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Clinical Applications of Phototherapy in Treating Skin Disorders

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Abstract

Introduction and Purpose: Phototherapy, involving the therapeutic use of ultraviolet and visible light, has been a cornerstone in dermatology for treating various skin disorders. This review aims to consolidate current knowledge on the mechanisms of action and clinical applications of phototherapy, with a focus on enhancing understanding among clinicians and researchers.

State of Knowledge: Phototherapy is particularly effective for chronic conditions such as psoriasis, vitiligo, and atopic dermatitis, where traditional therapies might not suffice. The mechanism involves modulation of immune response and inhibition of cellular proliferation, achieved through various wavelengths, including UVA and UVB. Recent advancements have introduced narrow-band UVB, which offers targeted therapy with fewer side effects compared to broad-band UVB. Moreover, the review explores innovations such as LED-based therapies and photodynamic therapy, expanding the spectrum of phototherapeutic options.

Summary: Phototherapy remains a vital and evolving treatment modality in dermatology, offering safe and effective management for multiple skin disorders. Its success hinges on precise application and adherence to treatment protocols. Future research should aim to optimize treatment regimens, reduce side effects, and enhance patient compliance to improve outcomes. By advancing our understanding and application of phototherapy, we can better tailor treatments to meet individual patient needs, thereby improving the quality of life for those afflicted with chronic skin conditions.

Key Words: Phototherapy; Skin Diseases; Ultraviolet Therapy

I. Introduction and purpose

1.1. Definition of phototherapy

Phototherapy, also known as light therapy, is a treatment method that uses electromagnetic radiation, especially ultraviolet (UV) light. It is used in dermatology mainly for the treatment of skin diseases such as psoriasis, atopic dermatitis, vitiligo or acne. There are different types of phototherapy, including UVB, UVA and PUVA (psoralen + UVA) therapy, which vary in wavelength and depth of skin penetration [1,2].

The history of phototherapy dates back to ancient times, when the Egyptians and Indians used sun baths in combination with plant extracts to treat skin diseases. However, modern phototherapy began at the beginning of the 20th century, when the Danish physician Niels Ryberg Finsen received the Nobel Prize in 1903 for the use of light in the treatment of skin tuberculosis. Since then, the technology and techniques of phototherapy have developed significantly, leading to the widespread use of this method in dermatology [3].

1.2. The importance of phototherapy in dermatology

Phototherapy plays a key role in dermatology, providing an effective and safe treatment for many chronic skin diseases. It is often used when other methods, such as topical treatment or pharmacotherapy, prove insufficient. Phototherapy has many advantages, including fast action, the ability to use it in patients of different ages, and minimal side effects compared to some drugs.

In dermatology, phototherapy is mainly used to treat psoriasis, where exposure to UVB or UVA helps reduce inflammation and accelerate skin regeneration. For atopic dermatitis, phototherapy reduces itching and improves the appearance of the skin. In vitiligo, UVB therapy may promote skin repigmentation, and in the treatment of acne, blue and red light may reduce the number of Propionibacterium acnes bacteria and inflammation.

Phototherapy is also used in other fields of medicine. In neonatology, it is used to treat hyperbilirubinemia in newborns, and in psychiatry, light therapy is effective in treating seasonal affective disorder (SAD). In addition, phototherapy has the potential to treat various pain conditions and sleep disorders [1,4,5].

