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Glucosamine Phonophoresis on Healing of Hand Flexor Tendon Post Repair

Ahmed Mohamed Elsayed Abo-Sleem [1], Amal Mohamed Abd El Baky [1], Husam–Eldin Hosny Abdulwahab[2], Ereny Sobhy Wahba Khalil[1]

[1]*Department of Physical Therapy for Surgery, Faculty of Physical Therapy, Cairo University, Egypt.*

[2]*Department of and Plastic Surgery, Faculty of Medicine, Cairo University, Egypt.*

Abstract

This study aimed to recognize the effect of glucosamine phonophoresis on healing of hand flexor tendon post repair. The study design was a randomized controlled trial (RCT). A Total of 60 male and female patients who experienced flexor tendon repair surgery, aged 25–45 years, were randomized into 2 equal groups. Group A was given Glucosamine phonophoresis and exercise program (passive, active range of motion (ROM) exercise for twelve weeks (3 sessions per week). Group B was given topical Glucosamine in addition to the same exercise given to group A for twelve weeks (3 sessions per week)**.** Dynamometer was used to measure hand grip post treatment at 12th week, ultrasonography measure continuity of intratendinous fibrillar pattern at baseline and at 4th and 12th week after treatment. Comparing groups, A and B at 12 weeks post-operatively, it was found that group A had a significantly higher hand grip ($p = 0.003$), but no significant difference was detected in median measurements of continuity of intratendinous fibrillar pattern ($p = 0.31$). It could be concluded that Glucosamine phonophoresis is effective in hand flexor tendon healing post repair.

Keywords: Glucosamine, Phonophoresis, Flexor tendon repair.

Full length article **Corresponding Author*, e-mail: a.abosleem1985@gmail.com

1. Introduction

Tendons are extremely important for movement and mechanics. They facilitate movement and posture maintenance by transferring the force generated by muscle contraction towards the skeletal levers. Because of the tendons, the muscle doesn't need to be too long between its origin and its insertion places to be at the ideal distance from the joint it works on [1]. An increasing number of individuals are seeking treatment for tendon injuries, which make up about 30% of all musculoskeletal diseases seen in large healthcare systems [2]. When deciding whether or not to repair a tendon, there are several factors to take into account. regarding flexor tendon injuries, primary surgical repair provides better functional outcomes than secondary repair (done more than three weeks after the initial injury) or tendon graft surgery [3]. Glucosamine is a building block of glycoproteins, which are present in connective tissue as well as synovial fluid within joints. It enhances sulfate absorption, which in turn stimulates chondrocyte stimulation and proteoglycan production, two processes essential for cartilage regeneration. Another way glucosamine helps joints last longer is by blocking matrix metalloproteinases [4]. Glucosamine chondroitin sulfate, more commonly known as glucosamine HCL-chondrotoitin sulfate (GlcN-CS) , is a popular choice for many common daily tasks. A decrease in chondromalacia and an inhibition of inflammation are both attributed to its ability to increase matrix proteoglycans as well as inhibit the cyclooxigenase-2 pathway, respectively [5]. Concurrently, GlcN-CS promotes the formation of collagen in fibrous tissues and tendons [6]. Results indicate that a combination of sodium-hyaluronata (NaH) and GlcN-CS may be useful for future clinical trials involving tendon ruptures, as it has the potential to restore the biomechanical and morphological characteristics of rabbits with injured superficial digital flexor tendon. Tendon, sodium-hyaluronate, healing, ultrastructure, histology, and biomechanics are all key words [7]. This research was based on the hypothesis that glucosamine and chondroitin sulfate could improve the tendon-to-bone interface's healing structure. to alleviate symptoms, this substance is recommended to individuals experiencing problems with their cartilage. Through its anti-inflammatory and collagen-stimulating effects on cartilage cells, the drug's impact provides symptom regression [8]. There have been

clinical applications of ultrasound therapy (US) to aid in tissue healing along with repair, promote blood flow and protein synthesis, promote extensibility of high collagenous tissues including tendons, and improve joint mobility. There is strong evidence from animal studies that therapeutic ultrasound can stimulate tendon regeneration and repair [9]. Further evidence suggests that US can enlarge damaged tendon fibers. The tendon's biomechanics will improve as a result of morphological improvements including larger collagen fibers, improved alignment of collagen fibers, and greater production of collagen [10]. Phonophoresis is a method of deep tissue stimulation and enhanced skin absorption of topically administered medications using ultrasonic energy. Ultrasound is most effective when administered to medications in a gel, liquid, or cream form, which allows them to permeate the skin. The physical characteristics of the materials involved determine how the ultrasonic energy is transferred from one to another [11]. This study aimed to recognize the impact of glucosamine phonophoresis on heling of hand flexor tendon post repair.

