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Innovative Light Therapy: 4. Influence of Polarization and Wavelength Range of Light on the Effectiveness of Its Pain Relief Action

Sergiy A. Gulyar[1, 2] and Zynaida A. Tamarova[1]

1. Department of Sensory Signaling, Bogomoletz Institute of Physiology, National Academy of Sciences of Ukraine, Kyiv 401601, Ukraine

2. International Medical Innovation Center Zepter, Kyiv 02152, Ukraine

Abstract: We studied the dynamics of the tonic pain response (formalin test) and changes in the pain threshold to electrical stimulation (vocalization test on an electric platform) in animals depending on the polarization and wavelength range of light. The study was carried out on 280 adult white male mice weighing 28-33 g. Each experimental series consisted of 10 animals, a placebo series (control without light)—20 animals. It has been experimentally verified that when polychromatic polarized light (PL) is used, pain weakened statistically significant due to local reactions from the locus of pain and systemic processes through pain points of acupuncture (AP). We revealed that the factors that significantly enhance the analgesic result of polychromatic light therapy are the polarization of light and the long-wavelength part of visible light.When applying different wavelength ranges of PL to the AP E-36, it was noted that all seven colors of the spectrum, as well as polychromatic (white) light, effectively suppressed pain. Analgesia was 36.1-54.4%, and no differences in statistical significance were found between the reactions. When PL in the long-wavelength range (red, yellow, orange) was applied to the pain locus, the pain response was shortened by 50.1-64.1%, while the other colors (blue, green, purple) weakened pain only by 31.5-44.3%. The differences between them and the most effective red light are statistically significant. Red light was also more efficient than polychromatic PL, and no significant differences were found between red, orange and yellow colors. The possibility of AP response to each of the main monochromatic ranges of sunlight and obtaining reactions that can be used for medicinal purposes has been experimentally verified. Clinical observations of human pain have shown dynamics similar to those obtained in animals. The analgesia caused by red light reached 48.2%. The importance of using photobiomodulation in clinical and home conditions is emphasized.

Key words: Photobiomodulation, Bioptron, polarized polychromatic light, red light, colour therapy, analgesia, acute pain, tonic pain, AP points, pain and non-pain behavioural reactions.

1. Introduction

White (polychromatic) light and its individual color (monochromatic) components in the wavelength range from 400 to 780 nm have been received by humans for medical purposes for many centuries. This physiotherapy direction has the general name actinotherapy with variations of light therapy, phototherapy, low-intensity laser therapy, color therapy, and photobiomodulation.

Corresponding author: Sergiy A. Gulyar, M.D., Ph.D., D.Sc., Prof., research fields: medicine (including environmental medicine), physiology, electromagnetic and light therapy (Bioptron, laser, LED).

There are no objections to the empirically established approaches to the treatment of psychoemotional disorders, insomnia, neonatal jaundice, prophylactic and pain-relieving light procedures, etc. [1-6]. The possibilities of light therapy have expanded since the advent of LASERs, which has drawn particular attention to a new kind of light. LASER creates coherent polarized light (PL) (monochromatic), the quanta of which propagated in a parallel stream. High-intensity LASER light is used for the surgical destruction of pathological foci [7]. Low-intensity LASER radiation is successfully used for therapeutic purposes in dermatology, rheumatology, wound

treatment, pain relief, etc. in humans and animals [8-10]. Low-intensity red LASER light has been shown to effectively suppress acute and chronic pain [11, 12]. However, LASERs have a drawback—a narrow wavelength range and the impossibility of simultaneously using the full palette of sunlight.

Bioptrons, as a separate group of light therapy devices that produce polychromatic PL, appeared in the late 80s. Last century [13, 14], however, their real implementation in medical practice occurred after the merger of the companies Zepter and Bioptron [15, 16]. At that time, the main arguments for the effectiveness of Bioptron-light were the hypothetical mechanisms of action of LASER light and the practical experience gained in the treatment of several cases of trophic ulcers of the leg [17]. But the first wave of results obtained in the 80-90s of the last century was characterized by heterogeneity in the selection of objects of observation, errors in the methodological base, empirical approaches and, ultimately, incomparability of data. Clinical observations due to the specificity of the human factor have demonstrated only relative evidence of the effectiveness of polychromatic PL.

As for the individual monochromatic spectral ranges of the Bioptron device (quasi-LASER light, color therapy), at the beginning of their application, the initial emphasis was shifted to the field of alternative medicine without obtaining an evidence base [18]. As a result, problems arose with the recognition of Bioptron-color therapy as a medical technology. At the same time, this path has already been passed by low-intensity laser medicine using color-PL. Methodological difficulties have also arisen due to the orientation of clinicians exclusively on the data obtained on patients with a specific disease. The implementation of such requirements is laborious and not possible for all diagnoses. Direct experimental results obtained in animals have not been properly accepted. The jealousy of fans of LASER medicine towards the young direction at that time is not excluded, which was expressed in ignoring the first results obtained at the level of case reports.

The fact of the presence of a statistical significance for analgesic effect of the polychromatic and monochromatic low-intensity PL of Bioptron device was first obtained in 1999 [19-20]. These experimental data suggested a marked suppression of pain by acting on antinociceptive APs [21].

Now one of the first necessary questions is to consider the significance of such a property of Bioptron light as polarization. This question was associated with the abundance of light technology used in physiotherapy, which also causes an analgesic effect, and the lack of clarity in understanding the differences between specific devices. The question of the presence or absence of a similar effect in unpolarized light, or of the exceptional property acquired by light after polarization, could be resolved by setting up a comparative study of the role of these two variants of light, provided they have the same power. This could be identified using different pain models: acute pain (vocalization on the electrode floor) and an artificially created locus of tonic somatic pain (formalin test).

Everyone understands that white light contains electromagnetic waves with different wavelengths and, perhaps, not all of them have the same analgesic effect. However, the evidence base on this topic is still practically absent. Hence, the relevance of the study of the analgesic effect of monochromatic color light ranges is clear.

Our goal was to apply a unified experimental methodological approach that would allow an objective assessment, with a minimum risk of errors, to determine the effectiveness of monochromatic light exposure on pain response. Such evidence cannot be obtained in human beings. It was important for us to obtain direct data and estimate the contribution of the polarization of poly- and monochromatic light. They would serve as the basis for further in-depth study of the differences for each of the polarized color ranges,

in particular, to find out the dependence of the analgesic effect on the PL wavelength. At the same time, it was important to find and quantify the ranges with the most noticeable analgesic effects.

2. Methods

We focused on the assessment of the analgesic response of polarized and unpolarized monochromatic and polychromatic light in different types of pain (tonic and acute) that arose after the application of a chemical or electrical stimulus in animals. The study also used the observation of the dynamics of post-traumatic pain in humans under the influence of PL.

2.1 Exposure to Polarized Light

We used Bioptron light: incoherent, low-energy (40 mW/cm^2) light (physical name PILER) with a wavelength range of 480-3,400 nm in the visible and near infrared spectrum. This light is also called Bioptron® Quantum Hyperlight®. The wavelength range of light could be modified by Colortherapy-Set monochromatic absorption filters (red, orange, yellow, green, cyan, blue, violet) (Fig.1). These filters are called Compact Set PAG-965, Manufacturer is Bioptron AG, Wollerau, Switzerland and are used with the Bioptron-Compact-1 and 3 devices. The polarization of light from a halogen lamp was created by reflecting it from a laminated glass located at the Brewster angle (linear polarization). Unpolarized light was obtained in a similar optical system of the Bioptron devices without a polarizer. Distance from the skin surface was 5 cm, exposure was10 min. The effects obtained with direct application of light to the locus of pain (inflammatory response) or distant exposure (response of acupuncture(AP)) were evaluated. The beam diameter was 5 mm (in animal experiments) or 5 cm (in human studies).

