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ORIGINAL RESEARCH

Evaluation of the Effectiveness of Using LED Light Combined With Chromophore Gel in Treating Acne Vulgaris – Preliminary Study

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Purpose: The aim was to quantitatively evaluate the effectiveness of LED light therapy combined with photoacceptor substances having anti-acne properties in reducing the symptoms of acne vulgaris.

Patients and Methods: 15 subjects aged 20 to 24 who suffered from moderate or severe acne lesions. The treatments were performed using a LED device (465-880 nm). Blue light - 465 nm in combination with red light - 640 nm in pulsed mode and nearinfrared light - 880 nm were used in the treatments. Each patient underwent 6 treatments, with intervals between treatments of 7 days. 3D images and biomechanical measurements were performed before first and fourth treatments and 6 weeks after the last. Additionally, photographic documentation was made 7 days after the 6th treatment.

Results: The series of treatments significantly influenced the clinical condition of the patients' skin. The treatments had a statistically significant impact on the intensity of erythema on the left and right cheeks. The hydration of the stratum corneum in all the examined areas of the face changed significantly after the treatments. Greater hydration was achieved six weeks after six treatments compared to the values obtained prior to treatment and after three treatments. The activity of sebaceous glands and, consequently, the amount of sebum on the epidermal surface in all the examined areas of the face changed significantly after the treatments. The treatments had a statistically significant impact on the volume of atrophic scars.

Conclusion: Therapy combining LED light with photoacceptor substances is an effective method of reducing the symptoms of acne vulgaris. The treatments lead to a significant reduction in erythema, reduction in the volume of atrophic scars, improvement of skin hydration and regulation of sebum secretion. These effects can be identified quantitatively. Further studies are necessary to confirm the long-term effectiveness and safety of this method.

Keywords: phototherapy, sebum, erythema, hydration

Introduction

Acne vulgaris is a common, chronic inflammatory dermatosis affecting the pilosebaceous unit.¹⁻³ Acne can be observed in every age group, but in most cases, it affects patients between 12 and 25 years of age. However, in recent years it has also more often affected people of mature age. Although it is most often diagnosed in women, the course of the disease is usually more aggressive in men.³ The clinical picture of acne vulgaris, depending on the advancement and clinical type, is characterized by the occurrence of comedones, papulopustular eruptions, purulent cysts, scars and post-inflammatory discolorations. The lesions mainly affect the skin of the face, chest and back, ie the areas with the greatest number of sebaceous glands.^{1–5}

Acne eruptions result from the coexistence of many factors, such as excessive production of sebum, excessive keratinization of the pilosebaceous follicle openings, colonization of the sebaceous glands by Cutibacterium acnes and excessive production of inflammatory mediators in the skin. Additionally, high concentrations of androgens contribute to increased sebum secretion by stimulating the receptors of sebaceous gland cells. Environmental factors such as stress and diet as well as disturbances in the balance of the skin and intestinal microbiomes also play an important role.^{1–10} Nowadays, the inflammatory basis of the disease and the immunological processes taking place in the skin affected by acne lesions are increasingly considered to be the key factors in the development of acne vulgaris, whereas disorders of keratinization seem to be less important.^{5,7}

Classic treatments of acne vulgaris include the use of topical medications and/or oral therapy. In less severe forms of acne, local treatment, involving mainly the use of agents with keratolytic properties (eg benzoyl peroxide, salicylic acid), topical antibiotics and retinoids, is often sufficient. General treatment is based on antibiotic therapy, hormonal treatment, especially in women with hormonal disorders, and isotretinoin therapy.^{5,11}

Despite the unquestionable effectiveness of antibiotics in the treatment of acne vulgaris, their excessive use has become a global problem, leading to the emergence of antibiotic-resistant strains. Additionally, it may result in permanent disturbances in both intestinal and skin microbiotas.^{7,12–14}

Due to the increasing antibiotic resistance of bacteria and the chronic and recurrent nature of acne vulgaris, both supportive and alternative methods of acne treatment are being sought. Methods that complement the classic acne therapy include the use of chemical peels, chemical skin stimulants, physical or mechanical peelings and methods based on phototherapy.^{15–20} The most popular methods using light include polychromatic light therapy and laser methods used to reduce atrophic scars. For several years, methods using blue light emitted by light-emitting diodes (LEDs) have been gaining popularity, as it has anti-inflammatory properties and limits excessive multiplication of skin bacterial flora.^{17–22}

The mechanism of action of light emitted by light emitting diodes is based on the induction of photobiochemical intracellular reactions. Under the influence of light with a wavelength ranging from 400 to 470 nm, endogenous porphyrins are stimulated (especially coproporphyrin III with the maximum absorption peak at 415 nm). They are produced by Cutibacterium acnes in the skin, which results in an endogenous photodynamic reaction with the production of singlet oxygen and/or free radicals, which can enhance the perifollicular inflammatory reaction and activate the expression of IL-8 derived from keratinocytes.^{18–22}

In experimental studies, photodynamic phenomena associated with endogenous porphyrins were most intense after irradiation with wavelengths of 407–420 nm. A significant reduction in the symptoms of acne vulgaris was also observed using light wavelengths of 465 nm and in the range of 400–450nm.^{20–22}

Red and near-infrared lights are also used in dermatology. Red light penetrates deeper than blue light. Studies have shown that red light stimulates microcirculation and stimulates fibroblasts to produce collagen, extracellular matrix components and growth factors.^{21–24}

In light therapy treatments, it is also possible to use dedicated preparations containing exogenous chromophores with antiinflammatory and antibacterial properties, reducing excessive activity of sebaceous glands activated by blue LED light. The use of exogenous chromophores may lead to the phenomenon of photobiomodulation, ie phototherapy capable of inducing photochemical and photophysical biological reactions in cells. The principle of operation of FLE (Fluorescent Light Energy) technology is based on fluorescent light energy (FLE), which is produced by excited chromophores absorbing blue light when illuminated by a multi-diode lamp. These reactions may generate free oxygen radicals capable of damaging bacterial cells, among others, Cutibacterium acnes, increase energy production at the cellular level, regulate inflammation, cell migration, proliferation, oxygenation, vascularization and antioxidant defence of skin cells.^{25,26}

The aim of the study was to quantitatively evaluate the effectiveness of LED light therapy combined with photoacceptor substances having anti-acne properties in reducing the symptoms of acne vulgaris.

