TÜBİTAK

Turkish Journal of Veterinary and Animal Sciences

http://journals.tubitak.gov.tr/veterinary/

Research Article

Turk J Vet Anim Sci
(2022) 46: 403-410

10.55730/1300-0128.4188

Comparison of low-level laser and dimethyl sulfoxide applications for the treatment of tendon injury in rabbits

Kardelen CEYDELİOĞLU[1], Gültekin ATALAN[2,*], Duygu YAMAN GRAM[3], Gökçen PERK[2]

[1]Ministry of Food, Agriculture, and Livestock Hilvan District Directorate, Sanliurfa, Turkey
[2]Department of Surgery, Faculty of Veterinary Medicine, Erciyes University, Kayseri, Turkey
[3]Department of Physiology, Faculty of Veterinary Medicine, Erciyes University, Kayseri, Turkey

Received: 09.12.2021 • **Accepted/Published Online:** 08.05.2022 • **Final Version:** 13.06.2022

Abstract: The aim of this study was to investigate and compare the effects of low-level laser therapy (LLLT) and dimethyl sulfoxide (DMSO) on tendon healing in rabbits. A total of 30 adult healthy New Zealand rabbits were used for this study. The rabbits were randomly allocated into 3 groups containing an equal animal number. The experimental tenotomy of the Achilles tendons was created on longitudinal aspect with 10 mm in length. During the postoperative 21-day of period, rabbits in Group I were exposed to laser beam at a rate of 10.8 J/cm^2 in 5 cm^2 area for 4 min. In the same period, 30% DMSO solution was applied externally to the injured tendon region for Group II. Saline solution was applied to the injured tendons area for Group III. Daily clinical examinations of each rabbit were recorded during the treatment period. At the end of the 21-day treatment period, all rabbits were euthanized and their tendons were examined macroscopically. Histopathological examination of the tendons was then carried out. Immature and mature connective tissue cells had an equal number of distribution in Group I; mild immature connective tissue cells and mostly mature connective tissue cells were observed in Group II, and partially longitudinal, scattered, and irregularly arranged, immature connective tissue cells (fibroblasts) were observed in Group III. As a result, satisfactory findings were obtained from LLLT and DMSO applications for the treatment of tendon injuries taking into consideration the histopathological and clinical findings. Moreover, DMSO provided a better recovery when these two applications were compared. However, it was suggested that combined application of DMSO and LLLT might have a strong positive effect on the healing process.

Key words: Tendon injury, laser therapy, dimethyl sulfoxide

1. Introduction

Tendons are anatomical formations that are involved in the attachment of muscles to bone, cartilage, or fasciae [1].

Tendon injuries occur when tendon fibers (fibrillar and fascicular) are torn as a result of excessive tensions and traumas. In these cases, there is swelling in a certain part or all of the tendon. The swelling has the character of edema and phlegmon, it is hot and painful. On palpation, the area where the fibrillar rupture is located is more sensitive. There is moderate and significant lameness occurring in a short time after the trauma [2, 3, 4].

In the period when acute tendinitis begins, buffers are applied to the area by diluting 1/3 of dimethyl sulfoxide (DMSO) locally. It is aimed to relieve inflammation, reduce pain in the region, and support the regeneration of the tendon by applying nonsteroidal antiinflammatory agents, analgesic drugs, polysulfated glucosaminoglycan (PSGAG) substances. Alternatively, therapeutic ultrasound, low-level laser therapy (LLLT), electromagnetic field therapy, bone marrow and stem cell studies have been reported in the treatment of tendinitis [5, 6, 7, 8, 9].

LLLT has been used widely in veterinary medicine, as it has effects such as increased blood circulation, collagen synthesis, increased energy, decreased inflammation, increased venous and lymphatic flow, and reduced pain [10, 11, 12, 13, 14]. Furthermore, the inflammation in the tendons can be reduced by laser treatment. Particularly in acute tendinitis, a positive result may be obtained due to the reduction of inflammation in the region and the increase in collagen tissue. LLLT also reduces pain in subacute and chronic tendinopathy when using in a valid treatment procedure and a specific dose [15, 16, 17, 18].

Therapeutic ultrasound provides thermal and nonthermal effects on cells and tissues, contributing to the tendon healing process. Therapeutic ultrasound is thought to accelerate repair by affecting cell activities [19, 20, 21].

Stem cell therapy has been reported as another treatment option in tendon damage. In this technique,

* Correspondence: gulty@hotmail.com

stem cells taken from the patient's own fat tissue were injected into the damaged tendon area and had a positive contribution to the repair of the tendon [22, 23].