2.2 Experiments on Animals

The study was performed on 280 adult white male mice weighing 28-33 g. All experiments were carried out in accordance with the Ethical Guidelines of the International Pain Association. As a model of tonic pain response, we used well described in the literature [22, 23] formalin test. The pain was induced by subcutaneous injection of a 5% formalin solution into the dorsum of the foot of the left hind limb. The experimental model was described in detail earlier [24]. Immediately after the formalin injection, a 10-minute application with the Bioptron device light to the pain locus or AP E-36 was performed. Each series of experiments consisted of 10 animals, and the placebo series (control without light) included 20 animals. With the help of a computer program, the duration of the painful behavioral reaction was calculated—licking the affected limb; as well as non-painful reactions (duration of sleep, eating, washing and running) for every consecutive 10 min during the 60 min observation period. Acute pain was induced by irritating the paws of animals with an electric current. The mouse was placed in a chamber with an electric floor. An unavoidable, gradually increasing electrical painful stimulation was applied and the threshold voltage (V) was recorded when the animal reacted by vocalization. The vocalization threshold was recorded before and after light application.

2.3 Research of Post-Traumatic Pain in Humans

In a patient diagnosed with a displaced fracture of the fifth metacarpal bone, we studied the effect of the red PL of the Bioptron device on the intensity of pain. Under local anesthesia, bone fragments were repositioned and fixed with a titanium plate. Severe pain syndrome was observed after the operation. To relieve it, the patient received 4 days of pharmacological analgesia (dexalgin). Then, instead of a pharmacological analgesic, treatment was performed with red PL (Bioptron device with a red absorption filter of glass blowing origin). Since the application of light to the locus of pain was impossible

due to the immobilizing dressing, the light was directed to AP GL-4 (He-Gu). The patient received a 10-min session of light therapy daily. Using a special computer program, the duration (s) of pain sensations was recorded for 30 min before the light was applied and for 30 min after the end of the light therapy session.

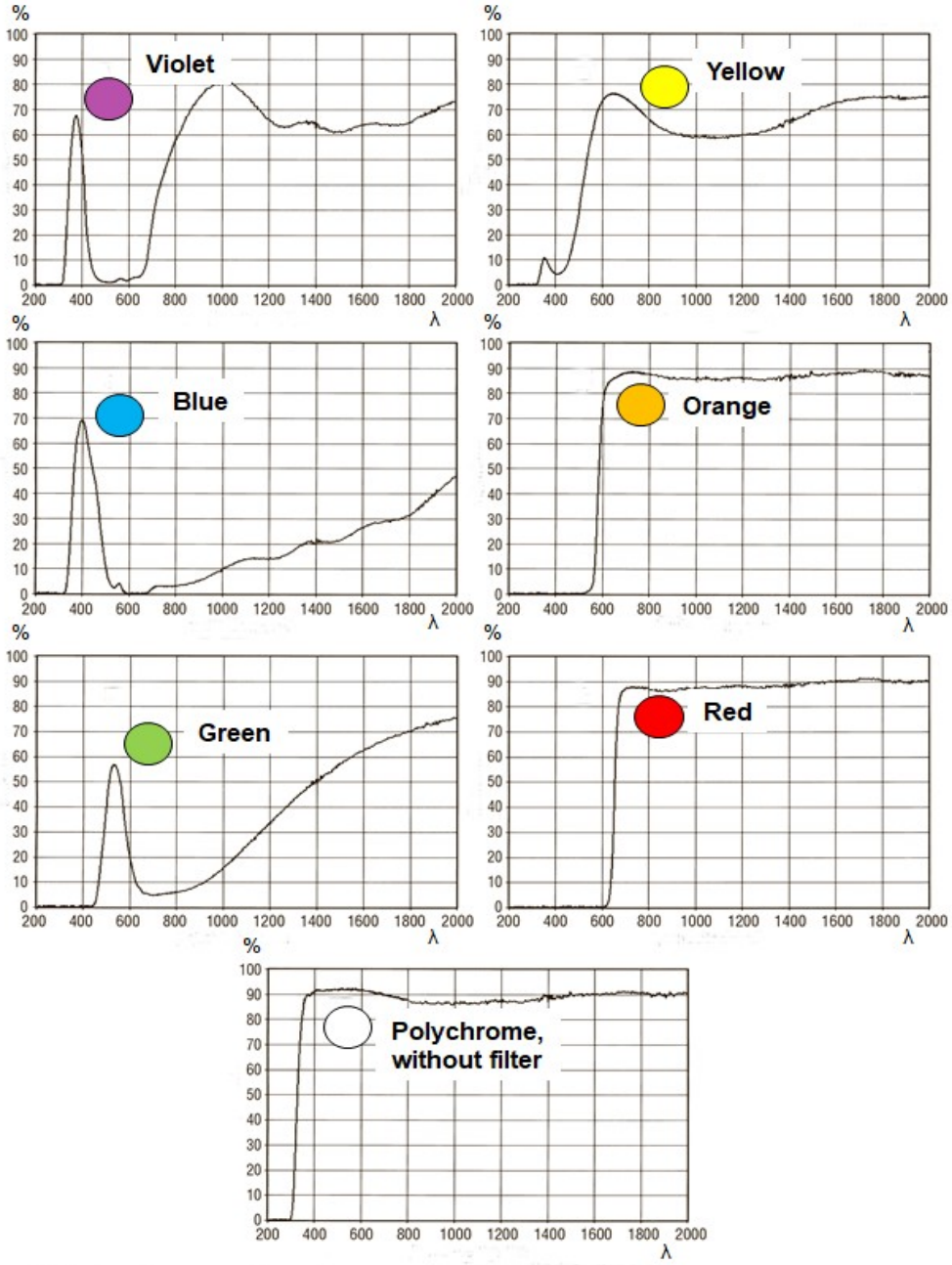

Fig. 1 Transmission spectra of Colortherapy-set filters.
Vertical—transmission percentage, %; horizontal—wavelength, λ.

2.4 Processing of Experimental Data

Data from animal and human studies were statistically processed. Results are presented as mean and standard error of the mean for each group (M ± m). The significance of the difference between the results before and after the application of light, as well

as between the groups where polarized and unpolarized light or light with different wavelengths were used, was assessed by the Student's test. The difference was considered significant at $p < 0.05$.

3. Results

3.1 Influence of Polychromatic PL on Pain and Non-pain Behavior of Animals

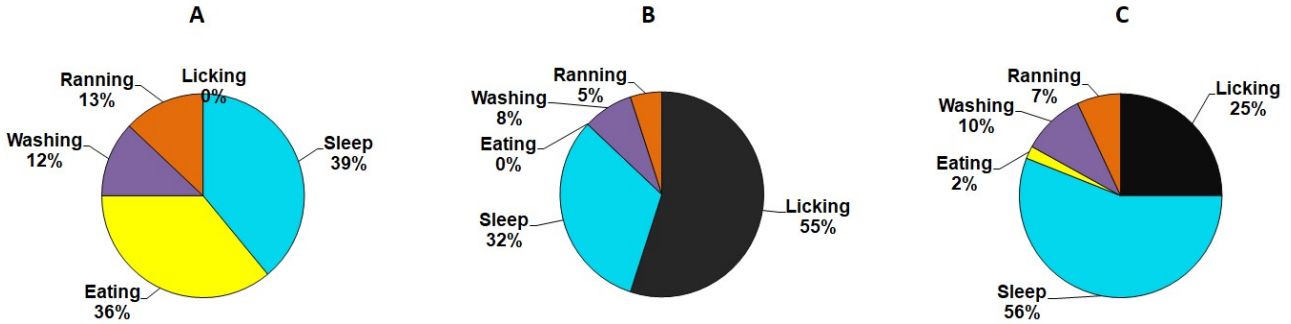

Fig. 2 The structure and duration of behavioral reactions in animals in a calm state (A—control group), in the presence of formalin-induced tonic pain before (B) and after 10-min application of polychromatic light to AP E-36 (C) [21].
Area of the whole circle was taken as 100%.

after the use of PL against the background of control data. This correlation makes it possible to assess the intensity of pain and, thus, to judge the presence of a biological response to a given type of light and specifically about the possibility of light analgesia.