Materials and Methods

The study included 13 women and 2 men who suffered from moderate or severe acne lesions located on the face, who had been struggling with acne for at least 3 years. The participants' age ranged from 20 to 24 years, with a mean \pm standard deviation of 21.6 ± 1.30 years. Patients primarily suffered from papulopustular acne. Single cysts were also observed on the skin of five patients. Acne in 10 patients was classified as 3 in the Investigator's Global Assessment (IGA) scale, while in 5 people it was classified as 4 in the IGA scale. The study included patients who had previously used topical and/or oral treatment. Information about previous treatment is provided in Table 1.

	Topical Medications						Oral Medications		
	Benzoyl Peroxide	Azelaic Acid	Salicylic Acid	Retinoids	Erythromycin	Clindamycin	Tetracyclines	Other Antibiotics	Isotretinoin
N	13	7	8	15	3	14	8	3	3
%	86.7	46.7	53.3	100.0	20.0	93.3	53.3	20.0	20.0

Table I Treatment Used by Patients Before Starting LED Light Therapy

Qualifications for treatments were performed by a dermatologist based on a protocol and taking into account the adopted inclusion and exclusion criteria. The inclusion criteria were as follows: patients over 18 years of age who could decide on their own about participation in the study, patients with inflammatory lesions in the course of acne vulgaris eligible for LED light therapy, no general or local antibiotic therapy in the area assessed (patients who had not used oral antibiotics for at least 12 weeks and topical antibiotics for at least 4 weeks), male and female patients, patients able to understand the purpose and risks associated with the study after signing the Patient Informed Consent form to participate in the study. The exclusion criteria included: pregnancy or breastfeeding, skin bacterial diseases other than acne vulgaris, active viral, parasitic, fungal infections - especially tuberculosis, HIV infection, HBV infection, people diagnosed with systemic lupus erythematosus, demyelinating diseases, active cancer and severe circulatory failure, lack of informed consent and cooperation of the patient, abuse of drugs or alcohol by the patient revealed in the interview.

The treatments aimed at reducing acne lesions were performed using a device emitting LED light in the range of 465 to 880 nm. Blue light with a wavelength of 465 nm in combination with red light with a wavelength of 640 nm in pulsed mode and near-infrared light with a wavelength of 880 nm (Celluma lamp, USA, built-in acne mode) were used in the treatments. Blue light constituted 80% of the emitted radiation beam, red light - 18%, infrared light - 2%. During six procedures, a preparation containing fluosin A, a chromophore with a precisely defined energy profile, was applied to the patient's skin. Then the skin was irradiated with light with a wavelength of 465 nm combined with red light with a wavelength of 640 nm and near-infrared light with a wavelength of 880nm. The energy density was 5–7J/cm², the treatment time was 20 minutes. Each patient underwent 6 treatments, with intervals between treatments of 7 days.

Photographic documentation, 3D images and biomechanical measurements of the patients' skin were performed before the first and fourth treatments and 6 weeks after the 6th treatment. Additionally, photographic documentation was made 7 days after the 6th treatment.

To prepare photographic documentation, the Fotomedicus clinical photography kit from Elfo (Poland), which allows for image acquisition in unpolarized and cross-polarized light, was used. 3D images of the skin surface, along with measurements of 6 skin parameters, were acquired using the Antera 3D device from Miravex Limited (Ireland). The severity of erythema was assessed by analysing images acquired with the Antera 3 D device. The area with the highest intensity of erythema and the scale of erythema intensity were determined in the entire area analysed. The scar depth was assessed by analysing images acquired with the Antera 3D device. In this way, the minimum and maximum erythema and the scale of erythema intensity were determined in the entire area analysed. The scar depth was assessed by analysing images acquired with the Antera 3D device. In each image, the area with the largest total volume of scars was selected on both the right and left cheeks.

Skin hydration and lubrication were measured using a corneometer and sebumeter from Courage-Khazaka Electronic (Germany). Measurements of skin hydration and lubrication were made in the entire area of skin irradiation, ie in the middle of the forehead between the base of the eyebrows, on the tip of the nose, in the middle of the chin, on the highest points of the zygomatic bone on both the right and left sides of the face.

The research was carried out after obtaining the written consent of volunteers who were familiarized with the purpose of the research and its course, and with the consent of the Ethics Committee of the Medical University of Silesia No. PCN/0022/KB1/11/I/20 of May 19, 2020. Study complies with the Declaration of Helsinki.

After performing the measurements, all results were placed in Excel sheets, and then exported to Statistica 13.3, where statistical analysis and figures were performed. Descriptive statistics were prepared, and then the normality of data distribution was assessed using the Shapiro–Wilk test. Due to the lack of normal distribution, the Friedman's Anova test

was used to observe the effects of the treatment over time, along with a post-hoc test dedicated to the program. The value of p < 0.05 was considered statistically significant.

Results

The series of treatments using the photo acceptor and LED light significantly influenced the clinical condition of the patients' skin (Figures 1–6).

The treatments had a statistically significant impact on the intensity of erythema on the left and right cheeks (p<0.001) (Figure 7). Compared to the initial state, a statistically significant reduction in erythema occurred after just three treatments (p<0.05) and decreased even more six weeks after six treatments (p<0.05). Statistically significant differences in the intensity of erythema were also revealed between measurements performed after three treatments and six weeks



Figure I Patient I, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



Figure 2 Patient I, left cheek, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



Figure 3 Patient 1, right cheek, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



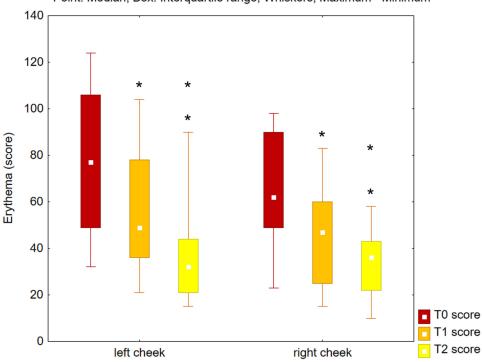
Figure 4 Patient 2, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



Figure 5 Patient 2, left cheek, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



Figure 6 Patient 2, right cheek, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments.