In this study, it was aimed to compare DMSO and LLLT applications on the healing processes in tendon injuries.

2. Materials and methods

2.1. Materials

The study was carried out in Erciyes University, Faculty of Veterinary Medicine, Department of Surgery. Study approval was obtained with the decision of Erciyes University Animal Experiments Local Ethics Committee (EUHADYEK).

2.1.1. Animal material

The animal material consisted of 30 adult (12 months and over), mixed-sex, New Zealand breed rabbits weighing an average of 2–4 kg. Three separate groups were created by randomly selecting 10 rabbits in each group, with equal number of male and female animals. The study was carried out on the right Achilles tendons. In addition, healthy left Achilles tendons of 6 rabbits randomly selected from the groups were also included in the study for histopathological comparison with injured tendons.

2.2. Method

2.2.1. Preparation for surgical Intervention

Rabbits were fasted and dehydrated 6 h before the operation. All animals were examined clinically for possible disease. Body temperature, respiration, and heart rate were measured.

In each rabbit, the area between genu and the tuber calcenei on right extremity was shaved and prepared for the operation.

2.2.2. Anesthesia protocol

For the premedication, xylazine hydrochloride (Xylazine Bio 2%, 20 mg/mL, Bioveta, Czech Republic) was administered to each rabbit intramuscularly (IM) at a dose of 5 mg/kg. Ketamine hydrochloride (Ketasol 10%, 100 mg/mL, Ricter Pharma, Austria) was injected IM at a dose of 35 mg/kg after 10 min of premedication.

2.2.3. Creation of tendon damage

After making a 2 cm long skin incision on the midline over the Achilles tendon, retraction of the subcutaneous connective tissues was performed, and the Achilles tendon was exposed. The fascia on the Achilles tendon was opened with blunt dissection and the tendon was reached.

After the damage was made by making a 1 cm length cut in longitudinal side with a scalpel (Figure 1), the subcutaneous tissues and then skin of the operation area were closed using polyglactin 910 usp: 2.0 (Vicryl, No: 2.0, Vauxhall Industrial Estate, United Kingdom) with a simple interrupted suture technique.

2.2.4. Groups

Thirty rabbits were allocated to three groups, each group consisted of 10 randomly selected rabbits.

Group I (LLLT group): The Maestro CCM brand laser device was applied to the 5cm² area daily for 21 days at a dose of 10.8 J/cm² for 4 min with a frequency of 3.0 Hz (Figure 2).

Group II (DMSO group): DMSO solution prepared was applied externally to the injured tendon area for 21 days. For this application, a 30% DMSO solution was prepared with 3 mL of DMSO and 7 mL of lactated Ringer's solution. The solution was applied once a day by massaging for 4 min.

Group III (control group): During the postoperative 21-day period, the damaged area was cleaned with physiological saline, and no other application was made.

2.2.5. Postoperative applications

In the postoperative period, 400,000 IU of iecilline (İ.E.ULUGAY, İstanbul, Turkey) was administered intramuscularly once a day for 5 days for the all groups.

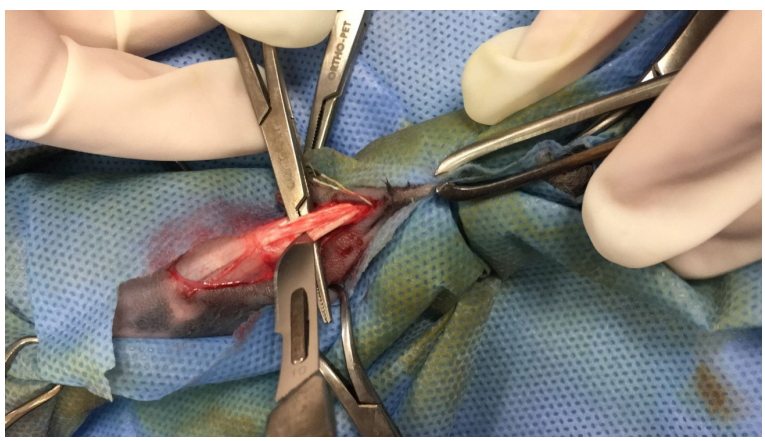

Figure 1. Creation of damage to the Achilles tendon with a longitudinal incision of 10 mm length.

