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Innovative Light Therapy: 3. Correction of the Acute Viral Respiratory Diseases Using Biophysical Capabilities of Bioptron-PILER-Light (Review)

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Abstract: The review contains information about a new therapeutic technology—light therapy, using Bioptron devices for the treatment of acute viral respiratory diseases including COVID-19. It is based on the use of a biophysical factor that weakens the course of the main pathological process: polarized polychromatic light (PL) with an infrared component. There are described mechanisms of correction of disorders at the expense of local cellular effects and systemic effects through the influence on blood structures and acupuncture points.

The positive contribution of PL applications to the airways during infection with high doses of influenza virus has been experimentally proven. There are described changes in immune variables, indicating the possibility of using percutaneous blood photo-modification to correct inflammatory processes, lipid peroxidation in erythrocyte membranes and plasma, and improve the rheological properties of blood. Evidence has been found that PL treatment in combination with other immunotropic drugs helps to restore immunological variables and reduce associated allergic reactions.

It is revealed the effectiveness of combined therapy by PL and antioxidants. In this case, the bronchial passability increased, the compensation of bronchial hyperreactivity improved, the respiratory moisture release and the content of immunoglobulins A and G in the blood serum increased.

The combined use of PL and a non-steroidal anti-inflammatory analgesic (ibuprofen) has also proved to be effective. The results of a comparative study indicate that the anti-inflammatory and analgesic effects of PL are comparable to the effect of moderate doses of this drug, and their combined use is more effective in suppressing pain than an isolated analgesic of the same dose.

It is confirmed the presence of biological responses arising from the application of PL to receptor zones (acupuncture points) sensitive to electromagnetic signals. By studying the responses to acute, tonic and visceral pain in animals, statistically significant analgesia was revealed after PL stimulation of acupuncture points. Application of PL to biologically active or indifferent areas in humans has shown the advantage of areas related to acupuncture. This expands the therapeutic possibilities arising from the use of active zones and allows obtaining reliable clinical results in patients with respiratory diseases. The possibility of using the monochromatic and fullerene PL ranges has been experimentally substantiated.

Among the personal protective equipment for the eyes of patients during light procedures, especially children, it is advisable to reduce the visual light load and protect the eyes by using glasses with fullerene filters.

This review is the evidence of testing polychromatic polarized light capabilities with a positive result, which is the basis for the inclusion of PL-therapy techniques in the protocol schemes for the prevention and treatment of acute viral respiratory diseases.

Key words: Bioptron® Quantum Hyperlight®, Tesla Hyperlight Eyewear®, THE®-glasses, fullerene, influenza virus, COVID-19, immunity, respiration, antioxidants, acupuncture point, light therapy, treatment of acute respiratory diseases.

1. Introduction

The COVID-19 influenza pandemic has forced humankind to mobilize overt and implicit reserves and turn to methods that were previously consistently ignored or not understood. A lot of fantastic recipes have surfaced, and in this heap of information, it is important not to lose pearls and diamonds.

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Physiotherapy methods include actinotherapy (treatment with different types of radiation), of which light therapy is a part. These methods are considered low intensity because the active factor, with the exception of the far UV ranges, does not have a damaging effect. Accordingly, the therapeutic effect after the first sessions may not be noticeable. Therefore, some specialists or official medical institutions that need a quick, intensive result ignore it. However, this does not mean that the therapeutic outcome does not exist.

Taking into account the specificity of the particularities of healthcare organization and approaches to the inclusion in treatment protocols in different countries indicates the diversity of lists of specific indications for which Bioptron light therapy can be used [1]. In some cases, experimental and clinical advances are being implemented with a delay, which reduces the effectiveness of medical care, especially when new diseases (COVID-19) appear, for which there are no sustainable treatment technologies.

Under these conditions, it is possible to apply the approach expressed in the Declaration on Good Off-Label Use Practice (GOLUP) [2]. These guidelines permit to prescribe off-label treatments, provided they comply with the ethical standards recommended by World Health Organization (WHO). The use of medicines and treatment methods for indications not approved by the state regulatory bodies and not mentioned in the instructions for use is advisable: (1) in case of a threat to the patient's life, (2) the absence of specific treatments, and (3) based on the analysis of scientific data on possible efficacy for a concrete patient. For example, in Ukraine, there is a Manual for Physicians approved by the Ministry of Health with a section and protocol for the treatment of influenza [3], experimental and clinical articles [4-9].

The personal experience of individual specialists is also presented, which characterizes the status of knowledge at the time of publication [10, 11].

1.1 Historical Steps

The first light source used for therapeutic or prophylactic purposes was sunlight. The scientific substantiation of this direction appeared at the beginning of the last century, when the Danish doctor N.R. Finsen was awarded the Nobel Prize for his contribution to the light therapy for skin diseases. In 50 years, the laser was invented and it turned out that its light could not only destroy, but also restore tissue. For medical purposes, narrow (monochromatic) ranges of red, ultraviolet, or infrared radiation spectra have proven to be effective. The researchers considered the light polarization to be an important indicator. In 1981, a group of Hungarian researchers created a device similar to a laser, with the difference that polarization was achieved in a more economical way, and the light was polychromatic, that is, it combined the visible and infrared ranges [12]. Based on this technical solution, the Bioptron family of light therapy devices was created.

1.2 Non-fiction Story

This happened in an ordinary kindergarten. In the fall, hardened and tanned children gather in a children's team in preschool or school institutions. The pink dreams of parents are shattered in a week or two, when someone starts to get sick, and the speed of micro-epidemics colds forces them to keep the child at home again and often treat hopelessly.

In one of the kindergartens in Kharkov, one of the nursery-teachers had a portable Bioptron device that produces healing light. The children of her group were sick like everyone else, but the wise nursery-teacher, every time the children returned from a walk with wet noses, shone on each nose, and it quickly stopped sniffing. When the results were summed up in the spring, it turned out that, in comparison with the control group, which was under normal conditions, acute viral respiratory infection was registered only in 67.5% of children, acute bronchitis—67.6%, otitis media—56.5%, sinusitis—58.3%, and in total 64.4% of children consulted a doctor [5]. Such a striking result has never been seen in the practice of nursing in a standard preschool institution.

The purpose of this review is to consider the possibilities of Bioptron technology from the point of view of prevention and treatment in the early stages of acute respiratory diseases, including the types of technology that provide this, what physical factors it creates and what mechanisms of local or systemic exposure cause positive effects. It is assumed that the characteristics of the optimal correction schemes are of practical importance for medical workers and users.

2. Methodical Aspect

2.1 General Possibilities of Devices Using Polarized Polychromatic Incoherent Light

The historically relatively short period of experimental and clinical observation [4, 13-21] showed that the effect of polychromatic polarized light on the human body is manifested by such preventive and therapeutic effects, as activation of regeneration processes, suppression of inflammation, pain, normalization of blood and immune processes. Such syndromes, in various combinations, are present in many diseases.

Therefore, in clinical practice, polarized polychromatic light has shown its effectiveness in desensitization, as a vasoactive, vegetotropic, psychotropic, analgesic agent, etc. The combination of this light with monochromatic or fullerene filters allows providing a narrowly targeted effect of a certain wave spectrum and getting the desired therapeutic effect [22-25]. This makes it possible to non-invasively enhance the influence of other physical methods, drug treatment, psychotherapy, physiotherapy exercises, rehabilitation, improve the care of patients of different ages by prescribing a variety of light therapy regimens [4, 25, 27, 28].

There are three models of certified light therapy devices, in which the light source is a broad-spectrum halogen lamp: Bioptron-MedAll, Bioptron-Pro-1 and Bioptron-2 (manufacturer: BIOPTRON AG, ZEPTER GROUP, Switzerland) [1]. Bioptron-MedAll (beam diameter 5 cm) is designed for small areas or for zone therapy targeting acupuncture points. Bioptron-Pro-1 (beam diameter 11 cm) provides higher performance of light therapy while maintaining compactness and mobility. Bioptron-2 (beam diameter 15 cm) due to the width of coverage is the best, for example, for the treatment of lesions of large areas of the skin, in burn therapy, for immune normalization and the like. Each of the Bioptron devices is equipped with a built-in timer that regulates the duration of the procedure; it can be used at home and in professional medical practice (polyclinic and inpatient medical institutions, children's institutions, cosmetology rooms, fitness centers, etc.).

2.2 Light Characteristics of Bioptron Devices

The light of Bioptron devices, which has the physical name PILER-light (PL) (Polarized, Polychromatic, Incoherent, Low Energy Radiation) [3, 4], or the general name Bioptron® Quantum Hyperlight® (hyperpolarized light) [1], has the same properties regardless of the model.

- *Polarization:* unlike the multidirectional multiple reflected motions of photons of ordinary scattered light, the polarized waves are ordered, unidirectional and vibrate in the same plane. This property causes a higher penetrating ability of light electromagnetic waves into the skin, superficial vascular and nervous structures without accompanying damage. The use of a fullerene filter adds toroidal hyperpolarization, which enhances the biological effect.
- *Polychromatic:* covers the full range of the visible and part of the infrared spectrum (480-3,400 nm). There is no ultraviolet radiation, but there is an additional opportunity to obtain the violet and near soft ultraviolet spectrum (UVA + PL, 320-3,400 nm), which are used with appropriate precautions in physiotherapy. The use of a fullerene filter creates a neutral + red spectrum (550-3,400 nm).
- *Incoherence:* PL electromagnetic waves are

unsynchronized, out of phase, that is, they oscillate at different frequencies.

- *Low energy:* in a wide electromagnetic range (visible light and near infrared radiation), each of the wavelength ranges does not add up. This means that the energies of individual wavelengths do not exceed the total energy of the total luminous flux. Therefore, light has a constant low energy density and is not biologically destructive. In the fullerene light, the energy of the entire spectrum is reduced and its blue part is absent.
- *Monochromaticity (optional):* depending on the color or structure of the light filter that can be used with the BIOPTRON device (red, orange, yellow, green, blue, indigo, violet), it is possible to obtain polarized monochromatic light of the corresponding part of the spectrum. Partially similar spectral packets can be obtained using LEDs or their combinations.

Physical characteristics of the PL (480-3,400 nm, polarization up to 95%, power density 40 mW/cm^2, light energy 2.4 J/cm^2/min, light intensity—10,000-2,000 Lx.

2.3 General Mechanisms of the PILER-Light Action

A change in the energy state of molecules can occur only upon absorption of a light quantum. The energy of absorbed quanta in biological molecules changes their functional state. This makes it possible to coordinate activity with numerous structures in living cells and provide activity of enzymes in them, metabolism, which has a decisive influence on the processes of restoring normal functions of the body.

The main mechanisms of PL biological reactions have been experimentally established: local (in the zone of light application) restoration of the functions of skin cells or mucous membranes, percutaneous influence on moving capillary blood, as well as on other structures of the dermal layer, and activation of reflexogenic zones (acupuncture points) [29, 30]. Thus, the biological effect of PL is manifested at the molecular, cellular and systemic levels. Experimental and clinical models are considered below, which made it possible to detail and describe the effects of PL.

3. The Main Areas of PILER-Light Application with Therapeutic and Prophylactic Purposes

The basic indications cover the main therapeutic possibilities of PL [3-9]. These include the correction of many types of pathology of the skin and mucous membranes, positive modification of immunodeficiency states, treatment of wounds and the consequences of trauma, pain relief, normalization of the electromagnetic balance of the visceral organs and the central nervous system. A large number of disorders fall within the scope of physical therapy. Specific therapeutic possibilities and indications are determined based on the understanding of PL action mechanisms in different spectral ranges (white polychromatic, seven color monochromatic, shortwave infrared, long wave ultraviolet, and fullerene). They, in turn, determine the lists of conditions and diseases, as well as treatment regimens that are recommended for practical use.

3.1 Colds: General Pathophysiology

Frequent diseases that are activated during the cold season are a variety of colds of the nose and sinuses, throat, ear, trachea, and lungs. Influenza belongs to acute respiratory diseases, among which it occupies a leading place. The causative agents of these disorders are adenoviruses, various strains of the virus influenza and coronaviruses, among which the most aggressive is *SARS-CoV-2* and its mutants [31].