Point: Median; Box: Interquartile range; Whiskers; Maximum - Minimum

Figure 7 Erythema score on the left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's ANOVA p<0.001, left and right cheek post-hoc *p<0.05 (T0vsT1), (T0vsT2), (T1vsT2)).

after six treatments (p<0.05). On the left cheek, the median erythema score before the procedure, after three treatments and six weeks after six treatments was: 77.0, 49.0 and 32.0, respectively, whereas on the right cheek: 62.0, 47.0 and 36.0, respectively.

The minimal values obtained from the measurement of erythema on the left and right cheeks changed statistically significantly over time (p<0.001) (Figure 8). On the left cheek, the minimal erythema score decreased significantly six weeks after six treatments compared to the minimal erythema scores obtained prior to treatment (p<0.05). On the right cheek, the minimal erythema score decreased significantly six weeks after six treatments compared to the minimal erythema scores obtained prior to treatment (p<0.05). On the right cheek, the minimal erythema scores obtained prior to treatment (p<0.05) and compared to the scores obtained after three treatments (p<0.05). On the left cheek, the median of the minimum erythema scores before the procedure, after three treatments and six weeks after six treatments was: 23.0, 20.2 and 18.3, respectively, and on the right cheek: 21.7, 20.5 and 18.7, respectively.

The maximal values obtained from the measurement of erythema on the left and right cheeks changed statistically significantly over time (p<0.001) (Figure 9). On the left cheek, the maximal erythema scores after three treatments (p<0.05) and six weeks after six treatments (p<0.05) were significantly lower compared to the maximal values obtained prior to treatment. On the left cheek, statistically significant differences in the maximal erythema scores were also revealed between the results obtained after three treatments and six weeks after six treatments (p<0.05). On the right cheek, the maximal erythema score six weeks after six treatments was significantly lower compared to the maximal values obtained values obtained prior to treatment (p<0.05) and after three treatments was significantly lower compared to the maximal values obtained prior to treatment (p<0.05) and after three treatments (p<0.05). On the left cheek, the median of the minimal erythema scores prior to treatment, after three treatments and six weeks after six treatments was: 50.5, 45.5 and 37.5, respectively, and on the right cheek: 51.7, 42.8 and 39.2, respectively.

The reduction in the severity of erythema is clearly visible in the images acquired with the Antera 3D device (Figures 10 and 11).

The treatments had a statistically significant effect on the number of inflammatory lesions in both the left and right cheek areas (p<0.001) (Figure 12). Post-hoc tests showed that after three treatments, the number of inflammatory lesions on both the left and right cheeks did not decrease significantly; however, when comparing the condition six weeks after

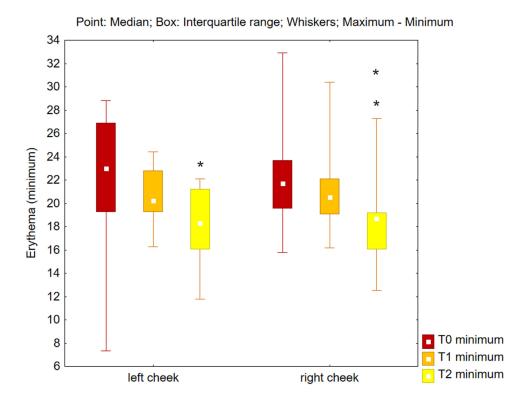


Figure 8 Minimal erythema scores on the left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's Anova p<0.001, left cheek post-hoc *p<0.05 (T0vsT2); right cheek post-hoc

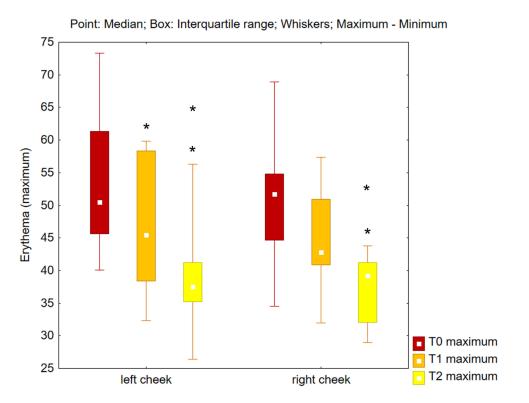


Figure 9 Maximum erythema score on the left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and 6 weeks after 6 treatments (T2), (Friedman's Anova p<0.001, left cheek post-hoc *p <0.05 (T0vsT1), (T0vsT2), (T1vsT2); right cheek post-hoc *p<0.05 (T0vsT2), (T1vsT2)).

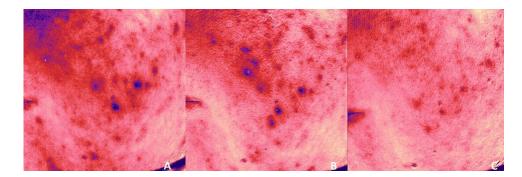


Figure 10 Intensity of erythema on the right cheek in Patient I, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments. Antera 3D view.

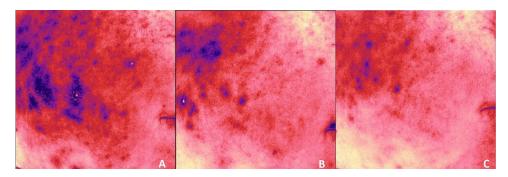


Figure 11 Intensity of erythema on the left cheek in Patient I, (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments. Antera 3D view.