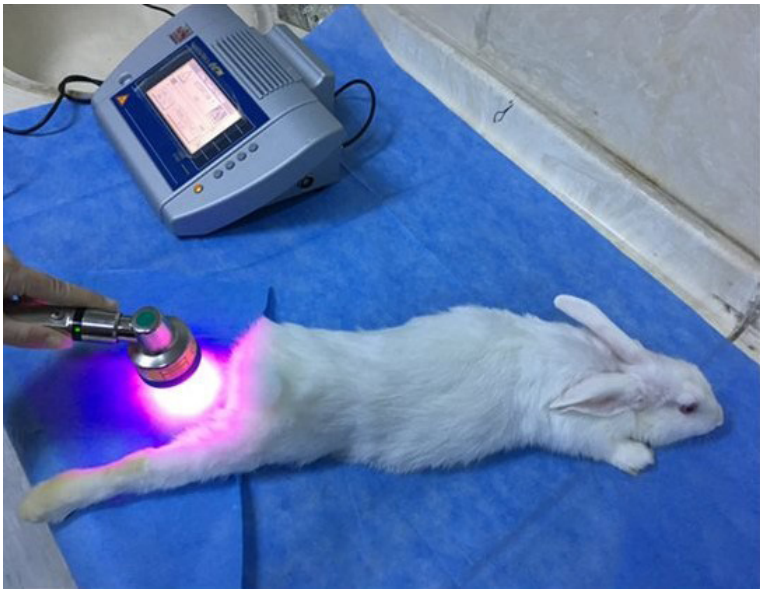

Figure 2. Application of the laser beams to the damaged area.

As an analgesic, butorphanol (Butomidor, 10 mg/mL, Richter Pharma AG, Austria) 0.1 mg/kg was administered intramuscularly once a day for 3 days.

2.2.6. Postoperative clinical evaluation

All rabbits were observed during the postoperative 21-day treatment period to evaluate the clinical findings. LLLT, DMSO, and control groups were examined separately for lameness and the following score table was created.

The degrees of lameness were graded as follows:

Grade 0: Absence of lameness,

1st degree: Mild lameness and can usually step on the foot,

2nd degree: Moderate lameness and occasional stepping on the foot,

3rd degree: Severe lameness and permanent hanging of the foot.

2.2.7. Histopathological examination

At the end of the postoperative 21-day period, all rabbits were euthanized by administering intravenous (IV) Na-pentobarbital at a dose of 50 mg/kg and their Achilles tendons were isolated for histopathological examination. Histopathological examination of the tissues for Group III was performed in order to compare them with the samples obtained from the LLLT and DMSO groups.

The tendons of rabbits were collected and fixed in buffered neutral formaldehyde, and then the specimens were thoroughly rinsed overnight under tap water. All tissue samples were dehydrated in graded alcohol and cleared in xylene, and embedded in paraffin using an automated Leica Tissue Processor, TP1020.Sections (4–5 µm) were prepared using a microtome. After staining with hematoxylin and eosin, the sections were examined under a light microscope and the degree of damage was scored.

Following hematoxylin and eosin staining, all sections were semiquantitatively evaluated for inflammatory response, immature connective tissue formation, and neovascularization. In the semiquantitative method, each injury parameter was scored by two pathologists in 10 different areas in a section for each animal's tendon, and the mean percentile values within the group were calculated. The mentioned parameters were accepted as 1 (mild) if they were less than 33%, 2 (moderate) if they were between 33% and 66%, and 3 (severe) if they were more than 66% (Table 1). The values obtained in each group were evaluated statistically and the statistical significance between the groups was recorded.

2.2.8. Statistical analysis

The conformity of the data to the normal distribution was evaluated with histogram, q-q graphs, and the Shapiro–Wilk test. Homogeneity of variance was tested with Levene's test. One-way analysis of variance (ANOVA) was used for quantitative variables in comparisons between groups of more than two. One-way analysis of variance (R-M ANOVA) was used for repeated measures in comparisons between measures. Bonferroni and Tukey's tests were used in multiple comparisons. The analysis of the data was carried out in TURCOSA (Turcosa Analitik Ltd Co, Turkey www.turcosa.com.tr) statistical software. The level of significance was accepted as $p < 0.05$.

3. Finding

3.1. Evaluation of clinical findings

From the first postoperative day of the study, all rabbits in the LLLT, DMSO, and control groups were walked on a flat platform and their lameness degrees were recorded.

Table 1. Tendon damage scoring table.

