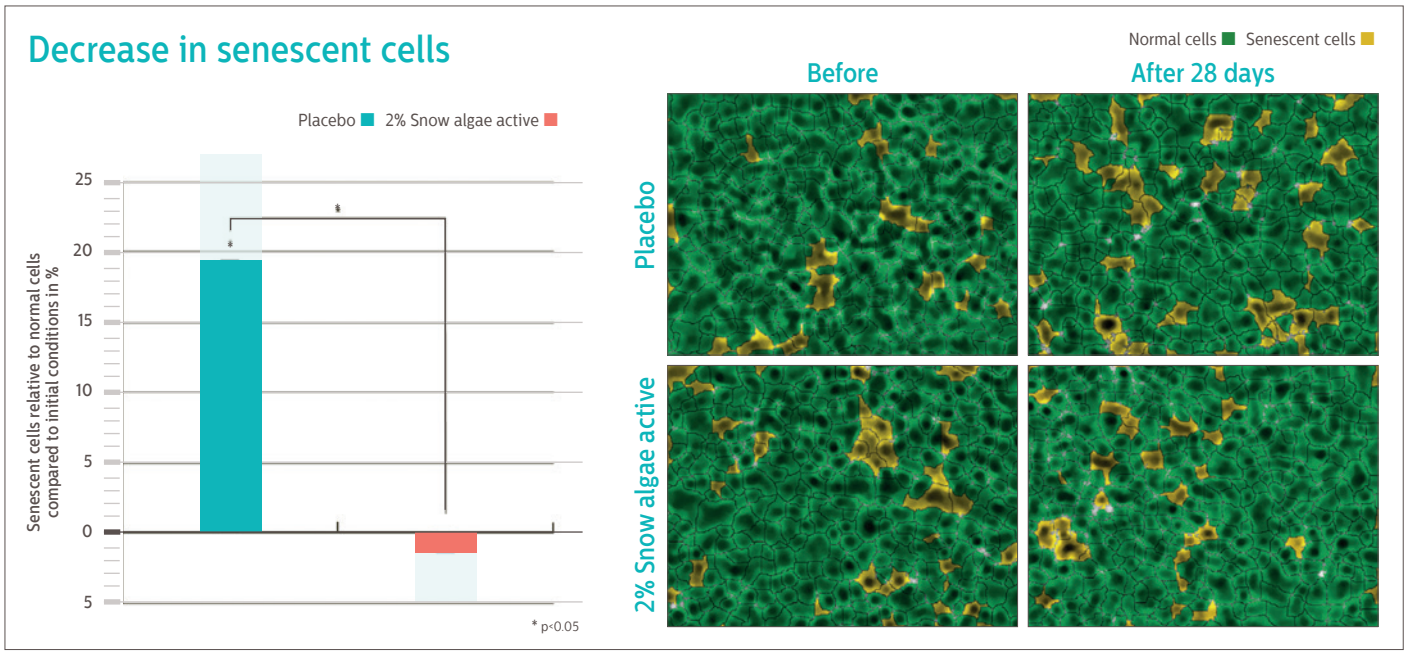


**Figure 6:** Snow algae extract prevents cellular senescence *in vivo*

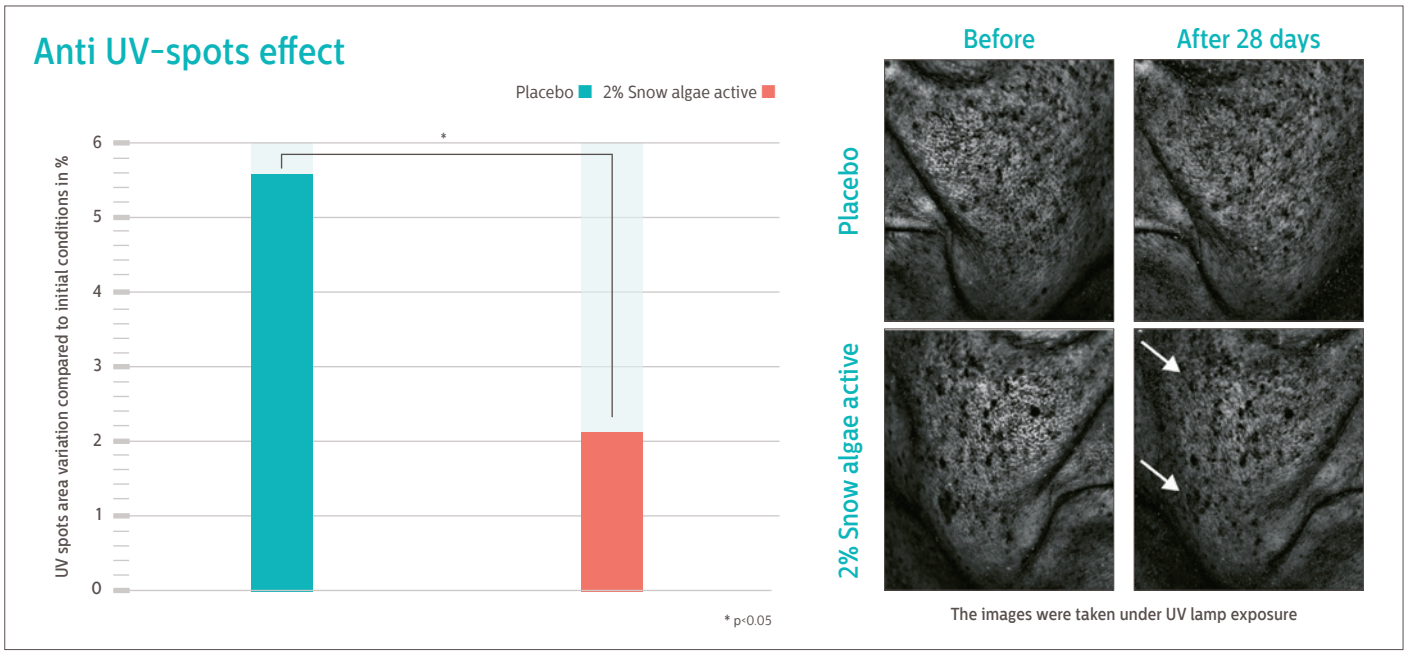


**Figure 7:** Anti-UV spots effect of snow algae active

This difference was statistically significant, and it can also be appreciated in exemplificatory pictures. By preventing the increase in senescent cells *in vivo*, snow algae active maintains a healthier cellular environment on the volunteers' skin.

During the previously described clinical study, high-definition photographs were taken both before and after treatment using the VISIA-CR system and a UV lamp. In these photographs, the area of UV spots was measured. These pigmented areas are induced by extensive exposure to the sun's UV rays and are a clear sign of photoageing.

Given that the study was performed during the summer, the UV spots area generally increased during the 28 days of the study duration. However, for the volunteers who applied the snow algae active, the area increase was significantly less than it was for the placebo-treated group (Figure 7). Therefore, snow algae active is able to reduce the UV spots area and thus prevent photoageing.

In another placebo-controlled clinical study performed during wintertime, transepidermal water loss (TEWL) was measured before and after treatment on the face (cheeks) using a tewameter. Winter weather conditions led to an increased loss of water by the skin, as shown with the placebo.