If to take the duration of all observed behavioral reactions as 100% (full circle), then changes in the ratio between pain and non-pain responses in different groups of animals will become obvious (Fig. 2). Under normal conditions (without any influences), the animals ate or slept 75% of the time (eating 36%, sleeping 39%), running and washing took them 25% of the time, there was no pain. In the group of animals that received formalin pain, but did not have the PL light application, we observed a decrease in sleep and a complete lack of interest in food. More than half of the time (55%) these animals licked the affected paw (pain locus). In the group that received formalin injection followed by a PL exposure (10 min) on AP E-36, the total time of licking the painful area significantly decreased (by 2.2 times) in comparison with the group without light application ($p<0.01$), which indicates pain relief. Sleep duration increased by 1.8 times ($p<0.05$). Some of the animals (6 out of 10) started eating food, but this was just a trend, like running or washing. We, subsequently, confirmed many times such patterns of behavioral reactions [19, 25-27].

Despite the fact that the above data convinced us of the effectiveness of the PL light, the question arose about the role of polarization in the development of the analgesic effect. The results of experiments carried out according to the method described above against the background of variations in pain syndromes, wavelength ranges and polarization, made it possible to verify the existence of differences in the case of using polarized and unpolarized light.

3.2 Comparison of the Effects of Unpolarized and PL on Acute and Tonic Pain

The effect of polychromatic unpolarized light on analgesic AP did not cause statistically significant changes in the pain threshold (acute pain) to electrical irritation of the soles of the feet (Fig. 3a). Its fluctuations did not exceed 6-11% of the initial values.

First of all, it is necessary to consider the correlation of pain and non-pain reactions in animals before and

Almost in the same range (5-8%), changes in the pain threshold were observed in the group that was not exposed to light (control). Curves of changes in the threshold current values in these two groups practically coincided. On the other hand, PL caused a noticeable increase in the pain threshold (by 34.2-59.1%). The analgesic effect lasted over 3 h. These results showed that only PL light had statistical significance of weakening the sensitivity to acute pain.

After illumination of AP E-36 with both polarized and unpolarized white light, tonic pain response (Fig. 3c) was lower than in placebo (50 and 67.9% of the control value). However, statistical analysis revealed an insignificant difference between the duration of licking the pain locus in the group where unpolarized light was used with the control group. On the other

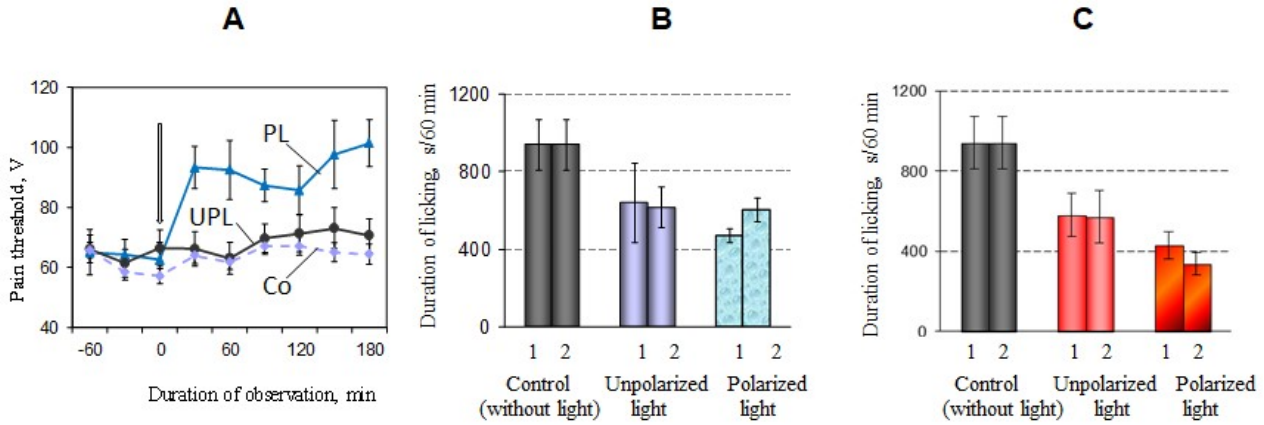

Fig. 3 Influence of polarized and unpolarized light in polychromatic (white) and monochromatic (red) variants on acute (A) and tonic (B, C) pain.

(A) The mean threshold of vocalization from the electrical stimulation of feet for three groups of mice with exposure of AP point E-36 to polarized white light (PL), or to unpolarized white light (UPL), and in the control group (Co) that was not exposed to light. The arrow indicates the beginning of exposure to light.

(B, C) Dependence of formalin-induced pain behavioral response (licking of the affected paw) on exposure of AP E-36 (1) or painful area (2) to polarized and unpolarized white (B) and red (C) light.

hand, PL significantly ($p< 0.01$) reduced the duration of the pain response.

If the polychromatic unpolarized light was directed right to the pain locus, then the duration of the pain reaction decreased in almost the same way as after exposure to the PL (65.4% and 64.2% of the control value), but due to the large scatter of individual values, the difference with the control turned out to be statistically insignificant. Only the increase in the duration of sleep compared to the control was significant ($p< 0.05$).

Monochromatic (red) PL, as shown above, reliably suppressed both acute and tonic pain. Since red PL had the greatest analgesic effect of the entire spectrum, it was advisable to compare the effectiveness of the use of unpolarized red and PL.

When studying the effects of monochromatic (red) light on a model of acute pain, an increase in the pain threshold was recorded after the exposure of AP E-36 to not only polarized, but also non-polarized red light. The threshold increased by 25.4% and 22%, respectively, compared with the control group. At the same time, polychromatic unpolarized light increased the pain threshold by a maximum of 11%, which did not differ significantly from the control.

In animals with an artificially created locus of tonic pain, a pronounced reduction in the duration of the pain reaction was observed after application of unpolarized red light to AP E-36 or to the locus of pain. The changes, however, were weaker in comparison with the effect of red PL (Fig. 3, C). This is clearly seen both in the dynamics and when

comparing the total (60 min of observation) values of pain reactions in different groups.

The nature of the changes in non-pain behavioral reactions is also noteworthy. In the group exposed to unpolarized red light, the duration of sleep and washing was shorter and the running time was longer than in the control animals. This meant that red PL suppressed tonic pain more noticeably than unpolarized red light.

So, comparative studies have shown that tonic and acute pain are most effectively alleviated by the action of PL (both poly- and monochromatic). Unpolarized light does not induce significant changes in sensitivity to acute or tonic pain.

These data reconcile with the results of Bolton et al. [28], who compared the effects of different polarization values of Bioptron light (95 and 14%) on the growth of macrophages in tissue culture. They found that under the influence of 1- and 2-min exposures, the reaction of macrophage proliferation was noticeable 4 days after application, and its degree (number of cells) was the greatest after exposure to PL (95%) for 2 min.

Our data showed that when unpolarized light acted on the locus of pain caused by inflammation, a more pronounced weakening of the behavioral pain response was observed than the response from AP E-36. It is known that hemogenic inflammation is characterized by the appearance of many inflammatory mediators, in particular, bradykinin and histamine, which stimulate nociceptive fibers and have a vasodilating effect, the development of edema, an increase in the permeability of the basement membranes of the skin, an increase in the metabolic rate by about one third, a decrease in the pH in the locus to 5.3, an increase in osmotic pressure, an increase in the concentration of K^+, Na^+, Ca^{++} ions by about 1.5 times [29, 30]. It was found that these and other pathological conditions were accompanied by changes in skin resistance. Thus, in a rabbit with experimental peritonitis for 7 days, areas with a strongly reduced resistance were noted on the auricles [31]. Skin areas with low resistance also appeared after the creation of an artificial gastric ulcer or upon stimulation of a number of visceral structures and the cerebral cortex [32]. This interesting fact suggests that the area of the skin outside the area of the AP point, altered as a result of hemogenic inflammation, acquires the properties of such a point and the ability to activate endogenous analgesic systems. In the practice of AP, these pathological extra-APareas are used to effectively suppress pain.

