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Optimizing Low-Level Light Therapy for Skin Rejuvenation: Efficacy of Wavelengths and Treatment Parameters in Collagen Synthesis and Aging Signs

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Abstract

Low-level light therapy (LLLT), particularly using light-emitting diode (LED) devices, has been an effective and non-surgical option for skin rejuvenation, treating signs of aging such as wrinkles, collagen loss, and pigmentation. Despite promising clinical outcomes, variability in treatment parameters such as wavelength, power density, fluence, and treatment regimens remains a challenge in optimizing the therapy for optimal results. Recent studies, including a prospective, randomized, placebo-controlled, double-blinded, and split-face clinical trial by Lee *et al.* (2007), have demonstrated significant improvements in wrinkle reduction and skin elasticity using 830 nm and 633 nm LED wavelengths. These findings highlight the importance of wavelength selection and treatment protocols in achieving consistent and effective outcomes. This biphasic dose-response characteristic of photobiomodulation suggests that treatment outcomes, particularly in collagen synthesis and the reduction of aging signs, can be optimized by adjusting these parameters. Red and near-infrared wavelength applications, in particular, have been shown to stimulate collagen synthesis and enhance skin texture. Inconsistency in device specification, treatment protocols, and study design nevertheless still precludes standardization of treatment protocols. However, inconsistencies in device specifications, treatment protocols, and study design still preclude standardization of treatment protocols. Based on the literature present, there is moderate evidence for the efficacy of LLLT for skin rejuvenation, but further, randomized controlled trials involving larger populations and better design are required to help refine protocols and establish standardized treatment guidelines. As LED technology continues to evolve, it has vast potential to revolutionize skin care by offering cheap, non-invasive treatments for skin aging.

Keywords

Low-Level Light Therapy, LED Therapy, Skin Rejuvenation, Collagen Synthesis, Photobiomodulation, Signs of Aging, Treatment Optimization

1. Introduction

Light therapy (LT) is a type of low-level light therapy (LLLT) utilizing low-energy lasers or light-emitting diodes in the 620 - 700 nm wavelength [1]. Red light therapy (RLT) offers the deepest penetration at 6 - 50 mm, reaching most dermal structures compared to its blue light counterpart [2]. It exerts its mechanism of action through photobiomodulation (PBM), which describes a process that causes effects at the molecular and cellular level. PBM provides dermatological benefits as mitochondrial chromophores, specifically cytochrome c oxidase, absorb the red light and excite electrons into a higher energy state. This causes activation of second messengers including reactive oxygen species (ROS), ATP, nitric oxide, and cAMP that can modulate the processes of proliferation, inflammation, and tissue repair [3]. Given the modulation of ROS, PBM does offer benefits to extrinsic skin aging that is often due to free radical damage. Recent advancements in LED phototherapy, such as those demonstrated by Lee *et al.* (2007), have shown that 830 nm and 633 nm wavelengths significantly increase collagen and elastic fiber production, reduce wrinkles, and improve skin elasticity without causing thermal damage [4]. These findings underscore the potential of non-thermal photobiomodulation as a safe and effective approach to skin rejuvenation.

The history of light therapy can be traced back to 1903 with the use of ultraviolet radiation to treat Lupus Vulgaris, which was subsequently awarded the Nobel Prize for Medicine at that time [5]. In 1968, low-level light therapy was also used to determine the relationship between low-energy red laser light and neoplastic changes by exposing the skin of a mouse to these beams of laser. The results of this study showed no correlation of the laser with neoplastic changes, but it was observed that the mice models had accelerated hair regrowth [6]. The National Aeronautics and Space Administration (NASA) simultaneously utilized LLLT for plant growth experiments in space, but incidentally, it was found that light therapy enhanced in vitro cellular proliferation and improved wound healing in clinical studies [7]. As the application of LT spread into the field of dermatology, acne vulgaris was one of the earliest conditions to have studies that supported a statistically significant benefit in treatment [8]. Overall, LT offers a multitude of benefits to patients, including accessibility and the non-invasive nature of the therapy itself.

Home-based devices utilizing LT continues to expand on the ease of accessibility for patients and can be utilized in various dermatological conditions including but not limited to skin aging [9] [10]. Oftentimes, LT requires multiple sessions on a weekly basis, and these home-based devices can also help improve patient adherence to treatment plans. Previous studies have also demonstrated no statistically significant adverse side effects associated with RLT, further encouraging its use in dermatological conditions [3]. LT additionally presents as an affordable and versatile option that can often be combined with pharmacotherapy to improve patient outcomes.

LT continues to show much promise in the continued and future practice of dermatology. It specifically has a huge potential to provide anti-aging and skin rejuvenation benefits. Previous studies in 2021 did show increased synthesis of type 1 collagen, type 3 collagen, and elastin in support of skin rejuvenation [11] [12]. LT overall shows much promise in treating skin rejuvenation, inflammatory conditions, and possibly dermatological autoimmune conditions.

2. Literature Review Methodology

A literature search was conducted to identify studies investigating the efficacy of low-level light therapy (LLLT) for skin rejuvenation, with a focus on collagen synthesis, treatment optimization, and aging-related skin changes. The electronic databases utilized included PubMed, Scopus, Web of Science, and the Cochrane Library, selected for their comprehensive coverage of biomedical and clinical research. The search strategy employed a combination of free-text terms and controlled vocabulary (MeSH terms) to enhance the specificity and sensitivity of results across databases.

