

New formulations of melatonin to prevent aging skin

Melatonin, a hormone produced by the pineal gland, has been also detected in multiple extrapineal organs and tissues at much more higher concentrations than in the pineal gland. Melatonin synthesis has been demonstrated in skin cells, and its expression was located in the upper layers of the epidermis, dermal structures, blood vessels and mast cells by immunocytochemistry. Melatonin is a potent free radical scavenger with antioxidant properties, which increases the expression and activity of the endogenous antioxidant enzymes. During its scavenging activity, melatonin generates a series of metabolites that are also free radical scavengers. Capable of crossing cell membranes, melatonin can reach all cell compartments, it is take up by mitochondria where it maintains mitochondrial homeostasis. Melatonin has also important anti-inflammatory effects, reducing the innate immune activation.

Recently, we have developed a pharmaceutical preparation of melatonin plus CoQ10 for the treatment and prevention of skin aging. The success of this preparation depends on its composition, which facilitates its transdermal adsorption, reaching both molecules all skin's layers. Moreover, the combination of both molecules favours their uptake by the mitochondria in all skin cells. The advantage of our product is that not only reverse the mitochondrial damage produced during cellular aging, but also improves skin healthy in many pathologies coursing with oxidative stress, inflammation, and mitochondrial impairment. Additionally, after reported a melatonin's gel that protects normal cells from oral mucositis induced by radio- and chemotherapy in head and neck human cancer.

Therefore, melatonin might be useful in the treatment of pigmentary diseases (e.g. vitiligo or hyperpigmentation), benign or malignant proliferative processes (melanoma, epidermal cancer or precancerous states), UVB-induced pathology, inflammatory dermatoses and, other skin pathologies, besides skin aging.



Figure 1: Melatonin prevents and recovers mitochondrial damage to the skin

Reference

1. Slominski A., Fischer TW, Zmijewski MA et al (2005) On the Role of Melatonin in Skin Physiology and Pathology. *Endocrine* 27: 137-148.
2. Slominsk A, Tobin DJ, Zmijewski MA et al. (2007) Melatonin in the skin: synthesis, metabolism and functions. *TRENDS in Endocrinology and Metabolism* 74:3913-3925.
3. Shen YQ, Guerra-Librero A, Fernandez-Gil BI et al (2017) Combination of melatonin and rapamycin for head and neck cancer therapy: Suppression of AKT/mTOR pathway activation, and activation of mitophagy and apoptosis via mitochondrial function regulation. *J Pineal Res* doi: 10.1111/jpi.12461
4. Abdel Moneim AE, Guerra-Librero A, Florido J et al (2017) Oral Mucositis: Melatonin Gel an Effective New Treatment. *Int J Mol Sci*. doi: 10.3390/ijms18051003
5. Fernández-Gil B, Moneim AE, Ortiz F, Shen YQ et al (2017) Melatonin protects rats from radiotherapy-induced small intestine toxicity. *PLoS One*. doi: 10.1371/journal.pone.0174474
6. Ortiz F, Acuña-Castroviejo D, Doerrier C et al (2015) Melatonin blunts the mitochondrial/NLRP3 connection and protects against radiation-induced oral mucositis. *J Pineal Res* 58:34-49.

Germaine Escames
Granada University School of Medicine, Spain