2. Subjects and methods

2.1. Study design

In this RCT, the patients were randomized into two equivalent groups (30 participants for every group) using closed envelope method.

2.2. Sample size

After collecting data about hand grip strength from a pilot study with 5 subjects in each group, the researchers used G*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) to determine that thirty participants per group would be needed for the full study. The values of α=0.05, power = 80%, and effect size = 0.74 were used for the calculation.

2.3. Participants

Sixty male and female participants who experienced flexor tendon repair took-part in this study. They were between the ages of 25 and 45. They were recruited from El AHRAR Teaching hospital and were randomized into two equivalent groups.

2.4. Randomization

Before signing the informed consent form, that indicates the intention to take part in the study, all participants received information on the study's purpose, the types of measurements taken, and the potential outcomes of any treatments. During the treatment period, they were told to report any adverse effects. Following randomization, no participants dropped from the study (Figure 1).

2.5. Outcome measures

Measurement of hand grip by Dynamometer, this measurement occurred only at 12th week of treatment for comparison between both groups (control and study group).
Assessment of continuity of intratendenous fibrillar pattern right after repair, 4th week and 12th week of treatment for comparison by Ultrasonography, the continuity of an intratendinous fibrillar echo texture was categorized as complete (3), incomplete (1), or absent (0) [12].

2.6. Intervention

Group A: (Study group): includes 30 flexor tendon repair participants who received Glucosamine phonophoresis and exercise program (passive and active ROM exercise). Patients were begun the treatment program at 7th postoperative day and were received three sessions a week for 12 successive weeks. Here are the ultrasonography parameters: treatment duration: 5 minutes, with a frequency of 1 MHz, and intensity of: 1 W/cm^2. The therapeutic ultrasonic instrument was PAGANI ultrasonic DT 20
Group B: (Control group): involves 30 flexor tendon repair participants who were received topical Glucosamine gel and exercise program (passive and active ROM exercise) for 12 successive weeks.

2.7. Statistical analysis

When comparing the groups according to age, we used an independent t-test; when comparing the groups according to gender and distribution of injured hands, we used a chi-squared test. An independent t-test was used to evaluate the groups' hand grip strength, while a Mann-Whitney U test was used to examine the groups' continuity of intratendinous fibriller pattern. Friedman and wilcoxon signed ranks tests were carried-out for comparison of continuity of intratendinous fibriller pattern between pretreatment, 4 weeks and 12 weeks after treatment in each group. All statistical tests were set to have a significance level of $p < 0.05$. The statistical program for social studies (SPSS) version 19 for windows (IBM SPSS, Chicago, IL, USA) was used for all statistical analysis.

3. Results and Discussion

3.1. Patients characteristics

The results for groups A and B were shown in Table (1). In terms of gender, age, and distribution of injured hands, no significant difference was seen among the groups ($p > 0.05$).

3.2. Comparison of hand grip between group

The mean difference in hand grip between groups was 2.03 kg. Following 12 weeks after treatment, group A had a significantly higher hand grip than group B ($p = 0.003$) (Figure 2, Table 2).

3.3. Effect of treatment on continuity of intratendinous fibriller pattern

No significant difference was detected in continuity of intratendinous fibriller pattern among before treatment and 4 weeks after treatment ($p > 0.05$), whereas a significant rise was detected in continuity of intratendinous fibriller pattern at 12 weeks after treatment when compared to before treatment and 4 weeks after treatment in both groups ($p < 0.01$). There was no significant difference in continuity of intratendinous fibriller pattern among group A and B before treatment, 4 weeks and 12 weeks after treatment ($p > 0.05$) (Table 3).

