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Comparative Biological Effects of Blue and Red Light (The "Battle of Lights") with Emphasis on Photobiomodulation Applications

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Abstract

Introduction: Light-based therapies, particularly photobiomodulation (PBM), have emerged as safe, non-invasive modalities with expanding applications in dermatology and rehabilitation medicine. However, substantial variability in treatment parameters and a lack of consolidated evidence continue to hinder their standardized clinical adoption. This review aims to synthesize the molecular mechanisms, biological effects, and clinical applications of light-based therapies in dermatology, with a focus on optimizing treatment protocols and improving skin health outcomes.

Methods: A narrative review was conducted to summarize experimental and clinical evidence on light-based therapies, including red light, blue light, near-infrared (NIR), LEDs, low-level laser therapy (LLLT), and photodynamic therapy (PDT). A comprehensive literature search was performed across PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar using the following keywords: Phototherapy, Photobiomodulation, Wound Healing, Radiation Therapy, Precision Medicine, and Skin Rejuvenation. Retrieved studies on molecular pathways, cellular responses, therapeutic efficacy, and clinical outcomes were critically appraised and narratively synthesized.

Results: PBM primarily acts via mitochondrial cytochrome C oxidase absorption, enhancing ATP production and modulating ROS and NO signaling. Red and NIR light promote collagen synthesis, angiogenesis, and tissue repair, while blue light exhibits antimicrobial effects against C. acnes and induces reparative macrophage polarization. PDT modulates inflammatory and regenerative pathways. Clinical data support the use of these therapies for radiation dermatitis, oral mucositis, acne, wound healing, and skin rejuvenation. Evidence for plaque psoriasis is limited, though combination with NB-UVB shows promise.

Conclusion: Light-based therapies offer effective, versatile options for tissue repair, inflammation control, and management of diverse skin conditions. Future integration of multi-wavelength technologies with biomarker-guided personalization is expected to enhance treatment precision and expand clinical applications.

Keywords: Phototherapy, Photobiomodulation, Wound healing, Radiation therapy, Precision medicine, Skin rejuvenation

Introduction

In recent years, phototherapy has gained increasing importance in medicine and rehabilitation because of its broad biological and therapeutic effects. Among light-based modalities, red, near-infrared (NIR), and blue light exert distinct clinical benefits through different mechanisms. Red and NIR light penetrate deeper into tissues, enhancing mitochondrial activity, ATP production, tissue repair,

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and anti-inflammatory responses, whereas blue light has limited penetration and primarily provides antimicrobial and immunomodulatory effects, making it particularly effective for acne and other dermatological conditions.[1]

Photobiomodulation (PBM), also known as low-level laser therapy (LLLT), is a safe, non-invasive modality that employs non-thermal red or NIR light (600–1100 nm).[2,3] Through photon absorption by mitochondrial chromophores, PBM enhances electron transport, ATP synthesis, and cellular metabolism.[4,5] Its biological effects include modulation of oxidative stress, inflammatory mediators, reactive oxygen species (ROS), and nitric oxide (NO), thereby promoting tissue repair, cellular protection, and regeneration.[2,6-9] An overview of these photobiomodulatory mechanisms and their corresponding clinical applications is illustrated in Figure 1. Increasing evidence supports its effectiveness in pain relief, wound healing, tissue regeneration, and inflammatory disorders.[2,10-13] PBM is also recommended by organizations such as NICE and MASCC for preventing and managing cancer therapy–related complications, particularly oral mucositis.[6] Furthermore, randomized clinical trials and recent meta-analyses have demonstrated its efficacy in reducing the severity of radiation-induced dermatitis and associated symptoms.[9,14-16]

Mechanistic studies further indicate that phototherapy regulates gene networks involved in inflammation, cell survival, and tissue repair. For example, narrowband ultraviolet B (NB-UVB) therapy modulates inflammatory and regenerative pathways in atopic dermatitis, supporting its role in promoting skin repair.[17]

In dermatology, PBM has shown significant therapeutic potential for hair disorders, acne, skin rejuvenation, and wound healing by stimulating the anagen phase of hair growth, enhancing collagen and elastin synthesis,[18] reducing inflammation,[19] and inhibiting Cutibacterium (Propionibacterium) acnes.[20,21] These effects are primarily mediated through activation of mitochondrial cytochrome C oxidase, leading to enhanced cellular metabolism and tissue regeneration.[22] As a safe, cost-effective, and non-invasive therapy, PBM can be used alone or alongside conventional treatments, with dermatologists playing a pivotal role in optimizing wavelength selection and treatment protocols.[23-26]

An important advantage of PBM is its ability to be tailored to individual skin characteristics and clinical indications, enabling personalized treatment while minimizing adverse effects. Its favorable safety profile makes it suitable for children, pregnant women, and patients with sensitive skin, and the growing availability of home-based phototherapy devices has further expanded its accessibility and clinical application.

