



Protecting the Natural Rhythm of Skin



Skin displays a remarkable rhythmic behavior related to exposure to environmental variations in temperature, humidity, and UV radiation (UVR) that corresponds to the 24 hour cycle of the day or circadian rhythm. Many cells including skin cells have a time-sensing mechanism (or clock) called a circadian oscillator that is coordinated by a central clock located in the brain called the suprachiasmatic nuclei. One of the biggest triggers for regulating this rhythm is light.

The skin barrier is important for protection from UVR, physical injury, microbial and chemical assaults and the maintenance of homeostasis related to body temperature and water

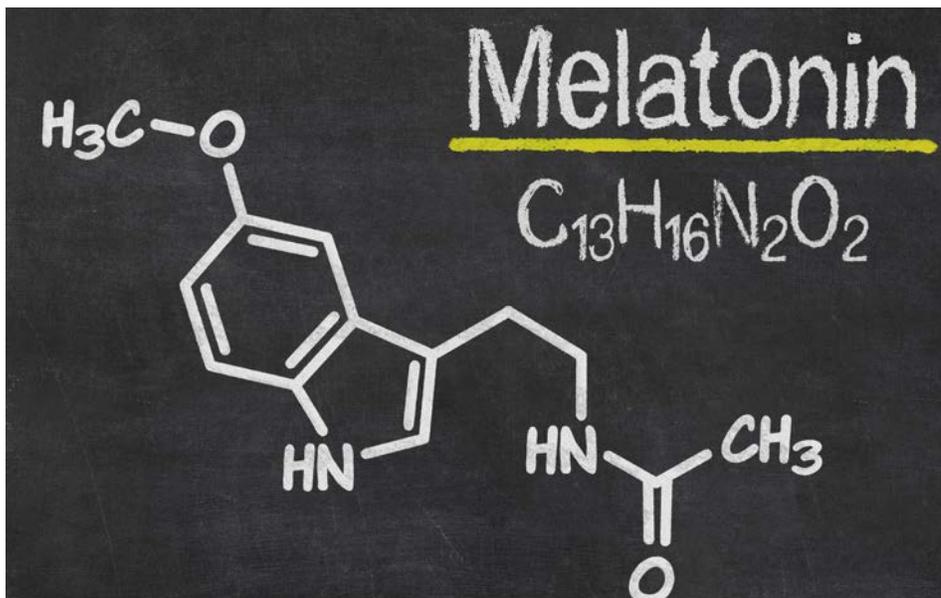
regulation. Healthy skin has decreased trans-epidermal water loss (TEWL), a well hydrated epidermis, and a slightly acidic pH. Several of these skin factors have been found to fluctuate in a circadian fashion, suggesting that the skin barrier function may be stronger during certain times of day than others. This mechanism probably evolved to provide optimal protection when UVR and other environmental insults are greatest. Further, DNA repair rates in skin have been found to be rhythmic with maximum repair occurring in the evening.

Viniferamine® skin and wound care products contain skin penetrating small molecule nutrients

including antioxidants like oleuropein from olives, resveratrol from grapes and epigallocatechin-3-gallate (EGCG) from green tea, as well as vitamins and amino acids that all help with skin repair and renewal. Viniferamine® Renewal Moisturizer contains a potent dose of Viniferamine® and all the other scientific ingredients. Each ingredient in Renewal Moisturizer is perfectly balanced to achieve maximum skin restoration. Viniferamine® Silicone Barrier includes a sophisticated silicone complex to protect skin from irritants that can damage skin. This non-occlusive “second-skin” provided by Silicone Barrier also protects compromised epidermis. The Viniferamine® enriched formula in Silicone Barrier allows delivery of nutrients that restore skin to a more healthy state.

Melatonin Helps Keep Things Balanced

Unfortunately, due to exposure to indoor lighting at all times of the day including night (when many individuals work), the natural rhythm of skin can be disrupted. Impairments in circadian rhythms in skin have been



reported to result in an imbalance in skin physiology that includes signs of premature aging. One of the beneficial ingredients found in Viniferamine[®] skin and wound care, melatonin, helps maintain the circadian rhythm and keep things balanced. Melatonin is a very important antioxidant that is in all animals and plants and even bacteria. Melatonin is found in the skin and can be produced by skin cells, however, normal aging is associated with a decline in its production. Melatonin helps preserve the natural circadian rhythm of cells and it has been shown to regulate the circadian rhythm of skin fibroblasts. In addition, melatonin enhances the skin barrier. It has also been shown that oleuropein enhances the skin barrier.