The search terms included combinations of "low-level light therapy," "LED therapy," "photobiomodulation," "collagen synthesis," "skin rejuvenation," "aging signs," "wrinkle reduction," and "treatment optimization," linked using Boolean operators (e.g., AND, OR). A representative query was constructed as follows: ("low-level light therapy" OR "LED therapy") AND ("collagen synthesis" OR "wrinkle reduction") AND ("treatment parameters" OR "fluence" OR "power density").

Filters were applied to refine search results by publication type, language, and study quality. Systematic reviews and randomized controlled trials were specifically queried in the Cochrane Library to ensure the inclusion of high-quality evidence. This methodology facilitated the selection of relevant and rigorous studies for analysis.

Inclusion Criteria:

- Studies published in peer-reviewed journals
- Research involving human participants or *in vitro*/*ex vivo* skin models
- Articles examining LLLT parameters, collagen synthesis, or clinical skin rejuvenation outcomes
- Quantitative studies with clearly defined methodologies

Exclusion Criteria:

- Non-English publications
- Editorials, case reports, or conference abstracts without original data
- Studies with small sample sizes or inadequate methodological transparency

Research in LLLT and dermatology is subject to various biases that may influence outcomes and interpretations. Selection bias is a significant concern, often resulting from non-representative study populations that lack diversity in skin types, age groups, or treatment conditions, limiting generalizability. Measurement bias arises due to inconsistencies in LLLT device specifications, including variations in wavelength, fluence, and power density. Furthermore, confounding factors such as baseline skin condition, concurrent skincare regimens, and environmental influences (e.g., sun exposure) are frequently underreported or uncontrolled, complicating direct attribution of observed effects to LLLT interventions. Lastly, publication bias may skew available literature, as studies with positive outcomes are more likely to be published than those reporting null or negative results.

Standardized frameworks were utilized to assess LLLT treatment parameters, collagen synthesis markers, and clinical skin outcomes to ensure consistency and reproducibility in data extraction. Wavelength efficacy was evaluated based on documented stimulation of fibroblast activity and collagen production, commonly measured via histological staining, hydroxyproline assays, and gene expression analysis. Quantitative data from randomized controlled trials and meta-analyses were synthesized where feasible to provide a comprehensive evaluation of treatment efficacy. Given the heterogeneity of study designs, treatment regimens, and outcome measures, a narrative synthesis approach was used to integrate findings. Where applicable, meta-analytical techniques were employed to aggregate quantitative data, stratifying key outcomes by wavelength specificity, treatment duration, and clinical efficacy in collagen remodeling and skin rejuvenation.

3. Discussion

3.1. Current Evidence and Applications

The use of light therapy, particularly low-level laser (light) therapy (LLLT), as a therapeutic intervention is a rapidly growing technology. LLLT was first discovered in the late 1960s and has recently evolved to include non-coherent light-emitting diode (LED) devices [5]. These devices serve as a non-invasive and convenient therapy for various skin diseases and skin rejuvenation. By delivering low-energy red and near-infrared (NIR) light, LLLT has applications in reducing pain and inflammation, promoting tissue repair and regeneration, and preventing tissue damage [3]. As LED devices become increasingly widespread and accessible for home use, a comprehensive evaluation of the clinical evidence and potential applications of this technology is essential.

3.1.1. Skin Rejuvenation

As we age, the skin begins to lose elasticity and collagen, leading to atrophy and disorganization of the epidermis, which results in the appearance of wrinkles and pigmentation [13]. In addition to decreased collagen synthesis, there is an upregulation of matrix metalloproteinases (MMPs), a group of collagenases involved in skin collagen turnover [14]. Due to the mechanism of action of low-level laser therapy (LLLT) and its evidence-based results, it is believed that this phototherapy could promote collagen production, aid in wound healing, and reduce epidermal signs of aging. A clinical study by Lee *et al.* (2007) demonstrated that LED phototherapy with 830 nm and 633 nm wavelengths significantly increased collagen and elastic fiber production, reduced wrinkles by up to 36%, and improved skin elasticity by up to 19% without adverse effects [4]. These findings align with earlier studies, such as Weiss *et al.* (2005), which showed that 96% of subjects experienced a reduction in signs of photoaging, including smoother skin texture, reduced redness, and decreased hyperpigmentation after treatment with 590 nm LED light [15]. Histological analysis revealed increased collagen in the papillary dermis and reduced MMP levels. Notably, no side effects or pain were reported.

Additional studies support these findings. A study conducted by Barolet *et al.* (2009) used tissue-engineered Human Reconstructed Skin (HRS) to evaluate histological and biochemical changes following 11 treatments with LED light at 660 nm or placebo [16]. Results showed a mean increase of 31% in procollagen levels and an 18% decrease in MMP levels in the LED-treated HRS compared to the placebo-treated HRS. No adverse effects were observed in this study either.

Recent research has further reinforced the regenerative potential of LLLT. Ablon (2018) conducted a randomized, double-blind, placebo-controlled study evaluating the effects of red and near-infrared LED therapy on skin aging [17]. The study reported a statistically significant improvement in skin roughness, hydration, and collagen density, with 87% of participants showing enhanced skin tone and firmness. Furthermore, LED therapy has been found to upregulate fibroblast proliferation, which is critical for long-term dermal remodeling and skin elasticity restoration [18].