At the same time, when studying changes in the pain threshold in experiments with acute pain, it was found that unpolarized light when applied to an AP is not able to cause a statistically significant suppression of the behavioral pain response, similar to that occurs after the application of PL of the Bioptron device [19]. It is known that in acute pain there is a natural physiological activation of nociceptive fibers, which is not accompanied by the development of local pathological changes in the skin. This fact confirms the conclusion that inflammation mechanisms underlie the increase in the sensitivity of ordinary skin to PL. There is evidence that under the action of PL on the skin of the paw of an anesthetized rat, a prolonged inhibition of the background activity in the afferent fibers of the cutaneous nerve was observed, while under the action of unpolarized light of the same intensity, biphasic changes in excitability occurred [29]. All this convinces us that only PL has the property of weakening sensitivity to acute and tonic pain, despite the presence of a general biological response to any light source. It can also be assumed that the best efficiency of red light was due to the absence in its spectrum of neutral and blue components that have antagonistic effects to it.

3.3 Influence of Monochromatic Spectral Ranges

Fig. 4 shows that after AP E-36 exposure to PL, statistically significant pain relief was provided by both polychromatic (white) and all ranges of colored

light. When acting on the pain locus, statistically significant pain relief took place after the application of white light and 5 variants of colored light, with the exception of blue (Fig. 5).

Regardless of whether the AP or the pain locus was illuminated, the shortest duration of the pain reaction was observed after the application by red light. The total time of licking the pain locus in these two experimental groups was 45.6±7% and 35.9±6.1% of the like indicator in animals not exposed to PL. Thus, the analgesic effect of the application of red PL to AP E-36 was 54.4%, and to the pain locus—64.1%. The red light is following in terms of efficiency of AP E-36 illumination then comes the white light (the duration of the pain reaction was 50% of the control), in case the locus of pain was illuminated by yellow 44.6% and by orange 49.9%. After application by the remaining colors of the spectrum, the pain response

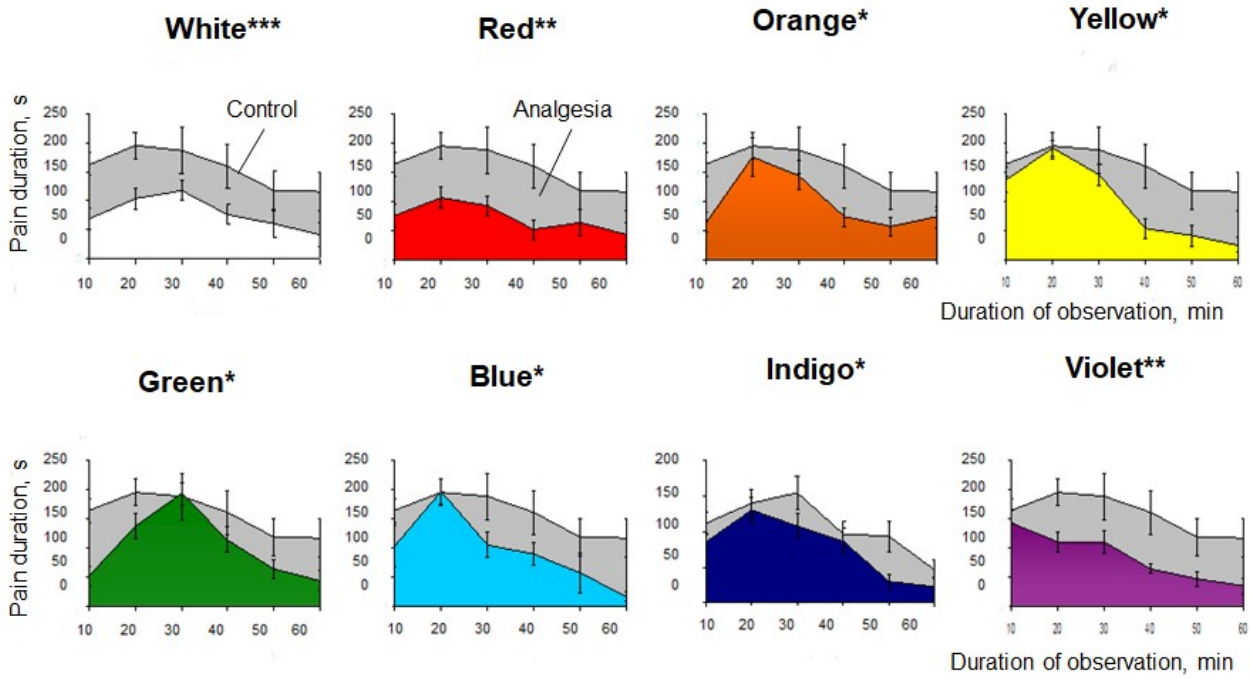

Fig. 4 Dynamics of pain response to tonic pain in animals after 10 min of AP E-36 exposure to poly- or monochromatic light of the Bioptron device.

The ordinate shows the duration of licking of the affected limb (s). The abscissa shows the observation duration (min).
Significance of difference with control over 60 min of observation: * $p< 0.05$; ** $p< 0.01$; *** $p< 0.001$.

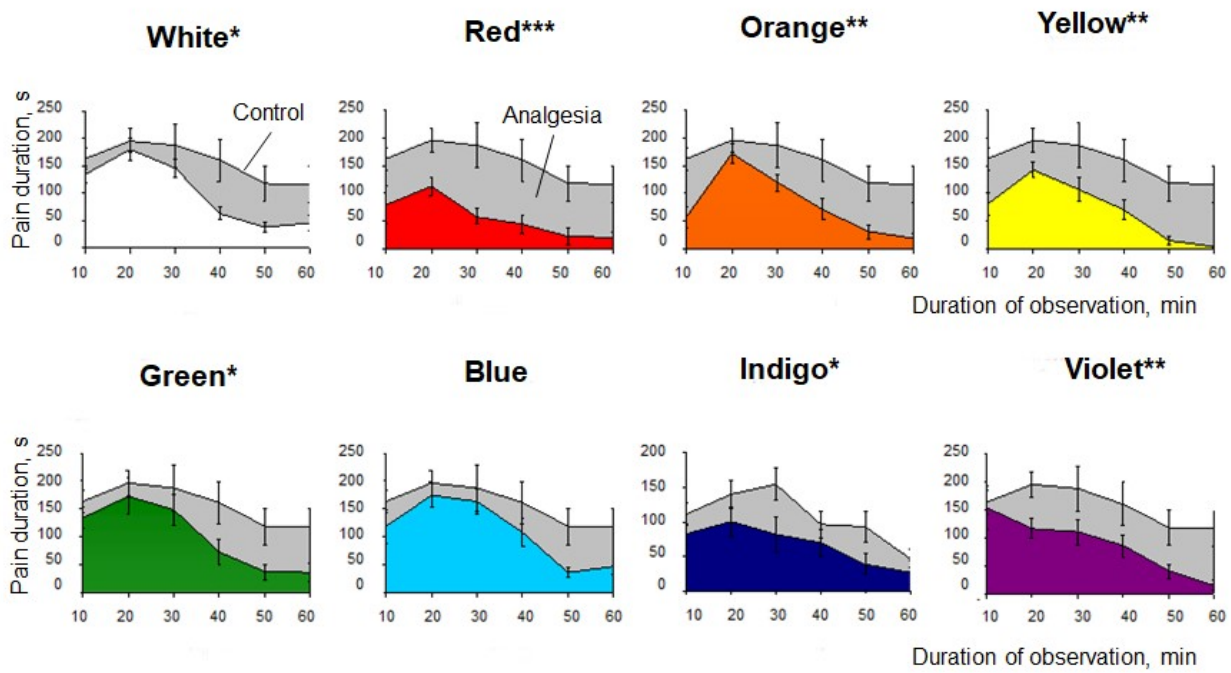

Fig. 5 Dynamics of pain response to tonic pain in animals after 10 min of the pain locus exposure to the poly- or monochromatic PL of Bioptron devices.