The danger of COVID-19 lies in its flu-likeness, but in fact, poly organics, i.e. ability to specifically affect not only the respiratory system, but also the kidneys, heart, liver, brain, blood, immune system, to create hypoxic and cytokine stress [32-34]. Influenza stimulates the synthesis of interferon, COVID-19 suppresses it, as it does to the entire immune system, and the cytokine storm is specific only for COVID-19

[11, 34, 35]. The main entrance gate is the epithelium of the airways, as well as the mucous membrane of the eye. As means of distribution, including for COVID-19, there are recognized air-drop, air-dust and contact. Influenza viruses undergo natural mutations every season. In this regard, those who become ill accumulate antibodies, but immunity arises only to a certain strain of the virus, and it is insufficient with the emergence of a new strain. The disease is characterized by acute rhinitis, high body temperature, catarrhal changes of the airways, and this is typical for both influenza and COVID-19. However, with COVID-19, the infected person is the most dangerous during the incubation period and in the first days of symptoms. The progress of the inflammatory process extends to the bronchioles and alveoli, gives rise to pneumonia. A feature of coronavirus infection is the primary lesion of the conductive zone of the lungs, causing a secondary violation of their respiratory function.

Against this background, in response to the action of circulating fragments of the virus increases the negative immune response (secretion of cytokines). The mosaicity of hypoxic zones in the whole organism increases, with microcirculation disorders in the lungs and parenchymal organs (kidneys, liver, etc.), especially if there are initial pathophysiological changes in them. The patient’s condition is aggravated by concomitant metabolic disorders, such as obesity. Lipid peroxidation increases, especially suffer the membranes of blood cells, in the first term erythrocytes, micro-thrombosis occurs. This significantly impairs the transport of oxygen and carbon dioxide. Hypoxemia and hypercapnia increase. As a response to inflammation, there develop fibrous growths, the endothelium is damaged, thrombosis increases, which further disrupt gas exchange in the lungs. There appears a pathological vicious circle.

All this is accompanied by the development of a stress state, one of the components of which is the systemic stress of adaptation processes and a violation of the electromagnetic balance. Each patient may have an individual pattern of disorders, but their dynamics obey the general laws first noticed by Selye [36]. A pandemic is an extreme event with a flexible scale from individual to population. Typical dynamics were noted under conditions of physiological stress (prolonged stay under water, hyperbaric chambers, in space, in extreme zones) and pathological stress (ionizing radiation, systemic diseases of internal organs) [21, 37-40].

With a favorable ending, there are naturally observed phases of initial adaptation, steady state (flowering of the clinical picture), initial disadaptation (fracture/degradation of the pathological process), readaptation with transitional states in the form of damped oscillations (with waves of micro-recurrences). The duration and severity of these phases depend on the characteristics of the stressor, its intensity and duration of action. They will be influenced by the individual capabilities of the body and therapeutic measures. At the population level, one can see similar dynamics, which, hypothetically, can be applied to the coronavirus pandemic process (Fig. 1). Thus, this scheme can be viewed from the point of view of a pandemic in a planetary aspect and from a narrowly individual position that reflects the dynamics in relation to a particular patient.

3.2 Possibilities of PILER-Light in the Treatment of Viral Etiology Diseases

Interest in the search for methods of prevention and adjuvant treatment of acute respiratory diseases has always existed, and it is increasing in connection with the emergence of new strains of “traditional” influenza viruses or previously unexplored aggressive types of it, such as SARS-CoV-2. We will review the results of studies that, although they are devoted to the previous generation of virus influenza, are nevertheless directly relevant to the topic of this review.

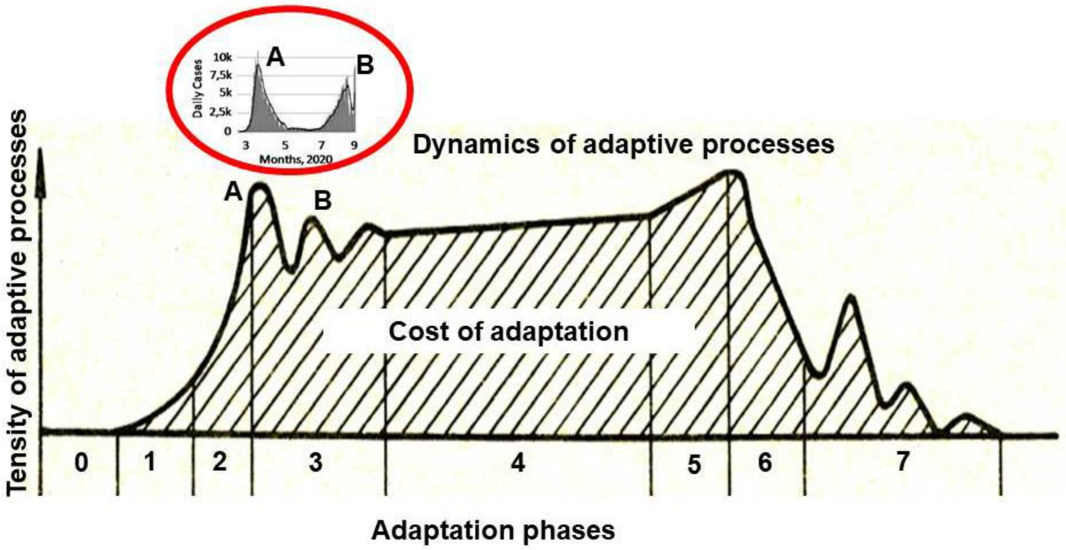
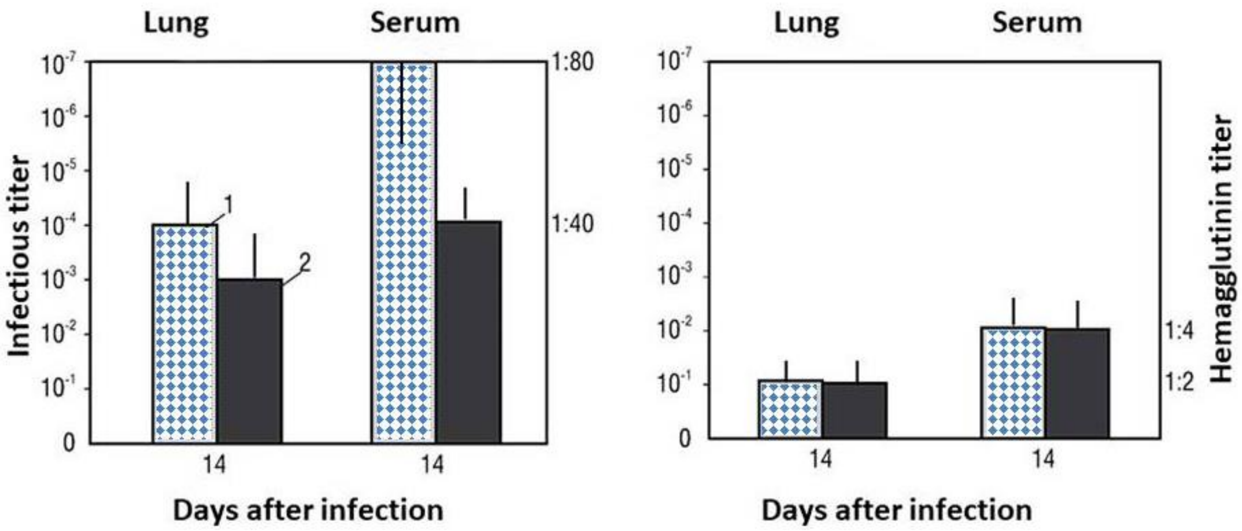


Fig. 1 Tension of individual-populate adaptation processes during extreme situations [37].
0—relative health, 1-2—incubation phase (infection and accumulation of the virus), 3—initial phase ("waves") of manifestations, 4—phase of the clinical picture flourishing, 5—phase of turning point/degradation of the process, 7—maladaptive-readaptation phase with waves of micro-recurrences; top—the number of the Daily Cases dynamics (incidence of COVID-19) for the period March-September (Spain) [41]: A—the first wave of the pandemic, B—the second wave of the pandemic.

There were investigated [6, 42] the consequences of laboratory animals (330 white Balb mice) infection with lethal and sublethal doses of influenza virus AP/R/8/34 (H1N1) depending on the PL applications. The adapted influenza virus (4 passages) had dilutions with infectious titers of 10-1 LD_{50} 0.1 mL (100% animal mortality) and 10-2 LD_{50} 0.1 mL (50% animal mortality). We used 6-minute daily PL sessions to the head area and mucous membranes and acupuncture points. Control/placebo groups received 0.9% NaCl solution, intact uninfected and infected groups without light applications. On days 5, 6, 7 and 14, animals were selected to determine in the lung homogenate and blood serum the protease and inhibitory activity of the virus, its hemagglutinin, protein, and the infectious activity of the virus. The influenza virus infectious titer in the lungs and blood serum was determined by infecting 160 of 10-11-day-old chicken embryos and evaluated in embryonic infectious doses at which 50% of the embryos die in response to the virus injection.

Studies have shown that with a lethal dose of the influenza virus, there was a rapid accumulation of infectious and hemagglutinating activity in the lungs, the total protein increased at the beginning of the infection, and by the time the animals died, its amount sharply decreased. The mortality rate of intact animals on the 6th day after infection was 100%. In the group with the use of PL applications, a delay in the multiplication of the virus was revealed in 1 day, when the infectious and hemagglutinating activity in the lungs became lower than the control data. As a result, 20% of the animals survived on the 14th day.

In Fig. 2 there are presented data on the use of PL at a sublethal dose of the virus. On the 14th day, 50% of the animals remained alive, in which the infectious titer of the virus in the lungs was 10^{-3}, and in the blood serum—10^{-4}. No changes in lung protein content were observed. Hemagglutinating activity in the lungs had a titer of 1:40, and in blood serum—1:80. In the group that received a sublethal dose of the virus, after a course of light therapy, 80% remained alive. In the lungs and blood serum of such animals, infectious/hemagglutinating activity was noted in insignificant amounts (10^{-1}/1:2 and 10^{-2}/1:4, respectively).



(a) (b)

Fig. 2 Infectious and hemagglutinating activity of lungs and blood serum of animals.
a—infected with sublethal dose of influenza virus AP/R/8/34 (control); b—those who underwent a course of treatment by PL [6]; 1—hemagglutinin titer, 2—infectious titer.

In separate series of studies carried out according to a similar scheme, the zone of light application was changed: the influence on acupuncture points XH1/14, XH1/4, VI 11/43, VII/43 [43] was applied. The effect of PL on the acupuncture points of mice had little protective effect as only 20% of the experimental animals survived, which the authors associate with a decrease in the surface area and radiation dose.

In studies on 50 volunteers [44] it was shown that due to the application of PL to the frontal and maxillary sinuses, tonsils and sternum in patients with determined diagnoses (acute adenovirus infection and seasonal flu), the duration of clinical and intoxication symptoms was reduced on the 2nd-3rd days. In patients with initial manifestations of a respiratory infection, positive dynamics was noted after 2-3 sessions: edema and hyperemia decreased, nasal breathing improved, which made it possible to refuse intranasal treatment with vasoconstrictor drugs in 50% of cases.

Additional evidence of the antiviral efficacy of PL is provided by clinical observations of 47 patients with herpes zoster [7]. Based on the dynamics of the clinical picture and immune variables, it was proven the acceleration of regression of herpetic foci by 19.7%, and the pain syndrome by 26.0%.

Thus, the results of virologic studies, which showed the reality of the therapeutic effect of PL even in animals infected with lethal and sublethal doses of the influenza virus, give rise to hope. Positive clinical results have also been observed in humans. The authors [7, 44] consider the main mechanism of the antiviral action of PL to be the activation of antiviral enzyme groups and stimulation of the immunity factors production.

3.3 Immune Hemic Aspect of PILER-Light Action

The therapeutic efficacy of PL is a consequence of many positive functional changes in the body. They are experimentally proven and are the basis for the use of PL for the purpose of biological correction [3, 4, 14, 15, 17, 19, 21, 24, 25, 45-48]. There is also evidence that a significant part of these effects is caused by a relatively small amount of photo-modified blood (about 2-3% of the total volume of circulating blood) [14, 49, 50]. The result is a structural change in the organization of blood cell membranes and activation of cellular function. Clinically important processes have been identified: proliferation, normalization of lipid peroxidation and antioxidant processes, activation of natural resistance factors, regulation of cellular and humoral immunity, etc. Many of them appear within a few hours after a phototherapeutic procedure. Corrective actions on the autonomic nervous, nociceptive and neurohormonal systems are realized through a different mechanism associated with the transport of electromagnetic signals through collagen structures [51-53].

Let us consider the experimental data revealing a block of hemic mechanisms that can be useful for the correction of respiratory disorders of viral etiology. A blood test was carried out in volunteers who received a single broad-beam light application (Bioptron-2) to the sacral zone. The authors [15, 50, 54-57] evaluated changes in the content of lipid peroxidation products in erythrocyte membranes and plasma (malondialdehyde), as well as in some rheological and immune variables of blood (*in vivo*). There were determined the coefficients of deformation and relative viscosity of erythrocytes. A similar study was also carried out *in vitro*. It was determined the phagocytic activity of monocytes, and calculated the integral coefficient of phagocytosis. It was studied the cytotoxic activity of natural cytotoxic cells, the content of proinflammatory cytokines (IL-1 and TNF-α) in plasma, and others. The control was a group of volunteers who were simulated by light application.

