ORIGINAL ARTICLES

EFFECT OF PHOTOBIOMODULATION THERAPY WITH LOW LEVEL LASER ON GINGIVAL IN POST-CURETTAGE PATIENTS

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Abstract

This research investigate how red laser treatment affects individuals who have had chemotherapy's ability to heal their wounds. The sixty individuals were split up into groups for treatment and control. On the third and fifth days, the treatment group had reduced signs of inflammation and enhanced recovery. The results point to possible advantages of red laser treatment for recovery after a cure. 60 patients were divided into 30 therapy groups and 30 control groups to investigate the role of photo biomodulation therapy in wound healing. The therapy groups had 60 seconds of light biomodulation therapy utilizing a 650 nm red laser at a dose of 3,5 J/cm^2. The gingival index, prostaglandin E2, human defensin 2, and interleukin-1β levels in the laser-treated and control groups' saliva were measured. The level of significance was set at $p < 0.05$. The result of this study on day zero after curettage showed that subjects treated with 650 nm laser levels of prostaglandin E2, human defensin 2, and interleukin-1β remained essentially the same as the control group subjects without therapy. On the third and fifth days after curettage, subjects treated with 650 nm laser showed lower levels of prostaglandin E2, human defensin 2, and interleukin-1β. They exhibited substantial differences from the control group subjects without therapy. The gingival index on post-curettage patients showed no significant differences between laser therapy and control groups on day zero but significantly differed on the third and fifth days. Photobiomodulation therapy with a red laser can help the healing of post-curettage subjects according to the analysis' findings of the gingival index, prostaglandin E2, human defensin 2, and interleukin-1β.

Key words: post curettage wound healing, 650 nm red laser, photo biomodulation, pro-inflammatory mediator.

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ВЛИЯНИЕ ФОТОБИОМОДУЛЯЦИОННОЙ ТЕРАПИИ С ИСПОЛЬЗОВАНИЕМ ЛАЗЕРА (650 НМ) НА СОСТОЯНИЕ ДЕСЕН ПОСЛЕ КЮРЕТАЖА

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Резюме

Изучено влияние лазера, излучающего в красной области спектра, на способность к заживлению ран после химиотерапии. В исследовании участвовали 60 человек, которые были разделены на две группы: лечения и контрольная. Пациенты из группы лечения получали 60-секундную световую биомодуляционную терапию с использованием красного лазера с длиной волны 650 нм и световой дозой 3,5 Дж/см^2. Были измерены десневой индекс, уровни простагландина E2, человеческого дефензина 2 и интерлейкина-1β в слюне пациентов из обеих групп. Принятый уровень значимости $p<0,05$. Результаты исследования после кюретажа показали, что у пациентов, получивших воздействие лазером с длиной волны 650 нм, уровни простагландина E2, человеческого дефенсина 2 и интерлейкина-1β оставались практически такими же, как и у пациентов контрольной группы без терапии. На 3-й и 5-й дни после кюретажа у пациентов группы лечения наблюдались более низкие уровни простагландина E2, человеческого дефензина 2 и интерлейкина-1β, чем в контрольной группе. Десневой индекс у пациентов после кюретажа не выявил существенных различий между группами лечения и контрольной группой в день лечения, но значительно отличался на 3-й и 5-й дни. В эти сроки в группе лечения наблюдалось уменьшение признаков воспаления и ускорение выздоровления. Результаты указывают на возможные преимущества лечения лазером, излучающим в красной области спектра, для восстановления после химиотерапии. Фотобиомодуляционная терапия красным лазером может способствовать процессам заживления у пациентов после кюретажа согласно результатам анализа десневого индекса, простагландина E2, человеческого дефенсина 2 и интерлейкина-1β.

Ключевые слова: заживление ран после кюретажа, лазер 650 нм, фотобиомодуляция, провоспалительный медиатор.

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Introduction

Curettage is a type of periodontal therapy that makes use of a tool or hand instrument to remove plaque, classified deposits, and smooth cementum around degenerated teeth. This is because plaque and deposits combined with bacteria cause periodontal tissue damage and stimulate the inflammatory process in the gingival tissue, which can damage the alveolar bone and cause tooth mobility in severe cases. After curettage, the healing process is a series of natural processes that occur in body cells damaged by trauma or anatomical traces. This process begins somewhere between the second and fifth days after curettage therapy. A healthy vascular system will hasten to heal. If there is a bacterial infection in the process, the process will be delayed or will not occur at all. The increased dentistry using lasers over the last few decades has led to amazing technological advancements that can be used in dental care. The CO_2, Neodymium: Yttrium-Aluminum-Garnet (Nd: YAG), and Erbium: Yttrium-Aluminum-Garnet (EYAG) lasers are the ones most frequently used to treat peri-dental illness (Er: YAG) [1]. During treatments like gingivectomy, curettage, and the elimination of melanin pigmentation, it is frequently utilized to remove calculus, simplify bone surgery, and lessen soft tissue injury [2]. In addition to providing an antiseptic effect on non-vascularized tissues (such as bone and dentin) and overcoming antibiotic resistance in subgingival biofilms, lasers are hypothesized to enhance decontamination during treatment [3,4].

Oral disorders like tooth decay, periodontitis, and gingivitis affect 3.47 billion people worldwide, causing non-fatal impairment. Patient assessment of treatment requirements and clinical results is crucial for maintaining oral health. Healthy living, including dental health, improves the quality of life, labour productivity, and learning capacity [5]. The absence of clinically detectable inflammation determines periodontal health and bacterial plaque plays a role in the development and maintenance of inflammation. Risk factors like diabetes, smoking, and hereditary variables can affect periodontal disease progression. Compliance with oral hygiene practices and periodontal maintenance can impact local bacterial infections [6].

The wound healing process consists of several phases from hemostasis, inflammation, cell movement, matrix- forming, and remodeling [7]. The wound healing process caused by periodontitis will differ from person to person, as many factors will influence the healing of wounds, including aging and medication use, tobacco use, and bacterial illnesses in which endotoxins can cause an extended rise of pro-inflammatory cytokines, interleukins-1β (IL-1β) and TNF-, thereby prolonging the inflammatory phase and other factors that can inhibit the wound healing process. Antibiotics are quite effective in the treatment of infections and can also prevent the onset of pain due to the wound healing process, even though the optimal dose has yet to be discovered [8].

Photo-biomodulation therapy (PBM) is a low-intensity light irradiation therapy used for medical and dermatological conditions [9]. It involves ingestion of photon energy by body tissues' natural chromophores. Near-infrared and red light are used for therapy in animals and patients, as haemoglobin and melanin absorb blue light at specific wavelengths [10].