The ordinate shows the duration of licking of the affected limb (s). The abscissa shows the observation duration (min).
Significance of difference with control over 60 min of observation: * $p< 0.05$; ** $p< 0.01$; *** $p< 0.001$.

was 53.7-68.5% of the similar response in animals not exposed to PL of the Bioptron device.

The reduction in the duration of the pain reaction after exposure to colored PL was especially noticeable in the second half hour. This is clearly shown in Fig. 6. The pain reaction of all the groups was more intense in the first 30 min. However, in the control mice, even in the second half hour, the duration of licking the pain locus remained rather long and was up to 394.8 sec (versus 547.3 s in the first 30 min). In mice that received a session of color therapy, this time was in the range of 86.7-190.2 s (after irradiation of the pain locus) or 118-256.2 s (after AP E-36 exposure to PL).

The results of our experiments showed that the monochromatic PL of all investigated wavelength ranges had statistical significance as to weaken pain. When PL was applied to AP E-36, analgesia ranged from 28% to 54.5%, and to the pain locus—from 31.5% to 64.1% (Fig. 7). In both cases, red light produced the most potent analgesic effect: 54.5% and 64.1%, respectively.

It was interesting to find out whether the differences between the most effective red light and other colors of the spectrum had statistical significance. The total (for 60 min of observation) values of the duration of licking of the affected limb (the main indicator of pain in the formalin test) are shown in Fig. 8 and in Table 1. When the pain locus was exposed to light directly,

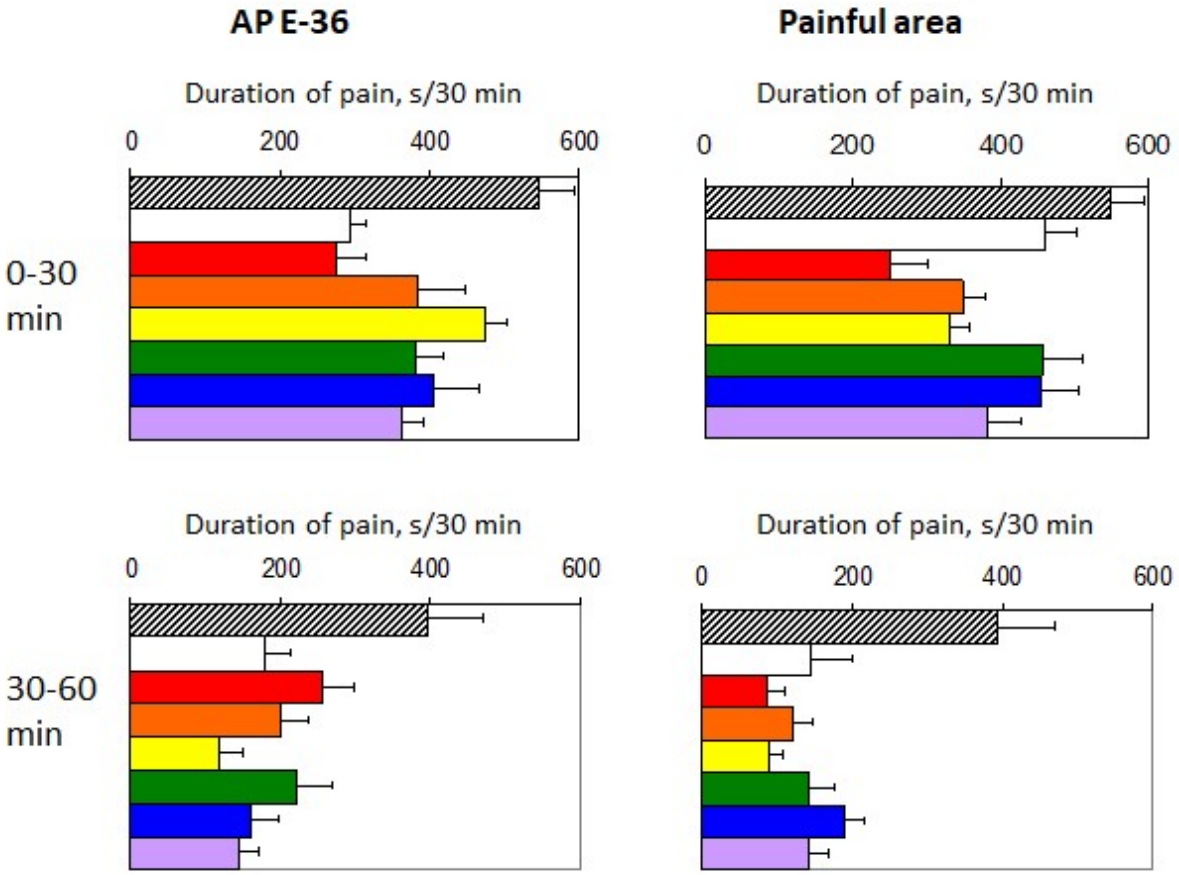

Fig. 6 The duration of the tonic pain reaction in animals in the first half hour and in the second half hour after 10 min of AP E-36 or the pain locus exposure to monochromatic light with different wavelengths.
For comparison, the response is shown in the group where polychromatic (white) light or no light was applied (shaded bar control).

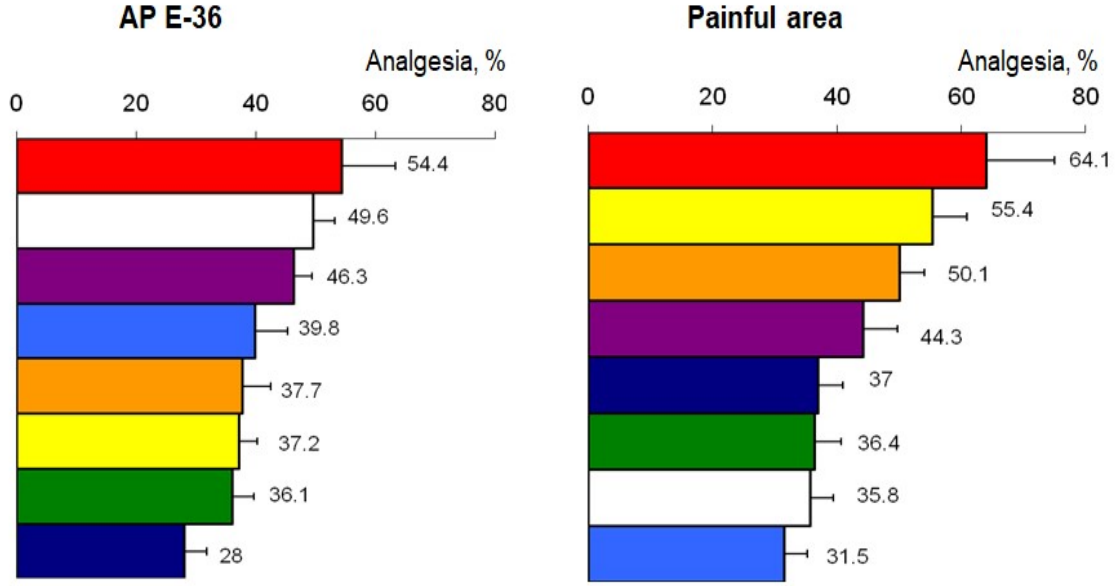

Fig. 7 Dependence of the analgesic effect of PL on monochromatic and polychromatic (white) wavelengths of BIOPTRON device [33].
Numbers above the bars—mean analgesia (%) in different groups.

