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EFFECT OF LASER, ANTIBIOTIC, PHOTOSENSITIZER AND THEIR COMBINATIONS ON THE HEALING RATE OF MICE WOUND INFECTED BY *STAPHYLOCOCCUS AUREUS*

[1]*Mohemid Maddallah Al-Jebouri, [2]Thamer Mutlek

[1]Department of Medical Laboratory Technology, College of Health and Medical Technology, Al-Qalam University, Kirkuk, Iraq.

[2]Department of Microbiology, College of Medicine, University of Tikrit, Tikrit, Iraq.

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***Corresponding Author**

Prof. Dr. Mohemid Maddallah Al-Jebouri

Department of Medical Laboratory Technology, College of Health and Medical Technology, Al-Qalam University, Kirkuk, Iraq.

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ABSTRACT

Background: Most workers in the field of laser stimulation for wound healing have applied wave length that presumably do not produce serious damage to the skin of the host. Laser stimulated several aspects of wound healing involving stimulation of blood clotting, phagocytosis by leucocytes, dilatation of blood vessels, hyperplasia, protein synthesis in fibroblast and growth of hairs. **Materials and Methods**: Different therapeutic interventions including cefotaxime, providine-iodine, laser irradiation and their combinations were carried out. a Helium-Neon (He/Ne) gas type was used. Providine-iodine (I. C. I., Britain) as a photosensitizer was used. Cefotaxime (SDI, Iraq) was utilized which was dissolved in phosphate buffer 6 and diluted with sterile distilled water. 420 Swiss albino mice of 25 gram weight were taken from the laboratory of the Biological and Pharmaceutical Quality Control(Baghdad). **Results:** The present study revealed that the rate of healing of mice wound after exposure to treatment by providine-iodine+cefotaxime and laser irradiation was 2.50 mm/day whereas the least healing rate was seen with infected wound without any sort of treatment or disinfection. The other combinations of treatment demonstrated different mean of healing**.** Treatments involving laser irradiation combined with cefotaxime and/or providine-iodine demonstrated markedly improved healing efficiency compared with single therapies or untreated controls. regression model explained

approximately 66.8% of the variability in healing rate. **Conclusions**: It was concluded that the rate of wound healing was 2.50 mm/day after treatment by cefotaxime and disinfectant with providine-iodine with exposure to laser light for 3 minutes, whereas this rate of healing was 1.46 mm/day after exposure to laser for 0.5 minute and subjected to the same disinfectant and antibiotic. The analysis demonstrated a significant negative correlation between treatment duration and healing rate ($p < 0.05$). Treatment durations were associated with higher wound healing rates. The L+PI+CEF combination produced the highest healing response (2.50 ± 0.23 Shorter mm/day) within only 7 days, indicating a strong synergistic therapeutic effect.

KEYWORDS: Mice, wound, infection, healing, laser, cefotaxime, providine-iodine.

INTRODUCTION

Most workers in the field of laser stimulation for wound healing have applied wave length that presumably do not produce serious damage to the skin of the host.[1] The effect of He/Ne laser with power of 1.0 mW, wavelength 632.8 nm and beam diameter of 0.6-1.0 nm that affecting wound healing by four mechanisms like mechanical, surface, thermal and chemical types which were applied to mice animal. The results revealed that the low dose of laser action exertion accumulative fashion or several phases of wound healing.[2,3,4] Laser stimulated several aspects of wound healing involving stimulation of blood clotting, phagocytosis by leucocytes, dilatation of blood vessels, hyperplasia, protein synthesis in fibroblast and growth of hairs. These stimulatory actions were histological substantiated and no abnormalities in cells were detected.[5,6] Isotomin et al. showed that the low-intensity laser have an effect on healing processes in intestinal sutures in rabbits[8] and in guinea pigs by 2-4 days faster compared to nontreated wounds by laser.[7,8] The Nd:YAG laser has been the subject of a number of studies regarding its possible application in dentistry. However, reports of its bactericidal effect are sparse. The viabilities of suspension of *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* were reduced only by energy doses greater than 600J(energy density equal to 1667J/cm^2) during a 10 second exposure. Light from the argon fluoride excimer laser can kill a range og Gram-positive and Gram-negative bacteria as well as the fungi *Candida albicans*. *S. aureus* developed resistance to many of the topical agents[4,9], several antibiotics, antiseptics and disinfectants emphasized the need to identify new techniques to eradicate this organism from infected wounds. Malik et al. described the lethal photosensitization of *S. aureus* using white light sources and