Despite substantial advances, a standardized assessment of the quality and consistency of evidence across the diverse applications of phototherapy remains limited. Therefore, this review integrates findings from fundamental photobiological research and clinical studies to provide an evidence-based overview of light-based therapies, clarify their therapeutic potential for improving skin health, and support their optimized integration into contemporary dermatological practice.

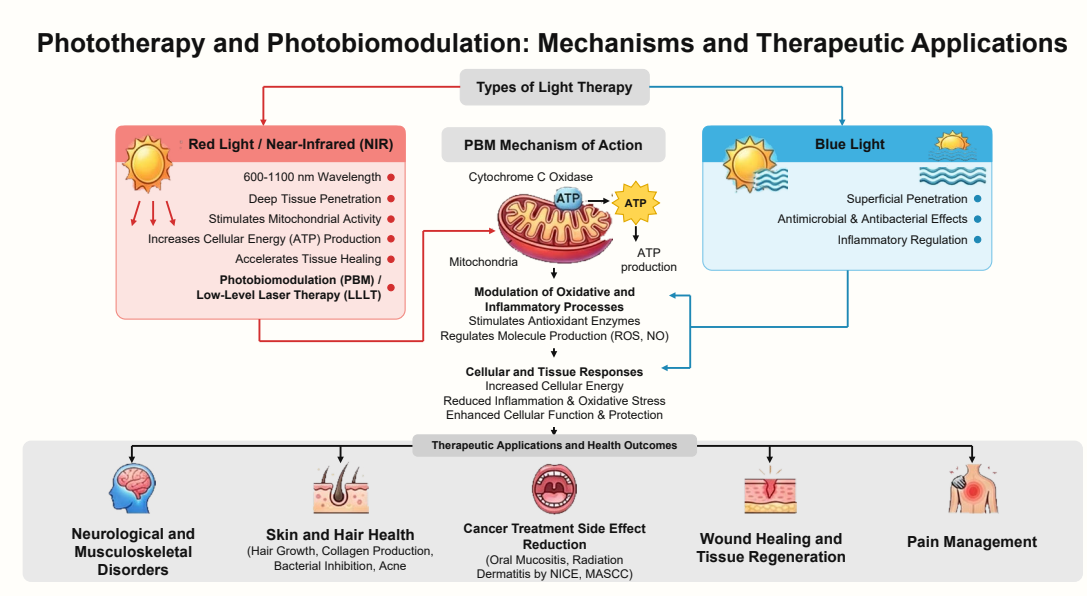


Figure 1. Mechanisms and therapeutic applications of phototherapy and photobiomodulation (PBM). Red and near-infrared (NIR) light (600–1100 nm) penetrates deeply into tissue, where absorption by mitochondrial cytochrome c oxidase enhances electron transport and ATP synthesis, accelerates tissue healing, and underlies the mechanisms of PBM/low-level laser therapy (LLLT). In contrast, blue light acts primarily at the tissue surface, exerting antimicrobial and anti-inflammatory effects. Both wavelength ranges converge on mitochondrial modulation of oxidative and inflammatory processes, stimulating antioxidant enzymes and regulating reactive oxygen species (ROS) and nitric oxide (NO) production. These molecular events translate into key cellular and tissue responses, including increased cellular energy, reduced inflammation and oxidative stress, and enhanced cellular function and protection. Collectively, these mechanisms underpin the diverse clinical applications of phototherapy, spanning neurological and musculoskeletal disorders, skin and hair health (including hair growth, collagen production, and bacterial inhibition in acne), reduction of cancer treatment side effects (e.g., oral mucositis and radiation dermatitis, as endorsed by NICE and MASCC), wound healing and tissue regeneration, and pain management.