Recent media interest has focused on photodynamic therapy (PDT), a minimally invasive therapeutic method, as a novel cancer treatment option. When a photosensitizer is exposed to certain light wavelengths, it combines with molecular oxygen to produce reactive oxygen species, which cause cell death in the target tissue [11]. Longer wavelengths of light (red and infrared) penetrate the tissue more effectively because the amount of light that is absorbed by the tissue reduces as the wavelength increases. The «network optical window» is the term for the 600 to 1200 nm wavelength range. The skin is more sensitive to light because the shorter wavelength (600 nm) penetrates less tissue and absorbs more energy. Longer wavelengths (850 nm) lack the energy to sufficiently create reactive oxygen species and excite oxygen in the singlet state. The highest tissue permeability consequently occurs between 600 and 850 nm [12].

The 405 nm and 649 nm diode laser has been demonstrated in aPDT15 and PBM investigations to expedite the proliferative process of wound healing following molar extraction based on the results of histological and immunohistochemical testing [1]. In a different study, 'bio stimulators' were low-level lasers and light-emitting diodes (LEDs) with less power than surgical lasers. A sort of light therapy called photo-biomodulation therapy (PBMT) encourages the growth of epithelial cells, an anti-inflammatory response, pain alleviation, and the prevention of scarring, all of which are necessary for wound healing [13]. Laser is a non-invasive, effective, safe, and inexpensive medical device based on aPDT and PBMT therapy for response accelerators for healing dental and oral diseases. Laser parameters and dose influence therapy results. Low-level laser therapy (LLLT) has short-term advantages in lowering pocket depth, but medium-term effects are not significant. Long-term benefits are unknown due to methodological weaknesses and a lack of studies [14]. Research on LLLT for wound healing continues [15].

Wound healing in the oral cavity involves repairing palate and gingival tissue without scar tissue, influenced by early inflammation, reduced immune mediators, fewer blood vessels, bone marrow-derived cells, quick re-epithelialization, and fibroblast proliferation [16, 17]. Microbial infection of the oral cavity is a common risk factor for periodontal disease, which can lead to gingival inflammation and if not treated promptly, may affect the periodontium in general [18]. Bacteria that cause gingival inflammation are *Streptococcus*, *Haemophilus* and *Neisseria species* [8]. *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, *Porphyromonas gingivalis*, *Campylobacter rectus*, *Prevotella intermedia*, and *Selenomonas species* are among the most prevalent subgingival bacterial species [11,19]. The duration of the natural wound healing process is mainly caused by both local and systemic disorders [20].

Local and systemic factors, such as poor blood flow, infection, and foreign substances, affect wound healing. To accelerate healing, therapeutic mechanisms like photo-biomodulation laser therapy and non-invasive approaches are needed. This study aims to determine the method of laser diode therapy and the irradiation time in root canal treatment.

Materials and Methods

Ethical Approval

The Ethics Committee of the Faculty of Dentistry at Airlangga University has accepted this study with the ethical number [551/HRECC.FODM/IX/2021].

Light Source

LLLT is a therapeutic advance that uses low-level infrared light spectrum lasers. The effect is related to tissue bio-stimulation, with photoelectric, photo energetic, and photochemical reactions eliciting a therapeutic response [21]. Photo biomodulation, on the other hand, uses a 650 nm-wavelength diode laser to induce a quicker healing process, as well as to reduce pain and inflammation by stimulating the cell's response to light. The diode laser spectrum and power were tested with the Jasco CT-10 and Thorlabs S140C chromate detectors. The results of laser characterization showed that the laser spectrum was 650 ± 0.05 nm, the power value was stable at 12.02 ± 0.01 mW, and the beam area was 0.20 ± 0.03 with a stable temperature of 32 °C during therapy. Therapy was carried out at a distance of 1 cm from the wound with an energy density of 3.5 J/cm^2 and a long exposure time of 60 seconds.

Treatments

The study involved 60 patients from the Dental and Oral Hospital's Periodontology section, divided into 30 therapy and control groups. The therapy group received a 650-nm red laser photo biomodulation therapy for 60 seconds, followed by curettage. Saliva samples were collected and transferred to ELISA plates. The samples were then blocked with 10% ovalbumin and 100 mL of hBD-1 mouse monoclonal antibody. The study aimed to understand the effects of laser therapy on gingival and salivary index in patients with periodontal cancer.

The study focuses on the characterization of a 650 nm diode laser used for photo biomodulation therapy, with the control group not receiving any treatment. The second phase is an experimental study examining the impact of specific factors on other variables. This study looked at gingival index and pro-inflammatory mediators in response to different types of therapy, specifically the administration of 650 nm diode laser photo biomodulation therapy and wound healing with antibiotics, in order to assess the level of effectiveness of the red-light diode laser or its effect on the tissue wound healing process in post-curettage patients. The test group patients underwent conventional non-surgical treatment associated with a laser irradiation session to eliminate the bacterial biofilm from the root surface and stop the inflammatory process. Prostaglandin E2 (PGE2), interleukin-1β (IL1β), and human beta defensin 2 (HBD2) concentrations were evaluated using the enymed-linked immunosorbent assay and the gingival index.

Enzyme-Linked Immunosorbent Assay (ELISA) Testing

By dilution, 120 l of Standard Solution into 120 l of standard diluent was used to create the standard and wash buffer. In deionized or distilled water, the wash buffer was diluted with 15 ml of the wash buffer concentrate before being mixed with 300 ml of water.

The sample well plate and standard well (not the blank, control well) each received 50 l of the standard, 40 l of the sample, 10 l of anti-PGE2 antibody (or anti-IL1β antibody or anti-Human antibody defensins 2), and 50 l of streptavidin-HRP. The wells were sealed with sealer and incubated for 60 minutes at 37 °C before being rinsed three times with wash buffer. The next step is to add 50 l of each of the following solutions to each well: 50 liters each of the substrate solutions A and B, 10 minutes of incubation at 37°C, and 50 l of stop solution (blue color will turn yellow). An Elisa reader operating at a wavelength of 450 nm was used to measure the optical density (OD) following the addition of the Stop Solution. Fig. 1 shows the diluting procedure for the sample.

Measurement of Gingival Index

Starting points included the third and fifth days after curettage, as well as the zero-day before and after, for dental index testing. A gingival index score of post-curettage research subjects on day zero, third and fifth following laser therapy is how the gingival index examination was done. The gingival index (GI), a metric developed by Leo and Stillness, is employed to evaluate the presence and degree of gingivitis in a community, group, or person. The following criteria were used to determine the gingival state and the gingival index score: 0 indicates normal gingiva, 1 indicates a mild inflammation with mild discoloration and mild edoema but no bleeding on probing, and 2 indicates a significant inflammation with redness, edoema, and glossy skin; bleeding on probing. 3 = significant redness, edoema, ulceration, and a propensity for spontaneous bleeding; severe inflammation.