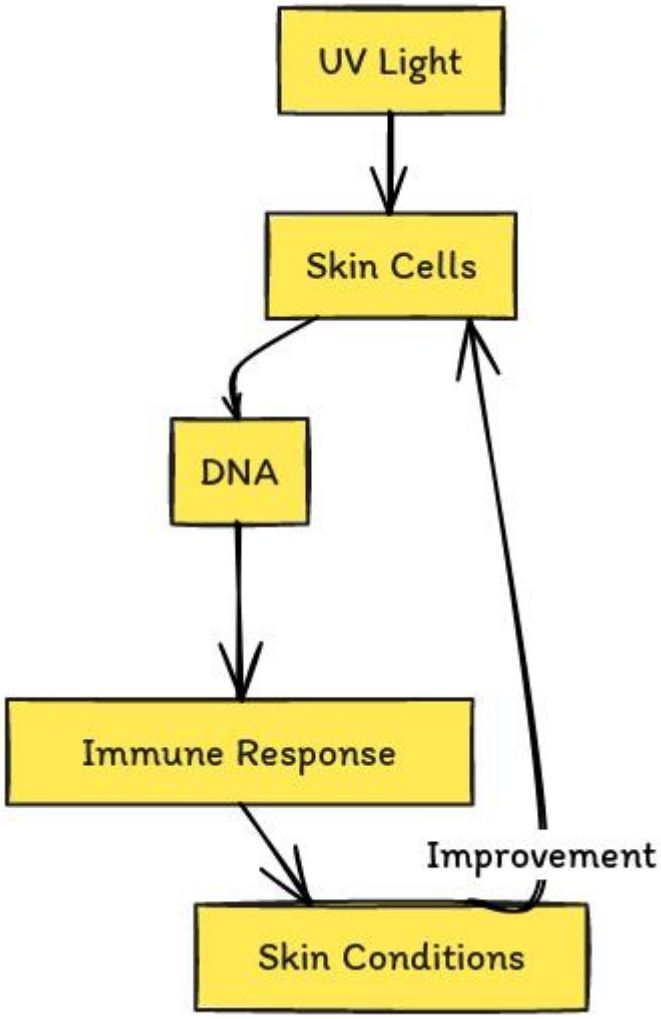

Figure 1. Scheme of action of phototherapy in skin diseases [1]

1.3. Purpose of the review work

The main objective of this review is to discuss in detail the mechanisms of action of phototherapy and its clinical application in the treatment of skin diseases. The aim of this work is to present the current state of knowledge on the efficacy and safety of phototherapy, to analyse different techniques and to review clinical trials related to its use.

II. State of Knowledge

Phototherapy, which uses light to treat various skin diseases, is based on complex physical and biological mechanisms. In order to fully understand how phototherapy affects the skin, it is necessary to thoroughly analyze the physical and biological basis of light response and its effect on the immune system.

2. 1. Physical basics of phototherapy

Different types of light used in phototherapy

Phototherapy in dermatology includes several types of light, each of which has unique properties and applications:

A) UVA (Ultraviolet A, 320-400 nm): UVA light penetrates deeper into the skin, reaching the dermis layer. It is used in PUVA therapy, which combines UVA light with psoralen, a chemical that increases skin sensitivity to light.

B) UVB (Ultraviolet B, 290-320 nm): UVB light mainly affects the epidermis. It is very effective in the treatment of psoriasis, atopic dermatitis and vitiligo. UVB can be used in a narrowband form (Narrowband UVB, 311-313 nm), which has a lower risk of burns and is more effective.

C) PUVA (Psoralen + UVA): This method combines UVA light with the intake or application of psoralen, which increases the skin's sensitivity to UVA radiation. PUVA is particularly effective in the treatment of psoriasis, eczema and vitiligo.

D) Lasers: Lasers emitting light in different wavelengths are used to treat specific skin conditions. Examples include excimer laser (308 nm) used for the treatment of vitiligo and psoriasis and pulsed dye lasers for the treatment of angiomas and rosacea [6-8].

Mechanisms of the influence of light on skin cells

Light used in phototherapy exerts its action through several mechanisms:

A) Light absorption by chromophores: Chromophores are particles in the skin that absorb light at specific wavelengths. The key chromophores are DNA, melanin, hemoglobin and porphyrins. Absorption of light by these chromophores initiates a variety of biological reactions.

B) DNA damage to skin cells: UVB light causes the formation of thymidine dimers in the DNA, which leads to cell cycle arrest and apoptosis of excessively proliferating cells, as in psoriasis.

C) Production of reactive oxygen forms (ROS): UV radiation can lead to the formation of

ROS, which act as signal mediators, modulating various cellular pathways, including those associated with inflammation and immune response [9-10].

2. 2. Biological mechanisms of action of light

Photochemical reactions in the skin

Photochemical reactions occurring in the skin are key to the therapeutic effects of phototherapy:

A) Formation of thymidine dimers: As mentioned earlier, UVB induces the formation of thymidine dimers in DNA, leading to cell damage and apoptosis, particularly in excessively proliferating psoriatic cells.

B) Photodegradation of Porphyrins: In the treatment of acne, blue and red light causes the photodegradation of porphyrins produced by Propionibacterium acnes bacteria, leading to ROS production and bacterial cell death [11-12].