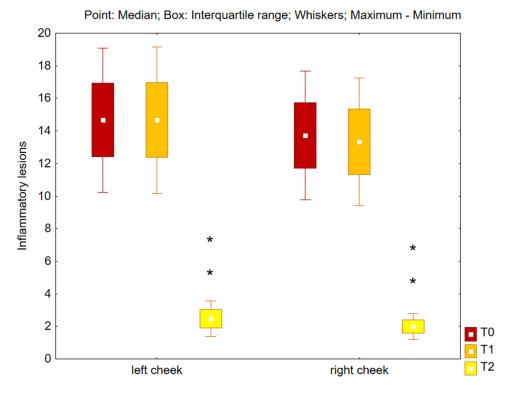


Figure 12 Number of inflammatory lesions on the left and right cheek, before treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's ANOVA p<0.001, left and right cheek post-hoc *p<0.001 (T0vsT2), (T1vsT2)).

six treatments to the initial state and the state after three weeks, statistically significant differences (p<0.001) were observed in both the left and right cheek areas. On the left cheek, the median number of inflammatory lesions before treatment, after three treatments, and six weeks after six treatments was 11, 10, and 2 respectively, while on the right cheek it was 10, 10, and 2 respectively.

The treatments had a statistically significant effect on the severity of acne according to the IGA scale (p<0.001) (Figure 13). Post-hoc tests showed that after three treatments, the severity of acne according to the IGA scale did not change significantly compared to the initial state, while the IGA acne severity values in the final measurement six weeks after six treatments differed significantly from both the initial state (p<0.001) and the state after three treatments (p<0.001). The median acne severity according to the IGA scale at successive measurement points was: 3, 3, and 1.

The treatments had a statistically significant impact on the volume of atrophic scars present on the left and right cheeks (p<0.001) (Figures 14–16). Both on the left and right cheeks, compared to measurements made prior to treatment, the volume of scars after three treatments (p<0.05) and six weeks after six treatments (p<0.05) decreased statistically significantly. Statistically significant differences in scar volume on both cheeks were also revealed in measurements taken after 3 treatments and 6 weeks after 6 treatments (p<0.05). On the left cheek, the median scar volume prior to treatment, after three treatments and six weeks after six treatments was: 1.15, 1.04 and 0.53, respectively, and on the right cheek it was: 1.13, 1.09 and 0.63, respectively.

The hydration of the stratum corneum in all the examined areas of the face changed significantly after the treatments (p<0.001) (Figure 17). Greater hydration was achieved six weeks after six treatments compared to the values obtained prior to treatment (p<0.05) and after three treatments (p<0.05). Such differences occurred in all the areas. The median skin hydration prior to treatment, after three treatments and six weeks after six treatments was: forehead - 53.5, 55.1, 61.7, nose - 45.2, 47.8, 54.3, chin - 53.1, 52.6, 60.3, left cheek - 54.2, 58.4, 67.2 and right cheek - 54.3, 56.7 and 70.4, respectively.

The activity of sebaceous glands and, consequently, the amount of sebum on the epidermal surface in all the examined areas of the face changed significantly after the treatments (p<0.001) (Figure 18). A reduction in the amount

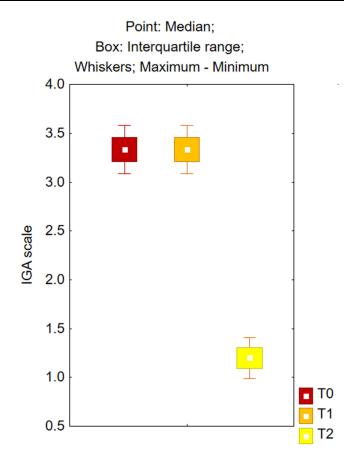
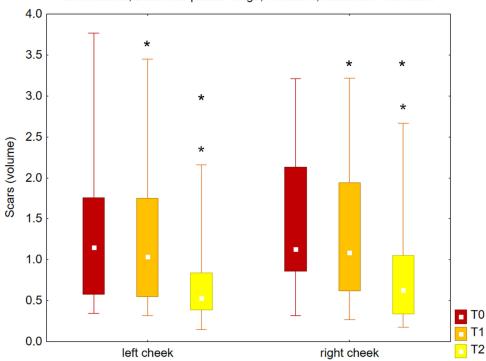


Figure 13 Acne severity in IGA scale before treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's ANOVA p<0.001, post-hoc p<0.001 (T0vsT2), (T1vsT2)).



Point: Median; Box: Interquartile range; Whiskers; Maximum - Minimum

Figure 14 Volume of scars on the left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's Anova p<0.001, left and right cheek post-hoc *p<0, 05 (T0vsT1), (T0vsT2), (T1vsT2)).

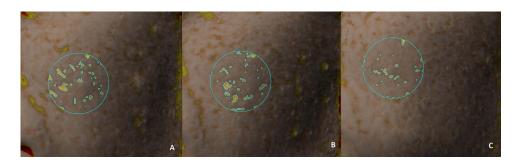


Figure 15 The volume of scars on the left cheek in Patient 1 (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments. Antera 3D view.

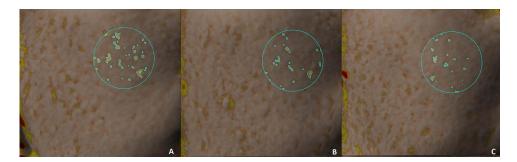
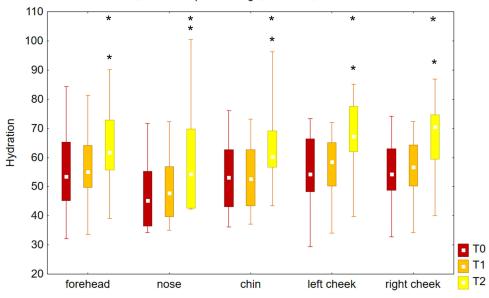


Figure 16 The volume of scars on the right cheek in Patient I (A) Prior to treatment, (B) After 3 treatments, (C) 6 weeks after 6 treatments. Antera 3D view.