Data Analysis

This study gathered information on the gingival index, proinflammatory markers such as PGE2, IL 1β, and HBD-2, as well as instrumentation tests using a diode laser. The Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. Individual sample T-Test can be used to do statistical analyses if the data are regularly distributed. The interval/ratio data scale, unpaired independent data groups, normal distribution of group data, and the absence of outliers in group data are necessary preconditions for using the independent sample T-Test.

Results

IL 1β protein testing was conducted to monitor inflammation during the wound healing process, both before extraction (day 0) and after extraction (day three and day five post-wound occurrence). In general, the observation results indicated a decrease in the levels of IL 1β. The normality test, performed using Kolmogorov-Smirnov, demonstrated that the data exhibited a normal distribution for the control group (without photobiomodulation therapy) with a significance level

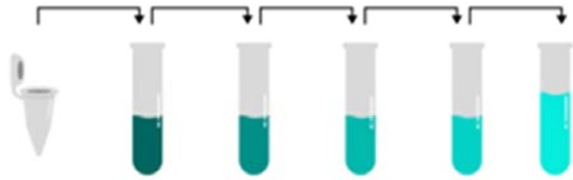

Рис. 1. Методика стандартного разведения.
Fig. 1. Standard dilution.

(α) of 0.300, while for the photobiomodulation therapy group, it was 0.115. Table 1 shows that post-extraction on day 1, day 3, and day five significantly impacted IL 1β levels ($p < 0.05$). All control group subjects exhibited higher IL 1β levels when compared to the photobiomodulation therapy group.

Enzyme-linked immunosorbent assay PGE2 test results

PGE2 protein levels fell from day zero to day five, which are significant mediators in the etiology of periodontitis and indications of inflammation in the healing phase of wounds. The independent T-Test was used to compare the PGE2 levels in the control and treatment groups to see if there were any variations in the mean values between the two unrelated sample groups. On the first, third, and fifth days, T-Tests were performed on all data collected in the control and treatment groups. On the first, third, and fifth post-curettage days, the mean PGE2 values in the control and treatment groups are displayed in Table 1.

PGE2 levels were measured in post-curettage subjects using the expression test, and the results showed greater levels in the laser therapy group but no statistically significant difference from the control group. The levels of PGE2 were lower in the laser therapy group on the first, third-, and fifth days following curettage, which was substantially different from the levels in the control group. Figure 2 shows visually the amounts of prostaglandin E2 at the zero, first, third-, and fifth-days post-curettage in patients.

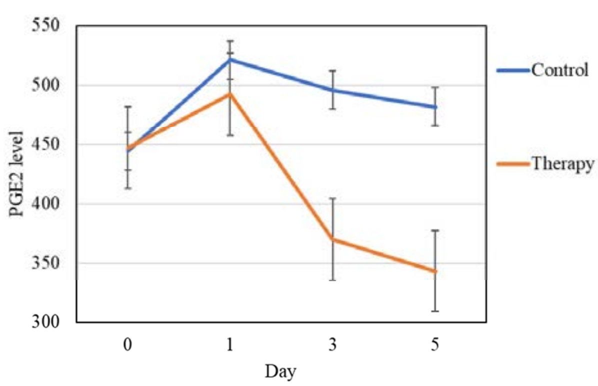

Рис. 2. Уровни простагландина Е2 в контрольной группе и группе лечения.
Fig. 2. Prostaglandin E2 levels against the control and therapy groups.

Таблица 1
Работа тока у больных с признаками воспаления кист поджелудочной железы и без признаков воспаления кист поджелудочной железы

Table 1
Electric current work in patients with signs of inflammation of pancreatic cysts and without signs of inflammation of pancreatic cysts

Дни Days	Группа Group	N	Значение Average	SD	Независимый Т-тест Independent T Test
0	Контроль Control	30	444.17	10.54	p = 0.277
	Лечение Therapy	30	447.20	10.85	
1	Контроль Control	30	521.13	36.79	p = 0.030*
	Лечение Therapy	30	492.20	26.86	
3	Контроль Control	30	495.93	36.78	p = 0.031*
	Лечение Therapy	30	369.77	36.90	
5	Контроль Control	30	481.73	40.02	p = 0.001*
	Лечение Therapy	30	343.13	22.33	

*Различия статистически значимы
*There is a different meaning

Enzyme-Linked Immunosorbent assay test results in Human defensin 2

Human defensin 2 protein levels, crucial for wound healing, decreased from day zero to day five, indicating a decline in pathogenic bacteria colonization in the oral cavity. The amount of human defensin 2 proteins in the control and therapy groups were compared using the Independent T-Test to determine the average difference between the two groups of unrelated samples. T-Tests were run for the control and treatment groups on the first, third, and fifth days. Table 2 shows the distribution of the mean values of human defensin 2 in the control and treatment groups in post-curettage patients on the zero, first, third, and fifth days after curettage.

Based on the test results, the therapy group's expression of Human Defensin 2 had higher levels on day zero of the wound-healing process in post-curettage individuals, but it was not statistically different from the control group. On the first, third, and fifth days, there was a substantially different expression of defensin 2 in the 650 nm red laser therapy group compared to the control group. Human Defensin 2 levels in post-curettage patients are depicted graphically in Figure 3 at zero, first, third-, and fifth days following curettage.

Enzyme-Linked Immunosorbent assay test results Interleukin-1β

Measurements of interleukin-1β levels revealed a decrease from day zero to day fifth. Then the results of assessing interleukin-1β protein levels in the control and therapy groups were compared using the Independent T-Test to determine the average difference between the two groups of unrelated samples. T-Tests for the control and treatment groups were run on the first, third, and fifth days. Table 3 displays the distribution of interleukin-1β in the control and treatment groups for post-curettage patients on the zero, first, third, and fifth days after curettage.

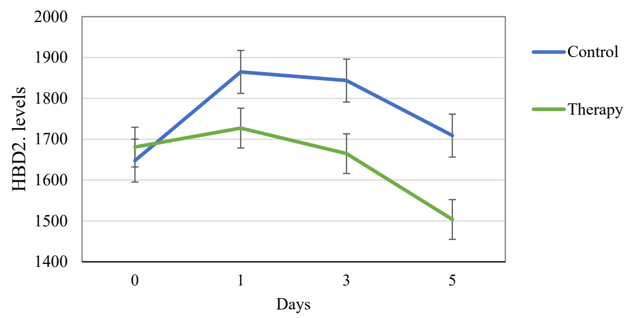

Рис. 3. Сравнение уровней дефензина 2 человека в контрольной группе и группе лечения в период с 0-го по 5-й дни.
Fig. 3. Comparison of Human defensin 2 levels against the control and therapy groups on zero-day to the fifth day.