It was revealed a systemic decrease in lipid peroxidation in the blood system. For example, 15-30 minutes after PL application (70 subjects), the content of malondialdehyde in erythrocytes and circulating blood plasma decreased (Fig. 3). The changes caused by PL were manifested in the structural transformation of membrane lipids, changes in the rheological variables of erythrocytes. In particular, during the day after the light application, the deformability of erythrocytes increased, and the viscosity decreased in the entire volume of circulating blood in 88 and 82% of the examined, respectively (Fig. 4). In parallel, platelet disaggregation and an increase in the anticoagulant activity of plasma components were observed, which characterized the development of antithrombotic effect. This mechanism was separately investigated [58] and it was found that under the transcutaneous action of light, excessive agglutination of erythrocytes is weakened and their mobility increases. This led to an increase in regional hemodynamics, for example, in the liver area by 29%. In addition, the diffusion

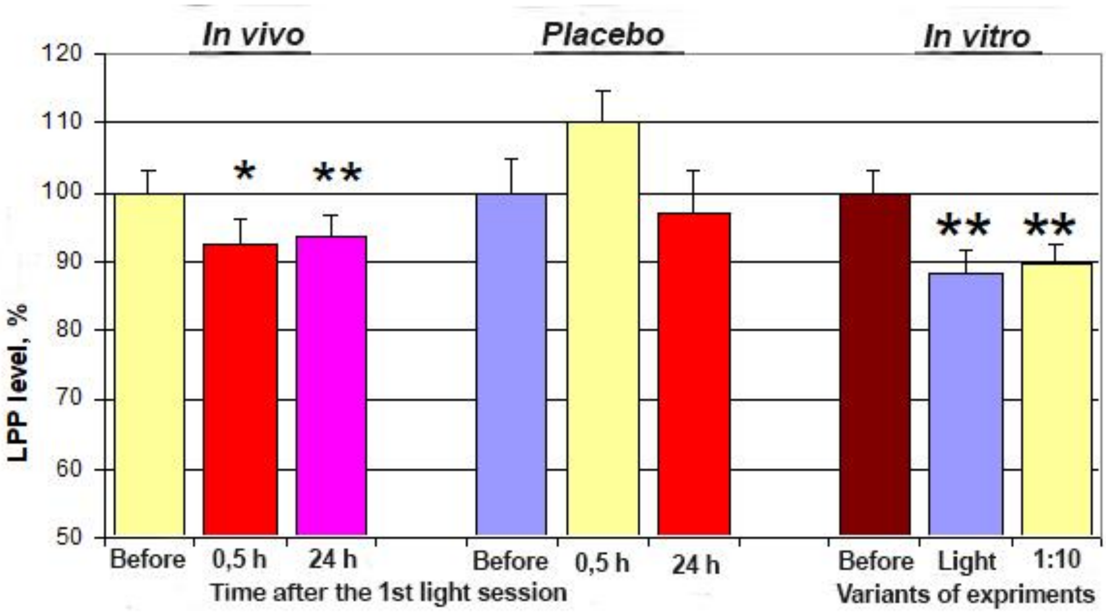


Fig. 3 Rapid decrease of the enhanced content of lipid peroxide products (LPP, m ± SE) in the surface membrane RBC [15]. Statistically significant difference from the initial level: * $p < 0.05$, ** $p < 0.01$.

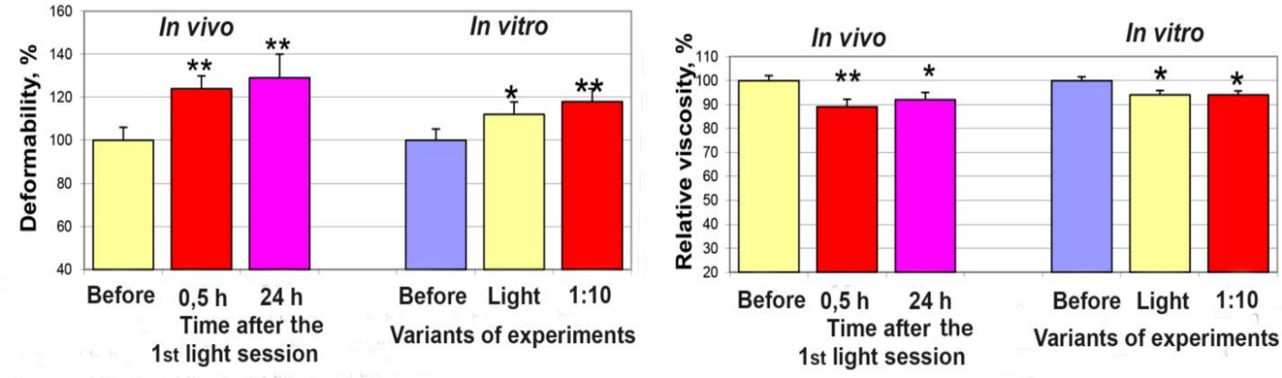


Fig. 4 Rapid improvement of rheological properties of RBC after irradiation with PILER-light of volunteers (*in vivo*) and their blood samples (*in vitro*) [15, 50].
Statistically significant difference from the initial level: * $p < 0.05$, ** $p < 0.01$.

surface of erythrocytes increased and their oxygen transport capacity improved. The resulting increase in microcirculation rate was also the result of activation of synthesis of nitric oxide (NO), a vasodilator secreted by vascular endothelial cells and platelets.

Against this background, the functional state of monocytes, natural cytotoxic cells and neutrophilic granulocytes and antioxidant activity of plasma normalized, and some shifts in the content of cytokines were also observed [15, 50, 54-57]. Individual differences in blood variables were revealed in subjects of both sexes and different ages (probably also with different health conditions). An inverse correlation was observed between the initial values of the indicators and their character, as well as the degree of their changes, after light applications. As a rule, initially low values blood variables increased after the PL session, while initially high values could decrease or remain at the same level. An analysis of variance of the studied variables revealed no decrease in their variability in 30 min after irradiation. However, after 24 hours, there was a tendency towards the normalization of such variables as the number of monocytes, natural cytotoxic cells and functional state of granulocytes: the Fisher coefficient increased from 1.15-1.81 (after 30 minutes) to 1.94-4.05 (after 24 hours).

Blood changes caused by transdermal exposure to PL were confirmed by the presence of similar changes resulting from *in vitro* blood irradiation. This allowed the authors to conclude that the observed changes were not the result of mediator's impact which were secreted by irradiated skin areas. Since light-induced changes in blood *in vivo* were also reproduced in *in-vitro* experiments, when irradiated blood was mixed in a ratio of 1:10 with non-irradiated autologous blood, the authors proposed a different mechanism of response. The processes observed in the entire volume of circulating blood are a consequence of the high activity of small portions of blood directly irradiated in the superficial skin vessels. Since the changes occurring in photo-modified blood *in vitro* and *in vivo* were very similar, this phenomenon was interpreted as a sign of the ability of blood to "relay" light-induced changes to the entire volume of intact circulating blood. This point of view was confirmed by similar data obtained earlier in patients after transfusion of a small amount of autologous blood irradiated under extracorporeal conditions with ultraviolet light (wavelengths 254, 280-400 nm) or laser irradiation of the visible range (633 nm) *in vivo* and *in vitro* [54-57].

The mechanism of "retransmission" of changes from irradiated blood to the entire volume of circulating blood can be explained as a result of direct contact of cells that play the role of signaling cells. It triggers modulation of the structural and functional state of non-irradiated cells. This is due to the modification of the surface of cells irradiated with light by changing the number of membrane markers and unmasking structural elements that are usually atypical for such cells in a “normal” state. Such modulations can include both glycoprotein changes on the cell surface and the release of various mediators and cytokines by activated blood cells [15]. As a result, the triggering role of cells that have received the energy of external quanta is to trigger many secondary positive functional changes in the body, for example, improving the rheological variables of blood and microcirculation, normalizing the transport of respiratory gases and gas exchange, detoxifying the blood, activating metabolic and proliferation processes, modulating nonspecific and antiviral protection.

Diseases characterized by various etiopathogenesis are accompanied by alterations in the structural and functional state of blood cell membranes. Rapidly developing changes in their membranes and membrane-dependent cellular functions are in most cases reversible; in this case, the duration of the effect was no more than 1-2 days. More stable alterations occurred after several transfusions of photo-modified blood. Analysis of variance confirmed not only the regulatory, but also the normalizing nature of such distant changes.

Among the changes developing in the entire circulating blood pool, it was found activation of all types of leukocytes (monocytes, lymphocytes, natural killer cells and granulocytes), which indicated the normalization of humoral immunity [15, 50, 54-57]. The functional state of monocytes, despite their relatively small number in the blood (3-7%), plays an important role in the formation of reactions of nonspecific resistance and immunity (control of proliferation, hemostasis, removal of old structures, as well as in the formation of a connection between the immune, nervous and endocrine systems). This group of mechanisms is important for obtaining a complete picture of defense processes. The activity and intensity of phagocytosis (the percentage of phagocytic cells and the average number of particles produced as a result of phagocytosis by each cell) were reflected through the integral index of phagocytosis. In 17 examined individuals, the activity and intensity of phagocytosis in 30 minutes after PL application increased in 62% of patients, and the integral phagocytosis index—in 69%.

The functional state of neutrophilic granulocytes, which make up 50-70% of all circulatory leukocytes, was assessed by their ability to degranulate and by an increase in the content of bactericidal cationic proteins, which are important in the system of nonspecific anti-infectious immunity. In 30 minutes after the PL session, a decrease in the content of bactericidal cationic proteins (by an average of 32%) occurred in almost 50% of the subjects. This undoubtedly indicated an increase in their content in blood plasma (in 33% of volunteers). Since the synthesis of all products secreted by granulocytes stops before their migration from the bone marrow into the bloodstream, the increase in the content of bactericidal cationic proteins cannot be explained by their *de novo* synthesis. The cytochemical detection of bactericidal cationic proteins depended not only on direct degranulation, but also on neutrophils, which are capable of other forms of secretory activity (release of granular products into the cytoplasm without increasing their content [59]). Both secretory processes were considered as signs of cellular activation, which, in relation to granulocytes, persisted after 24 hours in 55% of the volunteers.

The state of blood plasma also indicated normalizing modifications of humoral immunity. In particular, the immunoglobulins (IgA, IgG, IgM) synthesis increased (Fig. 5). The anti-inflammatory tendencies increased in the form of changes in the ratio of pro- and anti-inflammatory factors (cytokines) in plasma. The content of proinflammatory cytokines (TNFα, IL-6, IL-12, IFN) decreased and the content of anti-inflammatory factors in the blood (IL-10, TGFβ1) increased. PL is also noted as a potent inducer of

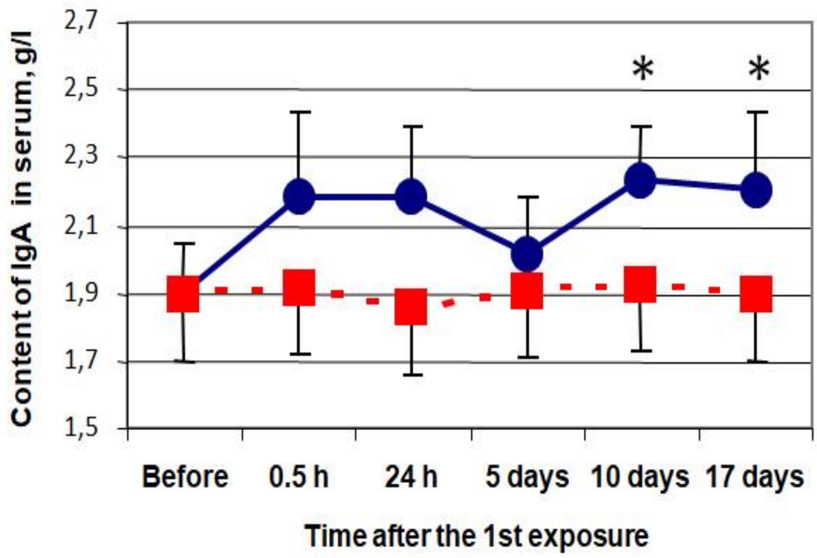


Fig. 5 Increase of IgA content in blood plasma after a single application of PL to the sacral zone in healthy individuals [15, 50].
Difference from the initial level: * $p < 0.05$.

interferon-γ. These effects may explain the significant suppression of inflammatory processes, which were especially noticeable in the immune compromised individuals. PL also increased blood levels of growth factors (PDGF, TGFβ1, EGF) capable of initiating cell proliferation, the main participants in wound healing (keratinocytes, fibroblasts and endothelial cells). This is important for the processes of regeneration in the internal (for example, lungs) and external (for example, skin and mucous membranes) zones of destruction.