Point: Median; Box: Interquartile range; Whiskers; Maximum - Minimum

Figure 17 Hydration of the stratum corneum on the forehead, nose, chin, left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and six weeks after 6 treatments (T2), (Friedman's Anova p<0.001, in all regions post-hoc *p < 0.05 (T0vsT2) and (T1vsT2)).

of sebum was achieved six weeks after six treatments compared to the values obtained prior to treatment (p<0.05) and after three treatments (p<0.05). Such differences occurred in all facial regions examined. Moreover, a statistically significant reduction in sebum content on the forehead and chin occurred after three treatments compared to the state prior to treatment (p<0.05). The median amount of sebum on the epidermal surface prior to treatment, after 3 treatments and 6 weeks after 6 treatments were: forehead - 150, 134, 97, nose - 142, 134, 98, chin - 175, 155, 110, left cheek - 106, 96, 69 and right cheek - 100, 91 and 67, respectively.

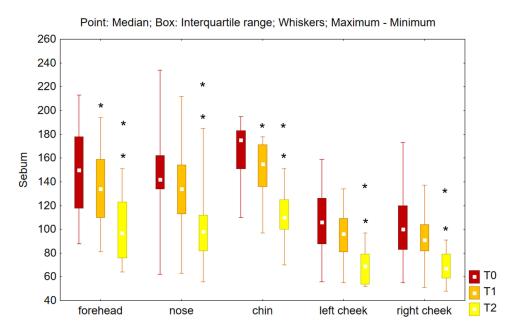


Figure 18 Amount of sebum on the forehead, nose, chin and on the left and right cheeks, prior to treatment (T0), after 3 treatments (T1) and 6 weeks after 6 treatments (T2), (Friedman's Anova p<0.001; in all treatment areas post-hoc *p<0.05 (T0vsT2) and (T1vsT2) and on the forehead and chin post-hoc *p<0.05 (T0vsT1).

Discussion

The use of blue LED light in reducing acne symptoms has been widely described in the scientific literature. Much fewer reports can be found about technologies combining light with active substances, among others, chromophores, especially in quantitative terms.

In studies conducted by Edge et al²² aimed at assessing the effectiveness of FLE (Fluorescent Light Energy) technology in reducing the symptoms of acne vulgaris, a significant reduction in the intensity of inflammation was observed after 6 treatments, as well as a significant reduction in the number of inflammatory lesions and the depth of atrophic scars. The authors of the study also identified stimulation of the angiogenic process. These findings confirm the results obtained, which revealed a very satisfactory clinical response after 6 weeks of irradiation. The study by Antoniou et al²⁵ showed that the use of blue LED light in combination with photoacceptor gel clinically significantly reduces the severity of acne vulgaris. In over 61% of patients, a change in the severity of acne was observed from severe to moderate (on the IGA scale), and in 45% of patients from moderate to mild. A reduction in the number of inflammatory lesions by at least 40% compared to the state prior to treatment was also observed. In turn, the study by Nikolis et al^{26} showed that a device with blue LED light using photoconverter chromophores can significantly reduce moderate to severe facial acne while providing an excellent safety profile. The greatest reduction in inflammatory lesions was observed in patients with severe acne (IGA - 4). However, the improvement in patients with moderate and mild acne was 81.8% and 58.3%, respectively. Thus, it can be stated that LED therapy using external chromophores is effective in a wide spectrum of acne severity, from severe to moderate, as in the study by Nikolis, as well as in mild acne, as in the other presented studies. We obtained similar results in our study, observing a significant reduction in the number of inflammatory lesions in all studied patients with both moderate (IGA-3) and severe acne (IGA-4). The median number of inflammatory lesions decreased from 11 before therapy to 2 six weeks after therapy. In 93.33% of patients, a two-unit change in acne severity was observed on the IGA scale. Most patients completed therapy with acne at level 1 or 2 on the IGA scale. Importantly, statistically significant changes were observed not only in the reduction of inflammatory lesions themselves, but also in other key parameters of acne-affected skin. The impact on a wide range of skin parameters indicates the influence of LED radiation supported by external skin chromophores on the basic mechanisms of acne formation, and thus makes the durability of the achieved effects probable. A significant reduction in the intensity of erythema was observed after just three treatments, and this effect was further improved after completing the full series of six treatments. Reduction in erythema was evident for both minimal and maximal scores, suggesting an overall improvement in skin inflammation. This effect can be attributed to the anti-inflammatory effects of blue and red light and the properties of the chromophore used. The anti-inflammatory effect of blue light and, consequently, the

reduction of erythema results from several mechanisms. Reactive oxygen species (ROS) and nitric oxide are produced in tissues, which in low doses may lead to reduced inflammation.²⁷ Moreover, long-term exposure to blue light affects the migration of neutrophils and macrophages in the skin, which may modulate inflammatory processes.²⁸ At the same time, blue light irradiation causes changes in the expression of genes related to the anti-inflammatory response, including B cell signalling pathways.²⁹ Blue light has a direct antimicrobial effect, which may help reduce inflammation associated with skin infections, which can also cause skin erythema.²⁷ A reduction in the level of pro-inflammatory Th2/Th17 cytokines and a reduction in the infiltration of inflammatory cells after blue light therapy are also observed.²⁸ However, it is important to remember that anti-inflammatory effects are mainly observed with low doses of blue light. Higher doses may be harmful to tissues and potentially exacerbate inflammation.²⁷

A very clinically important effect of the therapy was the reduction of acne scars. A significant reduction in the volume of atrophic acne scars was observed six weeks after six treatments. This effect may be related to the stimulating effect of red and near-infrared light on fibroblasts, which leads to increased collagen production and improved skin structure. Under the influence of red light, microcirculation also improves, which accelerates regenerative processes and provides more nutrients to tissues.^{22,24,30} Better blood supply promotes scar remodelling and improves the overall appearance of the skin.^{27–29} In addition, reducing inflammation in acne scars may contribute to making them shallower and less visible.³¹ Faster cell turnover leads to improved skin texture and smoother scar surface.