hematoporphyrin as a sensitizer.[10] Szuminsty et al. found that the high-voltage pulsed current produced antimicrobial action against *S. aureus, Ps. aeruginosa, Klebsiella* and *E.coli* promoted to using it in the healing of decubitcus ulcers and surgical wounds by further studies in vivo.[11,12,13] It appeared that S. aureus can be killed by short term exposure to light from 7-3mW He/Ne laser in the presence of toluidine blue O as an exogenous photosensitizer.[14] Also it was found that more than 90% of S. aureus suspension can be killed by short-term exposure to light from a 11-Mw gallium aluminum arsenide (Ga-Aa) diode laser with aluminum desulphonated phthalocyanine (ALPCS2) as an exogenous photosensitizer.[15,16,17] Methicillin-resistant *S. aureus* strain recently was killed by a short-term exposure to light from a low-power He/Ne laser in the presence of low concentration (12.5 mg/l) of toluidine blue O.[4] Providine-iodine is the best known iodophore, a complex of elemental iodine with a carrier, 1-vinyl-2-pyrrolidinone, which provides increasing solubility of the iodine and sustained-release of the iodine.[18] Al-Jebouri and Al-Obaidy found that the providine-iodine long exerts antimicrobial activities and consequently laser + providine – iodine combination was more effective in killing *S. aureus* compared to providine-iodine, laser, laser+ toluidine blue O combinations.[4] Al-Jebouri and Al-Obaidy found that the providine-iodine was more effective photosensitizer compared to toluidine blue O used by Wilson and Pratten.[14,15]

MATERIALS AND METHODS

Wound bacterial pathogen

The bacterial pathogen used for infection experiment of mice wound was *Staphylococcus aureus.* This bacterium was isolated from patient wound medicated in Tikrit teaching hospital and identified following other authors.[19,20]

Laser light

The laser was a Helium-Neon (He/Ne) gas type with a measured output of 5mW (Laser Beacon, I. N. C, Michigan, USA) used in the present study. The emitted light had a wavelength of 632.8 nm.[21,22]

Photosensitizer

Providine-iodine (I. C. I., Britain) was used.

Antibiotic

Cefotaxime (SDI, Iraq) was utilized which was dissolved in phosphate buffer 6 and diluted

with sterile distilled water.

Experimental animal

420 Swiss albino mice of 25 gram weight were taken from the laboratory of the Biological and Pharmaceutical Quality Control(Baghdad). They were housed in the animal house of Tikrit University Medical College. They were kept in plastic cages in groups of 5 mice with feed pellets from Iba Centre (Baghdad). The animals were kept at room temperature adjusted to 25 ^{0}C. They were allowed food and water.[8,23]

Infection of wounds with Staphylococcus aureus

One day prior to infection process, mice were anaesthetized by ether anesthesia.[8,24] The back of the mice was shaved with a fine-tooth electric clipper. On the day of infection, wound was made on the backs of the reanesthesized mice[25] by making a longitudinal midline incision one cm in length and extending down to the panniculus carnosus. The wound was infected by dipping a drop of Pasteur pipette by seeding 10^{5} colony forming unit(CFU) of *S. aureus*.[8,26]

Animal treatment design

After induction of the wounds, animals were divided into 9 groups as follow:

First group.80 mice were treated by intramuscular injection of 3 mg cefotaxime (16.67 mg/kg B.W./day) as a single daily injection. The wounds was flooded with photosensitizer of providine-iodine. The animals were subdivided into four subgroups 20 animals each prior to laser radiation for 0.5, 1, 2 and 3 minutes for one exposure for each 3 days.

Second group: 80 mice were treated by intramuscular injection of 3 mg cefotaxime (16.67 mg/kg B.W./day) as a single daily injection. The animals were subdivided into four subgroups 20 animals each prior to laser radiation for 0.5, 1, 2 and 3 minutes for one exposure for each 3 days.

Third group: The wounds of 80 mice were flooded with providine-iodine. The animals were subdivided into four subgroups 20 animals each prior to laser radiation for 0.5, 1, 2 and 3 minutes for one exposure for each 3 days.

Fourth group: 80 mice were subdivided into 4 subroups and the wounds were made and exposed to laser irradiation for 0.5, 1, 2 and 3 minutes as one exposure each 3 days.

Fifth group: 20 mice were treated by cefotaxime 3 mg(16.67 mg/kg.B.w./day) as a single daily intramuscular injection and the wound was flooded with providine -iodine.

Sixth group: 20 mice were treated by cefotaxime 3 mg only and the intramuscular injection was daily made.

Sevenxth group: 20 mice were treated by daily flooding the wounds by providine-iodine.

Eighth group: 20 mice with infected wounds but no treatment was made.

Ninth group: 20 mice with wounds but no infection by *S. aureus* was made.

