

# Effectiveness of platelet rich plasma injection for achilles tendon injury in wistar rats: An experimental study

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## ABSTRACT

Tendon injuries, particularly Achilles tendon ruptures, significantly impact athletes and labourers, affecting daily activities and quality of life. The platelet plasma rich (PRP) injections have emerged as a treatment option due to their abilities in stimulating growth factors, essential for the healing processes. This study investigates the effectiveness of PRP injections in healing Achilles tendon injuries in Wistar rats. Thirty male Wistar rats were divided into three groups: Group 1 received a 100 µL PRP injection, Group 2 received a 50 µL PRP injection, and Group 3 received a 100 µL NaCl injection as a control. The Achilles tendons were surgically transected and sutured using modified Kessler method, followed by PRP or NaCl injections. Rats were euthanized on days 15 and 30 for histological and biomechanical evaluations. This study found that PRP administration had a significant effect on histological tendon healing on the 15th and 30th, with the best improvement at a PRP dose of 100 µL, especially in the early phase of healing. PRP also had a significant effect on tendon healing in terms of biomechanical function on the 15th and 30th days, with the best improvement at a PRP dose of 100 µL, especially in the final phase of healing. This study provides detailed biomechanical and histological insights into the tendon healing process, which may be challenging to obtain in human studies due to ethical and logistical constraints. The PRP injection improves healing in the Achilles tendon rupture in Wistar rats.

Keywords: achilles tendon, rupture, PRP injection, Wistar rats

## INTRODUCTION

Achilles tendon lesions frequently occur in athletes and physical laborers, significantly impacting daily activities and quality of life. Tendons, primarily composed of type I collagen fibers, elastic fibers, tenocytes, and water, include the Achilles tendon, which is the strongest tendon in the human body.<sup>1,2</sup> Tendon injuries are a major cause of musculoskeletal morbidity, affecting both professional athletes and inactive middle-aged individuals. Approximately 30%-50% of sports injuries involve tendons, with Achilles tendon injuries accounting for 52% of these cases. Such injuries often necessitate prolonged periods of inactivity for athletes.<sup>3-5</sup> In the United States, the incidence of Achilles tendon rupture increased from 1.8 per 100,000 people in 2012 to 2.5 per 100,000 people in 2016. This condition occurs more frequently in men (ratio 3.5:1), particularly in those aged 20-39 years, while it is more common in women aged 40-59 years. The most common cause of this injury is participation in sports or recreational activities, with basketball being a predominant factor.<sup>6</sup>

The platelet rich plasma (PRP) injections have been introduced as a treatment for tendon injuries. PRP, obtained through blood centrifugation, contains growth factors such as insulin-like growth factors 1 and 2, transforming growth factor, vascular endothelial growth factor, fibroblast growth factor, dan hepatocyte growth factor. These growth factors can attach directly to the outside of the cell membrane to activate healing. They stimulate cellular signals that trigger angiogenesis, cell proliferation, cell differentiation, and matrix formation in the healing process. The application of PRP has been shown to stimulate the proliferation and migration of fibroblasts and tenocytes to the injured area, while enhancing collagen production through proper regulation. This process is further enhanced by the upregulation of type I collagen gene expression, resulting in the healing of tissue with improved biomechanical properties.<sup>2,4,7</sup>

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Several studies support the accelerated and strengthened healing of Achilles tendon ruptures. For instance, De Mos et al.<sup>8</sup> reported that PRP increases the number of human tenocyte cells. Lyras et al.<sup>9</sup> observed a significant increase in angiogenesis during the early phase of tendon healing following PRP injections and suggested that PRP might shorten the tendon healing duration. Conversely, other study by De Carli et al<sup>10</sup> found that administering PRP for surgical treatment of Achilles tendon tears does not yield better clinical and functional outcomes. Similarly, Schepull et al.<sup>11</sup> concluded that PRP is not beneficial for treating acute Achilles tendon tears in humans, based on mechanical strength and clinical results. Based on this background, this study will investigate the effectiveness of PRP injections on the healing of Achilles tendon injuries in Wistar rats.

