Natural extremolyte shows global anti-pollution and skin protection efficacy

KEYWORDS: Anti-pollution, blue-light protection, Ectoin, skin protection, natural molecule, epidermal barrier regeneration, skin care.

ABSTRACT

Scientific evidence confirms that chronic exposure to external stress factors including air pollution and blue-light irradiation contribute to premature skin aging and skin disorders. Protecting the skin and the prevention of cell damage seem to be logical and effective strategies to delay premature skin aging and damage. Extremolytes are the natural protection substances of extremophilic microorganisms and plants. The probably best-researched member of these also called “stress protection molecules”, Ectoin, has shown protection and regeneration properties against various urban stress factors and might therefore be an effective solution to prevent and treat environmentally stressed skin.

INTRODUCTION

Human skin is situated at the interface of the organism and its environment and is therefore constantly exposed to numerous extrinsic stress factors. Chronic exposure to environmental conditions, including ultraviolet light (UV), blue light and air pollution has been shown to have significant impact to skin health and aging. It is an indisputable fact that cutaneous aging is mainly driven by external stress factors, promoting the formation of reactive oxygen species (ROS), encouraging inflammation processes in tissues and cells and compromising the natural skin barrier. This results in an increase of trans-epidermal water loss, along with a decrease of skin thickness, skin elasticity and the occurrence of wrinkles and pigment spots. But also dermatoses like rash, eczema, allergies, psoriasis and atopic dermatitis are being caused or enhanced by external influences (1).

Protecting the skin from external stress-factors and the prevention of cell damage thus are logical and effective strategies to retard premature skin ageing and treat disease-affected skin.

In recent years, stress-protection molecules, so called extremolytes became popular as cosmetic active ingredients, e.g. bitop Ectoin® natural (in the following referred to as its INCI name “Ectoin”). Extremolytes are natural protection substances of so called extremophilic microorganisms and plants, which thrive in the most hostile environments our world provides - deserts, arctic ice, hot springs or the deep sea. Extremolytes stabilise and protect the biological structures of the microorganisms such as cell membranes, proteins or DNA, thus cellular stress reactions are significantly reduced (2). Some halophilic bacteria accumulate the extremolyte Ectoin to protect their cytoplasmic biomolecules against harmful environmental conditions like UV-light, heat, freezing, dryness and osmotic stress (3). The amino acid derivate Ectoin is a highly water-binding, organic molecule and compatible with the cellular metabolism without adversely affecting the biopolymers or physiologic processes (4). It can be isolated from halophilic bacteria on a large scale and thus is available as an active ingredient for skin care applications [3] with various positive effects including the reduction of wrinkles, restoring and stabilizing the skin barrier or the protection of skin-cells from the negative impact of external stress factors.

Furthermore, Unfried et al. (2016) demonstrated that inhaling Ectoin leads to a decrease of the inflammatory parameters in the sputum in neutrophilic pneumonia (5) and thus is used in medical inhalation products for the treatment of particle induced asthma or COPD. Ectoin also prevents the initiation of pro-inflammatory signaling cascades, such as intercellular adhesion molecule-1 (ICAM) on the surface of human keratinocytes (6). ICAM is a hallmark of inflammatory skin diseases (7). In this context, several studies have provided evidence that Ectoin is a therapeutic and side-effect free option for the treatment of atopic dermatitis (8-13).

The following study data and information is based on 100% pure and natural Ectoin (“bitop Ectoin® natural” manufactured by bitop AG, Dortmund Germany).

Skin barrier repair

The epidermal barrier function is key for both – healthy and compromised skin. Scientific research has defined clear connections between barrier impairments and compromised skin, including specific skin disorders like atopic skin and eczematous dermatitis (14).

A clinical study with 20 subjects demonstrated the effects of 1% Ectoin compared to 0.25% hydrocortisone cream (“Ebenol® Cream”) and placebo on skin with compromised epidermal barrier function. For this purpose, the skin was stressed with 2% sodium dodecyl sulfate (SDS) for 24h and then treated twice daily for seven days with the verum (1% Ectoin), placebo and the benchmark (cream with 0.25% hydrocortisone). The measured parameters were the improvement of skin redness (erythema) and TEWL (trans-epidermal water loss).
A negative impact on human skin was conducted by the first study showing that particulate matter (PM) has synergistic effects on skin aging and diseases. Also, the combination of sunlight and air pollution is most likely to have reactions on human skin due to interactions of pollutants (15). Factors might not be additive but might cause qualitative new factors that might not be additive but might cause qualitative new actions on the skin and that the sum of stress might not be additive but might cause qualitative new actions on the skin and that the sum of stress factors might not be additive but might cause qualitative new actions on human skin due to interactions of pollutants (15). Also, the combination of sunlight and air pollution is most likely to have synergistic effects on skin aging and diseases.