The treatment of all groups were continued till complete healing of the wounds. The length of the wound was measured daily. Healing rate represented the reduction in the length of the wound.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as means, standard deviations, and frequency distributions were computed to summarize the data.[27,28]

RESULTS

Effect of cefotaxime, providine-iodine and laser combination

It was concluded that the rate of wound healing was 2.50 mm/day after treatment by cefotaxime and disinfectant with providine-iodine with exposure to laser light for 3 minutes, whereas this rate of healing was 1.46 mm/day after exposure to laser for 0.5 minute and subjected to the same disinfectant and antibiotic (Table 1). A one-way ANOVA was carried out to evaluate the effect of different laser exposure times on the wound healing rate in *Staphylococcus aureus*-infected mice treated with cefotaxime, providine-iodine, and laser irradiation. The F-statistic was 1.015 with P value more than 0.05 indicating no statistically significant difference in wound healing rates among the different laser exposure times(Figure 1).

Table 1: Rate of mice wound healing infected with *Staphylococcus aureus* treated with a combination of cefotaxime, providine-iodine and laser irradiation.

Exposure time for laser	No. of animals	Rate of healing/day:									Mean ±SD
		1	2	3	4	5	6	7	8	9	
3 min.	20	2.36	2.96	2.12	2.30						2.50±0.23
2 min.	20	1.70	0.32	2.32	2.42	3.16					1.98±1.06
1 min.	20	1.70	0.60	1.38	1.70	4..06	2.36				1.96±1.17
0.5 min.	20	1.88	1.88	1.58	2.14	1.16	1.56	1.86	0.10		1.46±0.67

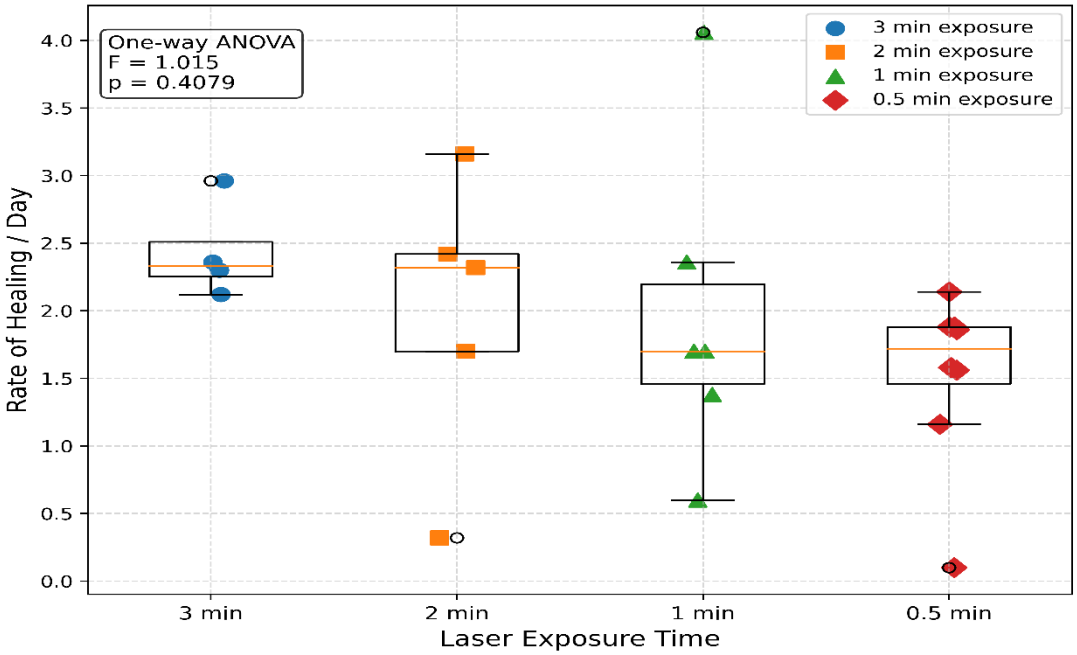

Figure 1: Effect of Laser Exposure Time on Wound Healing Rate in *Staphylococcus aureus*-Infected Mice Treated with Cefotaxime, Providine-Iodine, and Laser Irradiation.

Effect of cefotaxime and laser irradiation

The present study revealed that mean of wound healing was 1.45mm/day after treatment by cefotaxime and exposed to laser irradiation for 3 minutes, while when the exposure to the same combination for 0.5 minute was 1.08 mm/day. The of exposure of wound for irradiation for 2 and 1 minute was 1.90 and 0.96 mm/day respectively(Table 2). One-way ANOVA Results showed that F-statistic was 0.9399 and the P value was 0.4375 demonstrating no significant differences in wound healing rates among the different laser exposure durations (Figure 2).

Table 2: Rate of mice wound healing infected with *Staphylococcus aureus* treated with a combination of cefotaxime and laser irradiation.

Exposure time for laser	No. of animals	Mean ±SD								
		1	2	3	4	5	6	7	8	
3 min.	20	1.56	1.08	1.28	1.52	1.80				1.45±0.27
2 min.	20	1.30	1.40	0.26	0.84	0.78	0.94	2.12		1.90±0.58
1 min.	20	1.36	1.08	0.44	0.89	0.38	0.62	2.06		0.96±0.59
0.5 min.	20	1.54	0.96	0.64	0.94	0.94	1.02	1.86	1.20	1.08±0.28

The variations among groups were not significant (P< 0.05).