The data presented indicate the possibility of using PL for the correction of anti-infectious (as well as antitumor) immunity. Increased IgA content is useful for improving the protection of mucous membranes in the treatment or prevention of airways infections, and acute respiratory diseases. The same is true for allergic pathology, which is often accompanied by a decrease in IgA content. A decrease in the concentration of circulating immune complexes in the blood seems to be prognostically favorable, since this is one of the mechanisms of antigen elimination. A decrease in blood levels of certain pro-inflammatory cytokines (IL-6, IL-12 and TNF-α), prevention of the massive release of other inflammatory factors (IL-1β), as well as an increase in the content of anti-inflammatory cytokines (IL-10 and TGF-β1) can be an important mechanism of anti-inflammatory action of PL therapy [56]. The described possibility of correcting the variables of immune homeostasis is important not only in the treatment of one pathology or another, but also in cases where there are no pathological changes, i.e. useful for their prevention.

The anti-inflammatory effect of PL is also confirmed by the results of a study of cultured human monocytes U937 that received a long exposure to PL [60]. The cells were then analyzed for change in expression of genes and cell surface markers relating to inflammation. It was noted that 6 hours exposition to PL reduced the expression of the CD14, MHC I and CD11b receptors, and increased the expression of CD86. It was also shown that PL caused downregulation of the genes IL1B, CCL2, NLRP3 and NOD1, and upregulation of NFKBIA and TLR9. These findings imply that PL has the capacity for immunomodulation in human immune cells, possibly exerting an anti-inflammatory effect.

With regard to the search for antiviral technologies, the results of studies of the antitumor effect of PL [61-63] are of interest. A slowdown in the growth of hepatoma was found in mice after general light application and after direct influence of PL directly on tumor cells, followed by their transplantation into syngeneic mice. The authors believe that the mechanism of PL antitumor action was not associated with the cytotoxic or cytostatic effect of PL on cells, but was a consequence of structural changes in the surface of tumor cells, which enhanced their recognition by natural killer cells—the main effectors of innate antitumor immunity. An increase in the cytolytic activity of natural killer cells led to the death of PL-irradiated tumor cells. The same data, from the point of view of the authors, also indicate the oncological safety of PL.

The immune corrective effect of PL was noted when it was used in patients with infiltrative tuberculosis [64]. Against the background of the standard complex anti-tuberculosis chemotherapy, the use of a wide beam (Bioptron-2 device) on the reflexogenic zones of the chest caused stabilization of the variables of cellular and humoral immunity. The number of lymphocytes increased while the total number of leukocytes was preserved, the number of T-lymphocytes and their functional activity increased, i.e. normalization of the cellular link of systemic immunity was observed. There was no increase in the amount of immunoglobulins, and the number of circulating immune complexes had only a tendency to decrease. Phagocytosis changed most noticeably, the indicators of which (the absorption function of neutrophilic granulocytes, monocytes and the level of oxygen-dependent metabolism) significantly increased after a course of PL applications, while the functional activity of neutrophilic granulocytes increased.

The effectiveness of PL-therapy for complicated respiratory disorders was assessed on the model of immunosuppression caused by radiation exposure (the accident at the Chernobyl nuclear power plant) [65]. A contingent of 12 patients who received acute irradiation had dose loads on the thyroid gland of up to 980.0 cSv with total (external) irradiation of 1.0-5.0 cSv. The remaining 12 patients lived in areas of radionuclide contamination with long-lived radionuclides (chronic exposure). Thyroid doses were 30.0-3,000.0 cSv, total (external) irradiation doses were 0.2-11.5 cSv, doses from incorporated ^{137}Cs were 1.12-3.92 cSv, doses from incorporated ^{90}Sr—0.024-0.51 cSv, the total effective equivalent dose from external irradiation and irradiation from the incorporated radionuclides of cesium and strontium ranged from 2.5 to 11.91 cSv. Patients with abnormalities of the cardio-respiratory and immune systems were examined. We used PL applications on biologically active zones (sacrum and sternum), a total of 12 daily sessions with an exposure of 20 min (Bioptron-2 device). Preliminarily, it was found experimentally that the application of PL to these zones creates a better clinical effect in comparison with biologically indifferent zones [66].

An improvement in the functional state of the respiratory system has been established. This was manifested by an increase in the passability of the bronchi of medium and small diameter. In particular, in persons exposed to acute radiation exposure, there was a significant increase in maximum expiratory flow rate at the level of 50% of the forced vital capacity of the lungs (MEF_{50}) (by 28.6%; $p < 0.05$) and a pronounced tendency towards an increase of other indicators (respectively MEF_{25}—by 16.4% MEF_{75}—by 20.1%). In patients under the influence of chronic radiation, MEF_{25} and MEF_{75} significantly increased (by 40.8%; $p < 0.02$). The incidence of bronchospasm, which was initially 41.6-50.0%, decreased to 16.7% and in 33.3% bronchospasm was not detected at all. The function of the bronchial epithelium was restored: the specific respiratory moisture release increased by 30.6% ($p < 0.05$) after acute irradiation and by 50.3% ($p < 0.02$) after chronic irradiation.

It was observed normalization of the nervous regulation of cardiac activity during functional loads. The rate of normal response to the clinoortatic test tended to increase from 50.0 to 75.0% after 12 PL sessions. The balance of adaptive blood circulation mechanisms improved, which before PL-correction was observed in 41.7% of patients and in 58.3% after.

Under the influence of PL, there developed positive changes in peripheral blood, which were characterized by a normalization of the total number of leukocytes without shifts in the relative content of lymphocytes and neutrophils. So, against the background of initial leukopenia after acute radiation exposure, the average number of leukocytes increased by 16.3%; and after chronic—by 18.6%. For lymphocytes, this ratio was 16.4 ($p < 0.02$) and 18.1% ($p < 0.05$).

Assessment of the state of cellular immunity after PL-therapy showed an increase in the absolute number of T- and B-lymphocytes. For example, for T-lymphocytes, +24.4% ($p < 0.02$) and +23.1% ($p < 0.02$) were obtained, respectively, in acute and chronic irradiation, and for B-lymphocytes by +51.8% ($p < 0.05$), and +81.8 % ($p < 0.05$). When analyzing changes in the variables of humoral immunity, a tendency to an increase in the content of immunoglobulin G by 10.7% and immunoglobulin A by 8.5% after acute radiation exposure and, respectively, by 23.9% ($p < 0.05$) and 43.7% ($p < 0.02$) after chronic.

The intensity of peroxidation in blood serum, erythrocytes and exhaled air condensate decreased. There were estimated average indicators of the initiated chemiluminescence: light sum (S), i.e. integral indicator reflecting the rate of consumption of free radicals due to their interaction with antioxidants and the amplitude of the rapid flash (h), reflecting the content of lipid hydroperoxides in the studied substrate, inversely proportional to the content of antioxidants. In persons after acute radiation exposure, there was a decrease in blood serum S by 27.3% and h by 51.3%; ($p < 0.05$); in erythrocytes—a decrease in S by 58.8% ($p < 0.05$) and h by 55.4% ($p < 0.01$); decrease in S in the condensate of exhaled air—by 32.4% and h—by 6.0%. In patients with chronic irradiation, an antioxidant effect was also recorded after light therapy. They revealed in their blood serum a decrease in S by 49.5% ($p < 0.05$) and h by 13.5%; in erythrocytes—a decrease in S by 27.9% and h by 9.4%; in the exhaled air condensate—a decrease in S by 77.8% ($p < 0.05$) and h—by 35.4% ($p < 0.01$). An interesting detail was revealed: the antioxidant effect was more noticeable in individuals with high values of peroxidation (on average, 71.4%), while in individuals with low values—on average, 30.0% [65]. However, in general, it was found that the course of PL-therapy was statistically equally effective in case of respiratory, cardiac, hemic and oxidative disorders caused by acute and chronic exposure to ionizing radiation, which in terms of the degree of damaging effect is in many respects similar to COVID-19 pathology.

3.4 Allergic Disorders and Their Correction with PILER-Light

The accumulated experimental and clinical experience shows that PL in the polychromatic version provides a number of corrective and therapeutic effects: immuno-normalizing (local and systemic), antiallergic, analgesic (acute, tonic and visceral pain), anti-inflammatory, decongestant, antispastic, regenerative, as well as enhancing the local effect of drugs. When using monochromatic light combinations, accentuated analgesic, anti-stress, general stimulating, metabolic, and also optimizing the emotional state effects are achieved [67, 68].

Clinical evidence of antiallergic efficacy of PL was obtained in the treatment of respiratory and immune manifestations of bronchial asthma [4, 20, 21, 69, 70]. The authors applied zonal light applications [3] simultaneously with taking pharmacological (immunotropic) drugs (Imudon®, Broncho-munal P®, etc.). The results were compared with a control/placebo group of healthy individuals and a group of individuals receiving conventional therapy.

It was revealed that immunotropic therapy with Imudon® (an immune vaccine consisting of a mixture of lysates of bacteria predominantly of the intestinal group) in combination with PL is capable of increasing the number of T-lymphocytes (from 47.5 ± 1.2% to 56.7 ± 1.9% with norm 61.4 ± 0.8%) and their functional activity in the reaction of blast transformation of leukocytes to the nonspecific mitogen concanavalin A (Con A) at a concentration of 20 μg/mL (from 3.2 ± 0.1 to 5.1 ± 0.2 units). At the same time, the release of histamine from peripheral blood basophils induced by bacterial allergens decreased from 50.4 ± 5.6 to 15.1 ± 1.2%, the IgE content significantly decreased (from 91.4 ± 8.3 to 21.3 ± 9.1 KE/L, and there was also a tendency towards normalization of the IgA content (from 0.9 ± 0.2 to 1.4 ± 0.9 KE/L). The indices of the absorbing activity of neutrophils and alveolar macrophages, as well as the oxygen-dependent mechanism of phagocytosis (NST-test) were normalized.

These data indicated that in respiratory complications associated with bronchial asthma, PL and Imudon® treatment became more effective compared to the control group. The authors reported that improvement in the patients' condition was excellent in 38.0% of cases, good in 46.0%, satisfactory in 14.0%, and only in 3.0%—no effect, and after 6-12 months respectively 74.1; 12.1; 6.9%. This accounted for 85% of the overall positive result and contributed to a 25% reduction in hospital stays and an improvement in the patient's quality of life by 75%.

The immunological reactivity of the organism in case of bronchial asthma was assessed as an indicator of the effectiveness of PL in combination with Broncho-munal P®. It is based on a lyophilisate of bacterial lysates of predominantly pyogenic microflora, and in terms of the mechanism of action (has the properties of a vaccine) Broncho-munal P® is similar to Imudon®. A positive clinical result was confirmed by an increase in the number of T-lymphocytes (Table 1), normalization of the ratio of T-lymphocyte subpopulations, a decrease in the activity of the Th-2 component of the immune system, and normalization of the IL-4 content in the blood serum. Recovery of serum TNF-α, one of the factors that destabilize mast cells, was also seen as a beneficial effect of treatment.

Thus, we have found evidence that the use of PL in combination with other immunotropic drugs helps to restore immunological variables and reduce allergic reactions. Due to the normalization of the functions of the cell membrane, the activation of regenerative processes and the improvement of energy exchange in tissues, polarized light has advantages in eliminating allergic, immunodeficient and hypoxic conditions.

Table 1 The state of the B-link of immunity in patients with bronchial asthma during immunotropic and PL-treatment (M ± m).

Treatment options	$CD20^+$, %	IgG, %	IgE, KE/L
Control/placebo group (*n* = 20)	15.9 ± 3.2	11.4 ± 0.9	26.3 ± 1.5
PL application (*n* = 38)			
Before treatment	18.4 ± 1.2	[1]15.9 ± 0.7	[1]60.4 ± 2.1
After treatment	16.2 ± 1.1	[2]12.4 ± 0.5	[2]28.1 ± 1.8
Treatment with Broncho-munal P® (*n* = 29)			
Before treatment	18.1 ± 0.9	[1]15.7 ± 0.5	[1]63.5 ± 1.9
After treatment	17.1 ± 0.1	14.2 ± 0.1	56.4 ± 2.1
Treatment with Broncho-munal P® + PL (*n* = 35)			
Before treatment	18.7 ± 0.8	[1]15.5 ± 0.4	[1]59.3 ± 2.3
After treatment	[2]16.1 ± 0.5	[2]11.9 ± 0.2	[2]30.1 ± 2.9
Traditional treatment (*n* = 35)			
Before treatment	18.5 ± 0.4	[1]16. 1 ± 0.3	[1]64.8 ± 2.7
After treatment	17.9 ± 0.5	[2]15.1 ± 0.2	[2]49.4 ± 2.5

[1] Significance of differences with control ($p < 0.05$). [2] Significance of differences with before treatment data ($p < 0.05$).