The role of chromophores in light absorption

Chromophores are crucial for the absorption of light and the initiation of biological responses. Each chromophore has a unique absorption spectrum, which determines wavelengths that can be effectively absorbed and used therapeutically.

A) Melanin: Absorbs a broad spectrum of UV light, which protects the skin from damage, but also plays a role in repigmentation in case of vitiligo.

B) Hemoglobin: Absorbs light in the red spectrum, which is used to treat angiomas and other vascular lesions with pulsed dye lasers.

C) Porphyrins: They absorb light in the blue and red range, which is key in acne therapy [13].

Repair and regeneration processes of the skin under the influence of light

Light stimulates the repair and regeneration processes of the skin by:

A) Induction of apoptosis: UVB light can induce apoptosis of excessively proliferating cells, which is beneficial for the treatment of psoriasis and some skin cancers.

B) Stimulation of collagen production: Red and infrared light therapy can stimulate

fibroblasts to produce collagen, which improves skin elasticity and reduces scarring.
C) Reduction of inflammation: UVB and UVA light can reduce inflammation by modulation of cytokines and inflammatory cells [14-15].

2. 3. Effects on the immune system

Modulation of immune response by light

Phototherapy has a significant effect on the immune system, modulating the immune response through several mechanisms:

A) Reduction of T cell count: UVB and PUVA radiation can reduce the number of activated T cells in the skin, which is beneficial for the treatment of psoriasis and atopic dermatitis.
B) Induction of immune tolerance: Phototherapy may promote the development of immune tolerance by inducing regulatory T cells (Treg) that inhibit the inflammatory response.
C) Reduced production of pro-inflammatory cytokines: UV radiation reduces production of cytokines such as TNF-alpha, IL-17 and IL-23, leading to reduced inflammation in skin diseases [16-18].

Reduction of inflammation and effect on T cells

UV light has the ability to reduce inflammation by:

A) Inhibition of dendritic cell activation: UVB can inhibit dendritic cell activation, which reduces antigen presentation and T lymphocyte activation.
B) Induction of T lymphocyte apoptosis: UV light can lead to apoptosis of activated T lymphocytes, which is beneficial in autoimmune diseases such as psoriasis.
C) Changing the cytokine profile: UVB and PUVA can alter the cytokine profile in the skin, increasing the production of anti-inflammatory cytokines such as IL-10 [19-20].

3. Clinical application of phototherapy

Phototherapy plays a significant role in the treatment of various skin diseases, offering a wide range of methods and technologies that bring therapeutic benefits to patients suffering from chronic and acute dermatological conditions. Its clinical applications include the treatment of psoriasis, atopic dermatitis, eczema, vitiligo, acne and other conditions including

skin cancers, infections and wounds. Below is a detailed discussion of these applications, including efficacy, mechanisms of action, therapeutic protocols and clinical trial results [21].

3. 1. Phototherapy for the treatment of psoriasis

Psoriasis is a chronic inflammatory skin disease characterized by excessive proliferation of keratinocytes and the occurrence of erythematous-exfoliating skin lesions. Phototherapy is one of the main treatments for psoriasis and its effectiveness has been well documented in numerous clinical trials.

One of the most effective forms of phototherapy for the treatment of psoriasis is narrowband UVB (Narrowband UVB, NB-UVB). The use of NB-UVB at therapeutic doses reduces the proliferation of keratinocytes and inhibits the activity of T cells, which play a key role in the pathogenesis of psoriasis. NB-UVB is preferred due to its lower risk of burns and fewer side effects compared to Broadband UVB (Broadband UVB). A typical treatment regimen consists of three to five sessions per week for a period of several months until remission of the skin lesions is achieved.

Another popular approach is PUVA therapy, which combines the use of psoralen (a substance that increases skin sensitivity to UVA light) with exposure to UVA radiation. PUVA is effective for more severe psoriasis, but due to the higher risk of side effects such as photoaging and skin cancer, its use is limited to patients for whom other treatments have failed.

Studies comparing the efficacy of different phototherapy methods have shown that both NB-UVB and PUVA are effective, however NB-UVB is preferred due to its more favourable safety profile. The choice of method depends on the individual characteristics of the patient, the severity of the disease and the response to previous therapies [22-25].

3. 2. Atopic dermatitis and eczema

Atopic dermatitis (AZS) and eczema are chronic inflammatory skin diseases characterized by intense itching, dry skin and relapses of inflammation. Phototherapy, especially NB-UVB, is effective in reducing the symptoms of these diseases by reducing inflammation and improving the skin barrier.