3.1.2. Integration with Current Study Findings

The results of the studies align with the broader body of evidence supporting the efficacy of photobiomodulation in skin rejuvenation. The use of the Skin Light Dior × Lucibel mask, which employs red LED light, demonstrated significant improvements in skin parameters such as wrinkle depth, firmness, elasticity, and dermal density, consistent with the collagen-boosting and MMP-reducing effects observed in prior studies. Or instance, the 26.4% increase in dermal density after 28 days and the 47.7% increase after 84 days mirror the collagen-enhancing outcomes reported by Lee *et al.* (2007) and Barolet *et al.* (2009) [4] [16]. Similarly, the reduction in pore diameter (28.5% at 28 days) and sebum levels (34.9% at 28 days) suggests that photobiomodulation not only addresses structural aging but also improves skin texture and oil regulation, further supporting its multifunctional benefits.

Beyond its direct effects on collagen synthesis and MMP inhibition, LLLT has been found to enhance mitochondrial function in dermal fibroblasts. This leads to increased ATP production and cellular metabolism, which further supports tissue repair and anti-aging effects. Additionally, emerging evidence suggests that red and NIR LED therapy can modulate oxidative stress pathways by reducing reactive oxygen species (ROS) levels, thereby mitigating UV-induced skin damage and inflammation [19] [20]. These findings indicate that LLLT may have protective effects beyond rejuvenation, potentially serving as a preventive treatment for photoaging and environmental damage.

4. Treatment Parameters and Determinants of Efficacy

The efficacy of LED therapy is significantly influenced by critical treatment parameters, particularly peak wavelength. Red light typically falls within the wavelength range of 620 - 740 nm. A systematic review by Cios (2021) highlights the importance of wavelength, noting that red light, especially between 630 and 660 nm, penetrates the skin effectively to stimulate cellular processes [21]. Using RLT at these optimal wavelengths has been shown to enhance collagen synthesis and increase the production of collagen precursors while promoting the release of basic fibroblast growth factors. Collectively, these factors contribute to the anti-aging benefits associated with RLT. Lee *et al.* (2007) further demonstrated that combining 830 nm and 633 nm wavelengths yielded the greatest wrinkle reduction (36%) and improved skin elasticity (19%), suggesting that multi-wavelength approaches may optimize outcomes [4]. In contrast, wavelengths between 700 - 770 nm often yield less favorable results. However, higher near-infrared wavelengths, specifically those between 780 - 980 nm, are known to penetrate deeper tissues, offering advantages in wound healing and inflammation reduction [22]. While wavelengths from 780 - 980 nm may yield similar outcomes, their mechanisms of action differ. Near-infrared light around 780 nm stimulates mitochondrial activity and ATP production, while wavelengths closer to 980 nm enhance water absorption, activating heat-gated ion channels via the TRPV1 calcium ion channel pathway to promote cell proliferation [23]. These differences in therapeutic benefits and mechanisms emphasize the necessity for well-defined protocols in LED therapy applications.

Power density, defined as the amount of power delivered per unit area of skin at a given moment, plays a crucial role in determining treatment outcomes in LED therapy [24]. Fluence, in contrast, measures the amount of energy delivered per unit of skin over a period of time. Higher power densities can enhance photobiomodulation effects, but excessively high levels may inadvertently cause tissue damage or undesirable thermal effects. A study evaluating various power densities found that moderate levels of RLT, specifically around 20 - 100 nW/cm^2, yielded the most favorable results for skin healing and rejuvenation [25]. Treatment distance refers to the distance between the light source and the skin, which can impact both power density and fluence. Typically, closer distances yield higher power densities, enhancing the potential therapeutic effect. On the other hand, larger treatment areas can dilute the power density [24]. As a result of these findings, it is essential to consider both distance and area for optimal dosage of light.

Additionally, the method of light delivery, comparing pulsed versus continuous exposure, can influence treatment efficacy. Continuous wave treatment has shown effectiveness for more immediate results, whereas pulsed treatments may promote greater cellular repair over time by optimizing cellular energy absorption without adverse thermal effects [25]. Effectiveness is not merely contingent upon a single session; cumulative effects from repeated treatments can enhance results. Recommendations for treatment frequency may range from 2 - 3 times per week, with total sessions spanning several weeks or months for optimal skin rejuvenation depending upon the skin's condition [24]. More comparative studies are essential to determine the optimal mode of light delivery and treatment regimen for specific skin conditions to achieve the best outcomes.

Both coherent lasers and noncoherent LEDs are utilized in photobiomodulation therapy (PBMT), though they differ in their light properties. Lasers emit collimated, coherent light that penetrates deeper into tissues compared to noncoherent, noncollimated LED light. The coherent nature of laser light leads to interference patterns known as "laser speckles," which may be more effective in stimulating subcellular organelles like mitochondria due to their similar size scale [24]. Despite these differences, recent reviews suggest there may not be significant advantages of lasers over LEDs for PBM applications when other parameters are held constant.

5. Biphasic Dose-Response and the Need for Optimization

The biphasic dose-response concept in LLLT/photobiomodulation underlines such a relationship between fluence and biological outcomes. Most studies confirm that an optimal dose of photobiomodulation exists beyond which maximum beneficial responses are achieved. However, when this threshold is surpassed, the therapeutic benefits could be diminished and even adverse effects could be produced [22]. Three main factors may influence this biphasic dose response: excessive generation of reactive oxygen species (ROS), excessive nitric oxide (NO) release, and activation of cytotoxic pathways triggered by high fluence levels [26]. This duality of treatment outcomes emphasizes the necessity for practitioners to tailor RLT protocols to individual patients, maximizing therapeutic benefits while minimizing adverse effects. This may also be the reason for some of the RLT experiments that do not show improvements in patients.

