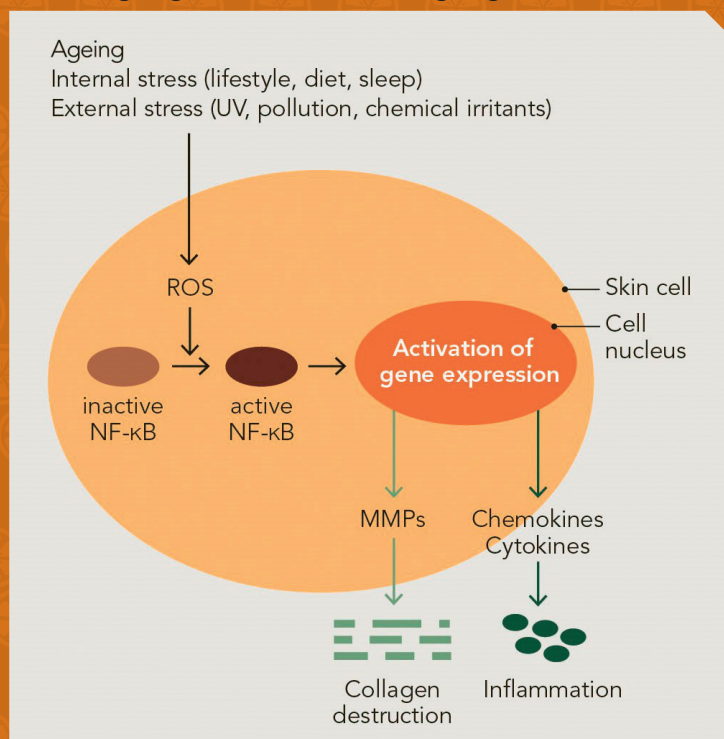


Upcycled Chios to Combat Inflammation

CALMandrin™ is our sustainable solution to soothe reddened skin and improve the signs of skin ageing. Thanks to its anti-inflammatory effect, **CALMandrin™** calms inflamed skin and markedly increases the firmness and density of the skin. The upcycled elixir **CALMandrin™** is based on the peel paste of organic mandarins used in the distillation process of fragrance production. The mandarins are grown exclusively in historic orchards on the Greek island of Chios

Inflammation contributes to skin ageing



The term “inflammation” was introduced two decades ago by Prof. Franceschi as a compound of the two words “inflammation” and “ageing”. Chronological ageing as well as intrinsic and extrinsic stress can lead to increased levels of reactive oxygen species (ROS) in the skin, resulting in activation of the NF-κB signalling pathway. Activated NF-κB induces the transcription of proinflammatory factors and metalloproteases. The human body’s ability to fight inflammation decreases with age and inflammatory processes can no longer be completely eliminated. Low-grade chronic inflammation occurs, contributing to the development of signs of ageing skin.

Mandarins from the Greek island of Chios

Mandarins are particularly rich in essential oils and antioxidants such as phenolic acids, flavonoids, limonoids and carotenoids. On the Greek island of Chios, mandarins were introduced in the

13th century after colonization by the Genoese. Chios mandarins grow exclusively in very mild climatic conditions in traditional organic cultivation. Unlike the modern industrially produced fruits, this ancient variety of mandarins contains many seeds. The mandarins of Chios are still highly appreciated for their excellent and intense aromatic properties and delicate fragrance as exquisite perfume essences.

Upcycled Chios mandarins – CALMandrin™

In a traditional small distillery, both the juice and the peel of the Chios mandarins are used for the gentle distillation process of organic fragrance production. The remaining rich and thick peel pulp (pomace) is the raw material for the production of CALMandrin™. Mibelle Biochemistry’s mission is to develop an active ingredient – CALMandrin™ – from this very special waste material through a gentle water-based upcycling process to extract the valuable antioxidants from these special mandarins for the skin.

Chios mandarin extract reduces NF-κB activation

The NF-κB signalling pathway is involved in immune regulation and contributes to the inflammation process. Therefore, we aimed to investigate the effect of Chios mandarin extract on the key inflammatory regulator NF-κB in human dermal fibroblasts. For this purpose, cells were pre-treated in the presence and absence of Chios mandarin extract. Inflammation was then induced and active NF-κB was analysed. Inflammation resulted in strong activation of NF-κB and its translocation to the nucleus. Pre-treatment with Chios mandarin extract significantly reduced NF-κB activation, demonstrating suppression of NF-κB signalling and consequently inflammation by Chios mandarin extract.

Chios mandarin extract reduces inflammatory response

To investigate the effect of Chios mandarin extract on inflammation, in vitro studies were performed using keratinocytes and dermal fibroblasts. For the keratinocyte assay, cells were treated with an inflammatory cocktail to stimulate chronic inflammation in the presence and absence of Chios mandarin extract. Analysis of genes important for the inflammatory response revealed that Chios mandarin extract decreased the expression of inflammatory markers in keratinocytes. In a second assay, dermal fibroblasts were treated with the secretion of UV-

Mandarins Immaging



stressed keratinocytes to simulate inflammaging conditions in the presence and absence of the Chios mandarin extract. Again, analysis of genes showed that the inflammatory response was reduced by treatment with Chios mandarin extract representing an anti-inflammatory effect.

Chios mandarin extract increases young collagen

Since the inflammatory response was reduced in keratinocytes and dermal fibroblasts, we wanted to test whether Chios mandarin extract had an effect on collagen deposition. Therefore, dermal fibroblasts were stressed with H_2O_2 in the presence or absence of Chios mandarin extract. Oxidative stress decreased the secretion of procollagen I whereas treatment with Chios mandarin extract counteracted this effect and increased procollagen I release compared with the stressed control. In addition, an ex vivo study was performed on skin explants with a cream containing 2% CALMandrin™ or the corresponding control. The treatment with CALMandrin™ for 7 days resulted in a visible increase in the ratio of young to mature collagen.

CALMandrin™ soothes reddened and irritated skin

To elucidate the calming and rejuvenating effect of CALMandrin™, a randomized placebo-controlled clinical study was conducted on a panel of volunteers with signs of skin redness as well as photo-ageing. Twenty women aged between 51 and 68 years (mean 60.9 years) applied a cream containing 2% CALMandrin™ or a corresponding placebo on each side of their face and on two separate areas on the forearms twice daily for 28 days. CALMandrin™ led to a visible improvement in skin redness

by -15.9% compared to initial conditions. Interestingly, facial skin redness was already decreased after 7 days of CALMandrin™-treatment demonstrating a fast-acting effect on reddened skin.

CALMandrin™ rejuvenates the skin

In addition to skin redness, the effect of CALMandrin™ on signs of ageing was investigated on the same panel of volunteers. Treatment with 2% CALMandrin™ increased skin elasticity by 29.5% and 29.3% after 7 and 28 days compared to initial conditions. Furthermore, CALMandrin™ enhanced skin firmness by 13.9% and 16.9% after 7 and 28 days, respectively. Only 7 days of CALMandrin™ application strongly improved skin elasticity and skin firmness, highlighting a rapid improvement of the skin parameters. Besides skin firmness and elasticity, 2% CALMandrin™ significantly improved skin density measured on the forearm by 11.1% after 28 days of treatment compared to initial conditions.

To summarize, CALMandrin™ counteracts the inflammatory immune response that results from both chronic ageing and extrinsic stress to win the race against inflammaging-induced signs of skin ageing.

Mibelle Biochemistry, Stand AA50