Mechanisms of action of phototherapy in the treatment of AZS include inhibition of keratinocyte proliferation, reduction of Langerhans cell and mast cell counts in the skin, and reduction of production of pro-inflammatory cytokines such as IL-4 and IL-13. The immunomodulatory effect of phototherapy also helps to restore the balance between Th1 and Th2 lymphocyte populations, which is key in the pathogenesis of AZS.

A review of clinical trials shows that phototherapy is effective in the treatment of moderate to severe AZS, with improvement seen in most patients after a few weeks of therapy. The standard treatment protocol includes exposure to NB-UVB two to three times a week for several months. The effectiveness of treatment is assessed by reducing the severity of clinical symptoms and improving the quality of life of patients [26-28].

3. 3. Vitiligo

Vitiligo is a chronic skin disease characterized by depigmentation caused by the loss of melanocytes. Phototherapy, especially NB-UVB, is one of the main treatments for vitiligo, aimed at stimulating skin repigmentation.

The use of NB-UVB in vitiligo is based on the ability of UV radiation to induce proliferation of melanocytes and their migration to depigmented areas. Phototherapy also increases the production of melanin, which leads to repigmentation. A typical therapeutic protocol involves exposure to NB-UVB two to three times per week for a period of several months to several years, depending on the patient's response to treatment.

Clinical studies indicate high efficacy of NB-UVB in the treatment of vitiligo, especially in areas such as the face and neck where repigmentation is most noticeable. PUVA is also used, particularly when NB-UVB is ineffective, but due to potential side effects, its use is limited [29-30].

3. 4. Acne

Acne is a common skin disease whose pathogenesis includes excessive sebum production, colonization of the skin by Propionibacterium acnes and inflammation. Phototherapy, especially blue and red light, is used to treat acne due to its antibacterial and anti-inflammatory properties.

The mechanisms of action of light in the treatment of acne include photodegradation of porphyrins produced by P. acnes, leading to the production of reactive oxygen forms (ROS) and the death of bacterial cells. Blue light, with a wavelength of about 415 nm, is particularly effective in eliminating P. acnes, while red light, with a wavelength of about 660 nm, penetrates deeper into the skin, reducing inflammation and promoting healing.

A review of available phototherapy methods for treating acne shows that both blue and red light are effective in reducing the number of acne lesions and improving the appearance of the skin. Therapy sessions usually take place two to three times a week for several weeks, depending on the severity of the acne and the patient's response to treatment [31-34].

3. 5. Other applications

Phototherapy is also used to treat other skin diseases, including cancers, infections and wounds. Dynamic phototherapy (PDT) is used to treat non-melanoma skin cancers such as basal cell carcinoma and spiked cell carcinoma. PDT involves the application of a photosensitizer to the skin, which, when activated by light, leads to the production of ROS and the destruction of cancer cells. PDT is effective, particularly in the treatment of superficial cancers and precancerous lesions such as solar keratosis [35-36].

Phototherapy is also used to treat skin infections, including fungal and bacterial infections. UV radiation has a bactericidal effect, reducing the number of pathogens on the skin surface and supporting the treatment of infections. In the treatment of wounds, red and infrared light is used due to its properties stimulating repair and regeneration processes. Light promotes angiogenesis, collagen production and fibroblast migration, which accelerates wound healing [37-38].

4. Effectiveness and safety of phototherapy

Phototherapy is a widely used treatment for many skin diseases due to its documented efficacy and relatively favourable safety profile. To evaluate its effectiveness and safety, it is necessary to review the results of numerous clinical trials, understand the potential side effects, and discuss the qualification requirements for healthcare professionals and patient monitoring procedures.

4. 1. Clinical efficacy

The clinical efficacy of phototherapy in the treatment of skin diseases such as psoriasis, atopic dermatitis, vitiligo and acne has been extensively documented in the scientific literature. Clinical studies clearly show a significant improvement in the skin condition of patients who received phototherapy compared to control groups who did not receive phototherapy. For example, in psoriasis, narrowband UVB (NB-UVB) and PUVA (psoralen + UVA) therapy have shown high efficacy in reducing skin lesions. Patients treated with NB-UVB usually experience improvement after a few weeks of regular sessions, as confirmed by the results of numerous clinical trials [39].