5.1. Explanation of Biphasic Dose-Response in Photobiomodulation

Photobiomodulation using red laser significantly increased cell proliferation across all irradiated groups compared to the control group. The biphasic dose response in PBM shows how different light dosages have diverse biological effects [27]. At lower doses, PBM stimulates tissue repair, proliferation, and collagen synthesis. This was demonstrated in our work and further proved by Serrage *et al.* (2019) and Fekrazad (2016) [28] [29]. Although optimum parameters of PBM are controversial, studies consistently show that red laser PBM enhances cell viability and proliferation. For instance, Eduardo *et al.* (2008) found that a 660 nm laser at 20 - 40 mW improved periodontal ligament cell proliferation and viability, which agreed with our findings [30]. Soares *et al.* (2015) observed that higher energy promoted proliferation in hPDLSC cells, while lower energy had limited effects [31]. However, as pointed out by Huang (2011) and Kreisler (2002), when energy exceeds an optimal threshold, aPBM may inhibit cellular functions [26] [32]. These data underline how important the optimization of the dose is in order to balance therapeutic benefits with adverse effects, such as metabolic inhibition and cellular damage [33]. The proper selection of parameters ensures efficacy but extends the application range of PBM in clinical and therapeutic settings.

5.2. The Importance of the Biphasic Dose-Response Curve

Understanding and optimizing the biphasic dose-response curve is critical to maximizing PBM's therapeutic benefits while minimizing risks [34]. This curve illustrates how low doses of light stimulate cellular functions, while higher doses may lead to inhibition or damage [26] [35] [36]. For example, lower doses generate beneficial reactive oxygen species (ROS) that enhance mitochondrial function, whereas excessive doses produce harmful ROS, impairing cellular processes [26]. These principles guided our findings, where repeated low-energy doses (0.56 J) yielded positive results, while higher single-session doses (5.04 J) caused inhibition. Careful parameter selection is thus essential for safe and effective PBM treatments, particularly as therapeutic goals vary. Clinicians can enhance outcomes by fine-tuning parameters like energy, wavelength, and application frequency to align with the desired therapeutic effect.

5.3. Importance of Matching Treatment Parameters to Therapeutic Goals

PBM's application for conditions like inflammation, wound healing, and skin rejuvenation requires precise matching of treatment parameters—such as wavelength, power density, and fluence—to therapeutic goals) [22] [37]. For inflammation, lower power densities and deeper-penetrating wavelengths are often ideal, whereas skin rejuvenation may require higher doses to stimulate collagen synthesis and cellular regeneration [38]. Tailored parameter adjustments ensure treatments align with individual needs, promoting optimal healing and rejuvenation. The absence of a universal approach highlights the importance of patient-specific regimens, particularly as each skin condition and response can vary. By focusing on precision in parameter selection, PBM therapies can achieve superior clinical outcomes and address diverse therapeutic objectives.

5.4. Tailoring LED Treatments and Addressing Variability in Clinical Outcomes

Tailoring LED treatments is essential to achieving specific outcomes, such as skin rejuvenation or anti-inflammatory effects. Higher light doses stimulate collagen production and cellular turnover, improving skin texture and reducing fine lines, while lower doses are better suited for reducing inflammation without overwhelming tissues [23] [39]. Dose optimization ensures the desired therapeutic effects are achieved safely and effectively. Mismatched parameters, such as unsuitable wavelengths or power densities, can reduce efficacy or even cause tissue damage [23]. For instance, light suited for superficial skin treatments may fail to address deeper tissue conditions. Studies consistently show better outcomes when PBM parameters are optimized [32]. Additionally, patient-specific factors like skin type and condition severity contribute to treatment variability [35]. Addressing these factors through personalized regimens ensures PBM's reliability and effectiveness.

6. Challenges and Limitations of Current Studies

Existing research highlights several limitations that hinder the establishment of standardized treatment protocols. One major challenge is the use of small sample sizes in many studies, which limits the generalizability of findings. For instance, Fan *et al.* (2024) explored red light therapy in the treatment of acne vulgaris with fewer than 20 individuals, while Kleinpenning *et al.* (2011) evaluated light therapy for the treatment of psoriasis with only 20 individuals [40] [41]. These small cohorts majorly restrict statistical power and generalizability to larger populations.

Another significant limitation of red light therapy studies is the lack of standardization in treatment protocols. This includes discrepancies in critical variables such as treatment duration, power density, and photodynamic therapy procedures. Couturaud *et al.* (2023) emphasized the importance of standardizing treatment power and duration, as inconsistencies create barriers to reproducibility and meaningful cross-study comparison [1]. These discrepancies also extend to the specification of the devices used and the distance between the device and the treatment site. Without uniform guidelines, researchers face difficulty in replicating results or synthesizing findings across studies. This variability ultimately hinders the development of evidence-based clinical practices and creates uncertainty about the therapy's efficacy. Addressing these gaps will require collaborative efforts to define and adhere to standardized protocols in future research. Doing so would enhance the reliability of findings and pave the way for broader clinical implementation.