Scoring table				
	None	Mild	Moderate	Severe
Immature connective tissue formation	0	1	2	3
Neovascularization	0	1	2	3

3.1.1. LLLT group (Group I)
The mean degree of lameness in the 1st week was recorded as 1.90 ± 0.74. In addition to mild and moderate lameness, low-intensity pain was detected, and no signs of inflammation were found.

At the end of the 2nd week, mean lameness grade was recorded as 0.50 ± 0.53. No signs of pain or inflammation on extremity were observed.

On the 21st day of the study, the lameness completely disappeared and no signs of pain and inflammation were visible.

3.1.2. DMSO group (Group II)
The mean degree of lameness in the 1st week was recorded as 1.80 ± 0.63 postoperatively. While mild and moderate lameness was observed, no significant difference was detected compared to Group I. There was no sign of inflammation and pain at the end of the 7th day.

At the end of the 2nd week, the mean lameness score was recorded as 0.30 ± 0.48. No sign of lameness was visible for 8 rabbits.

In the final evaluation on the 21st day of the study, lameness completely disappeared in all rabbits.

3.1.3. Control group (Group III)
The mean degree of lameness of the rabbits in the control group was noted as 2.50 ± 0.53 in the first week postoperatively. Moderate to severe lameness was observed. Rabbits held their leg and had difficulty in walking. Pain was determined, and moderate inflammation findings were observed.

At the end of the 2nd week, the mean degree of lameness was determined as 1.10 ± 0.74. Mild to moderate lameness was evident. However, regression in pain and inflammation was observed.

On the 21st day of the study, the lameness score was determined as 0.40 ± 0.52. Three rabbits had mild lameness. In other rabbits, lameness was gradually decreased with a rate of 0–1. At the end of the study, no signs of pain or inflammation were found for the any of the rabbits.

A statistically significant difference for lameness scoring was obtained between Groups I, II, and III at the end of the 1st week ($p < 0.05$), (Table 2).

A statistically significant difference was also found between Groups I, II, and III for the lameness scoring at the end of the 2nd week ($p < 0.05$).

3.2. Histopathological findings
At the end of the study, healthy tendons from euthanized rabbits were evaluated and the tendons were all macroscopically normal. Histopathological examination of tendons showed normal tenoblast and tenocyte formation (Figure 3A). The tendon damage parameters were evaluated for inflammatory response, immature connective tissue formation, and neovascularization, and the damage scores were found to be zero (Tables 3 and 4).

Following euthanasia, no macroscopic finding was observed in tendons in any of the groups (Groups I, II and III).

3.2.1. LLLT group (Group I)
Histopathological view revealed that the defect was filled with moderately connective tissue while immature and mature connective tissue cells in the area had almost equal distribution (Figure 3B). In addition, severe vascularization (Figure 3C) and moderate mononuclear cell infiltration consisting predominantly of lymphocytes was also observed.

3.2.2. DMSO group (Group II)
In the histopathological examination, mild immature connective tissue cells were found in the area, while most of the connective tissue cells were in mature morphology. In addition, no inflammatory cells were observed and the degree of vascularization was mild (Figure 3D).

3.2.3. Control group (Group III)
In the histological examination of the tendons, in the incision area, partially longitudinal, scattered, and irregularly arranged immature connective tissue cells (fibroblasts) with centrally located oval or flat nuclei resembling granulation tissue were observed (Figure 4A). However, mononuclear cell infiltration varying from mild to moderate severity (Figure 4B) and increased vascularization were observed in this area.

As a result of the semiquantitative evaluation of tendons, a statistically significant difference was observed between the groups in terms of immature connective tissue formation and neovascularization (Table 5), ($p < 0.05$). Besides, according to the histopathological examination, it was determined that they formed a collagen structure more similar to healthy tendon histology in Group II, while inflammation in minimal and most of the connective tissue cells were in mature morphology.

Table 2. Evaluation results of lameness scoring in rabbits (mean ± SD).

Lameness scoring		Group		p
	Group I (n: 10)	Group II (n: 10)	Group III (n: 10)	
1st week	1.90 ± 0.74^{abA}	1.80 ± 0.63^{bA}	2.50 ± 0.53^{aA}	0.044
2nd week	0.50 ± 0.53^{abB}	0.30 ± 0.48^{bB}	1.10 ± 0.74^{aB}	0.015
3rd week	-	-	0.40 ± 0.52^{C}	-
p* <0.001	< 0.001	<0.001		

· The p-value represents the intergroup significance for each week, and the p*-value represents the interweek significance of a group.
· The same superscripts letters on the same line indicate similarity between groups, and different letters indicate difference.
· The same capital letters in the same line indicate similarity between weeks, different letters indicate difference.
· Group I (LLLT group), Group II (DMSO group), Group III (control group)