3.4. Ethical approval

The research related to human use had complied with all the relevant national regulations and institutional policies; this trial was assented by the Ethical Committee of the Faculty of Physical Therapy, Cairo Univer¬sity (No:P.T.REC/012/003500).

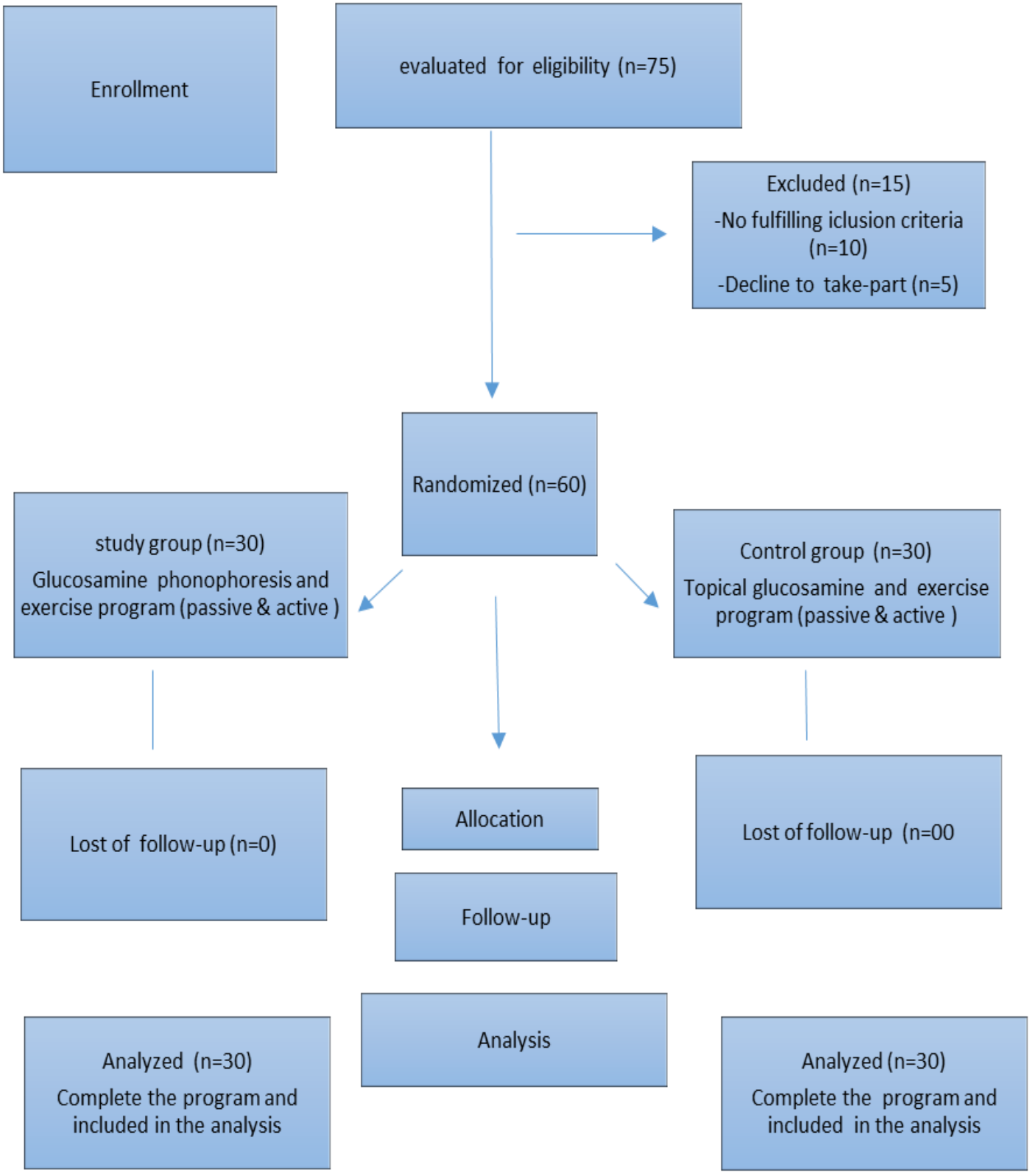

Figure 1: Flow chart of the study

Table 1: Comparison of subject characteristics between group A and B

	Mean ±SD		MD	t- value	p-value
	Group A	**Group B**			
Age (years)	35.40 ± 4.80	36.70 ± 5.09	-1.30	-1.02	0.31
Sex, n (%)					
Females	12 (40%)	13 (43%)		(χ^2 = 0.07)	.0.79
Males	18 (60%)	17 (57%)			
Injured hand, n (%)					
Dominant hand	19 (63%)	17 (57%)		(χ^2 = 0.27)	0.59
Non-dominant hand	11 (37%)	13 (43%)			