The long-term efficacy of phototherapy is also well documented. In many cases, patients who have achieved remission with phototherapy maintain improvement over a longer period of time, reducing the need for frequent medical interventions. However, to maintain the effects of treatment, periodic booster sessions are often recommended. For atopic dermatitis and eczema, regular NB-UVB sessions lead to a significant reduction in symptoms such as itching and inflammation, which translates into improved quality of life for patients.

Phototherapy also shows effectiveness in the treatment of vitiligo, where skin repigmentation is observed after several months of NB-UVB sessions. Although the rate of repigmentation may vary depending on the location of the skin lesions and the individual characteristics of the patient, the results of clinical studies confirm that phototherapy is one of the most effective methods of treating this disease. In the treatment of acne, blue and red light reduces the number of acne lesions and inflammation, which has been confirmed in numerous clinical studies. The effectiveness of phototherapy in the treatment of acne is often comparable to traditional pharmacological methods, but with a lower risk of side effects [39-41].

4. 2. Safety and side effects

The safety of phototherapy is one of the key aspects of its clinical application. Although phototherapy is generally considered a safe treatment, there are some potential side effects that should be considered. The most commonly reported side effects include erythema, dry skin, itching and in some cases sunburn. The risk of burns is particularly associated with

broadband UVB therapy and PUVA therapy, where the use of psoralen increases the sensitivity of the skin to UVA radiation.

Long-term use of phototherapy, particularly PUVA, is associated with an increased risk of photoaging and skin cancers, including melanoma. Therefore, patients undergoing long-term PUVA therapy require regular dermatological examinations for early detection of potential tumour changes. NB-UVB phototherapy is considered to be a safer option with a lower risk of skin cancer, but it is also necessary to monitor patients for side effects.

A review of the literature on the safety of phototherapy indicates that, with appropriate medical supervision and adherence to safety protocols, the risk of serious adverse reactions is relatively low. An important aspect is to individually adjust the radiation dose to the patient's skin phototype and gradually increase the exposure to minimise the risk of burns [42-44].

4. 3. Qualifications and medical supervision

The efficacy and safety of phototherapy depends to a large extent on the qualifications of the medical staff performing the procedures and patient monitoring procedures. Those responsible for performing phototherapy should have appropriate medical education and training in the use of phototherapeutic devices. Dermatologists and medical technicians specialising in phototherapy must be familiar with treatment protocols, safety rules, and methods of assessing and monitoring patients.

Patient monitoring procedures include regular clinical assessments to monitor treatment progress and identify possible adverse reactions. Patients should be informed of the risks associated with phototherapy and instructions for skin care after the sessions. Regular dermatological examinations are crucial for the early detection of skin lesions that may indicate the development of skin cancers.

Standard, evidence-based treatment protocols are recommended to ensure the highest level of safety. The treatment protocol should take into account the individual characteristics of the patient, such as skin phototype, age, health status and prior phototherapy experience. Gradually increasing the radiation dose and monitoring the patient's skin response minimizes the risk of adverse reactions and optimizes therapeutic outcomes [1,45].

5. Future Perspectives and Innovations in Phototherapy

Phototherapy, as a method of treating skin diseases, is constantly evolving thanks to advances in technology and clinical research. Recent years have seen a significant development of new devices and techniques, which opens up new opportunities in the field of dermatology.

5.1. New technologies in phototherapy

The development of new devices and techniques in phototherapy is one of the most dynamic areas in dermatology. Technological innovations are aimed at increasing the effectiveness and safety of phototherapy and expanding its clinical applications. Among the most important technological innovations, it is worth mentioning advanced laser systems and LED technologies.

Lasers are playing an increasingly important role in phototherapy, offering precise and effective treatment of many skin conditions. Lasers emitting light of specific wavelengths can be used to target cancer cells, reduce vascular lesions and stimulate collagen production. The excimer laser technology, emitting 308 nm light, is particularly effective in the treatment of vitiligo and psoriasis, allowing precise application of light to skin lesions without damaging healthy tissue. In addition, pulsed dye lasers are widely used in the treatment of angiomas and rosacea, providing effective therapeutic results with minimal risk of side effects.

LED (Light Emitting Diode) technologies are also gaining importance in phototherapy. LED devices emit light of different wavelengths that can be used to treat acne, improve skin texture and reduce scars. LEDs are particularly attractive because of their safety, ease of use and their ability to be used at home. LED phototherapy is also used to treat chronic wounds, accelerating the healing process by stimulating angiogenesis and collagen production [46-48].