However, snow algae active was shown to counteract this effect and even reduce TEWL (Figure 8). Therefore, even under challenging conditions, snow algae active is able to reinforce the skin barrier.

Finally, results showed the capacity of snow algae active to increase skin hydration after just two weeks of treatment. The skin hydration was significantly increased by almost 10% compared to the placebo and by almost 25% compared to untreated (Figure 8), and this moisturizing effect was observed in 100% of the subjects.

## Conclusion

The extract of the highly resilient snow algae provides an excellent ingredient for skin applications. By targeting seven hallmarks of ageing, snow algae active reduces biological age in skin cells, protects the skin from senescence and brings back the cells' proteomic profile to a young state.

*In vivo*, while preventing senescence in sun-exposed skin, it also hindered the formation of UV spots. In summary, snow algae active turns back the epigenetic clock and thereby rejuvenates the skin. **PCM**

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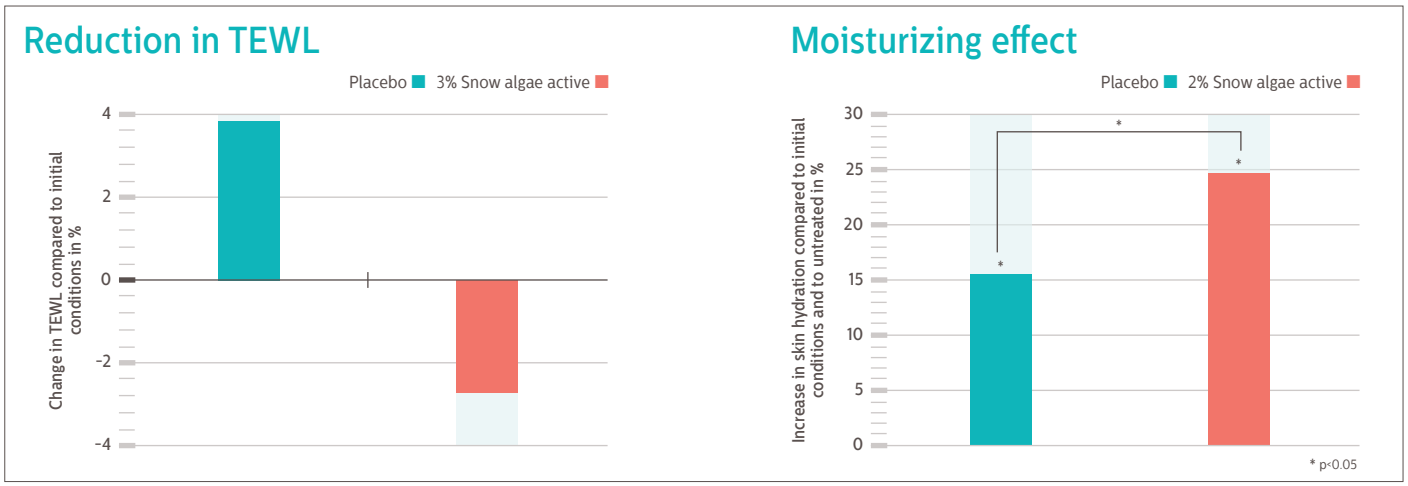


**Figure 8:** Snow algae active reduces TEWL and has a moisturizing effect