Biological and Molecular Mechanisms of Phototherapy

Photobiomodulation (PBM) was first introduced by Endre Mester in 1967 following the unexpected observation of enhanced hair growth and tissue regeneration during laser experiments in animal tumor models.[27] Since then, PBM has been extensively studied for the treatment of chronic wounds, scars, chronic pain, musculoskeletal disorders, and immune-mediated diseases.[28]

PBM regulates cellular activity through photochemical and photophysical interactions between visible or infrared light and endogenous chromophores. Accordingly, non-ionizing light sources, including low-level lasers, broadband light systems, and light-emitting diodes (LEDs), have been used to modulate cellular function without inducing thermal damage or cytotoxicity.[29,30] However, despite growing evidence supporting its therapeutic efficacy, the optimal irradiation parameters and the precise molecular mechanisms underlying PBM remain incompletely understood, limiting its clinical standardization and optimization.

Blue Light and LED Technology

Blue light (400–500 nm) is a high-energy component of the visible spectrum with significant biological activity.[31,32] Since the introduction of blue light-emitting diode (LED) technology in the early 1990s, its clinical applications have expanded considerably because of its focused emission, energy efficiency, and cost-effectiveness.[33,34] Blue light is readily absorbed by endogenous chromophores, enabling selective regulation of cellular processes involved in wound healing and tissue repair.[35]

Its biological effects are primarily mediated through the activation of heme-containing chromophores, including hemoglobin, cytochromes, and protoporphyrin IX, which enhance mitochondrial electron transport, ATP production, redox signaling, ROS homeostasis, and calcium regulation.[36-43] Blue light also promotes tissue repair by reducing inflammation, stimulating fibroblast activity and angiogenesis,[44,45] and inducing macrophage polarization toward the reparative M2 phenotype, thereby improving collagen deposition and tissue remodeling.[28,30,46,47]

Experimental and clinical studies have demonstrated the efficacy of blue light in wound healing, burns,[48] psoriasis,[49-51] eczema,[52] diabetic ulcers, acne, and scar management. However, excessive or prolonged exposure to high-intensity blue light, particularly from artificial light sources, may impair retinal structure and function.[31,53] Therefore, careful optimization of wavelength, dose, and exposure time is essential to maximize therapeutic benefits while minimizing adverse effects.

Photodynamic Therapy: An Emerging Approach for the Treatment of Diseases and Skin Disorders

Photodynamic therapy (PDT), first introduced by von Tappeiner and Jodlbauer,[54] is a minimally invasive treatment for malignant and non-malignant diseases.[55-57] PDT relies on the light activation of photosensitizers, particularly by red light (> 600 nm), after their selective accumulation in target tissues, leading to the generation of reactive oxygen species (ROS), including singlet oxygen ($^1O_2$). Controlled ROS levels promote cellular signaling and tissue repair, whereas excessive ROS induce phototoxicity, vascular destruction, and antitumor immune responses.

PDT is widely used for bacterial, fungal, viral, inflammatory, and immune-mediated skin diseases, as well as chronic wounds and skin rejuvenation.[58] The introduction of 5-aminolevulinic acid (ALA) has enhanced its dermatological applications through improved skin penetration and selective tissue accumulation.[59,60] Treatment efficacy depends on the light source and dosimetric parameters, with red light (600–800 nm) providing the greatest tissue penetration.[61-63]

Beyond its antimicrobial and cytotoxic effects, PDT promotes wound healing by inducing controlled inflammation, enhancing immune responses, and stimulating fibroblast activity.[64] It increases the release of regenerative mediators, including tumor necrosis factor-alpha (TNF-α), fibroblast growth factor (FGF), granulocyte-macrophage colony-stimulating factor (GM-CSF), transforming growth factor-beta (TGF-β), and interleukins, thereby regulating macrophage polarization, tissue remodeling, and regeneration.[65-69] Notably, increased TGF-β expression has been associated with accelerated wound closure by promoting keratinocyte migration, myofibroblast differentiation, and extracellular matrix remodeling.[59,66]

Overall, PDT exerts both immunostimulatory and immunoregulatory effects, influencing tissue repair and the mode of cell death. Emerging evidence also highlights the contribution of the nervous system and intact cutaneous innervation to immune regulation and efficient wound healing.[70-72]

Comparative Evaluation of LED and photobiomodulation Performance in Phototherapy

Photobiomodulation (PBM) is the modulation of biological processes through the interaction of non-ionizing light with cellular photoreceptors, producing beneficial cellular and tissue responses without causing thermal damage.[73] Its therapeutic effects depend primarily on wavelength, energy dose, and tissue characteristics rather than the light source, with low-energy irradiation promoting cellular signaling, metabolism, and tissue repair, whereas high-energy irradiation induces tissue destruction.

