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PHOTOBIOMODULATION OF NO BIOACTIVITY AND RELEASE IN THE SKIN

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Background: Nitric oxide (NO) is a very important signaling molecule for the cardiovascular system and impacts a series of other functions. NO is present in most living organism and tissues including human skin. It has been shown that UVA-mediated photolysis of cutaneous nitrite and/or nitrate can release NO from human skin. PBM may also release NO by photodissociation of NO from cytochrome c oxidase and from intracellular stores like nitrosylated forms of myoglobin and hemoglobin with less risk than UVA. The aim of the study was to determine if PBM can mobilize NO in the skin.
Study: Human skin samples were collected fresh from a face lift procedure and flash frozen on site and later mounted on microscope slides. The sections were then incubated in 4,5-Diaminofluorescein diacetate (DAF-2DA), a Nitric Oxide detecting fluorophore. Following this, half of these sections were irradiated with continuous wavelength light of 660 nm (10 mW/cm^2, 4 J/cm^2) and the other half were not irradiated. The slides from both groups were then treated with the NO Synthase inhibitor, L-NMMA, the NO scavenger, c-PTIO, or left untreated with these chemicals. The sections were examined using confocal microscopy to detect fluorescence.
Results: Confocal fluorescence microscopy studies of human skin pre-labeled with the NO-imaging probe DAF-2DA revealed that PBM-induced NO release occurs with the majority of the light-sensitive NO pool in the upper skin strata. Interestingly, in all samples, most of the fluorescence was observed in the epidermis as compared to the dermis.
Conclusion: Further studies are needed to measure the likely systemic rise in circulating nitrite and concurrent fall in plasma nitrate. This is consistent with the presence of NO storage forms mobilized by PBM in the epidermis reported in this study and the probable liberation of NO from these pools.

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UNDERSTANDING PHOTOBIOMODULATION FOR HUMAN WOUND HEALING

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Background: Visual and non-visual opsins (OPNs) and cryptochromes (CRYs), the putative transcription factors and circadian clock regulators have previously been suggested as mediators of photobiomodulation in human skin. Therefore, we have sought to localize their expression in human skin, in primary cells and in *ex vivo* wounds after 2 days in culture and determine changes in cell migration, metabolism and mRNA and protein expression in response to blue and red light.
Study: Expression of OPNs and CRYs in human female skin (n = 3) and *ex vivo* wounds was detected by immunohistochemistry. mRNA and protein expression in primary human dermal fibroblasts, DF, (n = 8) and epidermal keratinocytes, EK, (n = 3) was confirmed by qRT-PCR and immunocytochemistry. Different parameters of low-level red and blue light were used to modulate keratinocyte metabolism and migration (scratch assay). Knockdown of OPN3 was achieved using siRNA.
Results: CRY1 was expressed in the epidermis and dermis, OPN1-SW was expressed in the epidermal suprabasal layer and dermis, and OPN3 and OPN5 – in the epidermal basal layer. OPN3, but not OPN5 was expressed in the dermis. Expression mirrored in primary cultures of keratinocytes and fibroblasts. Photoreceptors were also expressed in the epithelial tongue of *ex vivo* wounds. Low doses of blue, red and IR light stimulated keratinocyte metabolism. High doses of IR inhibited keratinocyte metabolism, while medium doses of blue light had no effect on metabolism, but delayed migration. Silencing a blue light receptor (OPN3) with 98% efficiency increased cell migration. Furthermore, silencing OPN3 up regulated CRY1 and CRY2 in mechanically wounded keratinocytes.
Conclusion: The presence of different photoreceptors in human skin and *ex vivo* wounds suggests that light therapy may have diverse roles in wound healing. Different light parameters modulate keratinocyte metabolism and migration, which may be regulated by the blue light receptor OPN3. Further studies using light in combination of photoreceptor silencing will provide a better understanding of the molecular mechanisms of light therapy in wound healing for the development of reliable and efficient light-based treatments.

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A REVIEW OF FDA-CLEARED HOME-USE PHOTOBIOMODULATION DEVICES FOR TREATMENT OF ANDROGENETIC ALOPECIA

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Background: The market for home-use devices to treat androgenetic alopecia (AGA) has rapidly expanded, and the FDA has recently cleared many new photobiomodulation therapy devices for this indication. Photobiomodulation therapy has far-reaching biochemical effects that are thought to accelerate hair growth, induce and prolong anagen, and inhibit transition to catagen. The purpose of this review was to evaluate FDA-cleared commercially available home-use photobiomodulation devices for the treatment of AGA.
Study: A search of the FDA 510(k) Premarket Notification database was conducted to identify all home-use photobiomodulation therapy devices that have been FDA-cleared for the treatment of AGA.
Results: Thirteen devices were identified and compared. These devices emit visible red light with wavelengths ranging from 650 nm to 678 nm and have power classification of no more than five milliwatts (mW) per diode. The number of diode lasers or LEDs contained in the devices ranges from 7 to 272. The majority of these devices contain only diode lasers; however, two devices also incorporate pulsed emission LEDs. Device design varies and includes combs, headbands, caps, and helmets. Most home-use devices are available directly to consumers, but some must be obtained from an authorized physician. Retail cost of these devices