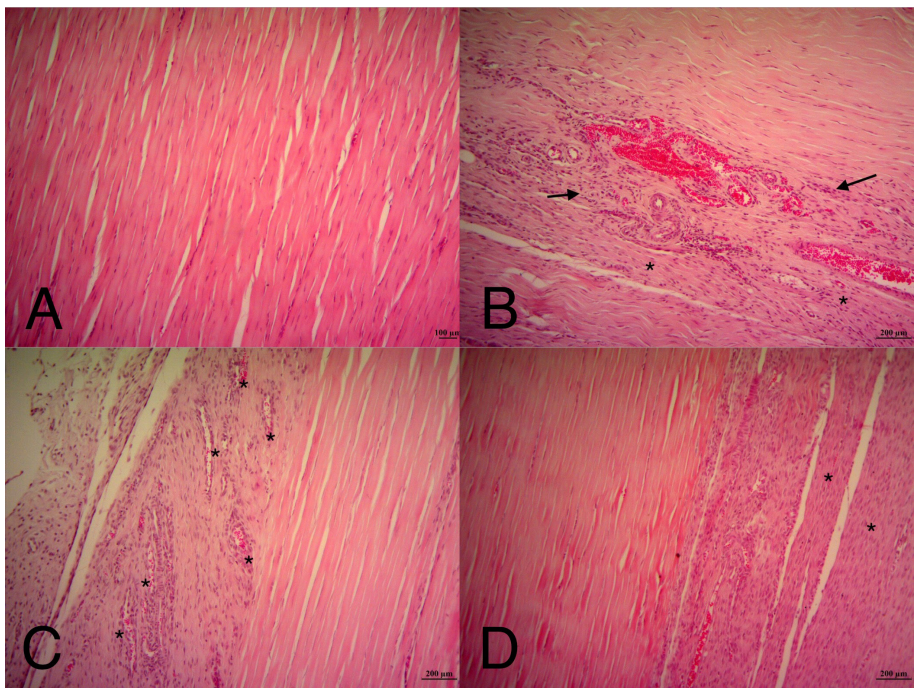

Figure 3. (A) Normal histological appearance of cells in healthy tendon, H&E, 40×, **(B)** Appearance of immature (arrows) and mature (asterisks) connective tissue cells at the injury site in Group I (LLLT group), H&E, 10×, **(C)** Appearance of new vessel formations (neovascularization) observed in the damaged site after 3 weeks in Group I (LLLT group) (asterisks), H&E, 10×, **(D)** Appearance of connective tissue cells, mostly mature morphology, filling the area in the damaged site in the Group II (DMSO group) (asterisks), H&E, 20×.

4. Discussion

In the present study, the effects of DMSO and LLLT applications for the healing of experimentally induced tendon injuries and the regaining of functional activity were examined [24].

Different methods have been reported for the treatment of tendon disorders. Treatment methods including LLLT, therapeutic ultrasound, stem cell therapy, platelet rich plasma (PRP) application, graft applications from various tissues, and different suture materials and techniques have been studied [9, 19, 22, 25].

Table 3. Semiquantitative scoring system for neovascularization in tendons.

Animal number	Group I	Group II	Group III
1	3	0	3
2	3	1	3
3	1	0	2
4	1	0	3
5	3	1	2
6	1	0	3
7	3	1	3
8	1	0	2
9	3	1	2
10	1	1	3

· Group I (LLLT group), Group II (DMSO group), Group III (control group)

Table 4. Semiquantitative scoring system for immature connective tissue formation in tendons.

Animal Number	Group I	Group II	Group III
1	2	1	3
2	2	1	3
3	1	1	3
4	2	2	2
5	2	1	1
6	2	1	2
7	1	1	3
8	2	2	2
9	2	1	2
10	2	1	1

· Group I (LLLT group), Group II (DMSO group), Group III (control group)