PBM is commonly delivered using lasers and light-emitting diodes (LEDs). Lasers emit coherent, focused light with high energy density, while LEDs provide non-coherent, broader illumination over larger treatment areas and typically require longer exposure times.[74,75] Although lasers have been more extensively studied, growing evidence indicates that LEDs are equally effective for PBM. Repeated treatment sessions are generally required, although standardized treatment protocols remain unavailable.

The biological effects of PBM are initiated by photon absorption by endogenous chromophores, including

melanin, hemoglobin, and water, rather than by thermal mechanisms. Because light penetration is wavelength dependent, red light primarily interacts with melanin and hemoglobin, whereas near-infrared (NIR) light penetrates deeper tissues and is predominantly absorbed by water.[76] In contrast, blue light exhibits limited tissue penetration and, owing to its higher photon energy and greater potential for adverse cutaneous effects, is generally less suitable for conventional PBM applications.

Applications of Light-Based Therapies in Dermatological Treatments

Photorejuvenation and Reduction of Skin Aging Signs

Photorejuvenation is a major dermatological application of photobiomodulation (PBM), aimed at reducing wrinkles, improving skin quality, and promoting tissue regeneration. Clinical studies have shown that red, near-infrared (NIR), and, to a lesser extent, amber light improve skin texture, firmness, elasticity, and photoaging, with red light being more effective for enhancing skin tone and reducing hyperpigmentation, whereas NIR light provides greater benefits for deeper wrinkles because of its superior tissue penetration.[77,78]

Combined red and NIR irradiation may further enhance clinical outcomes by increasing type I collagen synthesis and reducing extracellular matrix (ECM)-degrading enzyme activity. Overall, PBM is a safe, non-invasive, and well-tolerated strategy for skin rejuvenation; however, the lack of standardized treatment protocols and high-quality controlled studies highlights the need for further clinical investigation.

Stimulation of Collagen Synthesis and Modulation of Cellular Responses

Collagen, the major structural protein of the dermal extracellular matrix, is essential for maintaining skin strength and elasticity. Age-related collagen loss contributes to wrinkle formation and skin laxity, whereas photobiomodulation (PBM) promotes collagen synthesis and extracellular matrix remodeling by stimulating fibroblast activity and regenerative signaling.[79] Most studies have focused on red and near-infrared (630–950 nm) wavelengths because of their superior tissue penetration, although optimal treatment parameters remain to be established.

PBM enhances fibroblast proliferation and the synthesis of collagen, elastin, and other extracellular matrix components while suppressing matrix metalloproteinase (MMP) activity and improving mitochondrial function. These effects promote the expression of genes involved in tissue regeneration, antioxidant defense, and inflammation resolution.[80,81] Emerging evidence also suggests that light-based therapies may regulate pathways associated with oxidative stress, genome stability, and cellular longevity.[82]

Furthermore, PBM, particularly in combination with topical agents, may reduce ultraviolet-induced skin damage while enhancing collagen synthesis and growth factor expression. Through coordinated modulation of extracellular matrix remodeling, mitochondrial activity, and regenerative signaling, PBM improves skin firmness, elasticity, and overall dermal structure, supporting its role as a safe and effective non-invasive approach for skin rejuvenation.

Acne

Acne vulgaris is a chronic inflammatory skin disorder characterized by Cutibacterium acnes overgrowth, biofilm formation, sebaceous gland hyperactivity, and microbiome dysbiosis. Photobiomodulation (PBM) targets these pathogenic mechanisms by inducing reactive oxygen species (ROS) through activation of endogenous bacterial porphyrins, resulting in selective bacterial destruction.[83] PBM also suppresses sebaceous gland activity, normalizes follicular keratinization, and reduces the expression of pro-inflammatory cytokines, including IL-1α, IL-1β, IL-8, and TNF-α, thereby alleviating inflammation and acne lesions.[83,84]

Clinical studies have demonstrated that blue, red, and near-infrared light effectively improve inflammatory acne through complementary antimicrobial, anti-inflammatory, and sebostatic effects. Both low-dose laser systems and LED-based therapies, particularly combined red–blue light irradiation, significantly reduce inflammatory lesions and improve clinical outcomes.[85,86] PBM may further enhance treatment efficacy when combined with conventional therapies, such as photodynamic therapy and isotretinoin.[84] However, variability in irradiation parameters and the limited availability of high-quality randomized controlled trials highlight the need for standardized treatment protocols and further clinical validation.