According to the test results, the therapy group's post-curettage subjects had greater levels of interleukin-1β at day zero of the wound healing process than the control group, although this difference was not significant (p=0.127). On day first (p=0.043), third (p=0.029), and fifth (p=0.027), interleukin-1β expression in the 650 nm red laser treatment group was substantially different from that of the control group. Human Defensin 2 levels in post-curettage patients are depicted graphically in Figure 4 at zero, first, third-, and fifth days following curettage.

Gingival Index Test Results

The gingival index examination was conducted on day zero, with further assessments after three days. The condition index was calculated using measurements of fluid discharge, color, shape alterations, acute bleeding, and bleeding time. The study found that the control and therapy groups had mildly inflammatory gingival health on day zero, with the treatment group experiencing

Таблица 2
Сравнение результатов независимого выборочного Т-теста для уровней человеческого дефенсина 2 с контрольной группой и группой лечения в 1-й, 3-й и 5-й день после кюретажа

Table 2
Comparison of the results of the Independent Sample T-Test for levels of Human defensin 2 against the control group and the therapy group on day first, day third, and day fifth after curettage

Дни Days	Группа Group	N	Значение Average	SD	Независимый Т-тест Independent T Test
0	Контроль Control	30	1647.70	38.60	p = 0.687
	Лечение Therapy	30	1680.83	73.58	
1	Контроль Control	30	1864.77	32.51	p = 0.000*
	Лечение Therapy	30	1727.30	85.09	
3	Контроль Control	30	1843.60	38.79	p = 0.018*
	Лечение Therapy	30	1664.80	32.62	
5	Контроль Control	30	1709.00	43.12	p = 0.001*
	Лечение Therapy	30	1503.63	88.49	

*Различия статистически значимы
*There is a different meaning

Таблица 3
Сравнение результатов независимого выборочного Т-теста уровней интерлейкина-1β с контрольной группой и группой терапии на 0-й, 1-й, 3-й и 5-й дни после кюретажа

Table 3
Comparison of the results of the Independent Sample T-Test of interleukin-1β levels against the control group and the therapy group on the zero, first, third, and fifth days after curettage

Дни Days	Группа Group	N	Значение Average	SD	Независимый Т-тест Independent T Test
0	Контроль Control	30	1822.20	41.38	p = 0.127
	Лечение Therapy	30	1811.53	51.00	
1	Контроль Control	30	2223.97	88.53	p = 0.043*
	Лечение Therapy	30	1904.20	60.66	
3	Контроль Control	30	2086.90	91.59	p = 0.029*
	Лечение Therapy	30	1801.83	53.29	
5	Контроль Control	30	2000.30	87.03	p = 0.027*
	Лечение Therapy	30	1774.07	48.65	

*Различия статистически значимы
*There is a different meaning

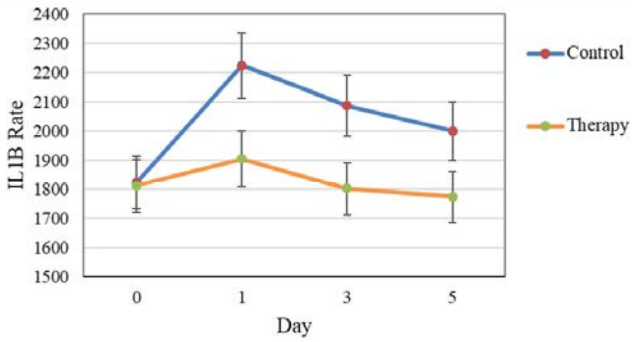

Рис. 4. Сравнение уровней интерлейкина-1β в контрольной группе и группе лечения в период с 0-го по 5-й дни.
Fig. 4. Comparison of interleukin-1β levels against the control and treatment groups on zero-day to the fifth day.

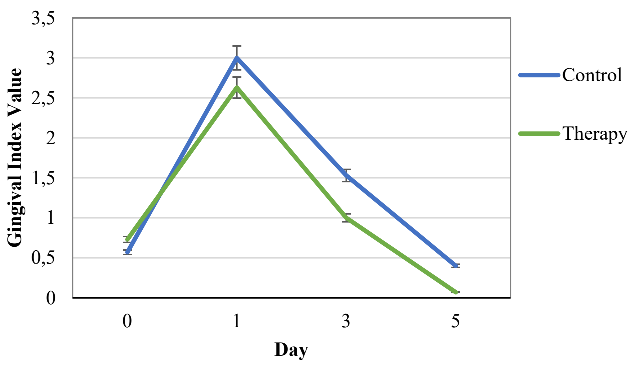

Рис. 5. Сравнение показателей десневого индекса в контрольной группе и группе лечения .
Fig. 5. Comparison of gingival index scores in the control group and the therapy group.

severe inflammatory health. On day 3, the control group deteriorated, while the treatment group showed moderately inflammatory health, with an average score of 1. The treatment group had a lower gingival index score of 0.07 on the fifth day, compared to the control group's average gingival score of 0.4, which showed that both groups were in good health. Figure 5 depicts the evaluation of the gingival index in the laser treatment and control groups on the first, second, third-, and fifth days following curettage.

The average number of gingival indices varies, as seen in Figure 9, but the shape and distribution of the data are the same. The median difference's significance is not evident. Since the Gingiva Index measurement in the control and therapy groups contains interval data, the Mann-Whitney U method is utilized for the Non-Parametric Test. The findings of the Mann-Whitney U test in Table 4 indicate that there is a different interpretation of the gingival index on the zero, first, third-, and fifth days following curettage in the control group compared to the treatment group in post-curettage patients ($p < 0.05$).

Discussion

Photobiomodulation therapy (PBMT) is a therapeutic approach using low-level infrared light spectrum lasers to stimulate tissue [22]. It works by absorbing photons by molecular photo acceptors or chromophores [23]. Effective tissue penetration occurs between 650 and 1200 nanometers, with absorption and scattering stronger in the blue section [24]. Most LLLT in animals and patients uses red light and near-infrared [25].