The first study showing that particulate matter (PM) has a negative impact on human skin was conducted by Vierkötter et al. in 2010. In this study with 400 Caucasian women, the association between PM exposure and pigment spot formation was shown (1). PM is a carrier for organic compounds like heavy metals and PAHs (polycyclic aromatic hydrocarbons). PAHs are highly lipophilic and thus easily penetrate the skin. PAH and PM are known to modify the expression and the release of POMC (pro-opiomelanocortin) and MMP1 (matrix metalloproteinase-1) resulting in the formation of pigment spots, collagen breakdown, and wrinkles (15, 16). Latest scientific research indicates that nitrogen dioxide [NO₂] might also have a negative impact on skin integrity. Hils et al. 2015 assessed the link between chronic exposure to NO₂ and pigment spot formation (17).

The clinical relevance of these scientific findings showing the damaging impact of air pollution on human skin touches upon aspects of both: prevention and therapy. Skin care and protection strategies which do not include pollution protection may need to be reconsidered.

One effective strategy to protect skin from air pollution is to maintain a healthy epidermal barrier function. Larger pollution particles like PM₁₀ and PM₂.₅ can thus be prevented from penetrating the skin. But air pollution is a very complex mixture of various chemicals and particles of different sizes. Given that particulate matter consists to 80% of ultrafine particles (UFP) like PM₀.₁ and smaller (18) and the highest level of concentration of toxic compounds like PAHs and heavy metals is related to ultrafine particles, anti-pollution strategies should particularly target ultrafine particles.

An ex vivo study with fresh epidermal keratinocytes from a female Caucasian and Asian donor has shown that Ectoin is capable to protect skin cells against the damaging impact of pollution particles of various sizes, particularly from ultrafine particles. Cells were untreated and pre-treated (24h) with 2 mM Ectoin solution. Afterwards, cells were stressed with fine and ultrafine carbon black particles and different surrogates for authentic street particulate matter such as SRM 1650 and SRM 2975.

After the particle stress, the expression of POMC mRNA was measured in keratinocytes by using real time PCR.

The results in figure 3 show that fine and ultrafine carbon black particles and diesel particulate matter induced POMC mRNA expression. POMC is known for melanogenesis stimulation in human melanocytes and to cause dark spot formations. It can therefore be used as a marker gene for pigmentation (16). Keratinocytes protected with Ectoin significantly down regulated PM induced over-expression of POMC mRNA in all tested cases by 100% or by 99%.

The TEWL is a parameter for the detection of compromised epidermal barrier function. Thus, the influence of the tested substances on the skin barrier could be directly demonstrated. The TEWL increased significantly after SDS treatment in all test persons.

For 1% Ectoin a decrease of TEWL by 28% after seven days of twice daily application was shown. After seven days, the efficacy of 1% Ectoin was higher compared to the results of treatment with 0.25% hydrocortisone cream.

**Anti-pollution efficacy**

In the past years, several epidemiological and mechanistic studies concluded a connection between pollutants and accelerating wrinkles as well as pigment spot formation. In some highly polluted areas like Beijing or New Delhi, air-pollution is most probably the main factor for premature skin aging, as pollutants and scattering particulates in the troposphere reduce the effects of shorter wavelength UVR and significant reductions in UV irradiance have been observed in polluted, urban areas. Air pollutants may not only induce skin aging but are also linked to causing or worsening acne, atopic dermatitis, eczema, allergic reactions or even skin cancer (1). Current research suggests that each individual pollutant has a specific toxic action on the skin and that the sum of stress factors might not be additive but might cause qualitative new reactions on human skin due to interactions of pollutants (15). Also, the combination of sunlight and air pollution is most likely to have synergistic effects on skin aging and diseases.

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Botta et al. (2008) demonstrated in an in vitro study set-up that Ectoin prevents oxidative damage in the skin induced by visible light irradiation. Here, Ectoin showed a protection level of up to 90% against the damaging impact of visible light on human keratinocytes (21).