Therefore, among the indications for the use of PL, respiratory disorders are natural (bronchial asthma, rhinitis and bronchitis of allergic or viral origin, etc.) [20, 68, 71]. These data also indicate the principal possibility of combining PL with antiviral vaccines (for example, influenza, COVID-19), although this will require special experimental confirmation.

3.5 Oxidative Stress and Antioxidants

To evaluate the effectiveness of combined therapy with PL and antioxidants, it was used a model of oxidative stress caused by exposure to ionizing radiation (the consequences of the Chernobyl disaster) [72]. Doses of thyroid gland irradiation in 29 patients ranged from 30.0 to 3,000.0 cSv, doses of total (external) irradiation—0.2-11.5 cSv, doses from incorporated ^{137}Cs—1.12-3.92 cSv, the dose from the incorporated ^{90}Sr is 0.024-0.51 cSv, the total effective equivalent dose from external irradiation and irradiation of the incorporated cesium and strontium radionuclides was from 2.5 to 11.91 cSv. Bioptron-2 device was used to the areas of the sternum and sacrum with an exposure of 15 minutes, a total of 12 sessions. At the same time, it was carried out a 3-week course of treatment with the drug “Sixth Element” containing pycnogenol, 25 mg 2 times a day.

It has been established an improvement in the functional state of the respiratory system. As seen from Fig. 6, the most noticeable increase in bronchial passability was revealed after a course of combined therapy. In the proximal bronchi of medium diameter and peripheral bronchi of small diameter, it was recorded an increase in the maximum volumetric flow rate of expiratory flows (MEF_{50} and MEF_{75}), respectively, by 25.8% ($p < 0.05$) and 30.2% ($p < 0.01$). Signs of bronchial hyperreactivity after PL-therapy were eliminated or decreased in 28.6% of patients. The specific respiratory moisture release increased (by 43.9%), which indicated an improvement in the functional state of the bronchial epithelium and the surfactant system of the lungs. Normalization of the adaptive mechanisms of blood circulation and autonomic regulation was observed during functional loads. The total number of leukocytes increased (by 18.6%) with an increase (by 5.8%) in the relative content of lymphocytes and a decrease in the relative content of segmented neutrophils (by 5.6%).

Immunological examination showed an increase in the absolute number of lymphocytes (by 12.7%). When assessing the state of cellular immunity, there was an increase (by 21.7%) in the absolute number of T- and B-lymphocytes (by 53.5%). On the part of humoral immunity, an increase in the content of immunoglobulins G (by 40.0%) and A (by 54.4%) was observed in the blood serum. The intensity of free radical processes in blood serum (by 47.0%), erythrocytes (by 51.6%), and exhaled air condensate (by 39.0%) decreased, as evidenced by a corresponding decrease in the light sum of the initiated chemiluminescence.

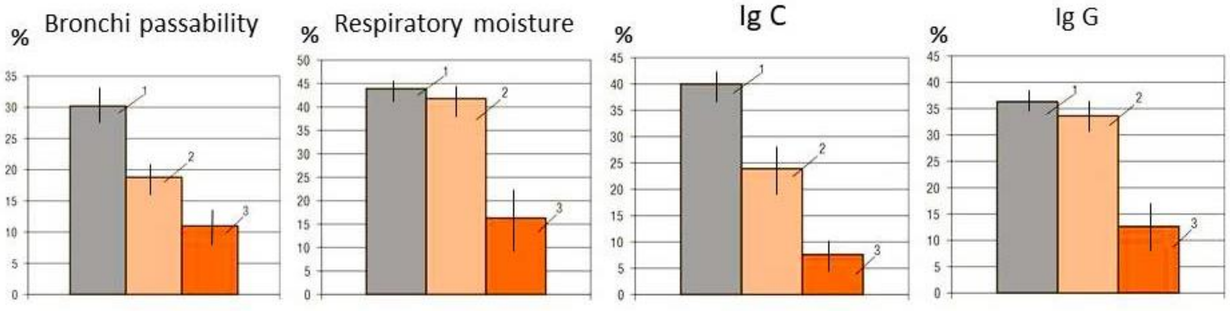


Fig. 6 The effect of combined therapy with PL and pycnogenol (1), in comparison with the isolated action of PL (2) and pycnogenol (3) on the variables of respiration and immunity in patients with oxidative stress caused by chronic ionizing radiation [72].

Table 2 Intensity of free radical oxidation in response to PL applications in combination with oral administration of the antioxidant pycnogenol.

#	Conditions of the experiments	*S*, impulses, Δ%; *p*	*h*, impulses, Δ%; *p*
1. Blood serum			
1.1	PL + pycnogenol (control)	54,316 ±4,810	194.3 ±11.2
1.2	PL + pycnogenol (after course therapy)	28,782 ±6,003 -47.0; $p < 0.01$	158.8 ±9.1 -18.0; $p < 0.05$
1.3	PL (control)	64,324 ±4,557	218.4 ±18.2
1.4	PL (after course therapy)	42,964 ±6,321 -49.5; $p < 0.05$	192.2 ±12.8 -13.5; $p > 0.05$
1.5	Pycnogenol (control)	40,166 ±3,810	144.3 ±18.6
1.6	Pycnogenol (after course therapy)	25,813 ±4,214 -35.3; $p < 0.05$	91.2 ±11.1 -36.7; $p < 0.05$
2. Red blood cells			
2.1	PL + pycnogenol (control)	62,729 ±8,317	250.6 ±14.9
2.2	PL + pycnogenol (after course therapy)	30,478 ±5,593 -51.6; $p < 0.01$	201.2 ±18.8 -19.6; $p < 0.05$
2.3	PL (control)	55,322 ±8,343	250.6 ±14.9
2.4	PL (after course therapy)	43,108 ±9,425 -27.9; $p > 0.05$	201.2 ±18.8 -19.6; $p < 0.05$
2.5	Pycnogenol (control)	49,169 ±7,188	278.3 ±39.4
2.6	Pycnogenol (after course therapy)	32,319 ±4,145 -35.5; $p < 0.05$	152.4 ±43.9 -45.6; $p < 0.05$
3. Exhaled condensate			
3.1	PL + pycnogenol (control)	41,558 ±5,143	128.8 ±7.9
3.2	PL + pycnogenol (after course therapy)	25,084 ±4,592 -39.0; $p < 0.05$	100.4 ±9.4 -21.9; $p < 0.05$
3.3	PL (control)	32,145 ±4,322	120.4 ±6.2
3.4	PL (after course therapy)	17,842 ±45,162 -77.8; $p < 0.05$	88.6 ±9.1 -35.4; $p < 0.01$
3.5	Pycnogenol (control)	42,198 ±5,793	132.6 ±9.2
3.6	Pycnogenol (after course therapy)	20,719 ±3,845 -50.1; $p < 0.01$	97.5 ±11.4 -27.1; $p < 0.05$

The dynamics of the antioxidant efficacy of isolated and combined therapy is noteworthy (Table 2). In all cases, there was a decrease in the intensity of free radical oxidation in biological media (serum and blood erythrocytes, exhaled air condensate). This was expressed in a decrease in the average indicators of the initiated chemiluminescence. These include the light sum (*S*), an integral indicator reflecting the rate of consumption of free radicals due to their interaction with antioxidants, and the rapid flash amplitude (*h*), reflecting the content of lipid hydroperoxides in the studied substrate, which is inversely proportional to the content of antioxidants.

When comparing the effectiveness of combined therapy courses and individual courses of phototherapy and the use of an antioxidant, it was found that against the background of the development of unidirectional therapeutic effects, there is a difference in the severity of shifts in the functional state of the respiratory system and humoral immunity. The combination of PL and antioxidants provided a more noticeable increase in the passability of the bronchi of medium and small diameter, an improvement in the compensation of bronchial hyperreactivity, an increase in respiratory moisture excretion, and an increase in immunoglobulins G and A in the blood serum. Since in acute respiratory diseases, for example, with influenza and COVID-19, in the pathogenesis there is an increase in peroxidation, bronchial dysfunctions, immunosuppression, etc., such a syndromic correction of disorders will be useful.

3.6 Potentiation of the Anti-inflammatory and Analgesic Action of Ibuprofen with PILER-Light

Respiratory disorders are usually accompanied by inflammatory processes, which are often the cause. Combined therapy with biophysical and pharmacological methods is an effective approach; however, the chemical load may be excessive. Of the large number of anti-inflammatory drugs, non-steroidal drugs are the most preferred due to the presence of concomitant analgesic action, lack of addiction and endocrine disorders. Ibuprofen, which is in this line, is included in the group of drugs used for viral respiratory diseases, in particular, with COVID-19.

A comparative assessment of the efficacy of PL and pharmacological analgesics [26] was performed on a model of inflammatory pain induced by subcutaneous injection of formalin (formalin pain model [73]). Full, half and combined with PL doses of ibuprofen (ibuprofen-solution, SIGMA-OLDRICH) were used.

The results indicate that the dual (anti-inflammatory and analgesic) effect of PL is comparable to the effect of moderate doses of non-steroidal anti-inflammatory drugs. Their combined use is more effective in suppressing pain than a single analgesic of the same dose. Thus, a 10-minute application of PL on the analgesic acupuncture point E-36 (AP) statistically significantly increased the analgesic effect of small doses of analgesics by 1.5-2 times. In contrast to animals in which analgesia was induced by the administration of high doses of analgesics, in the case of the use of low doses in combination with PL, there were no disturbances in motor activity and eating behavior (Table 3).

The clinical significance of the data presented is to prove the possibility of reducing the dose of analgesic drugs by applying PL, which reduces the risk of developing undesirable post-pharmacological side effects.

It follows from Table 3 that both painful and all non-painful reactions in the group of animals that received a half dose of ibuprofen in combination with PL application statistically significantly differ from similar reactions in the case of isolated use of an analgesic (taken as 100%). The pain was 68.7%, i.e. it was 1.5 times weaker than in animals receiving only an analgesic. At the same time, the duration of sleep increased by 2.9 times, which also indicated the weakening of inflammatory pain. Therefore, the combined use of ibuprofen and PL is more effective in suppressing pain than an analgesic alone. This means that a 10-minute application of PL to the AP allows, at a low dose of analgesic (50% dose), to obtain an effect comparable to the effect of twice the dose of an analgesic (Fig. 7).

Table 3 Comparison of the duration of painful and non-painful behavioral responses in two experimental groups, one of which immediately after the locus of pain creation received the ibuprofen injection (50% of a dose), and the second similar injection and a 10-min application of PL on acupuncture point.

Reaction	Effect of ibuprofen (15 mg/kg), *s*	Effect of ibuprofen (15 mg/kg) + PL on AP E-36, *s*
Pain	435.6 ±65 100%	299.3 ±38.6*** 68.7%
Sleeping	355 ±90 100%	1,023.6 ±175.8*** 288.3%
Washing	183.9 ±25 100%	129.5 ±27.8* 70.4%
Running	49.6 ±6 100%	77 ±27** 155.2%
Eating	7.4 ±5	6 ±3.6

The total duration of the reaction for 60 min of observation.

Reliability of the difference between the groups: *** $p < 0.05$; ** $p < 0.01$; * $p < 0.5$.