Таблица 4
Результаты U-теста Манна-Уитни на 0-й, 1-й, 3-й и 5-й дни после кюретажа
Table 4
Mann-Whitney U test results on zero, first, third, and fifth days after curettage

Дни Days	Группа Group	N	Значение Average	Критерий Манна-Уитни Mann-Whitney U
0	Контроль Control	30	0.57	p = 0.573
	Лечение Therapy	30	0.73	
1	Контроль Control	30	3.00	p = 0.000*
	Лечение Therapy	30	2.63	
3	Контроль Control	30	1.53	p = 0.001*
	Лечение Therapy	30	1.00	
5	Контроль Control	30	0.40	p = 0.002*
	Лечение Therapy	30	0.07	

*Различия статистически значимы
*There is a different meaning

This study aims to expedite healing and reduce pain and inflammation using photo biomodulation therapy using a diode laser with a characterization wavelength of 649 ± 0.05. The red laser light's energy and wavelength are 12.02 ± 0.01 mW at 650 nm [26]. The low-power dose of 3.5 J/cm² is crucial for the therapy, and the laser diode power characteristic test ensures maximum power stability at 60 seconds. The therapy is suitable for patients with various conditions [27]. Periodontal disease, causing tooth loss in adults, is primarily caused by bacterial buildup near teeth. Gingivitis and periodontitis are two types. Root planning and scaling are interconnected processes [28].

Curettage is a periodontal treatment that involves a change in microbiota and decreased inflammation. If inflammation persists, curettage can be performed. The depth of periodontal pockets can be significantly increased, depending on the damage. With proper care and maintenance, most patients can regain a 4 mm to 5 mm pocket depth. The study involved 60 patients, with 30 in the therapeutic group and 30 in the control group. After curettage treatment, the therapeutic group received red laser irradiation on the first day, followed by the control group on the third and fifth days. Samples were collected at each visit.

The collected samples were then tested for PGE2, IL-1β, and HBD-2 levels using an ELISA kit with 96 well plates. The ELISA kit used in this study has a sensitivity of 1.28ng/L for PGE2, 10.07 pg/mL for IL-1β, and 5.31 ng/L for HBD-2. One of the immunological techniques that aim to determine or measure levels of protein expression activity/response and immune reaction status from individual reactions/immune responses is the ELISA technique [30].

Wound healing involves fibrosis and regeneration, with fibrosis replacing damaged tissue with connective tissue [11, 31]. Laser biomodulation therapy enhances phagocytosis and lysosomal activity, activating Cytochrome Oxidase C and triggering downstream signaling cascades that promote protein synthesis, anti-inflammatory reactions, antioxidants, and cell proliferation [32].

Prostaglandin E2, a pro-inflammatory mediator, promotes the synthesis of inflammatory substances, particularly in periodontitis, particularly IL-1β [33]. Periodontitis patients have higher PGE2 levels, which can be blocked with anti-inflammatory medications to slow disease progression and reduce bone resorption, with faster decline in therapy groups [34]. Then the levels of PGE2, IL-1β, and HBD-2 in the samples were assessed using an ELISA kit with 96 well plates. The ELISA kit used in this study has a sensitivity of 1.28 ng/L for PGE2, 10.07 pg/mL for IL-1β, and 5.31 ng/L for HBD-2.

The ELISA technique assesses immune response status and protein expression activity. The study found that IL-1β concentration in gingival crevicular fluid (GCF) decreased after non-surgical periodontal therapy [35]. Laser phototherapy inhibited IL-1β production, affecting wound healing [36]. The study found differences in IL-1β protein levels during post-cartage wound healing using red laser photo biomodulation therapy at a 650 nm wavelength. The therapy group showed a faster decline than the control group [37].

The study shows that red laser photo biomodulation therapy significantly enhances wound healing in post-curettage patients, with a lower gingival index and faster decline in inflammation compared to the control group, indicating a positive healing effect [38]. Laser therapy wavelengths, particularly 600-700 nm, can stimulate cell proliferation and differentiation, regenerate tissue, reduce inflammation, and alleviate pain in chromophore cells [39]. The study demonstrates that red laser photo biomodulation therapy at 650 nm can accelerate wound healing in post-cursed patients, with significant reductions in test parameters [40]. This therapy accelerates fibroblast proliferation, which produces collagen and influences the epithelialization process, ultimately determining the outcome of wound healing [41].

According to the findings of statistical tests, there was a difference in post-curettage wound healing time between patients receiving photo biomodulation therapy and patients who did not receive photo biomodulation therapy with a probability value (p-value) of 0.05 in each pro-inflammatory mediator test (IL-1β, PGE2, and hB-2) and gingival index studies. If the P value is less than 0.05, the result is considered statistically significant. This value indicates that there is substantial evidence against the null hypothesis. As a result, the researcher discards the alternative hypothesis in favor of the null hypothesis. In comparison to patients who didn't get laser therapy, post-curettage patients who received a 650 nm diode laser showed faster-wound healing, according to the null hypothesis.

Conclusion

The findings of this study showed that levels of prostaglandin E2, human defensin 2, and interleukin-1β in participants treated with a 650 nm laser on the first day after curettage were not statistically different from those in the control group of subjects who received no therapy. On the third and fifth day after curettage, subjects treated with 650 nm laser showed lower levels of Prostaglandin E2, Human Defensin 2, and interleukin-1β and were distinct from the control group subjects without therapy. The results of the measurement of the gingival index on post-curettage patients on day zero showed that there was no significant difference between the control group and the laser therapy group, while on the third and fifth days there was a significant difference in the gingival index. Based on the examination of the gingival index, prostaglandin E2, human defensin 2, and interleukin-1β, photo biomodulation therapy with a red laser can aid in the healing of post-curettage individuals.