Psoriasis

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by excessive keratinocyte proliferation and erythematous, scaly plaques. Although photobiomodulation (PBM) has been investigated as an adjunctive therapy, current evidence is limited and inconsistent. Most studies have focused on pulsed dye laser (PDL) and Nd: YAG laser therapy, with findings indicating no significant advantage over conventional treatments, such as salicylic acid plus clobetasol propionate or narrowband ultraviolet B (NB-UVB) phototherapy for plaque psoriasis. Similarly, Nd: YAG laser therapy has demonstrated limited clinical efficacy.[87]

In contrast, PDL has shown promising results in nail psoriasis, where topical therapies and conventional phototherapy are often less effective because of limited drug penetration. Although PBM is not currently considered a standard treatment for psoriasis, it may provide a beneficial adjunctive option, particularly for patients with nail involvement.

Wound Healing

Chronic skin wounds fail to heal within 6–8 weeks because of persistent inflammation, infection, impaired cellular function, and underlying systemic disorders.

They remain arrested in the inflammatory phase, characterized by excessive inflammatory cell infiltration, increased protease and matrix metalloproteinase (MMP) activity, extracellular matrix degradation, reduced growth factor availability, microbial biofilms, and impaired fibroblast and keratinocyte function.[88,89] Normal wound healing involves four overlapping phases—hemostasis, inflammation, proliferation, and remodeling—regulated by coordinated interactions among inflammatory cells, fibroblasts, keratinocytes, endothelial cells, cytokines, and growth factors, including TNF-α, IL-1β, IL-6, TGF-β, PDGF, VEGF, and FGF.[89] Disruption of these pathways contributes to chronic wound persistence.[90]

Photobiomodulation (PBM) and photodynamic therapy (PDT) have emerged as promising adjunctive therapies by promoting tissue regeneration, modulating inflammation, and accelerating wound healing. PBM has also been investigated for hypertrophic scars and keloids, with most studies evaluating pulsed dye laser (PDL) and, less frequently, 1064-nm Nd: YAG laser therapy.[91,92] Current evidence indicates that PBM can reduce scar erythema, improve scar appearance, and enhance cosmetic outcomes, particularly when combined with conventional treatments such as silicone gel, intralesional corticosteroids, or 5-fluorouracil.[91] However, available evidence remains insufficient to establish PBM as a superior alternative to standard scar management, and it is currently best regarded as a complementary therapeutic approach.[92] Beyond these current applications, ongoing advances in PBM—particularly optimization of wavelength selection, multi-wavelength strategies, and the use of wavelengths beyond the near-infrared spectrum—as well as the growing role of NB-UVB in inflammatory and autoimmune skin diseases, continue to expand the therapeutic landscape of light-based therapies.[93,94] The principal dermatological applications of light-based therapies, along with their underlying biological mechanisms and clinical outcomes, are summarized in Table 1.

Future Perspectives

Development of Novel Approaches Based on Alternative Wavelengths

Future developments in photobiomodulation (PBM) are expected to focus on optimizing wavelength selection and implementing multi-wavelength strategies to enhance therapeutic efficacy and broaden clinical applications. Particular attention has been directed toward wavelengths beyond the near-infrared spectrum, which may improve tissue penetration through interactions with water molecules and induce distinct biological effects.[93] In addition, narrowband ultraviolet B (NB-UVB) continues to show considerable promise for inflammatory and autoimmune skin diseases through immune modulation and suppression of inflammatory signaling pathways.[94]

Blue light (400–470 nm) has also emerged as a promising antimicrobial modality by generating reactive oxygen species (ROS) that effectively inactivate bacteria, fungi, viruses, and certain parasites. Its antimicrobial activity is independent of conventional antibiotic resistance, with a low risk of resistance development following repeated exposure,[95] making it a valuable adjunct for managing cutaneous infections and promoting wound healing.[96]

Technological advances are further expanding PBM through the development of portable, intelligent, and multifunctional LED- and laser-based devices capable of delivering single- or multi-wavelength irradiation.[97] Integration of smartphone connectivity, digital monitoring, and user-friendly interfaces is expected to enable personalized treatment, remote patient management, and wider clinical adoption of PBM.[98]

Precision and Personalized Medicine in Dermatological Disorders

Personalized dermatology, integrating genomic information with individual skin characteristics, has the potential to improve treatment efficacy and clinical outcomes. Emerging evidence suggests that photobiomodulation (PBM) enhances genomic stability by activating DNA repair pathways and regulating genes involved in telomere maintenance, including TRF1 and TRF2.[99] Because genetic variability influences mitochondrial function, antioxidant defense, and inflammatory responses, incorporating