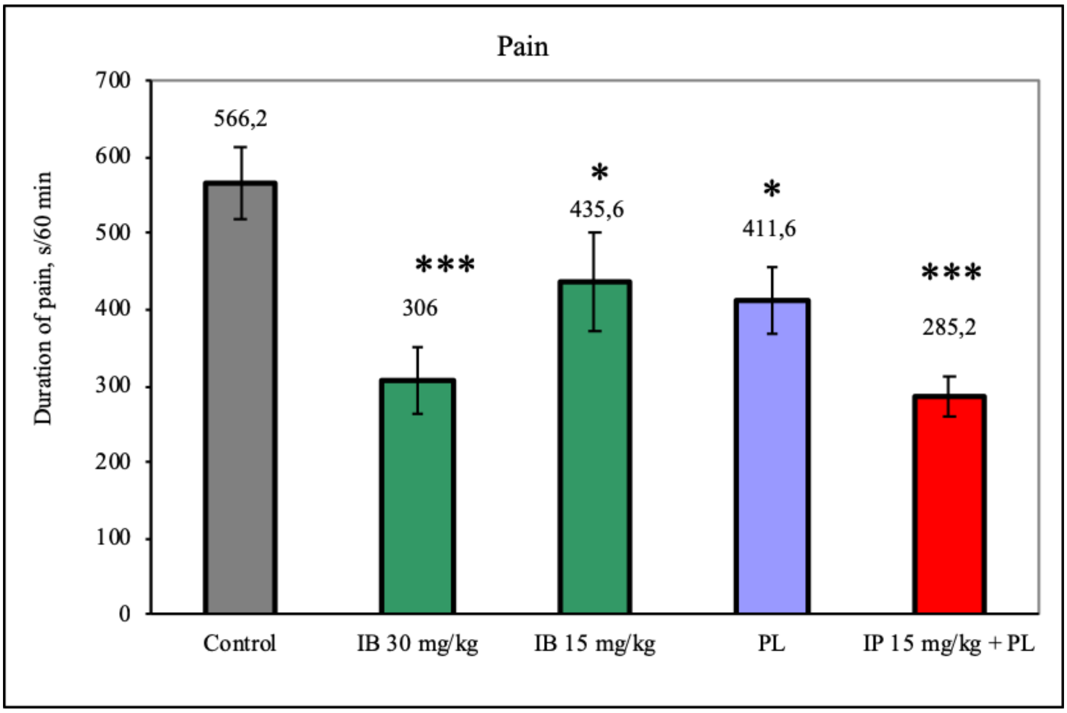


Fig. 7 The duration of the pain reaction during 60 minutes of observation in the control group (placebo) and in the four experimental groups that received the optimal (30 mg/kg) and 50% (15 mg/kg) dose of ibuprofen, 10 min application to AP E-36 by PL or combined use of ibuprofen (50% dose) and PL [26].

Reliability of the difference with the control: *** $p < 0.001$; ** $p < 0.1$.

Comparison of the intensity of the pain response in different experimental groups (Fig. 7) showed a significant reduction of pain under the action of both ibuprofen and PL. The effect of PL was about the same as that of a 50% dose of ibuprofen. But with their combined use, the analgesic effect was achieved almost the same as from ibuprofen in the optimal (twice as large) dose (30 mg/kg). Analgesia from the use of a 50% dose of ibuprofen was 23.1%, and from a combination with PL—47.1% (2 times more). This means that PL made it possible to halve the dose of ibuprofen, i.e. the effect of a 50% dose of ibuprofen can be potentiated by the action of PL on pain-relieving AP. Similar analgesic effects were also found with the use of other analgesic drugs (analgin and tramal), which were investigated using a similar technology [26, 74, 75].

When considering the mechanisms of PL antinociceptive action, it is advisable to pay attention to the involvement of the opioidergic system in the application of PL to AP. It is known [76] that some (analgesic) APs excite afferent nerves and induce intense production of neuromodulators in the brain stem structures. Endorphins produced by opioidergic neurons are involved in developing analgesia. It is possible to prove the presence of this process with the help of naloxone, which blocks it in the central nervous system. In medical practice, this phenomenon is known and used in the treatment of opiate addiction [77]. With regard to acupuncture technology, it was revealed [78] that naloxone blocked the transmission of afferent impulses from AP located on the limb (E-36) and, accordingly, analgesia, which increased depending on the dose. Therefore, there is direct evidence that the brain stem opioidergic system is involved in analgesia (and anti-inflammatory effect). However, it should be noted that even a high dose of naloxone did not completely eliminate the analgesic effect of PL. This indicated that other anti-pain brain systems, possibly serotonergic, dopaminergic, noradrenergic, and others, were involved in the implementation of the analgesic effect of PL. All of the above indicates that the analgesic + anti-inflammatory effect of low-intensity PL is comparable to the effect of moderate doses of nonsteroidal anti-inflammatory drugs [26].

The clinical significance of the data on the combined action of PL and non-steroidal anti-inflammatory drugs is to prove the possibility of reducing the dose of analgesics, which reduces the risk of developing undesirable post pharmacological side effects. Biological responses evoked by PL can be used for clinical purposes as ancillary physiotherapy technologies [3].

3.7 Contribution of the Light Puncture to Biological Effect

Mentioning of the presence of a positive effect in respiratory disorders is also based on the results of the use of light puncture. Although oriental medicine does not doubt the effectiveness of puncture technology, in European medicine skepticism is often manifested towards it. The main problem lies in the difficulty of obtaining objective experimental evidence of the biological effect of the acupuncture point exposure, on the one hand, and the methodological approaches adopted by experts from the East and West. Until now, the unity in understanding of the body structure has not been achieved, there are incompatible classifications of pathological conditions, the presence of acupuncture points and their anatomical and topographic localizations, there are many contradictions in explaining the mechanisms of obtaining a therapeutic effect, etc. Analysis of a huge array of heterogeneous information is not the task of this review, and the view of a physiologist was summarized by us earlier in a special review [79, 80]. One of his positions is that the acupuncture point has polymodal properties, i.e. it can respond to various physical factors: mechanical, thermal, vibrational, electrical, electromagnetic, light, etc., which is widely used in practice.

With regard to the electromagnetic aspect in the “light—acupuncture point—organism” system, a concept was formulated about the presence of a functional system for regulating the body's electromagnetic balance [52, 53, 81], which exists similarly to the known body systems (respiration, blood circulation, thermoregulation, etc.). Based on its provisions, light therapy (photo-biomodulation) is a process that uses evolutionarily formed and coordinately acting parts of a given system. The complete chain of its mechanisms begins with local and/or systemic exposure to polarized electromagnetic waves of the biologically necessary (solar) range using receptor or sensory gates, a transporting connective tissue framework and a cascade of photochemical reactions. The final address of delivery of electromagnetic energy is regulatory systems or areas experiencing its deficit or imbalance. The therapeutic effect of PL is due to the appearance and rehabilitation of the proper intensity of the resonance response of molecular structures that have an affinity for electromagnetic oscillations in the range of visible light and are in conditions of energy deficiency. At the same time, they suppress pathological and activate normalizing physiological regulatory and executive reactions at the atomic, subatomic, molecular, cellular and systemic levels. The consequence of this is the maintenance of the natural local and general electromagnetic balance [51-53, 82].

The evidence for the functioning of such a system is the presence of a biological reaction that occurs when PL is applied to the receptor zones (acupuncture points). To do this, let us analyze the results of a study of the effect of PL on acute (vocalization test for electrode flow) [74] and tonic (formalin test) pain [18, 48, 75]. Similar results have also been obtained for visceral pain [83]. In all cases, studies were carried out on animals (mice) to exclude emotional and individual artifacts inherent in experiments on humans.

It was shown that a single 10-minute exposure to PL of AP E-36 caused a statistically significant increase in the pain threshold upon electrical stimulation of the skin of the foot. The analgesic effect was 34.2-59.1% and lasted more than 3 hours.

Painful and non-pain behavioral responses of tonic pain were assessed by the action of PL on AP (E-36, V-60, V-56) or on an indifferent skin surface. Statistically significant changes were found only when the AP was exposed to light (Fig. 8). Suppression of painful behavioral reactions (licking the locus of pain) and lengthening of non-painful reactions (sleep, food intake, etc.) were found. AP E-36 proved to be more effective than AP V-60 or V-56 (pain relief reached 50%, 34.4% and 33.2%, respectively); however, we note the presence of a biological response for each of the studied APs. It was also revealed the dependence of analgesia on AP E-36 exposure. At 2-min and 6-min exposure to PL, analgesia was 7.6% and 30.9%, respectively, and at 10-min—up to 50%. Such antinociceptive effects were caused by the action of PL on AP E-36 of the paw with a painful area and the contralateral paw without it: pain relief was almost identical (50% and 51.2%, respectively). The simultaneous use of PL on both AP E-36 did not lead to increased analgesia. These results objectively prove the effect of pain suppression by the action of PL to AP and the fact that there is a biological response from AP light puncture in general.

Clinical evidence was obtained by assessing the dynamics of various diseases or conditions in response to the action of PL on one or more AP [3, 4]. Some data in relation to the topic of this article are given above [20, 65, 66]. Similar results were also found when using low-intensity laser (monochromatic) light. Studies of its antinociceptive action through AP [84-87] have shown that the therapeutic effect is carried out with the involvement of the brain stem opioidergic system and is accompanied by inhibition of the late (nociceptive) components of somatosensory evoked potentials. A similar effect arising under the influence of PL and proven with naloxone blockade is described above [78, 88]. Along with the pain relief caused by exposure of AP to low-intensity laser light, it was observed an increase in the synthesis of ATP and serotonin in cells, as well as a decrease in the inflammatory process [88].

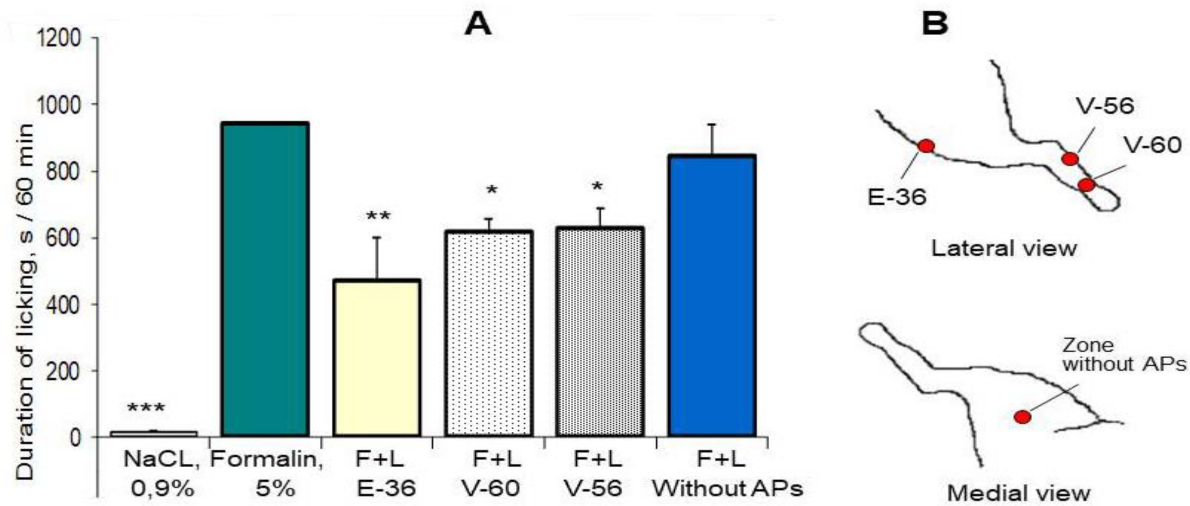


Fig. 8 Effect of PL on formalin-induced pain behavior in mice [48].
A: The mean (± SEM) duration (*s*) of licking the painful area for 60 min of observation in six groups of mice, which received: (1) injection of 0.9% NaCl in hind limb (placebo-1); (2) injection of 5% formalin (attenuated in 0.9% NaCl) in hind limb (placebo-2); (3-6) injection of 5% formalin in hind limb followed by polarized light exposure of one AP (E-36, V-60, V-56) or of a skin area without any analgesic APs. F + L—the mice with formalin injection into the hind limb followed by PL. Comparison with NaCl-evoked response. Significant difference from the control (formalin): *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$. B: Localization of the zone exposed to PL.

3.8 Contribution of Monochromatic (Colour) PILER-Light

Narrow polychromatic PL variants are of considerable clinical interest. These include modifications of PL that have passed through absorption, interference or fullerene filters. Attention to such PL variants, especially to the long-wavelength part of visible light and near infrared radiation, is due to their physical ability to penetrate deeper into the skin, at least the dermis, capillary network and nerve receptor structures. In this case, the antagonistic effects caused by the short-wavelength part of the spectrum are substantially eliminated. It was experimentally shown that pain of inflammatory origin caused by subcutaneous injection of formalin was most noticeably suppressed by red polarized light in combination with near infrared radiation (Bioptron-colour therapy set filters) [4, 22, 24, 25, 89]. The biological effect occurs under the action of any variant of PL, with red light occupying a leading position, although noticeable efficiency is noted with the use of polychromatic, orange, yellow, and fullerene light (Fig. 9). This indicates the advisability of using the long-wavelength range of the spectrum for the same purposes as PL.