REFERENCES

1. Astuti S. D. et al. An in-vivo study of photobiomodulation using 403 nm and 649 nm diode lasers for molar tooth extraction wound healing in wistar rats. *Odontology*, 2022, vol. 110 (2), pp. 240-253. doi: https://doi.org/10.1007/s10266-021-00653-w
2. Sağlam M. et al. Combined application of Er: YAG and Nd: YAG lasers in treatment of chronic periodontitis. A split-mouth, single-blind, randomized controlled trial. *Journal of periodontal research,* 2017, vol 52(5), pp. 853-862. doi: https://doi.org/10.1111/jre.12454
3. Astuti S.D. et al. The efficacy of photodynamic inactivation with laser diode on Staphylococcus aureus biofilm with various ages of biofilm. *Infectious disease reports*, 2020, vol. 12(S1), pp. 68-74. doi: https://doi.org/10.4081/idr.2020.8736
4. Astuti S.D. et al. Chlorophyll mediated photodynamic inactivation of blue laser on Streptococcus mutans. *In AIP Conference Proceedings*, 2016, vol. 1718(1), pp. 120001.
5. Daigo Y. et al. Wound healing and cell dynamics including mesenchymal and dental pulp stem cells induced by photobiomodulation therapy: an example of socket-preserving effects after tooth extraction in rats and a literature review. *International Journal of Molecular Sciences*, 2020, vol. 21(18), pp. 6850. doi: https://doi.org/10.3390/ijms21186850
6. de Paula Eduardo C. et al. Laser phototherapy in the treatment of periodontal disease. A review. *Lasers in medical science*, 2010, vol. 25 (6), pp. 781-792. doi: DOI 10.1007/s10103-010-0812-y
7. Eming S.A. et al. Wound repair and regeneration: mechanisms, signaling, and translation. *Science translational medicine*, 2014, vol. 6 (265), pp. 265sr6-265sr6. doi: DOI: 10.1126/scitranslmed.3009337
8. Mardianto A.I. et al. Photodynamic Inactivation of Streptococcus mutan Bacteri with Photosensitizer Moringa oleifera Activated by Light Emitting Diode (LED). *In Journal of Physics: Conference Series*, 2020, vol. 1505 (1), pp. 012061
9. Sutherland J.C. et al. Biological Effects of Polychromatic Light. *Photochemistry and photobiology*, 2002, vol. 76 (2), pp. 164-170. doi: https://doi.org/10.1562/0031-8655(2002)0760164BEOPL2.0.CO2
10. Astuti S.D. et al. Photodynamic effectiveness of laser diode combined with ozone to reduce Staphylicoccus aureus biofilm with exogenous chlorophyll of Dracaena angustifolia leaves. *Biomedical Photonics*, 2019, vol. 8 (2), pp. 4-13.
11. Correia J.H. et al. Photodynamic therapy review: Principles, photosensitizers, applications, and future directions. *Pharmaceutics*, 2021, vol. 13 (9), pp. 1332. doi: https://doi.org/10.3390/pharmaceutics13091332
12. Astuti S.D. et al. Combination effect of laser diode for photodynamic therapy with doxycycline on a wistar rat model of periodontitis. *BMC oral health*, 2021, vol. 21(1), pp. 1-15.
13. Hung C.M. et al. Gingyo-san enhances immunity and potentiates infectious bursal disease vaccination. Evid. *Based Complementary Altern Med*, 2011. doi: https://doi.org/10.1093/ecam/nep021
14. Plaetzer K. et al. Photophysics and photochemistry of photodynamic therapy: fundamental aspects. *J Lasers Med Sci*, 2009, vol. 24 (2), pp. 259-268.
15. Ren C. et al. The effectiveness of low-level laser therapy as an adjunct to non-surgical periodontal treatment: a meta-analysis. *J. Periodontal Res*, 2017, vol. 52 (1), pp. 8-20. doi: https://doi.org/10.1111/jre.12361
16. Gilowski L. et al. Amount of interleukin-1β and interleukin-1 receptor antagonist in periodontitis and healthy patients. *Arch. Oral Biol*, 2014, vol. 59 (7), pp. 729-734. doi: https://doi.org/10.1016/j.archoralbio.2014.04.007
17. Harvey J.D. et al. Periodontal microbiology. *Dent. Clin*, 2017, vol. 61 (2), pp. 253-269. doi: https://doi.org/10.1016/j.cden.2016.11.005
18. Iglesias-Bartolome R. et al. Transcriptional signature primes human oral mucosa for rapid wound healing. *Sci. Transl. Med*, 2018, Vol. 10 (451), pp. eaap8798. doi: 10.1126/scitranslmed. aap8798
19. Savitt E.D. et al. Distribution of certain subgingival microbial species in selected periodontal conditions. *J Periodontal Res*, 1984, vol. 19 (2), pp. 111-23. doi: https://doi.org/10.1111/j.1600-0765.1984.tb00800.x
20. Ismiyatin K. et al. Different 650 nm laser diode irradiation times affect the viability and proliferation of human periodontal ligament fibroblast cells. *Dent. J (Majalah Kedokteran Gigi*, 2019, vol. 52 (3), pp. 142-142.