Table 1. Summary of Major Dermatological Applications of Light-Based Therapies, Their Biological Mechanisms, and Clinical Outcomes

Dermatological Condition	Light-Based Modality	Primary Biological Mechanisms	Main Clinical Outcomes	Ref.
Acne vulgaris	Blue, red, and near-infrared (NIR) PBM	ROS-mediated *Cutibacterium acnes* inactivation, sebaceous gland regulation, suppression of pro-inflammatory cytokines	Reduced inflammatory lesions, erythema, and sebum production	83–86
Photorejuvenation	Red, NIR, and amber PBM	Fibroblast activation, collagen and elastin synthesis, reduced MMP activity, extracellular matrix remodeling	Improved skin elasticity and texture, reduced fine lines and wrinkles	77–82
Chronic wound healing	Red/NIR PBM; Photodynamic therapy (PDT)	Enhanced mitochondrial activity, angiogenesis, fibroblast proliferation, immune modulation, extracellular matrix remodeling	Accelerated wound healing and tissue regeneration	64–72, 88–89
Hypertrophic scars and keloids	Pulsed dye laser (PDL), Nd: YAG PBM	Collagen remodeling, vascular modulation, reduced inflammation and erythema	Improved scar appearance as an adjunctive therapy	91, 92
Psoriasis	NB-UVB, blue light, red/NIR PBM	Immune modulation, suppression of Th1/Th17 cytokines, regulation of keratinocyte proliferation	Reduced plaque severity and pruritus; improved quality of life	50, 91–94
Radiation dermatitis	Red/NIR PBM	Mitochondrial activation, anti-inflammatory effects, enhanced tissue repair	Reduced pain, erythema, lesion severity, and delayed skin toxicity	9, 14–16

patient-specific molecular profiles may facilitate precision PBM.

Advances in non-invasive biomarker detection, including skin sampling patches, have improved the diagnosis and monitoring of inflammatory skin diseases. Candidate biomarkers include NOS2, hBD-2, MMP8/9, filaggrin mutations, TARC, and IL-22.[100] In addition, polarized PBM alters the expression of genes associated with mitochondrial function and extracellular matrix remodeling, suggesting reduced cellular stress after treatment.[101]

Overall, biomarker-guided PBM may enable individualized optimization of wavelength selection, irradiation dose, and treatment duration. However, large-scale clinical studies are required to validate reliable non-invasive biomarkers and establish evidence-based personalized PBM protocols.

Treatment of Severe Skin Diseases

Psoriasis

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by genetic susceptibility, immune dysregulation, and environmental triggers. Activation of the NF-κB pathway and Th1/Th17 immune responses increases the production of IL-17, IL-22, and IL-23, leading to keratinocyte hyperproliferation and the development of erythematous, scaly plaques.

Phototherapy remains a cornerstone of psoriasis treatment. Narrowband UVB (NB-UVB, 311 nm) and the 308-nm excimer laser provide greater efficacy and safety than broadband UVB, making NB-UVB the first-line phototherapeutic option for plaque psoriasis.[102] Clinical outcomes may be further enhanced when combined with acitretin.

Red and near-infrared photobiomodulation (PBM) have shown potential as adjunctive therapies by modulating immune responses, suppressing inflammatory cytokines, and regulating keratinocyte proliferation. Combined 830- and 630-nm LED irradiation has demonstrated significant clinical improvement in treatment-resistant psoriasis.[103] Blue light (420–453 nm) also reduces Psoriasis Severity Index (LPSI) scores, pruritus, and lesion severity,[50,104] while the combination of curcumin with blue and red light further enhances anti-inflammatory and antiproliferative effects through inhibition of Akt/ERK and NF-κB signaling.[105]

Overall, PBM represents a safe and promising adjunctive treatment for plaque psoriasis; however, larger randomized controlled trials are required to establish standardized treatment protocols and define its role alongside conventional phototherapy.

Atopic Dermatitis

Atopic dermatitis (AD) is a chronic inflammatory skin disease caused by interactions among genetic susceptibility, environmental factors, and immune dysregulation. It is characterized by elevated IgE levels, Th1/Th2 imbalance, increased expression of pro-inflammatory cytokines (IL-4, IL-6, and TNF-α), reduced IFN-γ production, and activation of Langerhans cells and mast cells.[106] Photobiomodulation (PBM) has emerged as a promising adjunctive therapy by reducing inflammation, promoting skin barrier repair, and improving quality of life.