SD, Standard deviation; MD, Mean difference; χ^2, Chi squared value; p value, Probability value

Table 2: Mean hand grip of group A and B post treatment

	Group A	**Group B**			
	Mean ±SD	**Mean ±SD**	**MD**	**t-value**	**p value**
Hand grip (kg)	**17.43 ± 2.42**	**15.40 ± 2.63**	**2.03**	**3.11**	**0.003**

SD, Standard deviation; MD, Mean difference; p value, Probability value

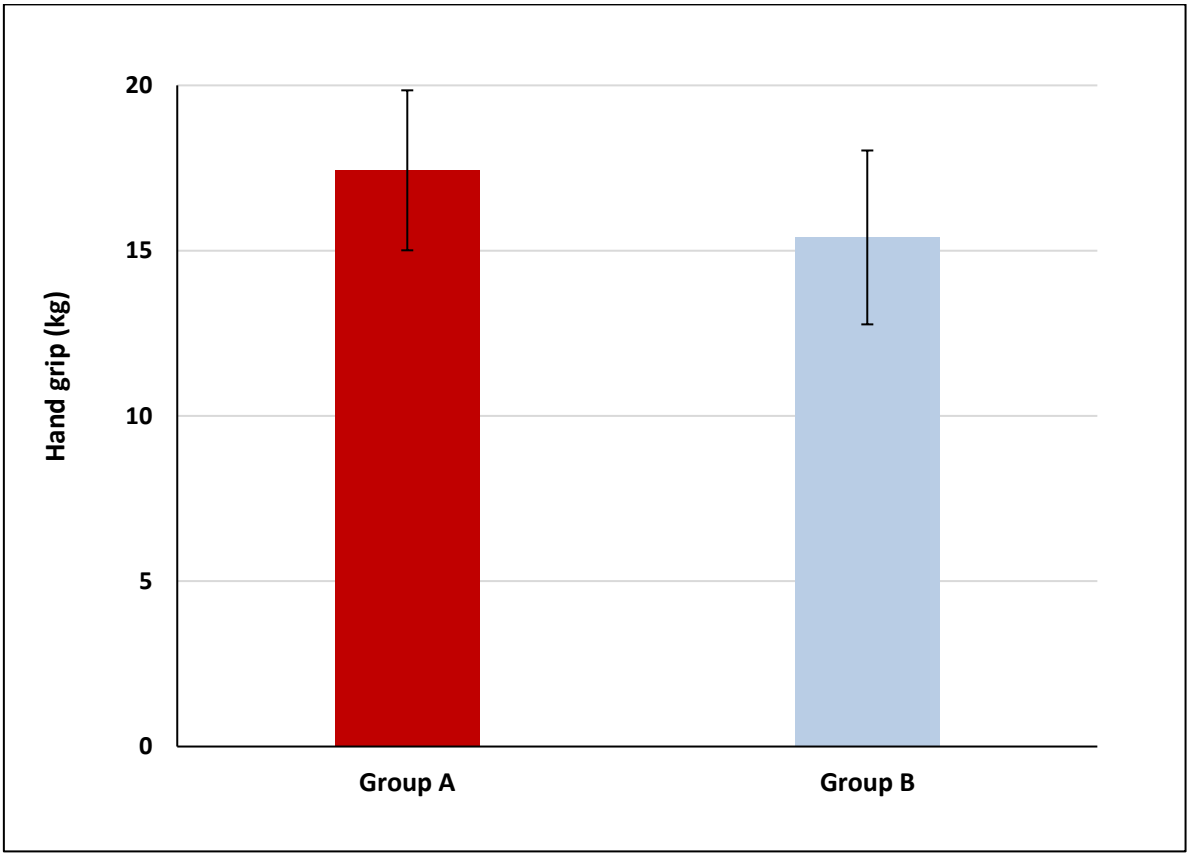

Figure 2: Mean hand grip of group A and B post treatment

Table 3: Continuity of intratendinous fibriller pattern pretreatment, 4 weeks and 12 weeks after treatment of group A and B