ЛИТЕРАТУРА

1. Astuti S. D. et al. An in-vivo study of photobiomodulation using 403 nm and 649 nm diode lasers for molar tooth extraction wound healing in wistar rats // Odontology. –2022. – Vol. 110 (2). – P. 240-253. doi: https://doi.org/10.1007/s10266-021-00653-w
2. Sağlam M. et al. Combined application of Er: YAG and Nd: YAG lasers in treatment of chronic periodontitis. A split-mouth, single-blind, randomized controlled trial // Journal of periodontal research. – 2017. – Vol 52(5). – P. 853-862. doi: https://doi.org/10.1111/jre.12454
3. Astuti S.D. et al. The efficacy of photodynamic inactivation with laser diode on Staphylococcus aureus biofilm with various ages of biofilm // Infectious disease reports. – 2020. – Vol. 12(S1). – P. 68-74. doi: https://doi.org/10.4081/idr.2020.8736
4. Astuti S.D. et al. Chlorophyll mediated photodynamic inactivation of blue laser on Streptococcus mutans // In AIP Conference Proceedings. – 2016. –Vol. 1718(1). – P. 120001.
5. Daigo Y. et al. Wound healing and cell dynamics including mesenchymal and dental pulp stem cells induced by photobiomodulation therapy: an example of socket-preserving effects after tooth extraction in rats and a literature review // International Journal of Molecular Sciences. – 2020. – Vol. 21(18). – P. 6850. doi: https://doi.org/10.3390/ijms21186850
6. de Paula Eduardo C. et al. Laser phototherapy in the treatment of periodontal disease. A review // Lasers in medical science. – 2010. – Vol. 25 (6). – P. 781-792. doi: DOI 10.1007/s10103-010-0812-y
7. Eming S.A. et al. Wound repair and regeneration: mechanisms, signaling, and translation // Science translational medicine. – 2014. – Vol. 6 (265). – P. 265sr6-265sr6. doi: DOI: 10.1126/scitranslmed.3009337
8. Mardianto A.I. et al. Photodynamic Inactivation of Streptococcus mutan Bacteri with Photosensitizer Moringa oleifera Activated by Light Emitting Diode (LED) // In Journal of Physics: Conference Series. – 2020. – Vol. 1505 (1). – P. 012061
9. Sutherland J.C. et al. Biological Effects of Polychromatic Light // Photochemistry and photobiology. – 2002. – Vol. 76 (2). – P. 164-170. doi: https://doi.org/10.1562/0031-8655(2002)0760164BEOPL2.0.CO2
10. Astuti S.D. et al. Photodynamic effectiveness of laser diode combined with ozone to reduce Staphylicoccus aureus biofilm with exogenous chlorophyll of Dracaena angustifolia leaves // Biomedical Photonics. – 2019. – Vol. 8 (2). – P. 4-13.
11. Correia J.H. et al. Photodynamic therapy review: Principles, photosensitizers, applications, and future directions // Pharmaceutics. – 2021. – Vol. 13 (9). – P. 1332. doi: https://doi.org/10.3390/pharmaceutics13091332
12. Astuti S.D. et al. Combination effect of laser diode for photodynamic therapy with doxycycline on a wistar rat model of periodontitis // BMC oral health. – 2021. – Vol. 21(1). – P. 1-15.
13. Hung C.M. et al. Gingyo-san enhances immunity and potentiates infectious bursal disease vaccination. Evid // Based Complementary Altern Med. – 2011. doi: https://doi.org/10.1093/ecam/nep021
14. Plaetzer K. et al. Photophysics and photochemistry of photodynamic therapy: fundamental aspects // J Lasers Med Sci. – 2009. – Vol. 24 (2). – P. 259-268.
15. Ren C. et al. The effectiveness of low-level laser therapy as an adjunct to non-surgical periodontal treatment: a meta-analysis // J. Periodontal Res. – 2017. – Vol. 52 (1). – P. 8-20. doi: https://doi.org/10.1111/jre.12361
16. Gilowski L. et al. Amount of interleukin-1β and interleukin-1 receptor antagonist in periodontitis and healthy patients // Arch. Oral Biol. – 2014. – Vol. 59 (7). – P. 729-734. doi: https://doi.org/10.1016/j.archoralbio.2014.04.007
17. Harvey J.D. et al. Periodontal microbiology // Dent. Clin. – 2017. – Vol. 61 (2). – P. 253-269. doi: https://doi.org/10.1016/j.cden.2016.11.005
18. Iglesias-Bartolome R. et al. Transcriptional signature primes human oral mucosa for rapid wound healing // Sci. Transl. Med. – 2018. – Vol. 10 (451). – P. eaap8798. doi: 10.1126/scitranslmed. aap8798
19. Savitt E.D. et al. Distribution of certain subgingival microbial species in selected periodontal conditions // J Periodontal Res. – 1984. – Vol. 19 (2). – P. 111-23. doi: https://doi.org/10.1111/j.1600-0765.1984.tb00800.x
20. Ismiyatin K. et al. Different 650 nm laser diode irradiation times affect the viability and proliferation of human periodontal ligament fibroblast cells // Dent. J (Majalah Kedokteran Gigi. – 2019. – Vol. 52 (3). – P. 142-142.

21. Politis C. et al. Wound healing problems in the mouth. *Front. Physiol*, 2016, vol. 7, pp. 507. doi: https://doi.org/10.3389/fphys.2016.00507
22. Popova C. et al. Correlation Between Healing Parameters and PGE2 Expression Levels in Non-Surgical Therapy of Chronic Periodontitis. *J of IMAB – Annual Proceeding Scientific Papers,* 2017, vol. 23 (4), pp. 1758-1764. doi: 10.5272/jimab.2017234.1758
23. Arjmand B. et al. Low-Level Laser Therapy: Potential and Complications. *J Lasers Med Sci*, 2021, vol. 12. doi: 10.34172/jlms.2021.42
24. Rosso M.P.D.O. et al. Photobiomodulation therapy (PBMT) in peripheral nerve regeneration: a systematic review. *J. Biomed. Eng*, 2018, vol. 5 (2), pp. 44. doi: https://doi.org/10.3390/bioengineering5020044
25. Farivar S. et al. Biological effects of low-level laser therapy. *J Lasers Med Sci*, 2014, vol. 5 (2), pp. 58.
26. Suhariningsih D. et al. The effect of electric field, magnetic field, and infrared ray combination to reduce HOMA-IR index and GLUT 4 in diabetic model of Mus musculus. *Lasers in Medical Science*, 2020, vol. 35 (6), pp. 1315-1321.
27. Astuti S.D. et al. Effectiveness Photodynamic Inactivation with Wide Spectrum Range of Diode Laser to Staphylococcus aureus Bacteria with Endogenous Photosensitizer: An in vitro Study. *Journal of International Dental and Medical Research*, 2019, vol. 12 (2), pp. 481-486.
28. Ren C. et al. The effectiveness of low-level laser therapy as an adjunct to non-surgical periodontal treatment: a meta-analysis. *J. Periodontal Res*, 2017, vol. 52 (1), pp. 8-20. doi: https://doi.org/10.1111/jre.12361
29. Setiawatie E.M. et al. An in vitro Anti-microbial Photodynamic Therapy (APDT) with Blue LEDs to activate chlorophylls of Alfalfa Medicago Sativa L on Aggregatibacter actinomycetemcomitans. *J. Int. Dent. Medical Res*, 2016, vol. 9 (2), pp. 118-125.
30. Sidharthan S. et al. Gingival crevicular fluid levels of Interleukin-22 (IL-22) and human β Defensin-2 (hBD-2) in periodontal health and disease: A correlative study. *J Oral Biol Craniofac Res*, 2020, vol. 10 (4), pp. 498-503. doi: https://doi.org/10.1016/j.jobcr.2020.07.021
31. Tang E. et al. Laser-activated transforming growth factor-β1 induces human β-defensin 2: implications for laser therapies for periodontitis and peri-implantitis. *J. Periodontal Res*, 2017, vol. 52 (3), pp. 360-367. doi: https://doi.org/10.1111/jre.12399
32. Muliani Izat W.O.A. et al. The Effectiveness of Sea Cucumber Extract (Holothuroidae Sp) on Interleukin-1β (IL-1β) Expression in Periodontitis (Research on Wistar Rats). *(Doctoral dissertation, Hasanuddin University)*, 2020.
33. Genco R.J. et al. Periodontal disease and overall health: a clinician's guide. *Yardley, Pennsylvania, USA: Professional Audience Communications Inc*, 2010, pp. 254-263.
34. Santosa B. et al. Elisa Method for Measurement of Metallothionein Protein in Rice. *Leaves Ir Bagendit*, 2020.
35. Sakurai Y. et al. Inhibitory effect of low-level laser irradiation on LPS stimulated prostaglandin E2 production and cyclooxygenase 2 in human gingival fibroblasts. *Eur. J. Oral Sci*, 2000, vol. 108 (1), pp. 29-34. doi: https://doi.org/10.1034/j.1600-0722.2000.00783.x
36. Hanna R. et al. Phototherapy as a rational antioxidant treatment modality in COVID-19 management; new concept and strategic approach: a critical review. *Antioxidants*, 2020, vol. 9 (9), pp. 875. doi: https://doi.org/10.3390/antiox9090875
37. Ebrahimi P. et al. Effect of photobiomodulation in secondary intention gingival wound healing a systematic review and meta-analysis. *BMC Oral Health,* 2021, vol. 21 (1), pp. 1-16.
38. Astuti S.D. et al. Effectiveness of 650 nm red laser photobiomodulation therapy to accelerate wound healing post tooth extraction. *Biomedical Photonics*, 2024, vol. 13 (1), pp. 4-15. https://doi.org/10.24931/2413-9432-2024-13-1-4-15
39. Genco R.J. et al. Periodontal disease and overall health: a clinician's guide. *Yardley, Pennsylvania, USA: Professional Audience Communications Inc*, 2010, pp. 254-263.
40. Avci P. et al. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring. *Semin Cutan Med Surg*, 2013, vol. 32 (1), pp. 41.
41. Rasouli M. et al. The interplay between extracellular matrix and progenitor/stem cells during wound healing: Opportunities and future directions. *Acta Histochemica*, 2021, Vol. 123 (7), pp. 151785. doi: https://doi.org/10.1016/j.acthis.2021.151785.

