

# Illuminating the Role of Visible Light in Dermatology

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**V**isible light is part of the electromagnetic spectrum and is confined to a range of 400 to 700 nm. Visible light phototherapy can be delivered across various wavelengths within this spectrum, with most research focusing on blue light (BL)(400-500 nm) and red light (RL)(600-700 nm). Blue light commonly is used to treat acne as well as actinic keratosis and other inflammatory disorders,<sup>1,2</sup> while RL largely targets signs of skin aging and fibrosis.<sup>2,3</sup> Because of its shorter wavelength, the clinically meaningful skin penetration of BL reaches up to 1 mm and is confined to the epidermis; in contrast, RL can access the dermal adnexa due to its penetration depth of more than 2 mm.<sup>4</sup> Therapeutically, visible light can be utilized alone (eg, photobiomodulation [PBM]) or in combination with a photosensitizing agent (eg, photodynamic therapy [PDT]).<sup>5,6</sup>

Our laboratory's prior research has contributed to a greater understanding of the safety profile of visible light at various wavelengths.<sup>1,3</sup> Specifically, our work has shown that BL (417 nm [range, 412-422 nm]) and RL (633 nm [range, 627-639 nm]) demonstrated no evidence of DNA damage—via no formation of cyclobutane pyrimidine dimers and/or 6-4 photoproducts, the hallmark photolesions caused by UV exposure—in human dermal fibroblasts following visible light exposure at all fluences tested.<sup>1,3</sup> This evidence reinforces the safety of visible light at clinically relevant wavelengths, supporting its integration into dermatologic practice. In this editorial, we highlight the key clinical applications of PBM and PDT and outline safety considerations for visible light-based therapies in dermatologic practice.

## Photobiomodulation

Photobiomodulation is a noninvasive treatment in which low-level lasers or light-emitting diodes deliver photons from a nonionizing light source to endogenous photoreceptors, primarily cytochrome C oxidase.<sup>7-9</sup> On the visible light spectrum, PBM primarily encompasses RL.<sup>7-9</sup>

Photoactivation leads to production of reactive oxygen species as well as mitochondrial alterations, with resulting modulation of cellular activity.<sup>7-9</sup> Upregulation of cellular activity generally occurs at lower fluences (ie, energy delivered per unit area) of light, whereas higher fluences cause downregulation of cellular activity.<sup>5</sup>

Recent consensus guidelines, established with expert colleagues, define additional key parameters that are crucial to optimizing PBM treatment, including distance from the light source, area of the light beam, wavelength, length of treatment time, and number of treatments.<sup>5</sup> Understanding the effects of different parameter combinations is essential for clinicians to select the best treatment regimen for each patient. Our laboratory has conducted National Institutes of Health–funded phase 1 and phase 2 clinical trials to determine the safety and efficacy of red-light PBM.<sup>10-13</sup> Additionally, we completed several pilot phase 2 clinical studies with commercially available light-emitting diode face masks using PBM technology, which demonstrated a favorable safety profile and high patient satisfaction across multiple self-reported measures.<sup>14,15</sup> These findings highlight PBM as a reliable and well-tolerated therapeutic approach that can be administered in clinical settings or by patients at home.

Adverse effects of PBM therapy generally are mild and transient, most commonly manifesting as slight irritation and erythema.<sup>5</sup> Overall, PBM is widely regarded as safe with a favorable and nontoxic profile across treatment settings. Growing evidence supports the role of PBM in managing wound healing, acne, alopecia, and skin aging, among other dermatologic concerns.<sup>8</sup>

## Photodynamic Therapy

Photodynamic therapy is a noninvasive procedure during which a photosensitizer—typically 5-aminolevulinic acid (5-ALA) or a derivative, methyl aminolevulinate—reacts

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with a light source and oxygen, resulting in reactive oxygen species.<sup>6,16</sup> This reaction ultimately triggers targeted cellular destruction of the intended lesional skin but with negligible effects on adjacent nonlesional tissue.<sup>6</sup> The efficacy of PDT is determined by several parameters, including composition and concentration of the photosensitizer, photosensitizer incubation temperature, and incubation time with the photosensitizer. Methyl aminolevulinate is a lipophilic molecule and may promote greater skin penetration and cellular uptake than 5-ALA, which is a hydrophilic molecule.<sup>6</sup>

Our research further demonstrated that apoptosis increases in a dose- and temperature-dependent manner following 5-ALA exposure, both in cutaneous and mucosal squamous cell carcinoma cells and in human dermal fibroblasts.<sup>17,18</sup> Our mechanistic insights have clinical relevance, as evidenced by an independent pilot study demonstrating that temperature-modulated PDT significantly improved actinic keratosis lesion clearance rates ( $P<.0001$ ).<sup>19</sup> Additionally, we determined that even short periods of incubation with 5-ALA (ie, 15-30 minutes) result in statistically significant increases in apoptosis ( $P<.05$ ).<sup>20</sup> Thus, these findings highlight that the choice of photosensitizing agent and the administration parameters are critical in determining PDT efficacy as well as the need to optimize clinical protocols.

Photodynamic therapy also has demonstrated general clinical and genotoxic safety, with the most common potential adverse events limited to temporary inflammation, erythema, and discomfort.<sup>21</sup> A study in murine skin and human keratinocytes revealed that 5-ALA PDT had a photoprotective effect against previous irradiation with UVB (a known inducer of DNA damage) via removal of cyclobutane pyrimidine dimers.<sup>22</sup> Thus, PDT has been recognized as a safe and effective therapeutic modality with broad applications in dermatology, including treatment of actinic keratosis and nonmelanoma skin cancers.<sup>16</sup>

**Clinical Safety, Photoprotection, and Precautions**  
While visible light has shown substantial therapeutic potential in dermatology, there are several safety measures and precautions to be aware of. Visible light constitutes approximately 44% of the solar output; therefore, precautions against both UV and visible light are recommended for the general population.<sup>23</sup> Cumulative exposure to visible light has been shown to trigger melanogenesis, resulting in persistent erythema, hyperpigmentation, and uneven skin tones across all Fitzpatrick skin types.<sup>24</sup> Individuals with skin of color are more photosensitive to visible light due to increased baseline melanin levels.<sup>24</sup> Similarly, patients with pigmentary conditions such as melasma and postinflammatory hyperpigmentation may experience worsening of their dermatologic symptoms due to underlying visible light photosensitivity.<sup>25</sup>

Patients undergoing PBM or PDT could benefit from visible light protection. The primary form of photoprotection against visible light is tinted sunscreen, which contains iron oxides and titanium dioxide.<sup>26</sup> Iron (III) oxide is capable of blocking nearly all visible light damage.<sup>26</sup>

Use of physical barriers such as wavelength-specific sunglasses and wide-brimmed hats also is important for preventing photodamage from visible light.<sup>26</sup>

## Final Thoughts

Visible light has a role in the treatment of a variety of skin conditions, including actinic keratosis, nonmelanoma skin cancers, acne, wound healing, skin fibrosis, and photodamage. Photobiomodulation and PDT represent 2 noninvasive phototherapeutic options that utilize visible light to enact cellular changes necessary to improve skin health. Integrating visible light phototherapy into standard clinical practice is important for enhancing patient outcomes. Clinicians should remain mindful of the rare pigmentary risks associated with visible light therapy devices. Future research should prioritize optimization of standardized protocols and expansion of clinical indications for visible light phototherapy.

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