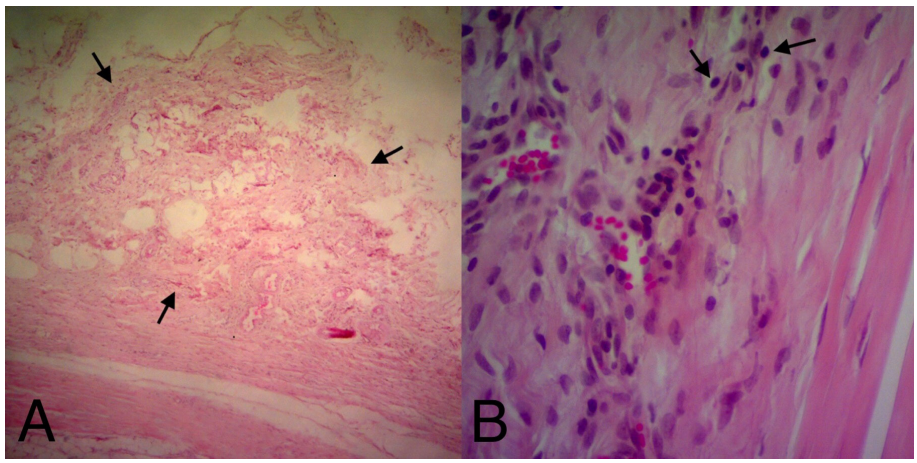

Figure 4. (A) The appearance of partially longitudinal, scattered, and irregularly arranged immature connective tissue cells (fibroblasts) resembling granulation tissue in Group III (control group) (limited area surrounded by arrows), H&E, 4×, **(B)** Appearance of moderate mononuclear cell infiltration mostly composed of lymphocytes (arrows) in Group III (control group), H&E, 40×.

LLLT applied to the tendon tissue caused a significant decrease in inflammation [25,26,27,28]. In application, laser beams reduce inflammation by decreasing prostaglandin (PGE_2) level and inhibiting cyclooxygenase-2 [29]. In a human study, LLLT reduced inflammation and pain in Achilles tendinitis when applied at a dose of 5.4 J/cm^2 [26]. In our study, LLLT in 10.8 J/cm^2 for 4 min for 21 days was applied to the tendon damaged area at a wavelength of 632 nm. While inflammation was not clinically observed in rabbits after 7th day of application, mild mononuclear cell infiltrations, the majority of which were lymphocytes, were observed in 4 out of 10 rabbits.

For the rabbits in Group II, no inflammation was found in clinical examination from the 7th day, and the presence of mononuclear cell infiltration was not detected in histopathological examinations. In this respect, although LLLT and DMSO had clinically similar inflammatory reactions, DMSO showed a more effective antiinflammatory property histopathologically.

In LLLT, photons increase neuron interaction by sending positive ions such as Ca to the applied areas and show analgesic effect [11]. Taking into consideration the appropriate dose and duration of LLLT application, it has been stated that LLLT reduces pain in subacute and

Table 5. Semiquantitative scoring system for tendon damage in groups (mean ± SD).

Groups				p
	Group I (n: 10)	Group II (n: 10)	Group III (n: 10)	
Immature connective tissue formation	1.80 ± 0.42^{ab}	1.20 ± 0.42^{b}	2.20 ± 0.79^{a}	0.002
Neovascularization	2.00 ± 1.05^{ab}	0.50 ± 0.53^{b}	2.60 ± 0.52^{a}	0.000

p-value expresses the significance between groups at 0.001.
· The same superscripts on the same line indicate similarity between groups, and different letters indicate difference.
· Group I (LLLT group), Group II (DMSO group), Group III (Control group).

chronic tendinopathy [15]. In Group III, pain continued until the 14th day. The use of right rate of laser beam dosage with a sufficient time significantly affects the healing. In addition, in studies where the application time and dosage are insufficient, tendon healing did not occur at the desired level [15, 30]. Ideal dose range of 1.4–14 J/cm² has been reported for irradiation in Achilles tendon with a wavelength of 632 nm [15]. In our study, irradiation was carried out close to the ideal dose range specified by the application of a laser beam at a dose of 10.8 J/cm².

LLLT has been applied in combination with PRP application for the rabbits with Achilles tendinitis. In the study, the radiation therapy was applied for 15 days at a dose of 1.8 J/cm² with a laser device with a wavelength of 650 nm. As a result, satisfactory improvement in tendon healing and clinical findings has been obtained by PRP and LLLT applications [25]. Our study differs from this study in terms of dosing and application times with lower dose and less application [25]. Taking into consideration lameness score, a good improvement was also obtained for the rabbits in Group II at the end of the study with less intense connective tissue formation than the other group. A satisfactory tendon healing reported by Allahverdi et al. [25] might be due to the effect of PRP combination besides LLLT.

Furthermore, lameness continued in 30% of the rabbits in Group II, 50% of the rabbits in Group I, and 80% of the rabbits in Group III between 7 and 14 days of the study. This indicated that the rabbits in Group II gained mobility more quickly.