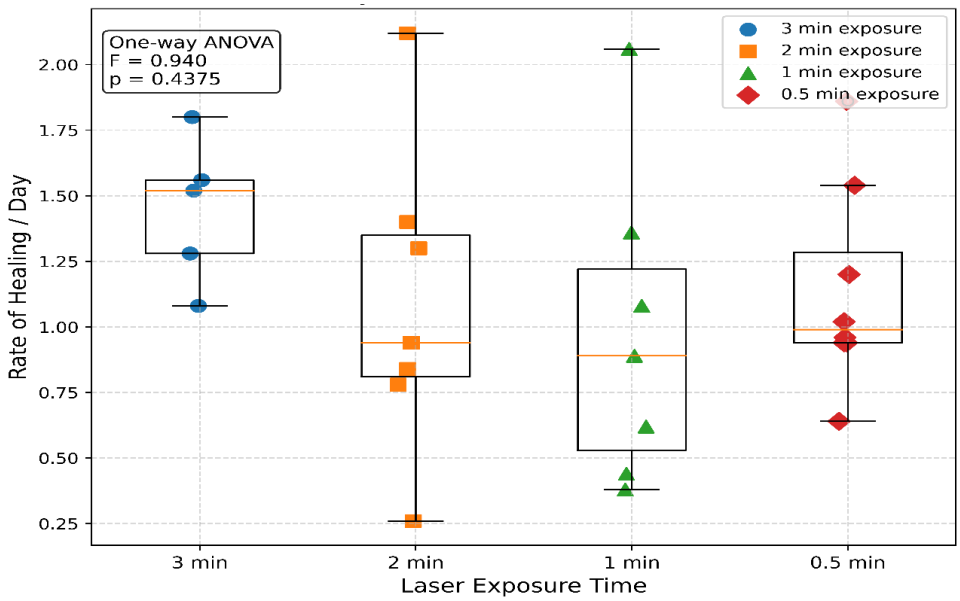

Figure 2: Effect of Cefotaxime and Laser Irradiation on Wound Healing Rate in *Staphylococcus aureus*-Infected Mice.

Effect of providine-iodine and laser irradiation

The rate of wound healing after exposure to providine-iodine and laser for 3,2,1 and 0.5 minute was 1.56,1.27, 1.29 and 1.29 mm/day respectively(Table 3). A one-way ANOVA was performed to determine the effect of different laser exposure durations on wound healing rates in *Staphylococcus aureus*-infected mice treated with providine-iodine and laser irradiation. This test revealed that F-statistic was 14.708 and P value was less than 0.0001. The analysis demonstrated a highly significant difference among the laser exposure groups ($p < 0.05$). The 3-minute laser exposure produced the highest wound healing rate with the lowest variability, indicating a more stable and effective therapeutic response. The 0.5-minute exposure demonstrated the lowest healing performance. Increasing laser exposure duration was associated with improved healing efficiency in mice treated with providine-iodine(Figure 3).

Table 3: Rate of mice wound healing infected with *Staphylococcus aureus* treated with a combination of providine-iodine and laser irradiation.

Exposure time for laser	No. of animals	Rate of healing (mm/day):							Mean ±SD
		1	2	3	4	5	6	7	
3 min.	20	1.48	1.66	1.62	1.49	1.53			1.56±0.08
2 min.	20	1.12	1.32	1.26	1.29	1.42	1.22		1.27±0.10
1 min.	20	1.22	1.21	1.16	1.16	1.16	1.28	1.26	1.29±0.16
0.5 min.	20	1.42	1.32	1.26	1.18	1.05	1.01	1.12	1.19±0.14

The variations among groups were not significant (P< 0.05).