5.2. Therapy personalization

Personalization of therapy is becoming an increasingly important aspect of medicine, including phototherapy. The personalized approach in phototherapy is to tailor the treatment to the individual characteristics of the patient, such as skin phototype, the type and severity of the disease, and the response to previous therapies. Personalization of phototherapy can significantly increase the effectiveness of treatment and reduce the risk of side effects.

One example of personalised therapy is the use of individually tailored doses of UV radiation to treat psoriasis. Lighter-skinned patients may require lower UV doses compared to darker-skinned patients to achieve optimal therapeutic results with minimal risk of burns. In addition, personalization may involve selecting the appropriate type of phototherapy, such as choosing between NB-UVB and PUVA, depending on the patient's response to prior treatment.

Therapy personalisation may also include the integration of new technologies, such as monitoring and data analysis systems. Mobile apps and wearables can track the skin's response to treatment, allowing the doctor to adjust the treatment on an ongoing basis. This approach can lead to more precise and effective treatment, minimising the risk of adverse reactions and improving overall therapeutic outcomes [49,50].

III. Summary

Phototherapy for the treatment of skin diseases is a method that uses the properties of electromagnetic radiation to bring relief to patients with various dermatological conditions. The mechanisms of action of phototherapy are complex and include both direct physical effects on skin cells and more subtle biological and immunological modulations. Phototherapy uses different types of light, including UVA, UVB and combinations such as PUVA, as well as lasers and LED technologies to tailor treatment to specific therapeutic needs. These mechanisms include absorption of light by chromophores in the skin, leading to photochemical reactions that can induce apoptosis of excessively proliferating cells, reduce inflammation, and modulate the immune response.

Clinically, phototherapy has shown significant efficacy in the treatment of many skin diseases, including psoriasis, atopic dermatitis, vitiligo and acne. In the treatment of psoriasis, both NB-UVB and PUVA are widely used due to their ability to reduce keratinocyte proliferation and inhibit T cell activity. In atopic dermatitis, phototherapy reduces inflammation and itching, which translates into improved quality of life for patients. Vitamins, characterized by skin depigmentation, benefit from NB-UVB therapy, which stimulates repigmentation through proliferation and migration of melanocytes. In the treatment of acne, blue and red light exhibits antibacterial and anti-inflammatory properties, which leads to a reduction in the number of acne lesions and an improvement in the condition of the skin.

The efficacy of phototherapy is well documented in numerous clinical trials. These studies confirm that phototherapy can lead to significant improvement in skin condition in a short time and maintain long-term therapeutic benefits. Regular therapy sessions, often requiring several months of treatment, are key to achieving and maintaining remission. Despite its effectiveness, the safety of phototherapy is equally important. Potential side effects include erythema, dry skin, itching and the risk of burns, especially with UVB and PUVA broadband therapy. Long-term use, particularly PUVA, is associated with an increased risk of photoaging and skin cancer, which requires regular monitoring of patients.

In the context of the future of phototherapy, the development of new technologies, such as advanced laser systems and LED technologies, offers new therapeutic opportunities. Lasers can be precisely used to treat specific conditions, such as vitiligo and psoriasis, without damaging healthy tissue. LED technologies, due to their safety and ease of use, are becoming more and more popular in both clinical and home environments. Personalisation of therapy, tailored to the individual characteristics of the patient, such as skin phototype and specific therapeutic needs, can significantly increase the effectiveness of treatment and reduce the risk of adverse reactions.

Prospects for the future in phototherapy also include research into new therapeutic indications. Phototherapy has the potential to treat autoimmune diseases, bacterial and viral infections, and can also be used in aesthetic dermatology to improve the appearance of the skin. Future directions of clinical research should focus on assessing the efficacy of phototherapy in these new areas and on developing more advanced technologies that can expand its clinical applications.

In summary, phototherapy is a versatile and effective method of treating many skin diseases. Its mechanisms of action include both physical and biological effects that lead to reducing inflammation, modulating the immune response and promoting the repair and regeneration processes of the skin. The clinical effectiveness of phototherapy has been confirmed in numerous studies, which makes it a valuable tool in dermatology. With proper medical supervision and personalized therapy, phototherapy can bring significant benefits to patients with a variety of skin conditions, offering new treatment options and improving quality of life.

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