	Pre treatment	4 weeks	12 weeks	Repeated measures		
	Median (IQR)	Median (IQR)	Median (IQR)	Pre - 4 weeks	Pre - 12 weeks	4 - 12 weeks
Group A	0(0-0)	0(0-0)	1 (1-0)	0.08	0.001	0.003
Group B	0(0-0)	0(0-0)	0 (1-0)	0.15	0.001	0.004
U- value	450	435	390			
P- value	1	0.64	0.31			

IQR, Interquartile range; U-value, Mann-Whitney test; p value, Probability value

Informed consent

Everyone who was a part of this study has given their informed consent. This study was done to determine the impact of glucosamine phonophoresis on healing of hand flexor tendon post repair as the treatment was begun at 7th day postoperative. The assessment of this study was done by dynamometer for hand grip and ultrasonogrhaphy for conitinuity of intratendinous fibriller pattern for all 60 participants of this study . The results revealed that a significant improvement has been detected in hand grip of group A when compared to that of group B at 12 weeks post treatment, and no significant difference was found in continuity of intratendinous fibriller pattern among group A and B at pretreatment, 4 weeks and 12 weeks post treatment. This study was significant and this agree with Silveira et al., 2013 [13] who reported that therapies related to phonophoresis have been suggested for the management of acute inflammatory disorders, with the goals of reducing tissue damage, accelerating the inflammatory response, and facilitating tissue healing. And other study by Wang et al., 2012 [10] that found that tendon biomechanics was improved due to morphological changes including greater production of collagen, larger collagen fibers, and improved alignment of collagen fibers. Further evidence that GA is a powerful agent in wound healing was provided by Soheil Ashkani et al., 2012 [14] in their study on the topic. And supported by Ozer et al., 2011 [8] who discovered that rats' Achilles tendon healing outcomes were better when given Glucosamine chondroitin sulphate. Reducing inflammation and increasing collagen formation might be the reasons behind this outcome. While GlcN-CS is typically prescribed to alleviate symptoms and signs of osteoarthritis, it has the potential to be more effective in treating soft tissue injuries sustained in athletic activities. Additionally, it was hypothesized that the combination of glucosamine as well as chondroitin sulfate may enhance the healing process at the tendon-to-bone interface. Patients suffering from cartilage issues often find relief with this substance. Through its anti-inflammatory and collagen-stimulating effects on cartilage cells, the drug's impact provides symptom regression. In addition, Oryan et al., 2011[7] proposed that future clinical trial research on tendon ruptures could benefit from combining NaH and GlcN-CS to restore the biomechanical and morphological features of wounded rabbit superficial digital flexor tendon.

The combined use of glcN and CS successfully induces neo synthesis of collagen in cell cultures of ligament, tendon, as well as cartilage tissue, according to another study by Lippiello L et al., 2007 [15]. In addition to targeting cartilage cells, this medication influences other cell types, including those found in ligaments and tenocytes**.**

Limitation

The study lacked a follow-up post treatment for 6 and 12 months after a treatment program to further assess the continuity of intratendinous fibrillar pattern by ultrasonography.

4. Conclusions

It was concluded that therapeutic effect of glucosamine phonophoresis had significant effect on healing of post–operative tendon repair than topical Glucosamine gel and exercise program (passive and active ROM exercise) only and had significant improvement in hand grip.

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Disclosure statement

There is no conflict of interest or financial gain for any of the authors involved in this study. **Conflict of interest**

Regarding this article, no possible conflicts of interest were disclosed.

References

[1] M.S. Tiwana, M.A. Sinkler, B. Bordoni. (2022). Anatomy, shoulder and upper limb, triceps muscle. In Stat Pearls [Internet]. Stat Pearls Publishing.