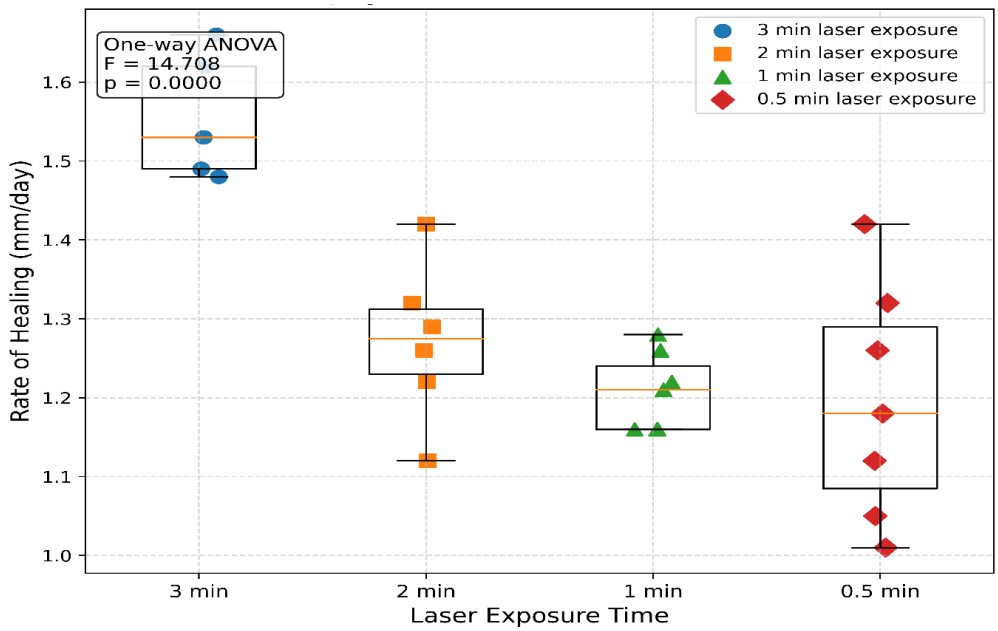

Figure 3: Effect of Providine-Iodine and Laser Irradiation on Wound Healing Rate in *Staphylococcus aureus*-Infected Mice.

Effect of laser irradiation

The rate of wound healing to laser irradiation for 3, 2, 1, and 0.5 minute was 0.86, 0.82, 0.74 and 0.7 mm/day respectively (Table 4).A one-way ANOVA was performed to evaluate the effect of different laser irradiation exposure periods on wound healing rates in *Staphylococcus aureus*-infected mice. This test showed that F-statistic was 0.602 and P value was 0.6172. The statistical analysis demonstrated no significant differences among the different laser exposure groups ($p > 0.05$). The 3-minute laser exposure produced the highest average wound healing rate. The 0.5-minute exposure demonstrated the lowest healing response and the highest variability. Although longer exposure periods tended to improve healing numerically, the differences were not statistically significant(Figure 4).

Table 4: Rate of mice wound healing infected with *Staphylococcus aureus* treated with different periods of exposure to laser irradiation.

Exposure time for laser	No. of animals	Rate of healing/day:													Mean ±SD
		1	2	3	4	5	6	7	8	9	10	11	12	13	
3 min.	20	2.30	1.02	1.00	0.64	0.84	0.60	1.06	0.64	0.64	0.46	0.56	0.56		0.86±0.49
2 min.	20	1.20	1.02	0.62	1.38	1.28	0.94	0.60	0.70	0.68	0.82	0.46	0.20		0.82±0.35
1 min.	20	0.66	0.90	0.94	0.84	0.80	0.64	1.06	1.32	0.10	0.30	0.54	024	0.35	0.74±0.32
0.5 min.	20	0.60	0.86	0.96	0.96	0.60	0.52	1.70	0.90	0.06	0.46	0.24	0.06	1.22	0.70±0.46

The variation among different groups were not significant (P>0.05).