## METHOD

### Study design

All procedures and protocols used in this investigation were reviewed and approved by the Ethics Committee of the Faculty of Pharmacy, Sumatera Utara University, in Medan, Indonesia. This research was conducted at the Integrated Laboratory of the Faculty of Pharmacy, Sumatera Utara University, over a period of two months (February 2024 – March 2024). The study population consisted of adult Wistar rats, obtained from the Integrated Laboratory of the Faculty of Pharmacy, Sumatera Utara University, in Indonesia. The inclusion criteria were healthy male Wistar rats (no fever, 38.3-40°C), weighing 300-400 grams, and aged 2-3 months. The exclusion criteria included any rats that died, experienced a rejection reaction during the study, or developed an infection during the healing process.

### Animals and studied groups

A total of thirty Wistar rats were included in the study and divided into three groups. In Group 1, PRP was injected at a dose of 100 µL on the first day after intralesional Achilles tendon repair. In Group 2, 50 µL of PRP was injected on the first day after intralesional Achilles tendon repair. In Group 3, 100 µL of 0.9% NaCl was injected on the first day after intralesional Achilles tendon repair. All three groups of rats were euthanized in the 15th and 30th days. The Achilles tendon tissue was then collected for histological examination. The rats underwent clinical examination and histological examination of Achilles tendon tissue.

### Preparation of PRP

After sedation, intracardiac blood was drawn from donor mice. The rat blood was then processed to obtain PRP. The PRP was prepared by mixing 3 ml of rat intracardiac blood aspiration with 0.5 ml of Anticoagulant Citrate Dextrose (ACD) solution through two intracardiac blood transfusions. The first centrifugation involved spinning at 4000 rpm for 10 minutes, which separated the intracardiac blood into three layers: the plasma layer, the buffy coat layer, and the erythrocyte layer. The top two layers, comprising the plasma and buffy coat, were transferred to another tube and centrifuged at 2000 rpm for 5 minutes during the soft spin centrifugation. This step resulted in two layers: a platelet-rich plasma layer at the bottom and a plasma layer containing a small number of platelets at the top. The top layer was removed, leaving a layer of platelet concentrate in the plasma. This platelet concentrate was then mixed with 0.1 ml of 10% calcium chloride (CaCl<sub>2</sub>) to activate the platelets.<sup>12</sup>



Figure 1. Preparation of PRP

### Surgical procedure

Thirty male Wistar rats weighing 200-300 grams were first acclimatized for 2 weeks in the laboratory of the Faculty of Pharmacy, University of Sumatera Utara, Indonesia. Six rats were housed per cage and provided with pellets and clean water ad libitum. The rats were then divided into three groups. Experimental rats were anesthetized intraperitoneally with ketamine (40 mg/kg) and midazolam (2 mg/kg), with tramadol (5 mg/kg) and gentamicin (4 mg/kg) administered subcutaneously 5 minutes before surgery. Gentamicin treatment continued for up to 5 days post-surgery. After anesthesia, the distal part of the right paw of each rat was disinfected with chlorhexidine and shaved. Aseptic techniques were followed using povidone iodine, and the rats were placed on a sterile area of the operating table, covered with sterile surgical drapes.

The process of Achilles tendon dissection and tendon rupture using the modified Kessler method can be seen in Figure 2.<sup>13</sup> The skin was incised longitudinally lateral to the midline and 5 mm proximal to the Achilles tendon insertion on the calcaneus. The Achilles tendon was completely transected transversely (transverse hemisection) using a No. 15 scalpel, 2.5 mm from the insertion point on the calcaneus and directed laterally to the Achilles tendon. This lateral transection aimed to avoid the flexor hallucis longus tendon medial to the Achilles tendon. After transection, the Achilles tendon was sutured using the modified Kessler method with 5.0 Prolene sutures for the core tendon, followed by circular stitching using continuous 6.0 Prolene sutures. The skin was closed with interrupted sutures using 5.0 Prolene and covered with a sterile dressing. Post-surgery, analgesics (paracetamol 200 mg/kg) were administered orally every 24 hours for three days. The rats were not immobilized with casting and received a 100  $\mu$ L PRP injection on the first day after surgery. The general condition of the



Figure 2. Achilles rupture, repair and PRP injection procedure

rats and the surgical wounds were monitored and evaluated daily.