Another challenge lies in the absence of blinding and placebo implementation, which introduces potential bias and reduces the reliability of study results. Many studies lack placebo-controlled designs, making it difficult to isolate the true effects of red light therapy from placebo effects influenced by visible and sensory characteristics of the intervention. Evers (2017) noted that psychological factors play a significant role in dermatological outcomes, particularly for conditions such as pruritus and erythema [42]. The absence of robust methodologies, such as sham placebos, compounds this issue by failing to account for such confounding variables. Furthermore, most studies do not adequately account for diversity in skin types, as defined by the Fitzpatrick scale, which limits their generalizability to broader populations. Fan *et al.* (2018) highlighted the importance of considering skin tone, oiliness, and dryness in evaluating therapeutic outcomes, as these factors significantly influence treatment response [43]. Without addressing these biases and gaps, current evidence on red light therapy remains incomplete and of limited practical value. Future studies must prioritize methodological rigor, including proper blinding, placebo controls, and diverse participant recruitment, to enhance the reliability and applicability of findings.

While a vast body of preclinical work supports the potential of red light therapy, clinical evidence remains inconsistent and varies in quality. Addressing these limitations will require larger sample sizes, a consensus on treatment parameters, and rigorous study designs to ensure standardization and reproducibility. Future studies must prioritize reproducibility and standardization to provide a complete understanding of standard protocols for skin rejuvenation and treatment for inflammatory skin conditions using red LED therapy.

7. Future Directions in Research and Clinical Practice

While randomized controlled trials (RCTs) are regarded as the gold standard in clinical research, their application to dermatological studies like low-level laser therapy (LLLT) presents unique challenges. Small sample sizes—often fewer than 20 participants—limit the accuracy and generalizability of results [44]. Moreover, rigid eligibility criteria often exclude participants with complex or atypical conditions, reducing the real-world applicability of findings. Paneth (2022) critiques the inflexible nature of RCTs, arguing that their overly regulated methodologies often detach them from clinical and biological realities [45]. This rigidity hinders the adaptability required for dermatological research, where individual variability in skin responses is significant. Additionally, RCTs frequently focus on short-term or surrogate outcomes, which may not fully capture the long-term efficacy of treatments for skin rejuvenation and anti-aging.

To enhance the practical value of LLLT research for skin aging interventions, researchers must adopt flexible designs that balance methodological rigor with real-world relevance. Future studies should prioritize long-term follow-ups to assess sustained improvements in collagen production, wrinkle reduction, and overall skin elasticity. These adaptations would help generate findings that are both reproducible and clinically meaningful.

7.1. Standardization of LLLT Protocols for Skin Aging

One of the major limitations of current research is the lack of standardized LLLT treatment parameters. A systematic review of existing studies reveals considerable variability in wavelength selection, fluence, power density, and treatment duration, which significantly impacts reproducibility and clinical efficacy. Without clear guidelines, dermatologists may struggle to translate research findings into effective treatments. Sadick (2021) underscores the importance of parameter standardization, noting that without precise definitions, replication is nearly impossible, delaying the translation of findings into practice [46] [47].

Key recommendations for future research and clinical practice include:

- Determining optimal wavelengths: Studies suggest that red (630 - 670 nm) and near-infrared (810 - 850 nm) light are most effective for stimulating collagen synthesis and reducing fine lines. Further research should refine the ideal range for different skin types and aging concerns.
- Optimizing treatment duration and frequency: There is no consensus on whether short, high-intensity sessions yield better results than prolonged, lower-intensity applications. Comparative trials should assess the efficacy of various treatment regimens for maximizing skin rejuvenation outcomes.
- Defining power densities and fluence: Excessive energy delivery can cause erythema or discomfort, whereas insufficient fluence may yield suboptimal results. Establishing evidence-based safety thresholds can mitigate these risks while enhancing therapeutic benefits [48].

7.2. Addressing Methodological Gaps: Placebo Controls and Temperature Regulation

Sham placebos are critical in LLLT research, as they help mitigate performance and detection biases. Many current studies fail to implement effective sham controls, undermining the reliability of their findings. Evers (2017) emphasized that psychological factors often influence the perceived efficacy of dermatological treatments, making it essential to isolate the true effects of LLLT [42].

Another key variable in dermatological studies is temperature control. Given that LLLT induces mild thermal effects, ensuring temperature-matched controls is crucial to differentiate treatment effects from heat-related skin responses. Berardesca (2013) highlighted the importance of these controls in maintaining uniform conditions across study groups. Future research should adopt stricter methodologies that incorporate sham treatments and temperature-controlled environments to improve study validity.

7.3. Personalized Approaches: Tailoring LLLT to Skin Types and Aging Severity

LLLT's effectiveness varies based on individual skin characteristics. Darker skin tones have higher melanin absorption, which may influence light penetration and heat generation, potentially increasing the risk of hyperpigmentation. Additionally, individuals with severe photoaging may require higher fluence or combined therapies for optimal results.

Key research priorities include:

- Stratifying treatment regimens by Fitzpatrick skin type: Studies should assess whether modifying wavelengths or fluence improves efficacy and safety for darker skin tones.
- Customizing LLLT protocols for aging severity: Individuals with mild aging signs may benefit from lower fluence and fewer sessions, whereas those with significant photodamage may require higher energy settings or adjunctive treatments like microneedling or topical retinoids.

8. Conclusions

The growing acceptance of LLLT for skin rejuvenation and aging highlights its potential as a non-invasive, effective modality for improving skin texture, reducing wrinkles, and enhancing overall dermal health. The mechanisms behind these benefits rely on light-induced biochemical processes that promote collagen production, fibroblast activation, and anti-inflammatory effects. Despite promising outcomes, several challenges persist that obscure LLLT's full integration into clinical practice. The lack of standardized protocols, small sample sizes, and inadequate placebo controls limit the generalizability and reliability of existing findings. Future research must address these limitations through rigorous methodology, including long-term trials, temperature-matched controls, and detailed parameter reporting.