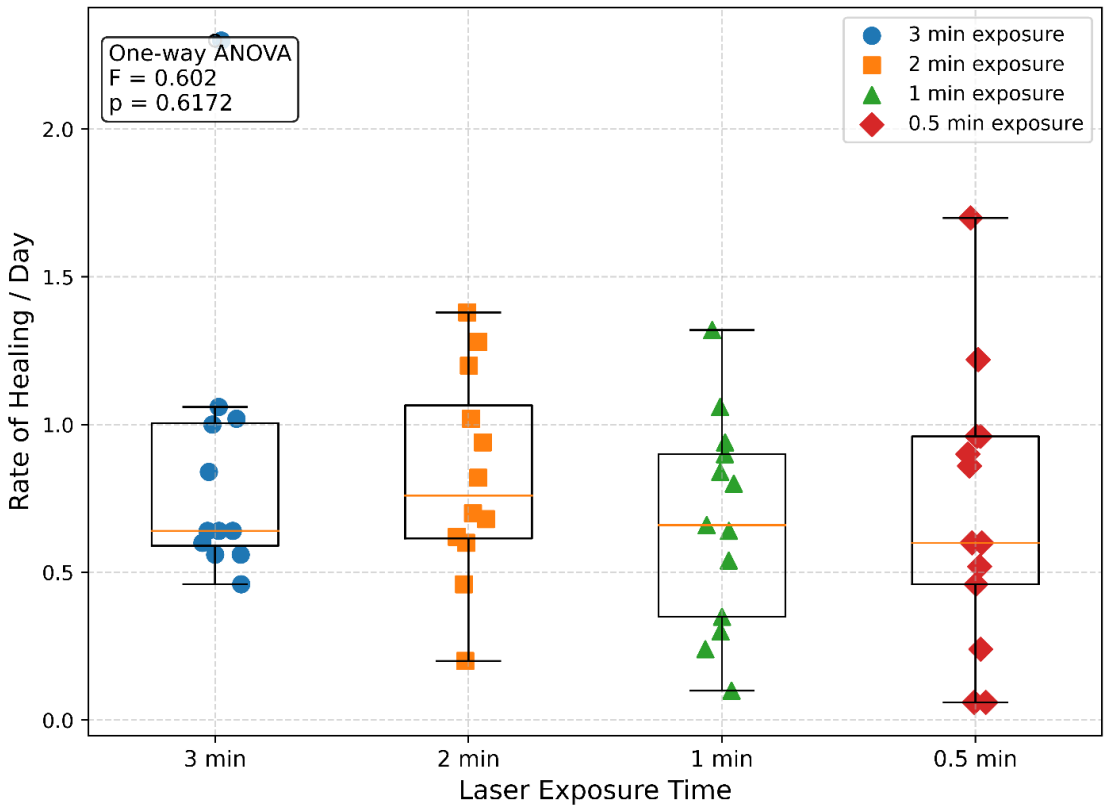

Figure 4: Effect of Different Periods of Laser Irradiation on Wound Healing in *Staphylococcus aureus*-Infected Mice.

Healing rate of mice wound subjected to different combinations of treatment

The present study revealed that the rate of healing of mice wound after exposure to treatment by providine-iodine+cefotaxime and laser irradiation was 2.50 mm/day whereas the least healing rate was seen with infected wound without any sort of treatment or disinfection. The other combinations of treatment demonstrated different mean of healing (Table 5). A linear regression and Pearson correlation analysis (y=−0.1380x+2.6490) were performed to evaluate the relationship between treatment duration and wound healing rate among different therapeutic combinations. This test revealed that correlation coefficient (R) was -0.817 and coefficient of determination (R^2) was 0.668 and the P value was 0.0072. The analysis demonstrated a significant negative correlation between treatment duration and healing rate ($p < 0.05$). Treatment durations were associated with higher wound healing rates. The L+PI+CEF combination produced the highest healing response (2.50 ± 0.23 Shorter mm/day) within only 7 days, indicating a strong synergistic therapeutic effect. Treatments involving laser irradiation combined with cefotaxime and/or providine-iodine demonstrated markedly improved healing efficiency compared with single therapies or untreated controls. regression model explained approximately 66.8% of the variability in healing rate(Figure 5).

Table 5: The mean of healing rate measured in millimeters of mice wounds treated with different combinations for different times.

Type of treatment	Days of treatment	Mean± SD*
Uninfected wound	14	0.73±0.021
Infected wound	16	0.61±0.32
CEF*	14	0.71±0.22
PI	15	0.61±0.19
CEF+PI	13	0.74±0.33
L	9	0.86±0.49
L+PI	7	1.56±0.08
L+CEF	7	1.45±0.27
L+PI+CEF	7	2.50±0.23

*= CEF, cefotaxime; PI, providine iodine; L, laser; SD, standard deviation.

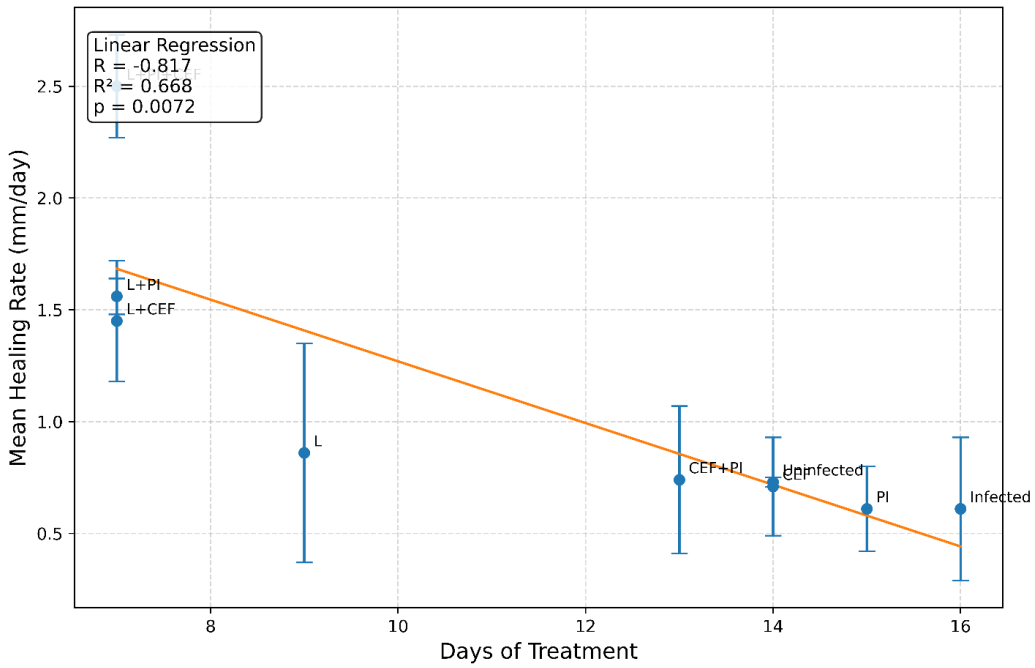

Figure 5: Linear Regression Analysis of Treatment Duration Versus Wound Healing Rate in Different Therapeutic Combinations.