LED therapy is often combined with other methods of treating acne scars, such as microneedling or fractional lasers, and it can be assumed that it may also be successfully combined with the use of photoconverters.^{24–27,30–33} The combination of these methods can increase the effectiveness of treatment by enhancing regenerative processes and stimulating collagen production. It is worth noting that the effects of LED therapy in reducing acne scars may be subtle and require a series of treatments. The best results are usually achieved with a combination of different treatment methods, adapted to the skin condition.

A significant increase in the hydration of the stratum corneum was also observed in all examined facial areas, especially after completing the full series of treatments. Optimal skin hydration is synonymous with its healthy and aesthetic appearance. Improved hydration may result from normalization of the skin barrier function and reduction of inflammation. LED light, especially red and infrared, stimulates fibroblasts to increase the production of collagen and elastin.^{22,24} These structural proteins are crucial for maintaining proper skin hydration because they create a "scaffold" for the skin that better retains water and improves skin elasticity, which affects its ability to retain moisture. In addition, LED therapy increases blood flow in the skin, thanks to which the skin is better nourished and hydrated, whereas toxins and metabolic products are removed.^{22,24,34} LED light can affect the production of natural moisturizing factors in the skin, such as hyaluronic acid. NMFs are crucial for maintaining the appropriate level of hydration in the skin.

The research also showed a regulatory effect on the activity of sebocytes. This may be due to the fact that certain wavelengths of LED light, especially blue, can regulate the functioning of the sebaceous glands. Balanced sebum production contributes to maintaining the proper hydrolipid barrier of the skin, which is important for its hydration. Additionally, it has been observed that LED light therapy can strengthen the epidermal barrier by stimulating the production of ceramides and improving the integrity of the stratum corneum, which reduces excessive transepidermal water loss (TEWL). It is worth emphasizing that the moisturizing effects of LED therapy are usually most visible with regular use and can be enhanced by proper skin care and hydration. Importantly, the therapy effectively reduced the amount of sebum on the skin surface in all tested regions. This effect was most visible after completing the full series of treatments, which suggests that regulation of sebum secretion requires a longer treatment period. LED light, especially blue light, directly affects the sebaceous glands, reducing their excessive activity, which leads to reduced sebum secretion.^{19,20} Moreover, LED therapy can regulate the expression of genes responsible for lipid synthesis in the sebaceous glands. LED light, especially red, has anti-inflammatory properties, which may indirectly affect the regulation of sebum secretion.³⁵ Some studies suggest that LED therapy may influence the activity of androgen receptors in the skin, the modulation of which may contribute to the regulation of sebum secretion. It is worth noting that the effects of LED therapy in regulating sebum secretion may vary from person to person and depend on many factors, including the wavelength of light, intensity and duration of therapy. The best results are often achieved when LED therapy is combined with other acne treatments and skin care treatments.

Considering the huge role of sebum in inducing acne lesions, even a relatively small quantitative impact on this parameter (sebum production and secretion) can significantly affect the clinical condition of acne patients.

To sum up, LED light therapy using external chromophores has a comprehensive effect on acne treatment, including reduction of inflammation, sebum production and acne scars, as well as improvement in skin hydration. Importantly, these effects can be assessed quantitatively, making it possible to compare, for example, various therapeutic protocols or correlate the effectiveness of therapy with the initial condition of the skin.

The effects of the therapy used should not be considered separately, as they complement and enhance each other, creating a synergistic healing mechanism. Reducing inflammation and regulating sebum secretion contribute to reducing the number of acne lesions, whereas improving hydration and stimulating collagen production support skin regeneration and scar reduction. A simultaneous impact on various aspects of acne pathophysiology leads to more effective and lasting improvement of the skin condition. This multidirectional therapy not only treats existing lesions, but also prevents the formation of new ones, offering a comprehensive approach to acne treatment. However, further studies involving volunteers are necessary, which will also verify the skin response depending on the dose and the proportions between the individual radiation ranges used in LED therapy.

In medical databases, there are few reports comparing the effectiveness of blue LED light with other acne therapy methods. Papageorgiou et al demonstrated in their study that the use of combined blue and red LED light (415 and 660 nm) and blue LED light alone (415 nm) after 12 weeks of therapy may be more effective in reducing inflammatory acne lesions than topical benzoyl peroxide.³⁶ In studies by Gold et al comparing the effectiveness of inflammatory lesion reduction in acne vulgaris using blue light and topical clindamycin, both methods showed skin improvement, with the reduction of inflammatory lesions being greater on the LED-illuminated side of the face (34%, compared to 14% with topical 1% clindamycin solution).³⁷ Russo et al³⁸ evaluated the efficacy and safety of combining low-dose oral isotretinoin with blue LED light illumination in conjunction with a photoacceptor gel. In their studies, they showed that the use of oral isotretinoin at 5mg per day combined with standard FLE technology yields very good therapeutic results. After 6 weeks of therapy, 50% of patients showed marked quantitative improvement measured as a 2-grade improvement according to the IGA scale, while the remaining 50% showed a 1-grade decrease according to the IGA scale. After 12 weeks from the start of therapy, 75% of patients showed a reduction in clinical severity to IGA 1. During assessment at weeks 33 and 52, patients treated with FLE in combination with isotretinoin achieved and maintained an IGA score of 0. Although the observed group consisted of only 9 patients, the researchers evaluated the therapy as safe, with the only side effects being skin dryness and transient erythema occurring in some patients immediately after treatment. Similar effects were obtained in studies by Li et al.³⁹ The researchers used oral isotretinoin at 10–20mg per day and illuminated half of the volunteers' faces with blue LED light, using a power density of 6–9 J/cm2, performing 4 treatments every 2 weeks. After 10 weeks, significantly greater improvement in skin condition was observed on the illuminated side. A reduction in papule count of 61.58% was achieved on the combination therapy side compared to 43.33% on the other side, and for comedones, a reduction of 63.15% compared to 43.30% for the non-illuminated side.