As LLLT continues to evolve, a patient-centered approach that tailors treatment regimens based on skin type and aging severity will be essential. Light therapy represents a transformative advancement in dermatological anti-aging treatments, promising to redefine non-invasive skin rejuvenation strategies. By standardizing treatment protocols and addressing existing research gaps, the dermatological community can enhance patient outcomes and establish LLLT as a cornerstone therapy for age-related skin concerns.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Couturaud, V., Le Fur, M., Pelletier, M. and Granotier, F. (2023) Reverse Skin Aging Signs by Red Light Photobiomodulation. *Skin Research and Technology*, **29**, e13391. https://doi.org/10.1111/srt.13391

[2] Austin, E., Geisler, A.N., Nguyen, J., Kohli, I., Hamzavi, I., Lim, H.W., *et al.* (2021) Visible Light. Part I: Properties and Cutaneous Effects of Visible Light. *Journal of the American Academy of Dermatology*, **84**, 1219-1231. https://doi.org/10.1016/j.jaad.2021.02.048

[3] Avci, P., Gupta, A., Sadasivam, M., Vecchio, D., Pam, Z., Pam, N. and Hamblin, M.R. (2013). Low-Level Laser (Light) Therapy (LLLT) in Skin: Stimulating, Healing, Restoring. *Seminars in Cutaneous Medicine and Surgery*, **32**, 41-52.

[4] Lee, S.Y., Park, K., Choi, J., Kwon, J., Lee, D.R., Shin, M.S., *et al.* (2007) A Prospective, Randomized, Placebo-Controlled, Double-Blinded, and Split-Face Clinical Study on LED Phototherapy for Skin Rejuvenation: Clinical, Profilometric, Histologic, Ultrastructural, and Biochemical Evaluations and Comparison of Three Different Treatment Settings. *Journal of Photochemistry and Photobiology B: Biology*, **88**, 51-67. https://doi.org/10.1016/j.jphotobiol.2007.04.008

[5] Glass, G.E. (2021) Photobiomodulation: The Clinical Applications of Low-Level Light Therapy. *Aesthetic Surgery Journal*, **41**, 723-738. https://doi.org/10.1093/asj/sjab025

[6] Mester, E., Szende, B. and Gärtner, P. (1968) The Effect of Laser Beams on the Growth of Hair in Mice. *Radiobiologia, Radiotherapia*, **9**, 621-626.

[7] Whelan, H.T., Smits, R.L., Buchman, E.V., Whelan, N.T., Turner, S.G., Margolis, D.A., *et al.* (2001) Effect of NASA Light-Emitting Diode Irradiation on Wound Healing. *Journal of Clinical Laser Medicine & Surgery*, **19**, 305-314. https://doi.org/10.1089/104454701753342758

[8] Ngoc, L.T.N., Moon, J. and Lee, Y. (2022) Utilization of Light-Emitting Diodes for Skin Therapy: Systematic Review and Meta-analysis. *Photodermatology, Photoimmunology & Photomedicine*, **39**, 303-317. https://doi.org/10.1111/phpp.12841

[9] Cohen, M., Austin, E., Masub, N., Kurtti, A., George, C. and Jagdeo, J. (2021) Home-Based Devices in Dermatology: A Systematic Review of Safety and Efficacy. *Archives of Dermatological Research*, **314**, 239-246. https://doi.org/10.1007/s00403-021-02231-0

[10] Mineroff, J., Maghfour, J., Ozog, D.M., Lim, H.W., Kohli, I. and Jagdeo, J. (2024) Photobiomodulation CME Part II: Clinical Applications in Dermatology. *Journal of the American Academy of Dermatology*, **91**, 805-815. https://doi.org/10.1016/j.jaad.2023.10.074

[11] Li, W., Seo, I., Kim, B., Fassih, A., Southall, M.D. and Parsa, R. (2021) Low-Level Red Plus Near Infrared Lights Combination Induces Expressions of Collagen and Elastin in Human Skin *in vitro*. *International Journal of Cosmetic Science*, **43**, 311-320. https://doi.org/10.1111/ics.12698

[12] Seaton, E.D., Mouser, P.E., Charakida, A., Alam, S., Seldon, P.E. and Chu, A.C. (2006) Investigation of the Mechanism of Action of Nonablative Pulsed-Dye Laser Therapy in Photorejuvenation and Inflammatory Acne Vulgaris. *British Journal of Dermatology*, **155**, 748-755. https://doi.org/10.1111/j.1365-2133.2006.07429.x

[13] Takema, Y., Yorimoto, Y., Kawai, M. and Imokawa, G. (1994) Age-Related Changes in the Elastic Properties and Thickness of Human Facial Skin. *British Journal of Dermatology*, **131**, 641-648. https://doi.org/10.1111/j.1365-2133.1994.tb04975.x

[14] Fisher, G.J., Varani, J. and Voorhees, J.J. (2008) Looking Older: Fibroblast Collapse and Therapeutic Implications. *Archives of Dermatology*, **144**, 666-672. https://doi.org/10.1001/archderm.144.5.666

[15] Weiss, R.A., McDaniel, D.H., Geronemus, R.G. and Weiss, M.A. (2005) Clinical Trial of a Novel Non-Thermal LED Array for Reversal of Photoaging: Clinical, Histologic, and Surface Profilometric Results. *Lasers in Surgery and Medicine*, **36**, 85-91. https://doi.org/10.1002/lsm.20107