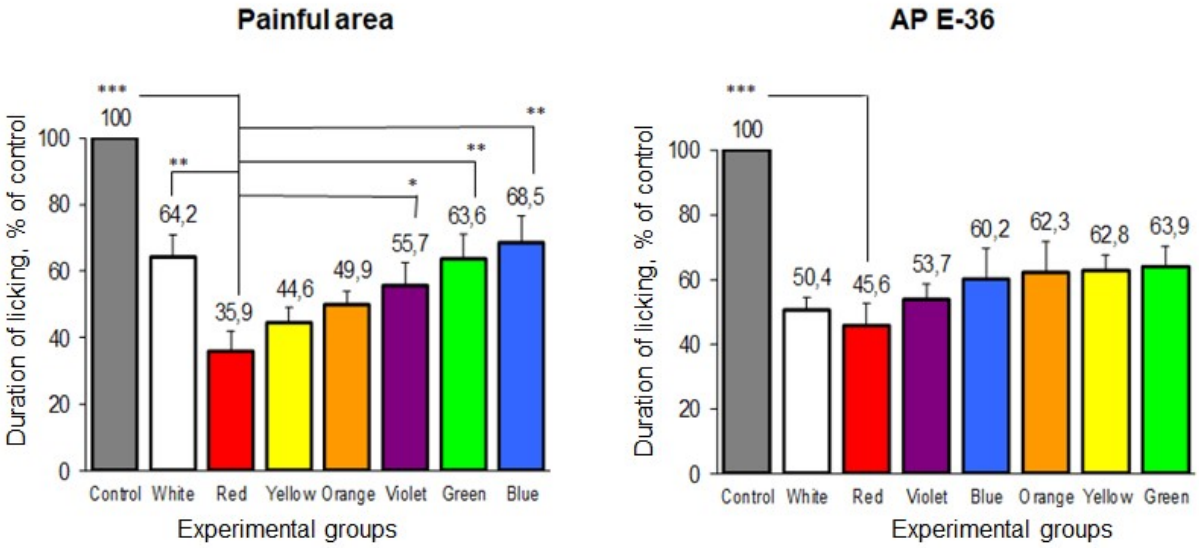

Fig. 8 Pain reactions in animals after application of different ranges of monochromatic or polychromatic (white) light in comparison with red light.

Mean (± SEM) values of licking time (% of the control value) for 60 min period of observation after exposures of painful area or AP E-36 to light.

Significant difference from the red light group: * $p< 0.05$, ** $p< 0.01$, *** $p< 0.001$.

differences were observed even within the color ranges. They were statistically significant when comparison was between the most effective red light and the three colors of the "cold" part of the spectrum (green, blue, violet). Red light had better statistical significance than polychromatic light ($p<0.01$). No significant differences were found between red and two other "warm" colors of the spectrum (yellow, orange); their analgesic efficacy was close to red light. They shortened the pain response by 50.1-64.1%, while the "cold" colors—only by 31.5-44.3%. These data indicate the leading role of red light in its topical

Table1 Differences between the duration of pain response in the group of mice exposed to the red color and in other experimental groups.

Color	After 10 min application of Bioptron light			
	To AP E-36		To the locus of pain	
	Licking, s	t-stud	Licking, s	t-stud
Red	429.8±65.8	-	338.2±57.4	-
White	471.3±38.0	0.55	604.7±63.5**	3.11
Orange	587.0±89.6	1.41	470.0±37.4	1.92
Yellow	591.4±44.7	2.03	420.6±41.2	1.17
Green	601.8±60.2	1.93	599.2±70.9**	2.86
Blue	566.9±88.6	1.24	645.1±76.5**	3.21
Violet	549.7±42.7	1.53	524.6±64.2*	2.16

Statistical significance of the difference between the group where the red light was used and other experimental groups: * $p< 0.05$; ** $p< 0.01$.

T-stud—student test.

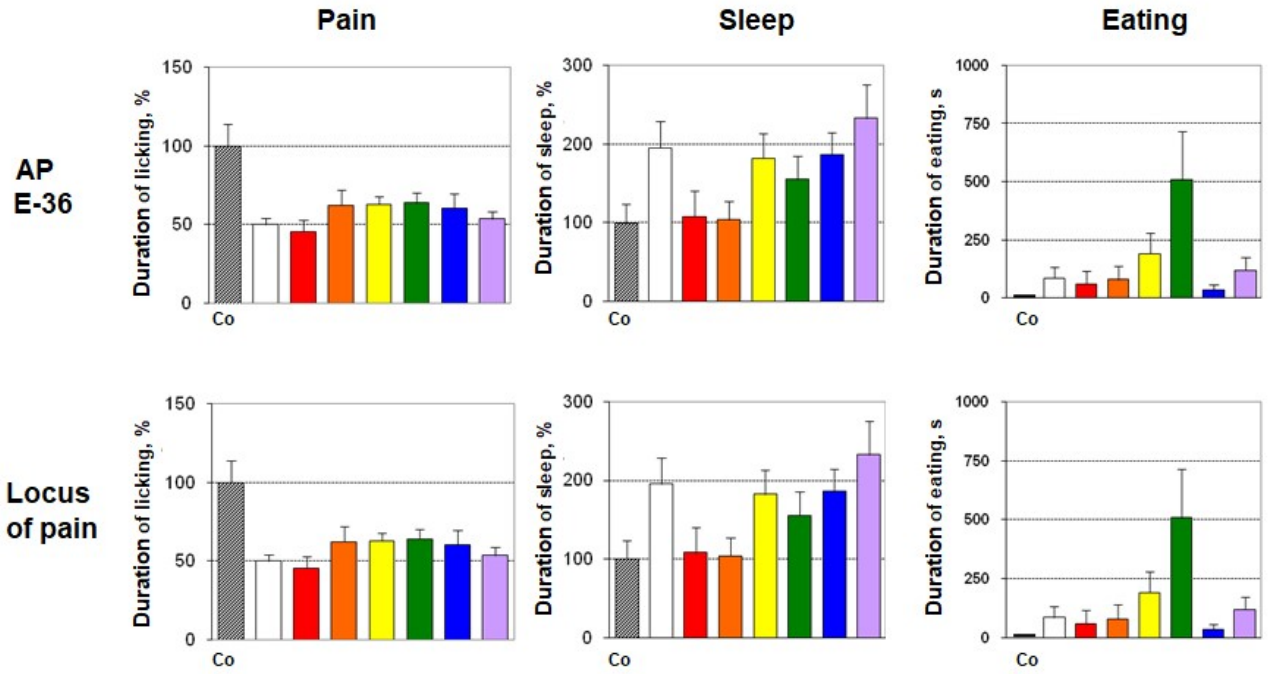

Fig. 9 Comparison of changes in the duration of pain and non-pain behavioral reactions in response to the action of poly- and monochromatic PL on the pain locus or AP E-36.

Co—data of the control group (pain without light application). The duration of taking food per hour of observation is indicated in s, the other two reactions are in % of control (taken as 100%).

application, and this was confirmed by the clinical experience gained with the use of red light of LASER or LED origin.

Under the influence of colored PL changes also occurred in non-pain behavioral reactions, in particular, eating behavior and sleep duration (Fig. 9).

Animals that received a 10-minute session of color therapy immediately after creating a locus of pain slept longer than control animals (Fig. 10). If in control animals the duration of sleep averaged 557.3 s, then in experimental animals it was: after AP E-36 exposure to PL—from 577.9 to 1,295.3 s, and after irradiation of the pain locus—from 757.2 to 1,271.2 s. It should also be noted that their sleep was calmer, without frequent shudders and awakenings, characteristic for the animals of the control group. This indicated a reduction in pain.