DISCUSSION

The pre sent study revealed that the rate of wound healing was 2.50 mm/day after treatment by cefotaxime and disinfectant with providine-iodine and exposure to laser light for 3 minutes, whereas this rate of healing was 1.46 mm/day after exposure to laser for 0.5 minute and subjected to the same disinfectant and antibiotic combination. However, A study conducted by De Angelis et al. revealed that all 11 participants completed the eight photobiomodulation sessions over a four-week period. However, two were lost to follow-up at twelve weeks: one participant died due to a cardiovascular event, and the other was

hospitalized with pneumonia. By the end of the photobiomodulation treatment (week four), nine hard-to-heal wounds had reduced in area, with a mean wound size of 9.5 cm2 (SD ± 11.4) and a mean percentage reduction of 24.6%(SD ± 47.6). However, the difference in wound area between baseline and at the end of biomodulation treatment (week four) was not statistically significant (p = 0.140). At the end of follow-up (week twelve), seven hard-to-heal wounds had reduced in area compared to baseline, with a mean wound size of 7.2 cm2 (SD ± 13) and a mean percentage reduction of40.5% (SD ± 45). A statistically significant reduction in wound area was observed at week12 compared to baseline (p = 0.04).[29,30,31,32] Moreover, the present study showed that a one-way ANOVA was carried out to evaluate the effect of different laser exposure times on the wound healing rate in *Staphylococcus aureus*-infected mice treated with cefotaxime, providine-iodine, and laser irradiation. The F-statistic was 1.015 with P value more than 0.05 indicating no statistically significant difference in wound healing rates among the different laser exposure times. A study conducted elsewhere it was demonstrated that at week 4, an area reduction was shown in 9 of 11 wounds (mean: 9.5 cm2, SD ± 11.4), though not statistically significant (p = 0.240). At week 12, a significant reduction was observed (mean: 7.2 cm2, SD ± 13; p = 0.04), with a mean percentage area decrease of 40.5%. Significant improvements were also noted in pain levels, exudate characteristics, and surrounding skin conditions over time.[29,33,34,35] Furthermore, the present study revealed that mean of wound healing was 1.45mm/day after treatment by cefotaxime and exposed to laser irradiation for 3 minutes, while when the exposure to the same combination for 0.5 minute was 1.08 mm/day. The of exposure of wound for irradiation for 2 and 1 minute was 1.90 and 0.96 mm/day respectively. Kandela et al. found that the wound healing rate was significantly stimulated in various phases of healing process by repeated exposure to laser irradiation.[36] Many mechanisms were given to laser as wound healing stimulators. Kandela et al. reported that this effect attributed to quicker response of phagocytic cell and initiation of fibroblastic reaction and rapid re-epithelization induced by laser.[36] Reid said that the increase in the healing rate of the wounds attributed to high sterilizing effect of laser compared to antiseptics.[37,38,39,40] Furthermore, the present study revealed that mean of wound healing was 1.45mm/day after treatment by cefotaxime and exposed to laser irradiation for 3 minutes, while when the exposure to the same combination for 0.5 minute was 1.08 mm/day. The of exposure of wound for irradiation for 2 and 1 minute was 1.90 and 0.96 mm/day respectively. One-way ANOVA Results showed that F-statistic was 0.9399 and the P value was 0.4375 demonstrating no significant differences in wound healing rates among the different laser exposure durations. On the other hand, Kuppa et al.