It is especially important to note the perspective of light modified by Nanophotonic Fullerene Filter (Tesla Hyperlight Optics®). This is a new direction in light therapy, which has declared its effectiveness. The physical ground is based on a hypothesis that theoretically substantiates the toroidal transformation of linearly polarized light in a layer of fullerene molecules of a certain thickness [90, 91]. The fullerene molecule has the form of a spherical polyhedron (truncated icosahedron). Light quanta, passing through its crystal lattice, are deflected (Faraday effect), and repeating such deflection creates a rotating flux of quanta, consisting of toroids following one after another in connection with the quantum structure of light. In addition to this, the distribution of toroidal structures in the light flux becomes uniform according to the Fibonacci law. Additional effects, due to fullerene, include elimination of the blue part of the spectrum and an overall reduction in light power density, which is used in the Tesla Hyperlight Eyewear® (THE® Glasses). The biological effect of fullerene light has been proven with extraocular action on the locus of pain and inflammation [25], with short and long-term exposures [92], as well as with ocular use—on the electroencephalographic correlators of the state of default brain systems in humans [93], speed and quality of information processing in the brain [94] and psychophysiological indicators of mental performance [95]. There are theoretical assumptions about the possibility of additional enhancement of biological effects due to the toroidal properties of PL [91], which requires confirmation studies and the accumulation of clinical experience.

Considering the role of monochromaticity in achieving a therapeutic result, we note that each of the ranges causes a more or less noticeable effect, which may be specific in relation to individual pathological syndromes (Fig. 9). If we specifically consider approaches to weakening respiratory disorders, especially with the consequences of viral, including COVID-19, invasions, then one should pay attention to the long-wavelength range of radiation (red + infrared or fullerene). For large areas of the chest covered with inflammation, exposure to deep penetrating radiation is important. This brings about healing effects, some of which are described above.

Clinical observations [96] have shown that monochromatic light of LED origin (red, blue) combined with infrared radiation is also useful in reducing the manifestations of acute respiratory diseases. In particular, a group of 62 (50 patients and 12 controls) children with acute viral and bacterial rhinosinusitis, acute otitis media and tonsilopharygitis was studied. As the light sources there were used devices Medolight-red (640 ± 30 + 880 ± 30 nm) and Medolight-BluDoc (470 ± 30 + 880 ± 30 nm)

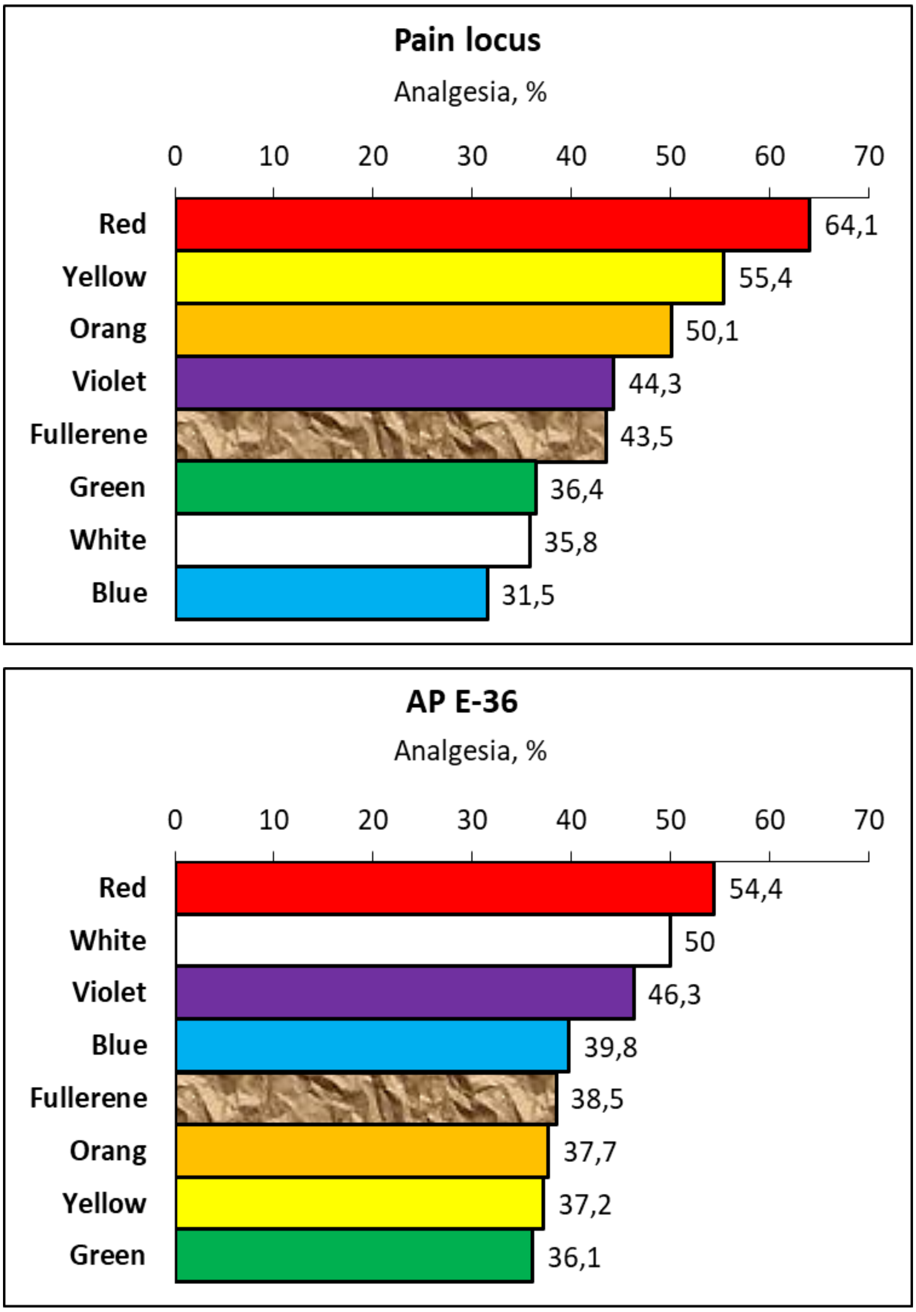


Fig. 9 Dependence of the analgesic/anti-inflammatory effect of polarized light on monochromatic wavelengths of BIOPTRON device [25].

Numbers to the right of the bars—mean analgesia in different groups.

(Bioptron AG by Zepter Group). It has been established that the use of red + IR in the treatment of patients with acute viral and bacterial rhino-sinusitis, acute otitis media, acute tonsillopharyngitis promotes a more rapid reduction of symptoms of the disease, pain syndrome, improvement of the function of ENT organs and accelerated recovery of patients' workability. The use of blue + IR contributed to a more rapid decrease in the acute manifestations of these diseases, suppression of inflammation, especially at the initial stage, a decrease in stress, and an overall improvement in the function of the ENT organs. In particular, it has been proven the expediency of reusable daily light applications at frequencies of 8,000 Hz.

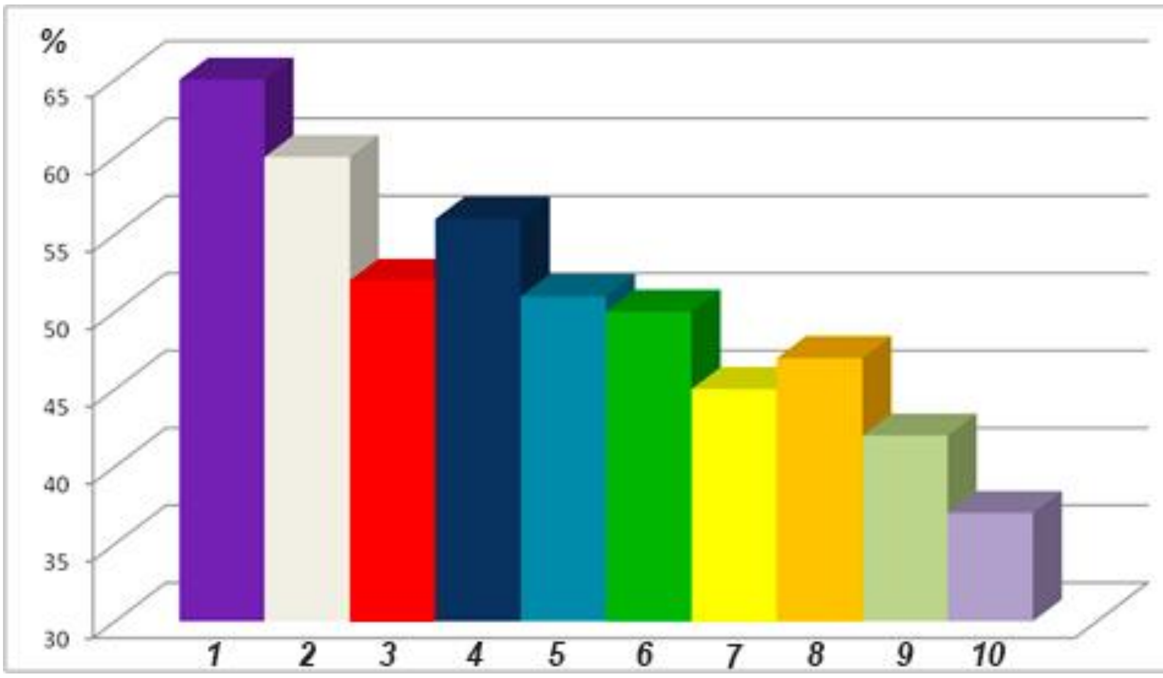


Fig. 10 Bactericidal activity of PL with different spectral ranges relative to *S. aureus* ATCC 25923 [98].
The relative data of the decrease in the growth rate of bacterial colonies in % compared to the control are presented. 1—violet, 2—320+ nm, 3—red, 4—indigo, 5—blue, 6—green, 7—yellow, 8—orange, 9—fullerene, 10—480+ nm.

Separately, we note the experimentally proven data (Fig. 10) on the inhibitory growth of microorganisms and the bactericidal effect of PL (polychromatic, monochromatic and fullerene) [97, 98]. In addition, it is of interest to increase the sensitivity of microorganisms to antibiotics under the influence of PL [99]. This PL property is important for antiviral non-contact treatment of skin and mucous membranes (e.g., nostrils, oral cavity, conjunctiva) and sterilization of the room air (Fig. 10).

4. Additional Therapeutic PILER-Light Correction for Viral Respiratory Disorders

Taking into account seasonal phasing and existence of epidemy, complex biophysical measures have recently been proposed to prevent, reduce symptoms and accelerate recovery of COVID-19, influenza and adenoviral respiratory diseases using Bioptron devices [3, 6, 8]. Standard protocol therapeutic and prophylactic measures for viral respiratory diseases contain the use of vaccines adequate to the virus strain, antiviral and antimicrobial (for secondary infection) drugs, antioxidant and symptomatic agents, rational nutrition, fortification, prevention of cooling against the background of isolation techniques together with individual disinfection, etc. In severe cases, oxygenation and resuscitation technologies are used. Below is a list of actions in the course of treatment of viral respiratory disorders, including COVID-19, based on the application of a biophysical approach, in particular, PL (Table 4).

Table 4 Supplementary protocol for preventive and therapeutic use of PL during influenza, adenoviral and other seasonal acute respiratory diseases [3, 6].

Phases	Stages	PILER-light applications (Bioptron devices)
1	Influenza virus infection threat	Preventive 10-minute PL applications (480+ nm or 550+ nm) on the nasal area (distance 5-10 cm, eyes closed) 1-2 times a day and after each stay outside home or in cold air. Application of PL (320+ nm) to the nostrils and lips (distance 2-5 cm, eyes closed, exposure 4 min) (Fig. 11). Ophthalmic instillation of antiseptics with antiviral effect (for example, okomistin).
2	The first signs of respiratory distress	Light applications to the nasal area (480+/550+ nm, eyes closed—10 min), into the oral cavity (320+ nm—2-4 min, 480+/550+ nm—8 min), to the sternum/trachea (480 +/550+ nm—20 min). Application of PL (320+ nm) to the nostrils (distance 2-5 cm, eyes closed—4 min) (Fig. 11, partially). Ophthalmic instillation of antiseptics with antiviral effect (for example, okomistin).
3	Influenza (including catarrhal disorders, rhinitis and bronchitis)	Light applications 2-4 times a day to the nasal area (480+/550+ nm, eyes closed—10 min), to the sternum and sacrum (480+/550+ nm—20 min each), to the projection of the roots of the lungs to the right and left, to the supraclavicular zone, auricles, hands, feet (480+/550+ nm—10 min each). A horizontal body position is advisable. In the presence of sinusitis (otitis media, sinusitis, frontal sinusitis), applications to the projection of the locus (480+/550+ nm—10 minutes each) in combination with the use of nasal vasoconstrictor agents (up to 3 days) (Fig. 12).
4	Rehabilitation	Light applications twice a day to the nasal area (480+/550+ nm, eyes closed—10 minutes) and after each stay outside home or in cold air; to the sternum and projections of the roots of the lungs (480+/550+ nm—10 min each) (Fig. 12). Breathing with dosed expiratory resistance. With the threat of complications— symptomatic treatment.