[2] R. Sheng, Y. Jiang, L.J. Backman, W. Zhang, J. Chen. (2020). The application of mechanical stimulations in tendon tissue engineering. Stem cells international.

[3] F. Bergamin, M. Civera, M.R. Reinoso, V. Burgio, O.G. Ruiz, C. Surace. (2023). Worldwide Incidence and Surgical Costs of Tendon Injuries: A Systematic Review and Meta-Analysis. Muscles, Ligaments & Tendons Journal (MLTJ). 13(1).

[4] A. Roda, L. Sabatini, A. Barbieri, M. Guardigli, M. Locatelli, F.S. Violante, L.C. Rovati, S. Persiani. (2006). Development and validation of a sensitive HPLC–ESI-MS/MS method for the direct determination of glucosamine in human plasma. Journal of Chromatography B. 844(1): 119-126.

[5] B.-C. Jang, S.-H. Sung, J.-G. Park, J.-W. Park, J.H. Bae, D.H. Shin, G.-Y. Park, S.-B. Han, S.-I. Suh. (2007). Glucosamine hydrochloride specifically inhibits COX-2 by preventing COX-2 N-glycosylation and by increasing COX-2 protein turnover in a proteasome-dependent manner. Journal of Biological Chemistry. 282(38): 27622-27632.

[6] A.L.M. Yamada, C. do Prado Vendruscolo, M.F. Marsiglia, E.D.P. Sotelo, F.R. Agreste, S.R.T. Seidel, J. Fülber, R.Y.A. Baccarin, L.C.L.C. da Silva. (2022). Effects of oral treatment with chondroitin sulfate and glucosamine in an experimental model of metacarpophalangeal osteoarthritis in horses. BMC Veterinary Research. 18(1): 1-14.

[7] A. Oryan, A. Shoushtari. (2009). Biomechanical properties and dry weight content of the developing superficial digital flexor tendon in rabbit. Comparative Clinical Pathology. 18: 131-137.

[8] H. Ozer, A. Taşkesen, O. Kul, H.Y. Selek, S. Turanlı, K. Köse. (2011). Effect of glucosamine chondroitine sulphate on repaired tenotomized rat Achilles tendons. Eklem hastaliklari ve cerrahisi= Joint diseases & related surgery. 22(2): 100-106.

[9] M.d.J. Moura Júnior, E.Â.L. Arisawa, A.A. Martin, J.P. de Carvalho, J.M.N. da Silva, J.F. Silva, L.

Silveira. (2014). Effects of low-power LED and therapeutic ultrasound in the tissue healing and inflammation in a tendinitis experimental model in rats. Lasers in medical science. 29: 301-311.

[10] J.H. Wang, Q. Guo, B. Li. (2012). Tendon biomechanics and mechanobiology—a minireview of basic concepts and recent advancements. Journal of hand therapy. 25(2): 133-141.

[11] B. Ortanca. (2016 Evaluation of the effects of steroid phonophoresis and therapeutic ultrasound applications in carpal tunnel syndrome .

[12] G.D. Puippe, N. Lindenblatt, R. Gnannt, P. Giovanoli, G. Andreisek, M. Calcagni. (2011). Prospective morphologic and dynamic assessment of deep flexor tendon healing in zone II by high-frequency ultrasound: preliminary experience. American Journal of Roentgenology. 197(6): W1110-W1117.

[13] P.C.L. Silveira, L.A. da Silva, C.A. Pinho, P.S. De Souza, M.M. Ronsani, D. da Luz Scheffer, R.A. Pinho. (2013). Effects of low-level laser therapy (GaAs) in an animal model of muscular damage induced by trauma. Lasers in medical science. 28: 431-436.

[14] S. Ashkani-Esfahani, Y. Emami, E. Esmaeilzadeh, F. Bagheri, M. Namazi. (2012). Glucosamine enhances tissue regeneration in the process of wound healing in rats as animal model: a stereological study. Journal of Cytology and Histology. 3(1): 150.

[15] L. Lippiello. (2007). Collagen synthesis in tenocytes, ligament cells and chondrocytes exposed to a combination of glucosamine HCl and chondroitin sulfate. Evidence-Based Complementary and Alternative Medicine. 4, 219-224.