Based on scientific research results available in medical databases and our own experience, it can be concluded that both the use of blue LED light and FLE technology can be good supporting methods in acne therapy. Combination therapies with low doses of isotretinoin appear particularly promising.

The Limitations of the Study

This study can be considered a preliminary study on the usefulness of blue LED light supported by chromophore gel in the treatment of acne vulgaris. We are aware of the limitations resulting from analyzing results in such a small group, therefore we plan to expand the research in the future. We will also introduce additional analyses, including the assessment of non-inflammatory lesions (open and closed comedones) to better discuss the impact on typical symptoms of acne vulgaris.

Conclusion

- 1. Therapy combining LED light with photoacceptor substances appears to be an effective method of reducing the symptoms of acne vulgaris.
- 2. The treatments lead to a significant reduction in erythema, reduce the number of inflammatory lesions such as papules, pustules, and cysts, reduction in the volume of atrophic scars, improvement of skin hydration and regulation of sebum secretion. These effects can be identified quantitatively.
- 3. Therapeutic effects are visible after just three treatments, but a full series of six treatments provides the best results.

- 4. This method may be a valuable supplement or alternative to conventional acne treatment methods, especially in the context of increasing antibiotic resistance.
- 5. Further studies involving a larger group of patients and with a longer follow-up period are necessary to confirm the long-term effectiveness and safety of this method.
- 6. It is worth considering comparative studies with other acne treatments to determine the relative effectiveness of this therapy.
- 7. The mechanism of action of this therapy requires further research at the molecular and cellular level, which may contribute to the optimization of treatment protocols.

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Disclosure

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References

- 1. Bhat YJ, Latief I, Hassan I. Update on etiopathogenesis and treatment of Acne. Indian J Dermatol Venereol Leprol. 2017;83(3):298–306. doi:10.4103/0378-6323.199581
- 2. Cong TX, Hao D, Wen X, Li XH, He G, Jiang X. From pathogenesis of acne vulgaris to anti-acne agents. Arch Dermatol Res. 2019;311 (5):337-349. doi:10.1007/s00403-019-01908-x
- 3. Kaur S, Verma P, Sangwan A, Dayal S, Jain VK. Etiopathogenesis and therapeutic approach to adult onset acne. *Indian J Dermatol.* 2016;61 (4):403–407. doi:10.4103/0019-5154.185703
- 4. Hazarika N. Acne vulgaris: new evidence in pathogenesis and future modalities of treatment. J Dermatolog Treat. 2021;32(3):277-285. doi:10.1080/09546634.2019.1654075
- 5. Kaszuba A, Maj J. Praktyka Dermatologiczna. In: Szepietowski J, Kapuścińska-Mrowiecka M, Kaszuba A, et al., editors. *Trądzik zwyczajny:* Patogeneza i leczenie. Konsensus Polskiego Towarzystwa Dermatologicznego. 1st ed. Poznań; 2016:75–80. [In Polish].
- Dréno B, Pécastaings S, Corvec S, Veraldi S, Khammari A, Roques C. Cutibacterium acnes (Propionibacterium acnes) and acne vulgaris: a brief look at the latest updates. J Eur Acad Dermatol Venereol. 2018;32(2):5–14. doi:10.1111/jdv.15043
- 7. Filo-Rogulska M, Wcislo–Dziadecka D, Brzezińska-Wicisło L. Rola mikrobiomu skóry w trądziku pospolitym [The role of the skin microbiome in acne vulgaris]. *Dermatologia Praktyczna*. 2017;10(3):27. [In Polish]. doi:10.26625/2017.10.3.02
- 8. Dréno B, Dagnelie MA, Khammari A, et al. The skin microbiome: a new actor in inflammatory acne. Am J Clin Dermatol. 2020;21:18–24. doi:10.1007/s40257-020-00531-1
- 9. Conforti C, Agozzino M, Emendato G, et al. Acne and diet: a review. Int J Dermatol. 2022;61(8):930-934. doi:10.1111/ijd.15862
- 10. Dréno B, Araviiskaia E, Berardesca E, et al. Microbiome in healthy skin, update for dermatologists. J Eur Acad Dermatol Venereol. 2016;30 (12):2038–2047. doi:10.1111/jdv.13965
- 11. Layton AM, Ravenscroft J. Adolescent acne vulgaris: current and emerging treatments. Lancet Child Adolesc Health. 2023;7(2):136-144. doi:10.1016/S2352-4642(22)00314-5
- 12. Karadag AS, Aslan Kayıran M, Wu C-Y, Chen W, Parish LC. Antibiotic resistance in acne: changes, consequences and concerns. J Eur Acad Dermatol Venereol. 2021;35(1):73–78. doi:10.1111/jdv.16686
- 13. Sardana K, Gupta T, Garg VK, Ghunawat S. Antibiotic resistance to Propionobacterium acnes: worldwide scenario, diagnosis and management. *Expert Rev Anti Infect Ther*. 2015;13(7):883–896. doi:10.1586/14787210.2015.1040765
- 14. Xu H, Li H. Acne, the skin microbiome, and antibiotic treatment. Am J Clin Dermatol. 2019;20(3):335-344. doi:10.1007/s40257-018-00417-3
- Al-Talib H, Al-Khateeb A, Hameed A, Murugaiah C. Efficacy and safety of superficial chemical peeling in treatment of active acne vulgaris. An Bras Dermatol. 2017;92(2):212–216. doi:10.1590/abd1806-4841.20175273
- 16. Nofal E, Nofal A, Gharib K, Nasr M, Abdelshafy A, Elsaid E. Combination chemical peels are more effective than single chemical peel in treatment of mild-to-moderate acne vulgaris: a split face comparative clinical trial. J Cosmet Dermatol. 2018;17(5):802–810. doi:10.1111/ jocd.12763
- 17. Lu L, Shi M, Chen Z. Efficacy of IPL therapy for the treatment of acne vulgaris: a meta-analysis. J Cosmet Dermatol. 2020;19(10):2596–2605. doi:10.1111/jocd.13586
- 18. Scott AM, Stehlik P, Clark J, et al. Blue-light therapy for acne vulgaris: a systematic review and meta-analysis. Ann Fam Med. 2019;17(6):545–553. doi:10.1370/afm.2445
- 19. Pei S, Inamadar AC, Adya KA, Tsoukas MM. Light-based therapies in acne treatment. Indian Dermatol Online J. 2015;6(3):145–157. doi:10.4103/ 2229-5178.156379
- 20. Elman M, Slatkine M, Harth Y. The effective treatment of acne vulgaris by a high-intensity, narrow band 405–420 nm light source. J Cosmet Laser Ther. 2003;5(2):111–117.