Among phototherapies, narrowband ultraviolet B (NB-UVB) and medium-dose UVA1 are established second-line treatments for moderate-to-severe AD because of their favorable efficacy and safety profiles.[107] Blue light (400–500 nm) exhibits both anti-inflammatory and antimicrobial effects, with clinical studies demonstrating significant reductions in disease severity, pruritus, and sleep disturbances.[108] Red and near-infrared light may further improve disease severity by suppressing inflammation, enhancing collagen synthesis, and restoring skin barrier function.[109] In addition, the antimicrobial activity of blue light (400–470 nm) against Staphylococcus aureus, including methicillin-resistant S. aureus (MRSA), may further support disease control.[110,111]

Although current evidence is promising, larger randomized controlled trials are needed to establish standardized treatment protocols and define the role of PBM in atopic dermatitis. The biological mechanisms, optimal wavelengths, and clinical applications of these light-based therapies are summarized in Table 2.

Safety and Limitations of Light-Based Therapies

Photobiomodulation (PBM), delivered by laser- or LED-based systems, is a safe and minimally invasive therapy when applied using appropriate treatment parameters. Current evidence indicates that red and near-infrared (NIR) light does not increase the risk of DNA damage or carcinogenesis and has been widely used in supportive cancer care, particularly for preventing and managing oral mucositis and radiation-induced dermatitis, without convincing evidence of increased cancer recurrence.[112] Nevertheless, therapeutic efficacy and safety depend on appropriate wavelength, irradiance, fluence, exposure time, and treatment protocols, emphasizing the need for evidence-based dosimetry.[113]

Special caution is required in certain patient populations. Individuals with darker skin phototypes may be more susceptible to erythema, hyperpigmentation, and localized heating because of increased melanin absorption.[4] In addition, excessive exposure to high-intensity blue light (400–440 nm) may induce oxidative stress, cellular toxicity, and potential retinal or tissue damage through overproduction of reactive oxygen species (ROS), highlighting the importance of careful dosimetric optimization.[114]

Despite encouraging clinical outcomes, the absence of standardized treatment protocols remains a major limitation. Variability in wavelength, fluence, irradiance, treatment frequency, and exposure duration has limited comparisons across studies and delayed the development of evidence-based clinical guidelines. Therefore, large-scale multicenter randomized controlled trials are required to establish optimal treatment parameters and confirm the long-term safety of PBM in dermatology.

Table 2. Biological Targets, Molecular Mechanisms, and Clinical Applications of Major Light-Based Therapies in Dermatology. For photodynamic therapy, the activation wavelength depends on the photosensitizer used; red light (approximately 630–635 nm) is most commonly employed clinically because of its superior tissue penetration.

Light-Based Modality	Wavelength (nm)	Primary Biological Targets	Major Biological Mechanisms	Main Dermatological Applications	Advantages / Limitations
Photobiomodulation (PBM)	600–1100	Cytochrome *c* oxidase, mitochondria, water, melanin	↑ ATP production, modulation of ROS/NO, activation of mitochondrial signaling, stimulation of fibroblasts, collagen synthesis, angiogenesis, and anti-inflammatory responses (NF-κB inhibition) [2,6–10,22,26]	Skin rejuvenation, chronic wound healing, hypertrophic scars, radiation dermatitis, acne (adjunctive), oral mucositis [9,14–16,77–82,83–86,88–92]	Deep tissue penetration; non-invasive, non-thermal, excellent safety profile; treatment parameters are not yet standardized.
Blue Light (LED)	400–500	Protoporphyrin IX, flavins, cytochromes, heme-containing proteins	ROS-mediated antimicrobial activity, *C. acnes* inactivation, macrophage polarization (M1→M2), modulation of inflammatory cytokines, stimulation of tissue repair [28,30,35–45]	Acne vulgaris, infected wounds, atopic dermatitis, psoriasis, wound healing [48–53,83–86,105,108–111]	Effective against antibiotic-resistant microorganisms; superficial penetration; prolonged high-intensity exposure may increase retinal phototoxicity.
Photodynamic Therapy (PDT)	Visible red light (>600 nm)	Photosensitizers (5-ALA/PpIX) in oxygenated tissues	Singlet oxygen ($^1O_2$) and ROS generation, selective cytotoxicity, vascular disruption, immune activation, mast-cell degranulation, TGF-β/TNF-α release [54–69]	Actinic keratosis, non-melanoma skin cancer, acne, chronic wounds, skin rejuvenation [55–69]	Highly selective and effective; efficacy depends on photosensitizer, oxygen availability, wavelength, and dosimetry.
Narrowband UVB (NB-UVB)	311	Keratinocytes, epidermal immune cells, DNA, T lymphocytes	Induction of immunomodulatory pathways, suppression of Th1/Th17 responses, reduced cytokine production (IL-17/IL-23), inhibition of keratinocyte hyperproliferation [17,94,95–102]	Plaque psoriasis, atopic dermatitis, other inflammatory dermatoses [94,95–101,102,107]	Strong clinical evidence and prolonged remission; cumulative UV exposure requires careful monitoring.