examined the effects of 630 nm red-light laser therapy on wound healing, with a focus on VEGF-mediated angiogenesis and collagen production. The effectiveness of red-light therapy is influenced by critical parameters, including treatment duration and distance, which often lack standardization across protocols. To address this, we conducted cell viability and scratch wound assays using NIH/3T3 cells in-vitro to identify optimal treatment conditions. Treatment durations of 10 s, 30 s, 60 s, and 5 min, along with distances of 3 cm and 5 cm, were evaluated. Following parameter optimization, the wound-healing efficacy of red-light therapy was assessed in-vivo using nude mice. Standardized 4 mm wounds were created using a biopsy punch, and healing was evaluated at 7 and 21-days post-intervention. Histological analysis was performed, and gene and protein expression levels of COL1A1, COL2A1, VEGF, and IL-1β, which are implicated in wound healing, were assessed via RT-PCR, western blotting, and immunohistochemistry. Results demonstrated that red-light laser therapy significantly upregulated collagen and VEGF expression while reducing IL-1β levels at the three-week time point ($p < 0.05$). Notably, these effects were comparable to hydrogel treatment, which served as a positive control to assess the efficacy of light-emitting diode (LED)-based therapy. These findings indicate that red-light therapy effectively promotes wound healing by enhancing collagen synthesis and VEGF-mediated angiogenesis within the wound bed.[41,42,43,44] Furthermore, The 3-minute laser exposure produced the highest wound healing rate with the lowest variability, indicating a more stable and effective therapeutic response. The 0.5-minute exposure demonstrated the lowest healing performance. Increasing laser exposure duration was associated with improved healing efficiency in mice treated with providine-iodine. The present study revealed that the rate of healing of mice wound after exposure to treatment by providine-iodine+cefotaxime and laser irradiation was 2.50 mm/day whereas the least healing rate was seen with infected wound without any sort of treatment or disinfection. The other combinations of treatment demonstrated different mean of healing. The analysis demonstrated a significant negative correlation between treatment duration and healing rate ($p < 0.05$). treatment durations were associated with higher wound healing rates. The L+PI+CEF combination produced the highest healing response (2.50 ± 0.23 Shorter mm/day) within only 7 days, indicating a strong synergistic therapeutic effect. Treatments involving laser irradiation combined with cefotaxime and/or providine-iodine demonstrated markedly improved healing efficiency compared with single therapies or untreated controls. regression model explained approximately 66.8% of the variability in healing rate. Moreover, Laser therapy has emerged as a preferred treatment for many types of scars.[45,46,47,48] The core mechanism of laser therapy for scarring is the synergistic effect of physical disruption,

molecular signal modulation and combination therapy to achieve collagen remodeling, vascular normalization and inflammation abatement, ultimately improving the appearance and function of the scar.[46,47, 50,51,52] However, the histologic and biochemical sequence of event in tissue wound healing is well characterized. Hyaluronic acid appears early in wound healing. Its subsequent degradation by the enzyme hyaluronidase is the triggering event for the subsequent stages of wound healing that lead to complete repair. In the early stages of wound repair, there is the deposition of high molecular weight hyaluronic acid at the wound site. The origin of this newly synthesized hyaluronic acid molecules is uncertain because there is very little hyaluronic acid circulating in the blood. In homeostasis, hyaluronic acid molecule bind to fibrinogen and act as a scaffold in the formation of a fibrin network. Hyaluronic acid also acts as a catalyst in fibrin clot formation subsequent to thrombin action. In the inflammatory response, hyaluronic acid enhances phagocytosis by monocytosis.[1,29,3942,50,53,54] Chronic wounds represent a major clinical challenge due to delayed healing, susceptibility to infections, and substantial functional and economic burdens.[55,56,57] Although this review presents consistent preclinical evidence, the relevance of these cellular responses to the context of chronic wounds is still uncertain, given that these models exhibit persistent inflammation, hypoxia, phenotypic alterations of fibroblasts, and vascular compromise. Therefore, the next translational step should focus on rigorously characterized chronic animal models capable of reproducing this pathophysiological complexity.[58,59,60,61,62,63] Therefore, we can conclude the enhancement of wound healing in the present study could be attributed to bactericidal effect of laser, effect of the laser on the viability and virulency of the bacteria, increase the sensitivity of the bacteria and enhancement of biochemical events participated in wound healing.[64,65,66,67,68,69,70,71] The Nd:YAG laser has been the subject of a number of studies regarding its possible application in dentistry. However, reports of its bactericidal effect are sparse. The viabilities of suspension of *Pseudomonas aeruginosa*, *Escherichia coli* and *Staphylococcus aureus* were reduced only by energy doses greater than 600J(energy density equal to 1667J/cm^2) during a 10 second exposure.[72,73,74,75,76]

CONCLUSIONS

The 3-minute laser exposure produced the highest wound healing rate with the lowest variability, indicating a more stable and effective therapeutic response. The 0.5-minute exposure demonstrated the lowest healing performance. Increasing laser exposure duration was associated with improved healing efficiency in mice treated with providine-iodine. It was

concluded that the rate of wound healing was 2.50 mm/day after treatment by cefotaxime and disinfectant with providine-iodine with exposure to laser light for 3 minutes, whereas this rate of healing was 1.46 mm/day after exposure to laser for 0.5 minute and subjected to the same disinfectant and antibiotic. The analysis demonstrated a significant negative correlation between treatment duration and healing rate ($p < 0.05$). Treatment durations were associated with higher wound healing rates. The L+PI+CEF combination produced the highest healing response (2.50 ± 0.23 Shorter mm/day) within only 7 days, indicating a strong synergistic therapeutic effect for eradication of *S. aureus* and healing of the infected wound.

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Statement of Ethics

All the procedures involving human participation were conducted in strict accordance with ethical standards of Institutional Research Committee, Department of Scientific Research, Tikrit University as well as the 1964 Helsinki Declaration and its subsequent amendments or equivalent ethical norms.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of Interest Statement

The author declares that he has no conflicts of interest, financial or otherwise.

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