In another study, Achilles tendon injury induced by experimental tenotomy was treated with a HeNe 632.8 nm laser device with a daily laser beam of 1.0 J/cm² for 14 days [31]. As a result, there was a 26% increase in collagen concentration with laser photostimulation, and a faster healing process was observed in the treated tendons compared to the control group [31]. Similarly, in a different study where both ultrasound and a laser device with a wavelength of 904 nm were applied with a dosage of 1 J/cm² and a frequency of 16 Hz, it was noted that the collagen level increased on the 10th and 21st days of the treatment [27]. Contrary to these studies, a higher amount of collagen increase was observed in Group II compared to Group I in our study, this might be also due to different dose and combined application for the mentioned studies.

As a result, successful results were obtained from LLLT and DMSO applications in the treatment of tendon injuries that may occur due to various reasons. It is thought that DMSO provides a better recovery when these two applications are compared. However, it is suggested that combined application of DMSO and LLLT may have a positive effect on the healing process.

References

1. Gültekin M. Evcil Memeli Hayvanların Karşılaştırmalı Myolagia'sı (Aktif Hareket Sistemi). Ankara, Türkiye: A Ü Basımevi; 1977 (in Turkish).
2. Dyson SJ. Tendon and ligament injuries. Part I. Equine Practice 1994; 10 (2): 273-487.
3. Seyrek İntaş D, Çelimli N. Atların tendinitislerinde iyileşme ve güncel sağaltım yöntemleri. In: 1st National Equine Symposium, Konya, Turkey; 1999. pp. 251-267 (in Turkish).
4. Silbersiepe E, Berge E, Müller H. Krankheiten an fesselgelenk und fessel. Lehrbuch der Speziellen Chirurgie für Tierärzte und Studierende, Stuttgart: Ferdinand Enke Verlag; 1986 (in German).
5. Li M, Zhu Y, Pei Q, Deng Y, Ni T. The 532 nm laser treatment promotes the proliferation of tendon-derived stem cells and up-regulates Nr4a1 to stimulate tenogenic differentiation. Shanghai Jiao Tong University, Shanghai, China, 2021. doi: 10.21203/rs.3.rs-960303/v2
6. Lin CC, Wu PT, Chang CW, Lin RW, Wang GJ et al. A single-pulsed electromagnetic field enhances collagen synthesis in tendon cells. Medical Engineering & Physics 2020; 77: 130-136. doi: 10.1016/j.medengphy.2019.12.001

7. Lui PPY. Mesenchymal stem cell-derived extracellular vesicles for the promotion of tendon repair-an update of literature. Stem cell reviews and reports 2021; 17 (2): 379-389. doi: 10.1007/s12015-020-10023-8

8. Tsai WC, Tang, ST, Liang, FC. Effect of therapeutic ultrasound on tendons. American Journal of Physical Medicine & Rehabilitation 2011; 90 (12): 1068-1073. doi: 10.1097/PHM.0b013e31821a70be

9. Yu H, Cheng J, Shi W, Ren B, Zhao F et al. Bone marrow mesenchymal stem cell-derived exosomes promote tendon regeneration by facilitating the proliferation and migration of endogenous tendon stem/progenitor cells. Acta Biomaterialia 2020; 106: 328-341. doi: 10.1016/j.actbio.2020.01.051

10. Karu T. Photobiological fundamentals of low powered laser therapy. IEEE Journal of Quantum Electronics 1987; 23 (10): 1703-1717. **doi:** 10.1109/JQE.1987.1073236

11. Laakso EL, Cramond T, Richardson C, Gallian JP. Plasma ACTH and ß endorphin levels in response to low level laser therapy for myofascial trigger points. Laser Therapy 1994; 6 (3): 133-141. doi: 10.5978/islsm.94-OR-07

12. Moshkovska T, Mayberry J. It is time to test low level laser therapy in Great Britain. Postgraduate Medical Journal 2005; 81 (957): 436-441. doi: 10.1136/pgmj.2004.027755

13. Parker S. Low level laser use in dentistry. British Dental Journal 2007; 202 (3): 131-138. doi: 10.1038/bdj.2007.75

14. Posten W, Wrone DA, Dover JS, Arndt KA, Silapunt S et al. Low-level laser therapy for wound healing: mechanism and efficacy. Dermatologic Surgery 2005; 31 (3): 334-340. doi: 10.1111/j.1524-4725.2005.31086