[16] Barolet, D., Roberge, C.J., Auger, F.A., Boucher, A. and Germain, L. (2009) Regulation of Skin Collagen Metabolism *in vitro* Using a Pulsed 660 Nm LED Light Source: Clinical Correlation with a Single-Blinded Study. *Journal of Investigative Dermatology*, **129**, 2751-2759. https://doi.org/10.1038/jid.2009.186

[17] Ablon, G. (2010) Combination 830-nm and 633-nm Light-Emitting Diode Phototherapy Shows Promise in the Treatment of Recalcitrant Psoriasis: Preliminary Findings. *Photomedicine and Laser Surgery*, **28**, 141-146. https://doi.org/10.1089/pho.2009.2484

[18] Whitley, R.J., Kimberlin, D.W. and Roizman, B. (1998) Herpes Simplex Viruses. *Clinical Infectious Diseases*, **26**, 541-553. https://doi.org/10.1086/514600

[19] Muñoz Sanchez, P.J., Capote Femenías, J.L., Díaz Tejeda, A. and Tunér, J. (2012) The Effect of 670-nm Low Laser Therapy on Herpes Simplex Type 1. *Photomedicine and Laser Surgery*, **30**, 37-40. https://doi.org/10.1089/pho.2011.3076

[20] Landthaler, M., Haina, D. and Waidelich, W. (1983) Behandlung von Zoster, postzosterischen Schmerzen und Herpes simplex recidivans in loco mit Laser-Licht. *Fortschritte der Medizin*, **101**, 1039-1041.

[21] Cios, A., Ciepielak, M., Szymański, Ł., Lewicka, A., Cierniak, S., Stankiewicz, W., *et al.* (2021) Effect of Different Wavelengths of Laser Irradiation on the Skin Cells. *International Journal of Molecular Sciences*, **22**, 2437. https://doi.org/10.3390/ijms22052437

[22] Hamblin, M.R. (2017) Mechanisms and Applications of the Anti-Inflammatory Effects of Photobiomodulation. *AIMS Biophysics*, **4**, 337-361. https://doi.org/10.3934/biophy.2017.3.337

[23] Zein, R., Selting, W. and Hamblin, M.R. (2018) Review of Light Parameters and Photobiomodulation Efficacy: Dive into Complexity. *Journal of Biomedical Optics*, **23**, Article 120901. https://doi.org/10.1117/1.jbo.23.12.120901

[24] Jagdeo, J., Austin, E., Mamalis, A., Wong, C., Ho, D. and Siegel, D.M. (2018) Light-Emitting Diodes in Dermatology: A Systematic Review of Randomized Controlled Trials. *Lasers in Surgery and Medicine*, **50**, 613-628. https://doi.org/10.1002/lsm.22791

[25] Hashmi, J.T., Huang, Y., Sharma, S.K., Kurup, D.B., De Taboada, L., Carroll, J.D., *et al.* (2010) Effect of Pulsing in Low-Level Light Therapy. *Lasers in Surgery and Medicine*, **42**, 450-466. https://doi.org/10.1002/lsm.20950

[26] Huang, Y., Chen, A.C.-H., Carroll, J.D. and Hamblin, M.R. (2009) Biphasic Dose Response in Low Level Light Therapy. *Dose-Response*, **7**, 358-383. https://doi.org/10.2203/dose-response.09-027.hamblin

[27] Flores Luna, G.L., de Andrade, A.L.M., Brassolatti, P., Bossini, P.S., de Freitas Anibal, F., Parizotto, N.A., *et al.* (2020) Biphasic Dose/Response of Photobiomodulation Therapy on Culture of Human Fibroblasts. *Photobiomodulation, Photomedicine, and Laser Surgery*, **38**, 413-418. https://doi.org/10.1089/photob.2019.4729

[28] Serrage, H., Heiskanen, V., Palin, W.M., Cooper, P.R., Milward, M.R., Hadis, M., *et al.* (2019) Under the Spotlight: Mechanisms of Photobiomodulation Concentrating on Blue and Green Light. *Photochemical & Photobiological Sciences*, **18**, 1877-1909. https://doi.org/10.1039/c9pp00089e

[29] Fekrazad, R., Asefi, S., Allahdadi, M. and Kalhori, K.A.M. (2016) Effect of Photobiomodulation on Mesenchymal Stem Cells. *Photomedicine and Laser Surgery*, **34**, 533-542. https://doi.org/10.1089/pho.2015.4029

[30] Eduardo, F.P., Mehnert, D.U., Monezi, T.A., Zezell, D.M., Schubert, M.M., Eduardo, C.P., *et al.* (2007) Cultured Epithelial Cells Response to Phototherapy with Low Intensity Laser. *Lasers in Surgery and Medicine*, **39**, 365-372. https://doi.org/10.1002/lsm.20481

[31] Soares, D.M., Ginani, F., Henriques, Á.G. and Barboza, C.A.G. (2013) Effects of Laser Therapy on the Proliferation of Human Periodontal Ligament Stem Cells. *Lasers in Medical Science*, **30**, 1171-1174. https://doi.org/10.1007/s10103-013-1436-9