In an ex vivo study, human living skin explants were pre-treated with 1% Ectoin and exposed to visible light (65J/cm²). Afterwards the parameters Nrf2 and MC1R were evaluated by immunostaining. Nrf2 is a key transcription factor in the cellular response to oxidative damage induced by reactive oxygen species (ROS). Nrf2 content in the cell increases automatically, when the skin is exposed to visible light or other stress factors.

The anti-pollution activity was evaluated by analysis of barrier lipid oxidation levels (measured by malondialdehyde, MDA) of ex vivo samples from the skin surface. MDA results from lipid peroxidation of the polyunsaturated fatty acids of the skin and is one of the reactive electrophile species that cause toxic stress in skin cells. Therefore MDA can be used as a marker for air pollution induced damage.

The study demonstrated the reduction of the cell’s stress response to oxidative stress induced by visible light irradiation due to Ectoin pre-treatment. The presence of Ectoin decreased the need of Nrf2 in the cell (figure 6). The results indicate that Ectoin can protect the skin from visible light induced skin damage and photo-aging.

Visible light has been reported to induce both, transient (22) as well as long lasting pigmentation in human skin (23). MC1R is a marker for skin pigmentation and its activation leads to eumelanin production. Visible light increases MC1R content, which consequently leads to pigmentation of the skin. The results of the latest ex vivo study (figure 7) indicate a reduction of visible light induced melonogenesis due to Ectoin pre-treatment.

CONCLUSION

The natural extremolyte Ectoin shows comprehensive skin protection efficacy against multiple external stress factors including particulate matter and blue-light irradiation. It effectively improves epidermal barrier function and stratum

Figure 4. In vivo study design: smoke application with standardized chamber system.

Figure 5. The pollution induced MDA content in the skin was reduced by 48% in the areas treated with 1% Ectoin compared to the placebo treated skin areas.

Figure 6. Nrf2 immunostaining of the negative control, placebo and 1% Ectoin pre-treatment batch with and without visible light irradiation.

Figure 7. MC1R immunostaining of the negative control, placebo and 1% Ectoin pre-treatment batch with and without visible light irradiation.

Five days of cream application with 1% Ectoin showed a positive anti-pollution effect. The pollution induced MDA overexpression was 48% lower compared to placebo and 47% lower compared to untreated but stressed control (figure 5).

Blue-light protection

The visible light spectrum responds to wavelengths from about 390 to 700 nm, and includes blue-light (450 to 495 nm) which is also emitted by digital devices like PC screens.

Various studies have shown negative effects to be exerted by visible light irradiation including erythema, pigmentation, thermal damage and free radical production. Visible light can also induce indirect DNA damage due to the generation of reactive oxygen species (ROS) (20).

Most of the currently available UV-filters, organic and inorganic, offer, if any, weak protection against visible light. This limited effectiveness indicates the need for further protection concepts.

CONCLUSION

The natural extremolyte Ectoin shows comprehensive skin protection efficacy against multiple external stress factors including particulate matter and blue-light irradiation. It effectively improves epidermal barrier function and stratum
corneum hydration - even on atopic skin - enhances general skin condition and reduces skin irritations due to its anti-inflammatory properties.

Ectoin is capable to protect skin and skin cells from the whole spectrum of air pollution induced aging and damage. This includes PAHs, heavy metals as well as PM of all particle sizes. The anti-pollution efficacy of Ectoin has been demonstrated in vivo on skin by analysis of barrier lipid oxidation levels from the skin surface as well as in human lungs for therapeutic and preventative applications. Several studies indicate that Ectoin is able to protect the skin from pollution and blue-light induced skin pigmentation.

Furthermore, Ectoin is supported by more than 15 years of published clinical data that proves its safety and efficacy for various applications including its therapeutic use in medical products for all skin types, which need to match various effective active ingredients, very well-suited for cosmetic applications including its therapeutic use in medical products.

In conclusion, the natural extremolyte Ectoin is a safe and effective active ingredient, very well-suited for cosmetic formulations for all skin types, which need to match various consumer demands and market trends.

REFERENCES


ABOUT THE AUTHOR

Janina Kienemund works as Junior Business Development Manager at bitop AG. She started her career as registered surgical nurse, afterwards completed a Master of Science degree in Microbiology successfully. During studies she already focused on extremophile and medically relevant microorganisms with regards to their positive and negative impacts to human health.

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