21. Politis C. et al. Wound healing problems in the mouth // Front. Physiol. – 2016. – Vol. 7. – P. 507. doi: https://doi.org/10.3389/fphys.2016.00507
22. Popova C. et al. Correlation Between Healing Parameters and PGE2 Expression Levels in Non-Surgical Therapy of Chronic Periodontitis // J of IMAB – Annual Proceeding Scientific Papers. – 2017. – Vol. 23 (4). – P. 1758-1764. doi: 10.5272/jimab.2017234.1758
23. Arjmand B. et al. Low-Level Laser Therapy: Potential and Complications // J Lasers Med Sci. – 2021. – Vol. 12. doi: 10.34172/jlms.2021.42
24. Rosso M.P.D.O. et al. Photobiomodulation therapy (PBMT) in peripheral nerve regeneration: a systematic review // J. Biomed. Eng. – 2018. – Vol. 5 (2). – P. 44. doi: https://doi.org/10.3390/bioengineering5020044
25. Farivar S. et al. Biological effects of low-level laser therapy // J Lasers Med Sci. – 2014. – Vol. 5 (2). – P. 58.
26. Suhariningsih D. et al. The effect of electric field, magnetic field, and infrared ray combination to reduce HOMA-IR index and GLUT 4 in diabetic model of Mus musculus // Lasers in Medical Science. – 2020. – Vol. 35 (6). – P. 1315-1321.
27. Astuti S.D. et al. Effectiveness Photodynamic Inactivation with Wide Spectrum Range of Diode Laser to Staphylococcus aureus Bacteria with Endogenous Photosensitizer: An in vitro Study // Journal of International Dental and Medical Research. – 2019. – Vol. 12 (2). – P. 481-486.
28. Ren C. et al. The effectiveness of low-level laser therapy as an adjunct to non-surgical periodontal treatment: a meta-analysis // J. Periodontal Res. – 2017. – Vol. 52 (1). – P. 8-20. doi: https://doi.org/10.1111/jre.12361
29. Setiawatie E.M. et al. An in vitro Anti-microbial Photodynamic Therapy (APDT) with Blue LEDs to activate chlorophylls of Alfalfa Medicago Sativa L on Aggregatibacter actinomycetemcomitans // J. Int. Dent. Medical Res. – 2016. – Vol. 9 (2). – P. 118-125.
30. Sidharthan S. et al. Gingival crevicular fluid levels of Interleukin-22 (IL-22) and human β Defensin-2 (hBD-2) in periodontal health and disease: A correlative study // J Oral Biol Craniofac Res. – 2020. – Vol. 10 (4). – P. 498-503. doi: https://doi.org/10.1016/j.jobcr.2020.07.021
31. Tang E. et al. Laser-activated transforming growth factor-β1 induces human β-defensin 2: implications for laser therapies for periodontitis and peri-implantitis // J. Periodontal Res. – 2017. – Vol. 52 (3). – P. 360-367. doi: https://doi.org/10.1111/jre.12399
32. Muliani Izat W.O.A. et al. The Effectiveness of Sea Cucumber Extract (Holothuroidae Sp) on Interleukin-1β (IL-1β) Expression in Periodontitis (Research on Wistar Rats) // (Doctoral dissertation, Hasanuddin University). – 2020.
33. Genco R.J. et al. Periodontal disease and overall health: a clinician's guide // Yardley, Pennsylvania, USA: Professional Audience Communications Inc. – 2010. – P. 254-263.
34. Santosa B. et al. Elisa Method for Measurement of Metallothionein Protein in Rice // Leaves Ir Bagendit. – 2020.
35. Sakurai Y. et al. Inhibitory effect of low-level laser irradiation on LPS stimulated prostaglandin E2 production and cyclooxygenase 2 in human gingival fibroblasts // Eur. J. Oral Sci. – 2000. – Vol. 108 (1). – P. 29-34. doi: https://doi.org/10.1034/j.1600-0722.2000.00783.x
36. Hanna R. et al. Phototherapy as a rational antioxidant treatment modality in COVID-19 management; new concept and strategic approach: a critical review // Antioxidants. – 2020. – Vol. 9 (9). – P. 875. doi: https://doi.org/10.3390/antiox9090875
37. Ebrahimi P. et al. Effect of photobiomodulation in secondary intention gingival wound healing a systematic review and meta-analysis // BMC Oral Health. – 2021. – Vol. 21 (1). – P. 1-16.
38. Astuti S.D. et al. Effectiveness of 650 nm red laser photobiomodulation therapy to accelerate wound healing post tooth extraction // Biomedical Photonics. – 2024. – Vol. 13 (1). – P. 4-15. https://doi.org/10.24931/2413-9432-2024-13-1-4-15
39. Genco R.J. et al. Periodontal disease and overall health: a clinician's guide // Yardley, Pennsylvania, USA: Professional Audience Communications Inc. – 2010. – P. 254-263.
40. Avci P. et al. Low-level laser (light) therapy (LLLT) in skin: stimulating, healing, restoring // Semin Cutan Med Surg. – 2013. – Vol. 32 (1). – P. 41.
41. Rasouli M. et al. The interplay between extracellular matrix and progenitor/stem cells during wound healing: Opportunities and future directions // Acta Histochemica. –2021. – Vol. 123 (7). – P. 151785. doi: https://doi.org/10.1016/j.acthis.2021.151785.