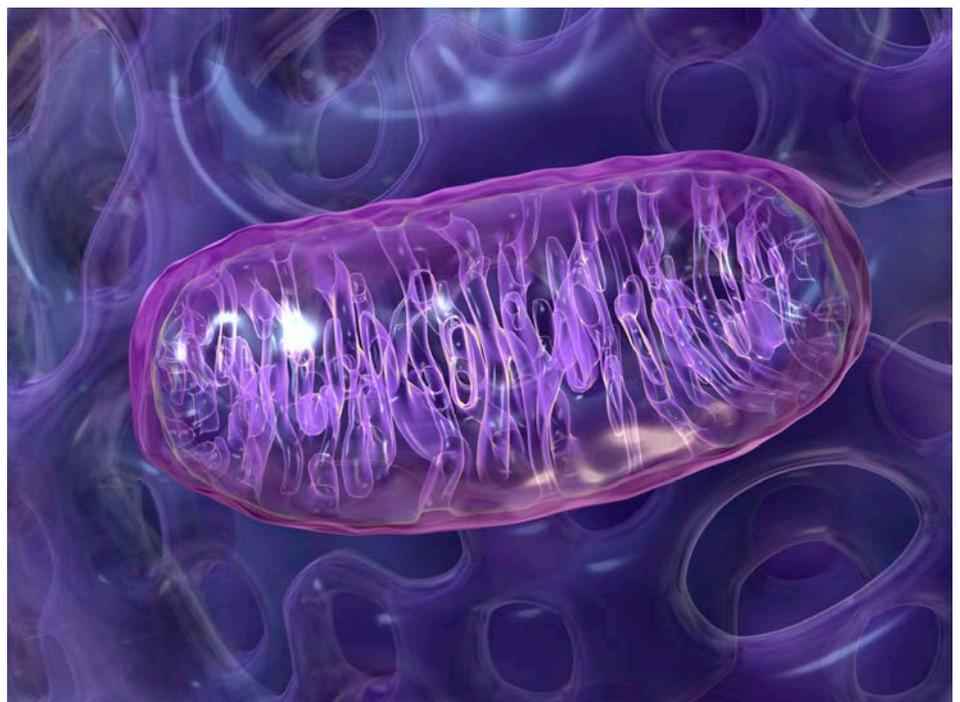
Protecting Mitochondria and Skin from Oxidative Stress

Mitochondria are the cell's powerhouses that produce energy including in skin cells. Recent studies have demonstrated that the circadian clock controls the activ-

ity of sirtuin deacetylase (SIRT) enzymes that regulate mitochondrial functions. This indicates that there is a strong interconnection between circadian and metabolic processes, shown by the fact that humans have more metabolic regulation in the morning than in the evening, which makes sense since humans are normally more active in the day than the evening. More metabolic activity during the day also means more free-radicals including reactive

oxygen species (ROS) produced (as side products of metabolism) that can cause oxidative stress. Viniferamine[®] skin and wound care products contain many antioxidants that counteract oxidative stress including melatonin and oleuropein, resveratrol, and EGCG, as well as L-glutathione. In fact, oleuropein, EGCG, resveratrol and melatonin also activate the important oxidative defense enzyme superoxide dismutase (SOD). Furthermore, resveratrol and EGCG activate SIRT1.

Skin cells are also vulnerable to oxidative stress caused by exposure to many irritants including, UVR, pollution and harmful chemicals. Oxidative stress has been associated with aging and mitochondrial dysfunction. Damaged or dysfunctional mitochondria produce more ROS that can lead to more oxidative stress. In contrast, when mitochondria are healthy and ROS levels are normal, ROS are important for controlling signaling and normal pro-



cesses such as wound healing. In fact, emerging evidence indicates that mitochondria are important regulators of skin physiology. Mitochondria metabolism also regulates keratinocyte differentiation and in addition, mitochondria are involved in melanocyte function.

More Protection for Mitochondria

Some of the antioxidants in Viniferamine® skin and wound care products have been found to specifically protect mitochondria. EGCG has shown to suppress radiation-induced damage to human epidermal keratinocyte mitochondria by turning on the

important antioxidant enzymes, superoxide dismutase 2 (SOD2) and heme oxygenase-1 (HO-1). Resveratrol has been shown to suppress macrophage mitochondrial damage. Melatonin can penetrate skin cells to access mitochondria and melatonin has been shown to prevent mitochondrial dysfunction caused by oxidative damage by preserving an important lipid found in mitochondria known as cardiolipin. Abnormalities in cardiolipin have also been associated with aging.

Viniferamine® skin and wound care products including Renewal Moisturizer and Silicone Barrier contain ingredients that help the

circadian clock regulate important functions like barrier function and skin repair. Viniferamine® skin and wound care products also include ingredients that enhance the skin barrier. In addition, some of the beneficial ingredients in Viniferamine® skin and wound care products help protect cells and mitochondria (the cell's powerhouse) from oxidative stress and dysfunction.

It's good to know that Viniferamine® skin and wound care products can help preserve the natural rhythm of skin to help skin protect us from environmental insults like UVR and pollution.

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