At all stages of treatment, it is advisable for the patient to stay in the rooms where the Therapy Air Ion air purifier is installed. It is useful during light applications to use Tesla Hyperlight Eyewear® (THE® Glasses) with fullerene filters (to eliminate the blue range and reduce the light load on the eyes in general [100].

These measures do not exclude the application of the main Protocol for the treatment of the corresponding disease [11, 31-34].

It is assumed the simultaneous use of antioxidants and non-steroidal anti-inflammatory drugs containing ibuprofen.

(480+ nm)—standard polychromatic light of the Bioptron device (480-3,400 nm);

(550+ nm)—polychromatic light passed through a fullerene filter (550-3,400 nm);

(320+ nm)—extended range of polychromatic light (device without filter).

The duration of the course of treatment is at least 10 days, as well as at least 10 days after the disappearance of all symptoms.

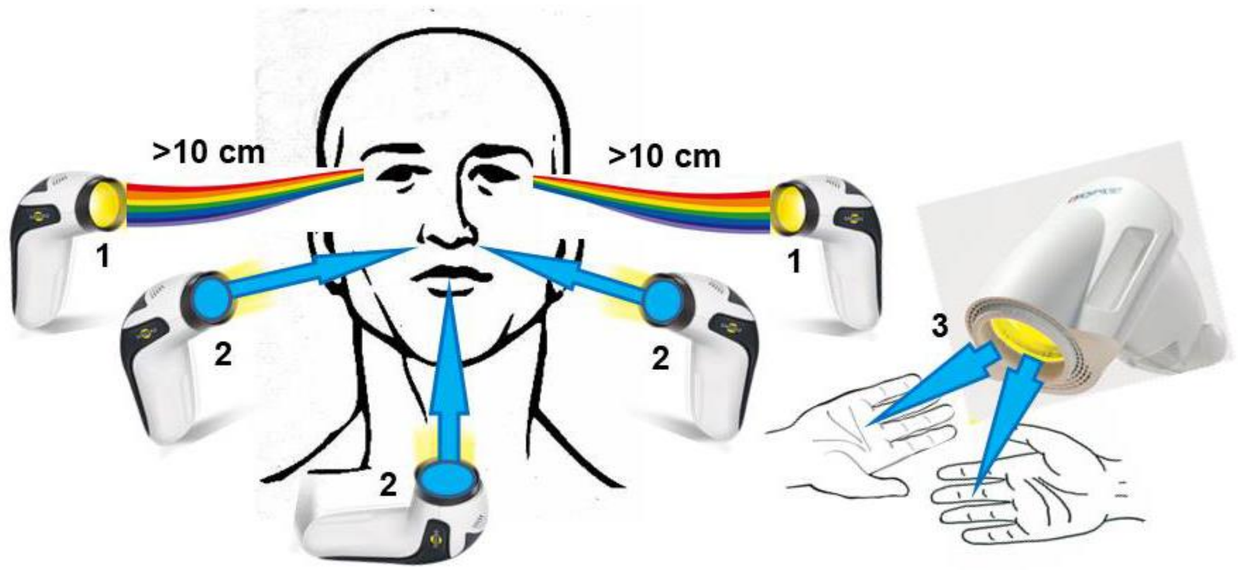


Fig. 11 The scheme of zones for active local PL protection of the mucous membranes in case of threat or consequences of contact with a virus-containing environment.

1—applications of PL to the lateral surface of the conjunctiva of the open eye (the beam is directed from the side from a distance of more than 10 cm), 2—applications of PL 320+ nm or violet light to the nostrils and oral cavity, 3—palms and other direct contact areas are treated by PL 320+ nm. Exposition up to 10 min [100].

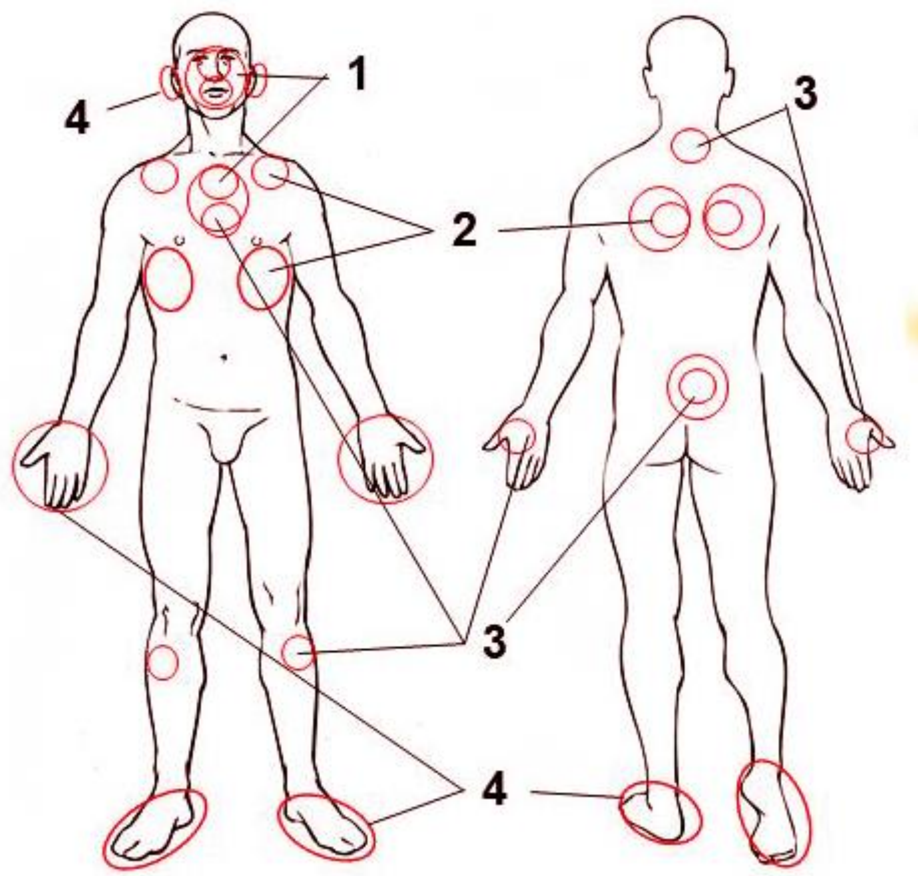


Fig. 12 The main areas used for correction of acute respiratory diseases by PL.
1—zones anatomically associated with the upper respiratory tract; 2—zones of the pulmonary structures' projection (apex, roots, separate lobes of the lungs); 3—reflex-therapy zones for immune normalization: sternum, sacrum; 7th cervical vertebra, Zu San Li (E-36) and He Gu (Gl-4) acupoints; 4—multifunctional zones (auricles, palms, soles of the feet) [100].

Exposure time is 10-20 minutes per zone. For light applications, it is advisable to use polarized polychromatic light (for example, Bioptron devices), polarized monochromatic light + infrared radiation (for example, Bioptron device equipped with sorption color or fullerene filters), red monochromatic light of halogen and LED (Medolight devices) origin. It is important that the area of the light spot is not less than 12 cm^2, and the light power density is not less than 30-40 mW/cm^2.

Auxiliary treatment or prevention/rehabilitation schemes are drawn up based on the indications, the patient's condition and the individual effectiveness of a particular type of light. During the cold season, it is advisable contactless non-invasive prophylaxis of colds using PL, which allows you to weaken the pharmacological load on the body. The main treatment should be based on the guidelines of the current Protocols.

For the child's body, it is important the bio-normalizing effect of PL, since the most important vital processes of the growing body are activated [8]. Under the influence of PL, protective capabilities increase by strengthening the immune processes, phagocytic activity of leukocytes, increasing of the nervous processes tone, accelerating maturation of the individual tissues or joints, normalization of the endocrine glands, phosphorus-calcium metabolism activity, etc.

The peculiarity of using PL in children is that the duration of the application, despite its low intensity, changes with age. This creates additional safety for the procedures. For infants and little children (0-3 years) in the treatment of bronchitis, atopic dermatitis, diaper rash and urticaria, it is advisable to use smaller exposures (2-6 minutes), for school age—6-10 minutes.

Eye protection is important, for example with Tesla Hyperlight Eyewear® (THE® Glasses), which use fullerene filters. The duration of the course of treatment depends on the type of disorders, their localization, the rate of reparative processes and individual photosensitivity and ranges from one to several weeks or months, and also without time limits (for example, for the prevention of autumn-winter respiratory morbidity).

5. Conclusions

The arsenal of medical measures for colds and respiratory diseases has expanded due to a new medical technology—light therapy with the help of BIOPTRON devices, which is in the phase of growth and accumulation of scientific baggage. It already has experimental and clinical evidence, some of which is given above. The technology is based on the use of a biophysical factor that weakens the course of the main pathological process (acute viral respiratory diseases, including COVID-19). The therapeutic effect develops due to the action of biologically active polarized polychromatic light with an infrared component. It can be modified into seven linearly polarized monochromatic (laser-like, with a narrowed wavelength spectrum) ranges, into an extended palette with the addition of near ultraviolet light, and into the fullerene range with toroidal polarization. Direct correction of pathology occurs due to local effects on the part of cells and light-sensitive molecules. Indirect systemic effects are a consequence of the electromagnetic balance normalization in many biological structures through the impact on the structures of moving blood. Additional impulses to trigger the transmission of electromagnetic signals along the collagen system are provided by the reactions of acupuncture points. The low intensity of the luminous flux eliminates the risk of negative tissue side effects, while in deep structures it approaches the fluctuations of natural bioluminescent processes.

The positive contribution of polychromatic polarized light applications to the upper respiratory tract during infection with high doses of the influenza virus has been experimentally proven.

It was revealed the evidence about changes in immune variables, indicating the possibility of systemic use of percutaneous photo-modification of blood for the correction of inflammatory processes, lipid peroxidation in erythrocyte membranes and plasma, and improvement of rheological properties of blood. Rheological efficacy is hypothesized to be synergic with anticoagulant therapy. It was found that the course of PL-therapy is equally effective in acute and chronic exposure to ionizing radiation.

Evidence has been found that the use of PL in combination with other immunotropic drugs contributes to the restoration of immunological variables and a decrease in the associated allergic reactions. This substantiates the presence of PL-light in indications for the use of respiratory disorders (bronchial asthma, rhinitis and bronchitis of allergic or viral origin, etc.).

On the model of respiratory pathology under oxidative stress caused by ionizing radiation, it was revealed the effectiveness of combined therapy with PL and antioxidants. The improvement in the functional state of the respiratory system in this case occurred due to an increase in bronchial passability, improvement in compensation of bronchial hyperreactivity, an increase in respiratory moisture release and an increase of immunoglobulins G and A in the blood serum.

It was revealed the efficacy of the combined use of PL and pharmacological agents (non-steroidal anti-inflammatory analgesic ibuprofen); it was proven in a comparative study on the model of formalin inflammatory pain. The results indicate that the anti-inflammatory and analgesic effect of the polychromatic PL is comparable to the effect of moderate doses of non-steroidal anti-inflammatory drugs, and their combined use is more effective in suppressing pain than an isolated the same dose analgesic.

There are presented results of experimental studies of one of the leading percutaneous mechanisms of the clinically positive action of PL. The presence of biological responses arising from the application of PL to receptor zones (acupuncture points) sensitive to electromagnetic signals has been confirmed. By studying the reactions to acute, tonic and visceral pain with an inflammatory component, statistically significant analgesic responses were revealed due to the non-contact action of PL on acupuncture points in animals. In this case, there were eliminated errors caused by emotional and individual artefacts inherent in humans. Application of PL to biologically active or indifferent zones in humans has shown a difference in the intensity of clinical responses in humans and the advantage of zones related to acupuncture. This expands the therapeutic possibilities arising from the use of active zones and allows to obtain reliable clinical results in patients with respiratory diseases.

Among the personal protective equipment for the eyes of patients during light procedures, especially for children, it is advisable to reduce the visual light load and protect the eyes by using glasses with fullerene filters.

These data are not specific for COVID-19, since they have been shown to be effective for respiratory viral diseases in their broad sense. However, no limitations have been identified for the use of this technology in COVID-19.

This review is evidence of the testing of the capabilities of polychromatic polarized light with a positive result, which is the basis for the PL-therapy techniques inclusion in the protocol schemes for the prevention and treatment of acute respiratory diseases.

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