15. Bjordal JM, Couppé C, Ljunggren AE. Low level laser therapy for tendinopathy. Evidence of a dose–response pattern. Physical Therapy Reviews 2001; 6 (2): 91-99. doi: 10.1179/ptr.2001.6.2.91

16. Dever M. What's in a laser beam for pain therapy? Pain 1990; 43 (2): 139. doi: 10.1016/0304-3959(90)91065-Q

17. Lögdberg-Andersson M, Mützell S, Hazel A. Low level laser therapy (LLLT) of tendinitis and myofascial pains a randomized, double-blind controlled study. Laser Therapy 2004; 14 (2): 79-84. doi: 10.5978/islsm.14.0_79

18. Moritz U, Sjolund B. Kan laser lindra smarta'? Fa kontrollerade studier och osakra resultat. Lakartidningen 1990; 87(26-27): 2261-4 (in Swedish).

19. Denegar CR, Saliba E, Saliba S. Therapeutic Modalities for Musculoskeletal Injuries. 4th ed. Human Kinetics; 2015.

20. Ganidağlı E, Güzel R. Arşiv Kaynak Tarama Dergisi 2013; 22 (2): 170-183.

21. Kalyon TA. Ultrason. In: Tuna N (editor). Elektroterapi. İstanbul, Türkiye: Nobel Tıp Kitabevi; 2001. pp. 129-41 (in Turkish).

22. Kokubu S, Inaki R, Hoshi K, Hikita A. Adipose-derived stem cells improve tendon repair and prevent ectopic ossification in tendinopathy by inhibiting inflammation and inducing neovascularization in the early stage of tendon healing. Regenerative Therapy 2020; 14: 103-110. doi: 10.1016/j.reth.2019.12.003

23. Ricco' S, Renzi S, Del Bue M, Conti V, Merli E et al. Allogeneic adipose tissue-derived mesenchymal stem cells in combination with platelet rich plasma are safe and effective in the therapy of superficial digital flexor tendonitis in the horse. International Journal of Immunopathology and Pharmacology 2013; 26 (1) (Suppl.): 61-68. doi.org/10.1177%2F03946320130260S108

24. Cihan M, Özaydın İ. Koyunlarda fibrin adeziv (tisseel) ile deneysel tenografi. Kafkas Üniversitesi Veteriner Fakültesi Dergisi 1999; 5: 103-112 (in Turkish).

25. Allahverdi A, Sharifi D, Takhtfooladi MA, Hesaraki S, Khansari M et al. Evaluation of low-level laser therapy, platelet-rich plasma, and their combination on the healing of Achilles tendon in rabbits. Lasers in Medical Science 2015; 30 (4): 1305-1313. doi: 10.1007/s10103-015-1733-6

26. Bjordal JM, Lopes-Martins RAB, Iversen VV. A randomised, placebo controlled trial of low level laser therapy for activated Achilles tendinitis with microdialysis measurement of peritendinous prostaglandin E2 concentrations. British Journal of Sports Medicine 2006; 40: 76-80. doi: 10.1136/bjsm.2005.020842

27. Demir H, Menku P, Kirnap M, Calis M, Ikizceli I. Comparison of the effects of laser, ultrasound, and combined laser + ultrasound treatments in experimental tendon healing. Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery 2004; 35 (1): 84-89. doi: 10.1002/lsm.20046

28. Nascimento LDS, Nascimento KFS, Pessoa DR, Nicolau RA. Effects of therapy with light emitting diode (led) in the calcaneal tendon lesions of rats: a literature review. The Scientific World Journal 2019. doi: org/10.1155/2019/6043019

29. Çetiner S, Kahraman SA, Yücetaş S. Evaluation of low-level laser therapy in the treatment in the treatment of temporomandibular disorders. Photomedicine and Laser Surgery 2006; 24: 637-641. doi: 10.1089/pho.2006.24.637

30. Tumilty SI, Munn J, McDonough S, Hurley DA, Basford JR et al. Low level laser treatment of tendinopathy: a systematic review with meta-analysis. Photomedicine Laser Surgery 2010; 28 (1): 3-16. doi: 10.1089/pho.2008.2470

31. Reddy GK, Stehno-Bittel L, Enwemeka CS. Laser photostimulation of collagen production in healing rabbit Achilles tendons. Lasers in Surgery and Medicine: The Official Journal of the American Society for Laser Medicine and Surgery 1998; 22 (5): 281-287. doi: 10.1002/(sici)1096-9101(1998)22:5<281::aid-lsm4>3.0.co;2-l