Fig. 8 shows that different wavelengths of light significantly altered the feeding behavior of animals. Of the 10 control individuals, only one touched food for a very short time. In the experimental groups grew the number of animals taking food (up to 5-7); the duration of their feeding process also became longer. The activation of the eating behavior indicated that the pain relieved after the light applications. Let us especially note the role of green color, under the influence of which food consumption increased. This is important for the clinical setting because patients can, through the activation of appetite, more easily compensate the consequences of pathological process.

4. Discussion

Prior to the beginning of our studies, there was no objective evidence of the effect of colored PL on experimentally induced pain syndromes. The above data are the first to reveal the analgesic effect of the main monochromatic ranges of light, as well as to conduct a comparative quantitative assessment of the effectiveness of PL with different wavelengths. In animals that received a single 10-minute exposure to color PL on AP or on the pain locus, according to the data obtained, a decrease in pain response was

observed within 10-20 min, whereas in the control group, the pain increased during this period of time. In the case of analgesic AP E-36 exposure to all wavelength ranges, we recorded statistical significance of pain relief. If the light was directed right to the locus of pain, a significant analgesic effect was also obtained. However, for the blue color, despite the shortening of the duration of the pain reaction (up to 645.1±76.5 s), the difference with the control (941.1±130.9 s) did not have statistical significance (p>0.05). Perhaps, in this case, the lower power density is of importance, which has arisen due to the attenuating effect of the blue filter. This is confirmed by special measurements: if for most ranges it was recorded within 23.0-51.0 mW/cm^2, for blue, only a value of 15.0-16.0 mW/cm^2 was obtained.

We drew attention to the fact that when the PL color was applied to the analgesic AP, there were no statistically significant differences between the effects of the use of different wavelength ranges: they all weakened the pain response by 36.1-54.4%. This fact confirms our earlier proposed hypothesis [34] that APs are electromagnetoreceptors. This hypothesis is also supported by experimental data of a high analgesic effect in cases of AP E-36 exposure to PL and in cases of exposure to electromagnetic waves of other frequencies [35-37]. Apparently, AP can be activated by electromagnetic waves of different (including light) ranges, but the final effect is due to the triggering of the brain's own pain-relieving systems, which leads to suppression of the transmission of pain impulses at the neural level. This mechanism has been verified in relation to electroacupuncture [12, 38]. Recent human studies have shown that the PL of the Bioptron device alters the conductivity of AP [39].

If we consider the effect of colored PL on the pain locus, we can see that a statistically significant analgesic effect was obtained for both poly- and all other monochromatic light variants studied by us, with the exception of blue.

The mechanism of the local analgesic effect of light in the case of its application to the locus of pain differs from the systemic (acupuncture) one. In this case, local changes play the main role. It is known that when applied to the skin, PL improves blood and lymph circulation, activates metabolic processes, and accelerates tissue metabolism [40]. This results in an anti-inflammatory effect, which in turn leads to a decrease in tissue edema and pain relief.

On the other hand, recent studies have shown that a decrease in the sensitivity of nerve endings is determined at the locus of exposure to PL [40]. For example, when the skin of the paw of an anesthetized rat was exposed to PL, we observed a prolonged inhibition of the background activity in the afferent fibers of the cutaneous nerve, while when this locus was exposed to unpolarized light of the same intensity, biphasic changes occurred [41]. When the synthesis of nitrogen monoxide was blocked, afferent impulses were also suppressed [42].

In our experiments, when PL was exposed directly to the pain locus, warm colors of the spectrum (red, yellow, orange) shortened the pain response by 50.1-64.1%, while cold colors (blue, green, violet) only by 31.5%-44.3%. The differences between the most effective red light and the three colors of the cold spectrum (green, blue, violet) were statistically significant.

Red PL light had more efficient statistical significance than polychromatic PL, although the power density of these two versions of light was the same (45.0 mW/cm^2). No significant differences were found between red and two other warm colors of the spectrum (yellow, orange). These data suggest that there are combinations in the skin that provide selective filtering of frequencies in the optical range. It is possible that this selectivity is provided by numerous carotenoids, which have been shown to perform a number of independent biological functions, including spectral filtering [11, 43]. Retinylidenes of photoreceptor cells, which are found not only in the

retina of the eye, but also in various tissues, including the skin of animals and humans, can also carry out partial filtering of light waves. Retinylidenes are suggested to include photo signal-driven ion transport, as well as a number of other processes [44].

The greatest analgesic effect of red light is possibly due to the fact that, along with the above mechanisms of action, together with the presence of near infrared radiation, it has a certain warming effect, which increases the blood flow rate, changes the rheological properties (increases fluidity) of blood [45] and creates an additional anti-inflammatory effect. Although the light of the Bioptron device, due to its low intensity (about 40 mW/cm^2), increases the skin temperature at the locus of exposure insignificantly, the thermal effect is undoubtedly present. It is caused by the presence of electromagnetic radiation in polychromatic light with wavelengths corresponding to the red and infrared spectrum.

The results of this work indicate that monochromatic fragments of PL have higher therapeutic potential than polychromatic PL [46, 47]. This can be explained by the removal of mutual neutralization of the red and blue parts of the spectrum, as a result of which the properties of each isolated range appear more noticeably. This confirms the previously existing empirical experience of using colored light in practical medicine.

5. Clinical Aspect of PL Color Therapy

Based on the foregoing, the use of specialized treatment regimens (programs) for clinical practice becomes justified. We regard the term “Program” as a specific set of factors, the use of which leads to a clinical outcome. Mandatory use of the main components of the Program supposes: “color + frequency + exposure + localization of the application + number of sessions”. Within each Program, variations are created (for example, by color, localization of the application, etc.), specific to the treatment of specific disorders. According to this scheme, we have previously prepared Treatment Programs for the light of the Bioptron, Medolight-Z4L and Medolight BluDoc Z5L-C [48-50] devices. The experience of their application has shown the feasibility of this approach. For doctors working in a narrow specialization, there is considerable scope for professional creativity and accumulation of experience.

Here is one of the schemes according to which clinical experience has been accumulated in relation to Bioptron devices (Fig. 10).