Discussion

This review demonstrates that the therapeutic effects of light-based interventions are primarily mediated through photochemical and photobiological mechanisms rather than thermal effects. Accumulating molecular and clinical evidence indicates that specific wavelengths regulate distinct cellular pathways, supporting the growing role of photobiomodulation (PBM) and related technologies in modern dermatology.

Wavelength-Dependent Biological Responses

One of the principal findings of this review is that therapeutic outcomes are highly wavelength-dependent. Red and near-infrared (NIR) light penetrate deeper tissues and primarily enhance mitochondrial function, increasing ATP production, promoting collagen synthesis, and facilitating tissue regeneration. In contrast, blue light acts predominantly within superficial skin layers, where it exerts antimicrobial, anti-inflammatory, and immunomodulatory effects through controlled ROS generation, inhibition of Cutibacterium acnes, and modulation of macrophage polarization. These complementary biological properties explain the broad therapeutic applications of different wavelengths across dermatological disorders.

Clinical Translation of Light-Based Therapies

Current evidence supports PBM as a safe, non-invasive therapeutic strategy that can be delivered using both laser- and LED-based systems. While laser devices provide precise energy delivery, LEDs offer broader tissue coverage, lower cost, and greater accessibility, making them particularly attractive for repeated and home-based treatments. Photodynamic therapy (PDT) represents a distinct therapeutic approach in which controlled ROS generation, immune activation, and tissue remodeling contribute to its effectiveness against selected dermatological disorders. However, successful clinical outcomes depend on careful optimization of irradiation parameters to maximize efficacy while minimizing excessive oxidative stress and tissue injury.

Challenges and Future Perspectives

Despite encouraging clinical evidence, the lack of standardized treatment protocols remains the major barrier to the widespread clinical implementation of PBM. Variability in wavelength, fluence, irradiance, treatment frequency, and treatment duration limits direct comparison among studies and hinders the development of evidence-based guidelines. Future research should therefore prioritize multicenter randomized clinical trials using standardized dosimetric protocols together with molecular profiling approaches. Biomarkers related to mitochondrial activity, oxidative stress, inflammation, and extracellular matrix remodeling may facilitate individualized selection of wavelength and irradiation dose, while intelligent multi-wavelength devices integrated with digital monitoring platforms could further advance personalized phototherapy and improve treatment outcomes.

Conclusion

Photobiomodulation (PBM) and related light-based therapies have transitioned from complementary tools to evidence-based dermatological strategies, supported by robust preclinical and clinical data. Their effects are mediated through mitochondrial modulation, ATP enhancement, ROS regulation, suppression of inflammatory pathways (e.g., NF-κB), and promotion of growth factor-driven tissue repair.

These mechanisms underpin their efficacy in conditions such as acne, wound healing, skin rejuvenation, psoriasis, and radiation dermatitis. However, heterogeneity in treatment parameters, study designs, and a shortage of large controlled trials continue to limit protocol standardization and broad clinical adoption.

Future research should prioritize the integration of molecular profiling with standardized dosimetry to advance precision photomedicine. Biomarkers reflecting mitochondrial activity, oxidative stress, inflammation, ECM remodeling, and angiogenesis can help tailor wavelength selection—e.g., red/NIR for mitochondrial and regenerative effects, blue light for antimicrobial action—and guide adjustments in fluence, irradiance, and treatment intervals to optimize efficacy and minimize adverse effects.

Additionally, genetic pathways such as Nrf2, NF-κB, TGF-β/SMAD, and MMP may serve as predictive markers of treatment response, enabling personalized parameter adjustments. Combining these molecular and genetic signatures with intelligent multi-wavelength systems holds promise for individualized PBM protocols, improved outcomes, reduced variability, and broader translation of precision photomedicine into routine dermatology practice.

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Ethical Approval

This study is a review article and did not involve human participants or animals; therefore, ethical approval and informed consent were not required.

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