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Editorial

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Photobiomodulation for Skin Pigmentation Disorders: A Dual-Function Treatment

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Skin pigmentation is a highly controlled complex process involving keratinocytes, melanocytes, and fibroblasts that communicate with each other through several secreted mediators and their receptors. These interactions then affect signaling pathways and lead to activation of transcription factors.[1] The main evolutionary purpose of skin pigmentation is to protect the skin against the short- and long-term damaging effects of exposure to ultraviolet (UV) light contained in solar radiation. Skin color is the main phenotypic variable, which characterizes human beings originating from different parts of the world, especially different latitudes.

Melanin is a polymeric macromolecule biosynthesized by melanocytes starting from L-tyrosine, secreted inside melanosomes and then taken up by keratinocytes. The most common form is the darker pigment eumelanin, whereas pheomelanin is a lighter pigment containing additional cysteine residues. The signaling pathways involved in melanogenesis are based on α-melanocyte stimulating hormone (α-MSH), a peptide that is formed by cleavage of proopiomelanocortin (POMC) produced in the pituitary gland. α-MSH binds to the melanocortin 1 receptor (MC1R), a G-protein coupled receptor expressed on melanocytes and upregulated by UV exposure. The microphthalmia-associated transcription factor (MITF) regulates the transcription of melanogenesis-related enzymes as well as the expression of MC1R in melanocytes.[2]

Disorders of pigmentation are highly distressing for their sufferers, even though they are unlikely to be life-threatening and are not generally classified as serious diseases. They can reduce the quality of life, especially when located on the face, hands, or other visible parts of the body. Disorders of pigmentation can be broadly divided into two opposite types of pathology. The first is a patchy type of depigmentation called vitiligo, which involves the loss of functional melanocytes in the affected skin areas. The second involves the appearance of hyperpigmented spots called solar lentigenes (age or liver spots). There are also hyperpigmented patches called melasma. Melasma often occurs in sun-exposed skin, or arises in women due to pregnancy or birth control hormones.

The intriguing topic that will be addressed as follows is that photobiomodulation therapy (PBMT) may be able to treat both types of pigmentation disorders and exert seemingly opposite effects depending on the result required. PBMT is a rapidly growing approach to the treatment and/or prevention of a multitude of diseases and disorders. PBM involves the application of relatively low levels of visible and/or near-infrared light to the human body, frequently to the skin even though it is intended to treat something beneath the skin. PBMT is rapidly being adopted in cosmetic and esthetic medicine due to its efficacy, safety, noninvasive nature, and relative cost-effectiveness.

Vitiligo is an autoimmune disease in which autoreactive CD8-positive T cells attack and destroy melanocytes in the skin.[3] The incidence of vitiligo is between 0.1% and 2% in different populations. Vitiligo has a genetic component involving mutations in several genes related to various aspects of the immune system, and sufferers and their close families have a greater incidence of other autoimmune diseases, including autoimmune thyroid disease, pernicious anemia, Addison's disease, systemic lupus erythematosus, and alopecia areata.[4]

A variety of treatments have been tested for vitiligo.[5] These include narrow band ultraviolet B (UVB), psoralen and ultraviolet A (PUVA) phototherapy, topical agents such as glucocorticosteroids, immunosuppressive agents, calcineurin inhibitors, and vitamin D. The suboptimal results obtained with these approaches has led to the introduction of molecular targeted therapies, including JAK (Janus-activated kinase) inhibitors and a wide range of monoclonal antibodies targeting various aspects of the immune system.

PBMT using a He–Ne laser (632.8 nm) has been shown to help with repigmentation in vitiligo patients. The mechanism of action of this effect was investigated in depth by Yu et al. in Taiwan.[6] They proposed that PBMT stimulated melanocyte stem cells in the hair follicles to give rise to melanoblasts (MBs). These MBs then proliferated, migrated out of the outer root sheath to the perilesional skin, where they differentiated into melanocytes. These effects were accompanied by activation of CREB (cyclic adenosine monophosphate response element binding protein), a pleiotropic transcription factor. There were also increases in nerve growth factor and basic fibroblast growth factor. It is

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also possible that the antiapoptotic effects, anti-inflammatory effects, and antioxidant effects of PBMT could have played a role by inhibiting the autoimmune disease process. More research is still needed to identify the best PBM wavelengths and dosimetric parameters for the repigmentation of vitiligo.

PBMT has been widely employed for skin rejuvenation and cosmetic dermatology, especially on the face, mediated by various wavelengths and power densities of light-emitting diode (LED) devices.[7] In addition to the expected effects on collagen production in dermal fibroblasts leading to a reduction in fine lines and wrinkles, beneficial effects on hyperpigmented spots have also been observed. Similar to vitiligo, a wide range of pharmaceutical approaches have been investigated for the treatment of hyperpigmentation.[8] These agents include inhibitors of tyrosinase activity and/or stability, melanosome maturation, transfer and trafficking, and melanogenesis-related signaling pathways. However, the nonpharmaceutical nature of PBMT might be preferred by dermatologists and patients in clinical cosmetic practice.

How PBMT might reduce melanin production in the skin was investigated at a mechanistic level by Oh et al.[9] PBMT using 660-nm LEDs inhibited α-MSH-induced tyrosinase activity in B16F10 mouse melanoma cells. They also found that 660-nm LEDs decreased MITF and tyrosinase expression and induced the activation of ERK (extracellular regulated kinase). Lee et al. described a wearable patch formed from surface-lighting micro-LEDs (SμLED) at 630 nm for reducing hyperpigmented spots.[10] The mechanistic investigation showed a lower melanin content in a human skin equivalent model, along with reductions in melan-A (a melanocyte differentiation marker), tyrosinase, and MITF expression.

Barolet reported that PBMT using 940 nm LEDs at 90 mW/cm^2 and a dose of 13.5 J/cm^2 combined with microdermabrasion significantly improved facial melasma in a spilt-face trial in patients who had failed prior treatments.[11] Dai et al. used 590 nm LEDs at 20 mW/cm^2 and a dose of 20 J/cm^2 to treat melasma in patients.[12] In a mechanistic investigation they showed that PBMT had antiangiogenic effects by reducing expression of vascular endothelial growth factor and stem cell factor in endothelial cells, triggering autophagy in melanocytes, and upregulating the long noncoding RNA H19, and its associated exosomal microRNA-675 in keratinocytes.

PBMT using fairly similar parameters may, therefore, be able to produce opposite effects in the skin, either lightening it or darkening it depending on what is required for optimum cosmetic outcomes.

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