- De Lucca AJ, Carter-Wientjes C, Williams KA, Bhatnagar D. Blue light (470 nm) effectively inhibits bacterial and fungal growth. Lett Appl Microbiol. 2012;55(6):460–466. doi:10.1111/lam.12002
- 22. Edge D, Mellergaard M, Dam-Hansen C, et al. Fluorescent light energy: the future for treating inflammatory skin conditions? J Clin Aesthet Dermatol. 2019;12(5):61-68.
- Glass GE. Photobiomodulation: the clinical applications of low-level light therapy. Aesthet Surg J. 2021;41(6):723–738. [Erratum in]: Aesthet Surg J. 2022;12:42(5):566. doi: 10.1093/asj/sjab396. doi:10.1093/asj/sjab025
- Couturaud V, Le Fur M, Pelletier M, Granotier F. Reverse skin aging signs by red light photobiomodulation. Skin Res Technol. 2023;29(7):e13391. doi:10.1111/srt.13391
- 25. Antoniou C, Dessinioti C, Sotiriadis D, et al. A multicenter, randomized, split-face clinical trial evaluating the efficacy and safety of chromophore gel-assisted blue light phototherapy for the treatment of acne. *Int J Dermatol.* 2016;55(12):1321–1328. doi:10.1111/ijd.13349
- 26. Nikolis A, Fauverghe S, Scapagnini G, et al. An extension of a multicenter, randomized, split-face clinical trial evaluating the efficacy and safety of chromophore gel-assisted blue light phototherapy for the treatment of acne. Int J Dermatol. 2018;57(1):94–103. doi:10.1111/ijd.13814
- 27. Zhang D, Leong ASW, McMullin G. Blue light therapy in the management of chronic wounds: a narrative review of its physiological basis and clinical evidence. *Wounds*. 2023;35(5):91–98. doi:10.25270/wnds/22097
- Magni G, Tatini F, Siena G, et al. Blue-LED-light photobiomodulation of inflammatory responses and new tissue formation in mouse-skin wounds. *Life*. 2022;12(10):1564. doi:10.3390/life12101564
- 29. Rossi F, Magni G, Tatini F, et al. Photobiomodulation of human fibroblasts and keratinocytes with blue light: implications in wound healing. *Biomedicines*. 2021;9(1):41. doi:10.3390/biomedicines9010041
- 30. Nikolis A, Bernstein S, Kinney B, et al. A randomized, placebo-controlled, single-blinded, split-faced clinical trial evaluating the efficacy and safety of KLOX-001 gel formulation with KLOX light-emitting diode light on facial rejuvenation. *Clin Cosmet Invest Dermatol.* 2016;9:115–125. doi:10.2147/CCID.S100697
- 31. Khatri KA, Mahoney DL, McCartney MJ. Laser scar revision: a review. J Cosmet Laser Ther. 2011;13(2):54-62. doi:10.3109/14764172.2011.564625
- 32. Alam M, Han S, Pongpruthipan M, et al. Efficacy of a needling device for the treatment of acne scars: a randomized clinical trial. *JAMA Dermatol.* 2014;150(8):844–849. doi:10.1001/jamadermatol.2013.8687
- 33. Phothong W, Wanitphakdeedecha R, Sathaworawong A, Manuskiatti W. High versus moderate energy use of bipolar fractional radiofrequency in the treatment of acne scars: a split-face double-blinded randomized control trial pilot study. *Lasers Med Sci.* 2016;31(2):229–234. doi:10.1007/s10103-015-1850-2
- 34. Azmahani A, Nakamura Y, McNamara KM, Sasano H. The role of androgen under normal and pathological conditions in sebaceous glands: the possibility of target therapy. *Curr Mol Pharmacol.* 2016;9(4):311–319. doi:10.2174/1874467208666150710120217
- Lee SY, You CE, Park MY. Blue and red light combination LED phototherapy for acne vulgaris in patients with skin phototype IV. Lasers Surg Med. 2007;39(2):180–188. doi:10.1002/lsm.20412
- 36. Papageorgiou P, Katsambas A, Chu A. Phototherapy with blue (415 nm) and red (660 nm) light in the treatment of acne vulgaris. *Br J Dermatol*. 2000;142(5):973–978. doi:10.1046/j.1365-2133.2000.03481.x
- 37. Gold MH, Rao J, Goldman MP, et al. A multicenter clinical evaluation of the treatment of mild to moderate inflammatory acne vulgaris of the face with visible blue light in comparison to topical 1% clindamycin antibiotic solution. J Drugs Dermatol. 2005;4(1):64–70.
- 38. Russo A, Mellergaard M, Pellacani G, Nisticò S, Nielsen MCE. Fluorescent light energy combined with systemic isotretinoin: a 52-week follow-up evaluating efficacy and safety in treatment of moderate-severe acne. *Clin Case Rep.* 2021;9(4):2057–2068. doi:10.1002/ccr3.3944
- 39. Li Y, Xia J, Zhu Y, et al. Efficacy and safety of low-level light therapy by delicate pulsed light combined with low-dose oral isotretinoin for the treatment of acne vulgaris: a randomized split-face study. *Lasers Med Sci*. 2022;37(8):3221–3229. doi:10.1007/s10103-022-03606-z

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