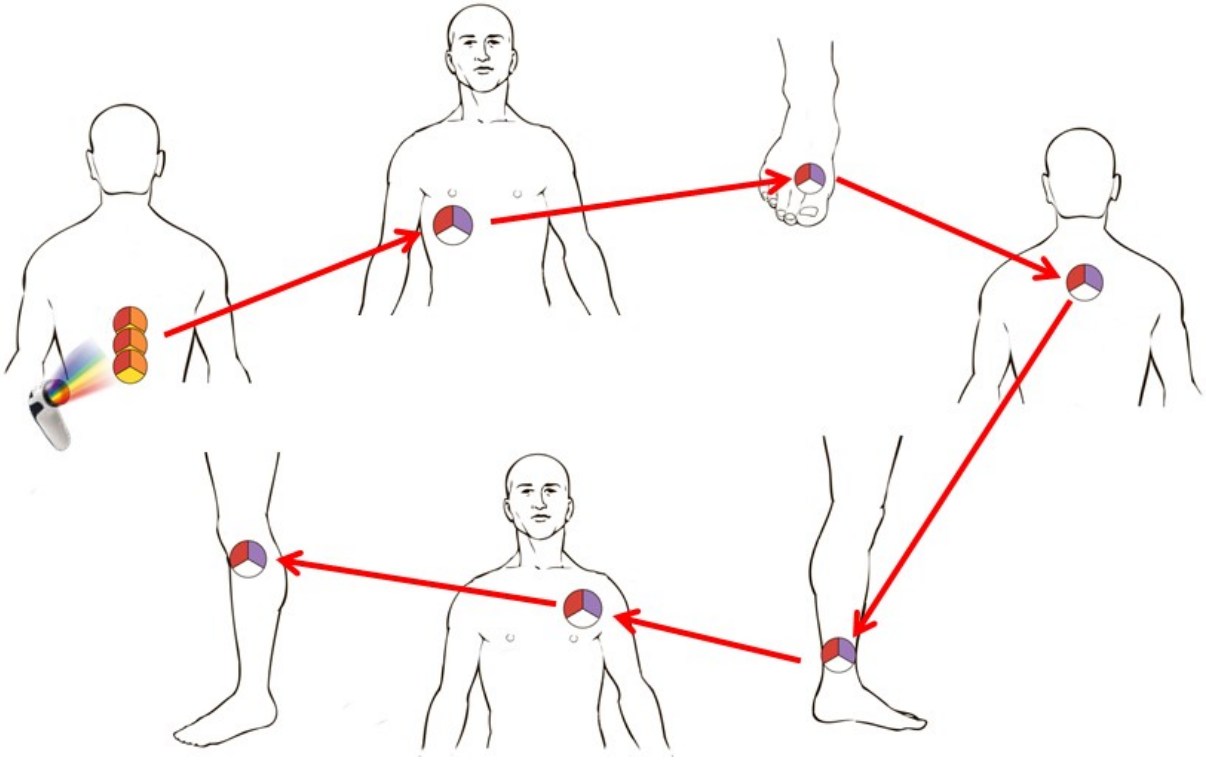

Fig. 10 Treatment scheme for acute intercostal neuralgia [48].
The primary application is aimed at the pain center, the subsequent ones—at the zones of pain irradiation and pain-relieving AP points. One of the indicated colors (red, orange, white, violet) is used; the exposure of each zone is 10 min. Possible fixation of the effect with drugs containing ethereal oils.

Clinical experience shows that it is problematic to obtain objective data on the severity of pain or the effectiveness of an analgesic factor in humans. The visual analogue scale (VAS pain) is often used [51], although everyone understands that subjective data inherent in a particular patient will be obtained.

Here is a case report on the result of analgesic treatment for a patient with a diagnosis “Shrapnel fracture of the fifth metacarpal bone with displacement”. Under local anesthesia, reduction of bone fragments and their fixation with a titanium plate was done. After the operation severe pain syndrome was observed. To relieve pain, the patient received pharmacological analgesia for the first 4 days (dexalgin). Then, instead of a pharmacological analgesic, treatment was performed with red PL (Bioptron device with a red absorption filter of a glass blower origin). The application of light to the locus of pain was impossible due to the immobilizing dressing. Each day, the patient received one 10-minute session of red PL on AP Gl-4 (He-Gu).The duration of pain was measured using special computer program, which made it possible to assess pain quantitatively (in seconds for 30 min of registration). For 3 days of observation, pain decreased by 48.2% in relation to the control data, as well as a progressive reduction of pain during the first 3 days of color therapy (Fig. 11).

The arsenal of a specialist in physical rehabilitation (physiotherapist) has increased due to the expansion of variations in physical factors (color of light, their frequency and exposure), combined into targeted treatment programs. The creation of such programs, taking into account the diagnoses and the duration of the courses, is a separate large task. However, now we can already predict that the indications for color therapy may include pain syndromes, inflammatory skin disorders, skin manifestations of allergic conditions, cosmetic defects, inflammatory joint disorders, consequences of musculoskeletal system injuries, inflammatory diseases of the nose,

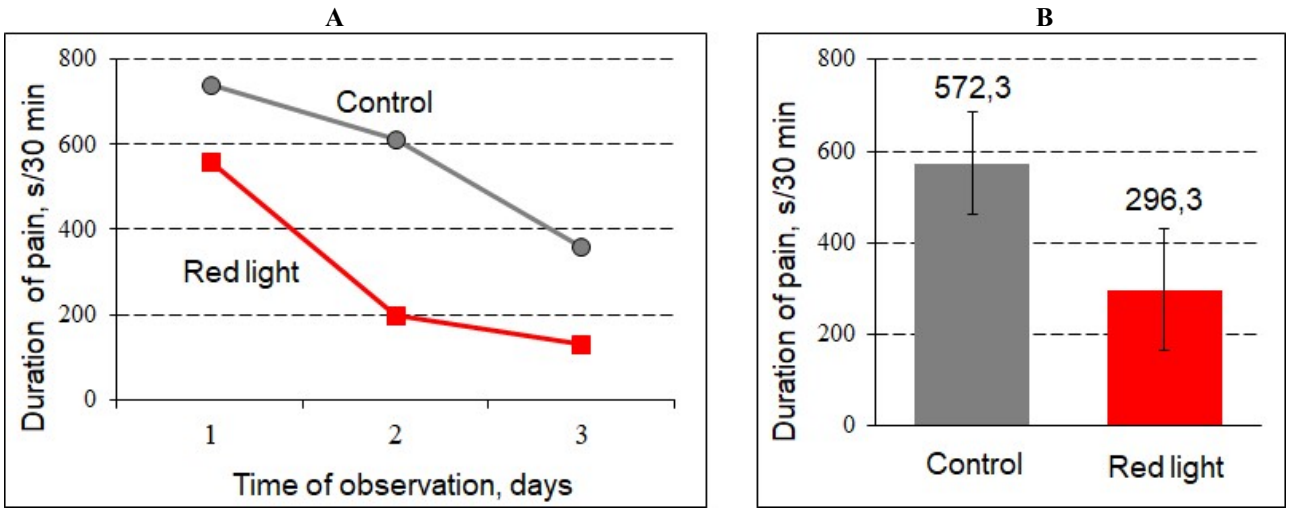

Fig. 11 Influence of red polarized light of the Bioptron device (10-minute application on AP He-Gu) on postoperative pain syndrome in patient T.

(A) Dynamics of the pain process; (B) The average values of the duration of pain before and after the session of light therapy.

throat, earand mouth, glaucoma, inflammatory and degenerative eye diseases, stress and depressive conditions, neonatal jaundice, disorders that are traditionally corrected by the polychromatic light of Bioptron devices (wound treatment, immunocorrection, etc.).

Opportunities have appeared for the targeted use of the full palette of PL wavelengths to activate multifunctional zones in order to obtain effects at the level of the whole organism. On the other hand, approaches for the prevention of acute respiratory diseases, including COVID-19, have become popular by using the bactericidal effects of shortwave (blue) and polychromatic ranges of polarized or LED light [50, 52-54]. It is important for clinicians to understand the possibility of using local applications, activating biologically active zones and AP points, transcutaneous blood photomodification and combinations of these approaches to achieve the optimal therapeutic effect [55].

6. Conclusions

It has been experimentally verified that application of polychromatic PL pain weakened, statistically significant weakened pain, due to local reactions from the locus of pain and systemic processes triggered through the analgesic APs.

We revealed that the factors that significantly enhance the analgesic result of PL therapy are the polarization of light and the presence of the long-wavelength part of visible light.

When applying different PL wavelengths to AP E-36, it was noted that all seven colors of the spectrum, as well as polychromatic PL, effectively suppressed pain; analgesia was 36.1-54.4%, and no statistically significant differences were found between the reactions.

It has been experimentally proven that APs can respond to each of the main monochromatic ranges of sunlight and receive reactions that can be used for medicinal purposes.

When PL is applied to the pain locus in the long-wavelength range (red, yellow, orange), the pain response was shortened by 50.1-64.1%, while the other colors (blue, green, purple) weakened pain only by 31.5- 44.3%. The differences between them and the most effective red light are statistically significant. Red light was also more effective than polychromatic PL, and no significant differences were found between red, orange and yellow colors.

Clinical observations of human pain before and after the application of PL revealed dynamics similar to those obtained in animals. Analgesia after 3-day application of red light to AP He-Gu in a patient with post-traumatic pain reached 48.2%. We emphasize the efficacy, simplicity and safety of the PL color clinical application.

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