[32] Kreisler, M., Christoffers, A.B., Al-Haj, H., Willershausen, B. and d'Hoedt, B. (2002) Low Level 809-nm Diode Laser-Induced *in vitro* Stimulation of the Proliferation of Human Gingival Fibroblasts. *Lasers in Surgery and Medicine*, **30**, 365-369. https://doi.org/10.1002/lsm.10060

[33] Karu, T. (1987) Photobiological Fundamentals of Low-Power Laser Therapy. *IEEE Journal of Quantum Electronics*, **23**, 1703-1717. https://doi.org/10.1109/jqe.1987.1073236

[34] Nie, F., Hao, S., Ji, Y., Zhang, Y., Sun, H., Will, M., *et al.* (2023) Biphasic Dose Response in the Anti-Inflammation Experiment of PBM. *Lasers in Medical Science*, **38**, Article No. 66. https://doi.org/10.1007/s10103-022-03664-3

[35] Hawkins, D. and Abrahamse, H. (2006) Effect of Multiple Exposures of Low-Level

Laser Therapy on the Cellular Responses of Wounded Human Skin Fibroblasts. *Photomedicine and Laser Surgery*, **24**, 705-714. https://doi.org/10.1089/pho.2006.24.705

[36] Huang, Y., Sharma, S.K., Carroll, J. and Hamblin, M.R. (2011) Biphasic Dose Response in Low Level Light Therapy—An Update. *Dose-Response*, **9**, 602-618. https://doi.org/10.2203/dose-response.11-009.hamblin

[37] Yamaura, M., Yao, M., Yaroslavsky, I., Cohen, R., Smotrich, M. and Kochevar, I.E. (2009) Low Level Light Effects on Inflammatory Cytokine Production by Rheumatoid Arthritis Synoviocytes. *Lasers in Surgery and Medicine*, **41**, 282-290. https://doi.org/10.1002/lsm.20766

[38] Tatmatsu-Rocha, J.C., Ferraresi, C., Hamblin, M.R., Damasceno Maia, F., do Nascimento, N.R.F., Driusso, P., *et al.* (2016) Low-Level Laser Therapy (904nm) Can Increase Collagen and Reduce Oxidative and Nitrosative Stress in Diabetic Wounded Mouse Skin. *Journal of Photochemistry and Photobiology B: Biology*, **164**, 96-102. https://doi.org/10.1016/j.jphotobiol.2016.09.017

[39] Migliario, M., Pittarella, P., Fanuli, M., Rizzi, M. and Renò, F. (2014) Laser-Induced Osteoblast Proliferation Is Mediated by ROS Production. *Lasers in Medical Science*, **29**, 1463-1467. https://doi.org/10.1007/s10103-014-1556-x

[40] Fan, H., Tuo, H., Xie, Y., Ju, M., Sun, Y., Yang, Y., *et al.* (2024) Comparison of Blue Laser and Red Light-Emitting Diode-Mediated Aminolevulinic Acid-Based Photodynamic Therapy for Moderate and Severe Acne Vulgaris: A Prospective, Split-Face, Nonrandomized Controlled Study. *Photodiagnosis and Photodynamic Therapy*, **49**, Article 104325. https://doi.org/10.1016/j.pdpdt.2024.104325

[41] Kleinpenning, M.M., Otero, M.E., van Erp, P.E.J., Gerritsen, M.J.P. and van de Kerkhof, P.C.M. (2011) Efficacy of Blue Light vs. Red Light in the Treatment of Psoriasis: A Double-Blind, Randomized Comparative Study. *Journal of the European Academy of Dermatology and Venereology*, **26**, 219-225. https://doi.org/10.1111/j.1468-3083.2011.04039.x

[42] Evers, A.W.M. (2016) Using the Placebo Effect: How Expectations and Learned Immune Function Can Optimize Dermatological Treatments. *Experimental Dermatology*, **26**, 18-21. https://doi.org/10.1111/exd.13158

[43] Fan, L., Yin, R., Lan, T. and Hamblin, M.R. (2018) Photodynamic Therapy for Rosacea in Chinese Patients. *Photodiagnosis and Photodynamic Therapy*, **24**, 82-87. https://doi.org/10.1016/j.pdpdt.2018.08.005

[44] Saldanha, I.J., Skelly, A.C., Ley, K.V., *et al.* (2022) Inclusion of Nonrandomized Studies of Interventions in Systematic Reviews of Intervention Effectiveness: An Update. Agency for Healthcare Research and Quality (US). https://www.ncbi.nlm.nih.gov/books/NBK579970/

[45] Paneth, N.S., Joyner, M.J. and Casadevall, A. (2022) The Fossilization of Randomized Clinical Trials. *Journal of Clinical Investigation*, **132**, e158499. https://doi.org/10.1172/jci158499
Sadick, N.S., Weiss, R.A. and Goldman, M.P. (2009) Advances in Laser and Light Source Treatments. *Dermatologic Clinics*, **27**, 105-113.

[46] Sadick, N., Schecter, A. and Sigal, L. (2014) A Study to Determine the Efficacy of Combination LED Light Therapy (633 nm and 830 nm) in Facial Skin Rejuvenation. *Journal of Cosmetic and Laser Therapy*, **16**, 208-213. https://doi.org/10.3109/14764172.2014.942663

[47] Goldberg, D.J. (2012) Laser Dermatology: Pearls and Problems. Wiley-Blackwell.

[48] Berardesca, E., Farage, M. and Maibach, H. (2012) Sensitive Skin: An Overview. *International Journal of Cosmetic Science*, **35**, 2-8. https://doi.org/10.1111/j.1468-2494.2012.00754.x