The sampling schedule for the research rats was conducted on the 15th and 30th days. Rats were euthanized by administering an intravenous injection of Euthal at 150 mg/kg into the antebrachial cephalic vein area. Once the pupils of the eyeballs had constricted, and breathing and heartbeat had ceased, the rats were then necropsied after disinfection with 70% alcohol. The right leg was dissected to isolate the gastrocnemius and soleus muscles while maintaining the continuity of the Achilles tendon and its insertion on the calcaneus. The tendon and plantaris muscle were incised and removed. The specimen was then covered with moist normal saline gauze and stored in a formalin tube.

### Biomechanical evaluation

The tensile test was performed on the Achilles tendon of the left leg of each experimental animal, conducted in three stages. Firstly, specimen preparation involved clamping the specimen in a vise and smoothing out any treatment or dissection marks that could affect measurement accuracy. This process was



Figure 3. Biomechanical evaluation of the Achilles tendon using tensile test

repeated for all specimens. Secondly, the gauge length and specimen dimensions were measured using pins to mark two points on each specimen, followed by measuring its dimensions. This step was also repeated for all specimens. Finally, testing was conducted on a tensile testing machine by applying continuous load until the specimen fractured. The load at yield, ultimate load, and fracture load were recorded from the load monitor. These procedures were repeated for each specimen to

ensure consistency and accuracy in the test results.

### Histological evaluation

The bone tissue pieces were fixed in 10% neutral buffered formalin and transported to the laboratory. Longitudinal histological examinations were conducted using a microtome. The tissue sections were affixed to slides and stained with hematoxylin-eosin (H&E). Histological analysis was performed under a microscope, and the network was evaluated and scored based on the Movin score. Subsequently, tendon examination was magnified, and areas showing the most significant changes in cell morphology were identified and evaluated using the Movin score.

Tissue blocks were sliced to a thickness of 3-5 microns, mounted on glass slides, and incubated overnight. Staining commenced with xylene rehydration in three stages, followed by sequential immersion in absolute alcohol three times, and then in decreasing concentrations of alcohol (96%, 90%, 80%, and 70%), ending with water. Hematoxylin staining lasted for 3 minutes, followed by a 5-minute tap water rinse and subsequent washing with distilled water. Eosin staining continued for 1 minute, followed by three washes each of 70%, 80%, 90%, 96% alcohol, and absolute alcohol, then three immersions in xylene. After fixation and covering with a cover glass, the slides were observed under a microscope.

Parameter	Group	Score (Mean $\pm$ SD)	
		Day-15	Day-30
Fiber Arrangement	PRP 100 $\mu$ L	1.4 $\pm$ 0.547	0 $\pm$ 0
	PRP 50 $\mu$ L	1.6 $\pm$ 0.547	0.4 $\pm$ 0.894
	NaCl 0.9%	1.8 $\pm$ 0.447	0.6 $\pm$ 0.894
Fiber Structure	PRP 100 $\mu$ L	2 $\pm$ 0	1 $\pm$ 0
	PRP 50 $\mu$ L	2 $\pm$ 0	1 $\pm$ 0
	NaCl 0.9%	2 $\pm$ 0	1.2 $\pm$ 0.447
Angiogenesis	PRP 100 $\mu$ L	1.2 $\pm$ 0.447	1 $\pm$ 0
	PRP 50 $\mu$ L	1.8 $\pm$ 0.447	1.6 $\pm$ 0.547
	NaCl 0.9%	2 $\pm$ 0.447	1.8 $\pm$ 0.447
Nuclear Rounding	PRP 100 $\mu$ L	1.2 $\pm$ 0.447	1 $\pm$ 0
	PRP 50 $\mu$ L	1.8 $\pm$ 0.447	1.2 $\pm$ 0.447
	NaCl 0.9%	2.4 $\pm$ 0.547	1.6 $\pm$ 0.547
Cell Density	PRP 100 $\mu$ L	2 $\pm$ 0	2 $\pm$ 0
	PRP 50 $\mu$ L	2.2 $\pm$ 0.447	2 $\pm$ 0
	NaCl 0.9%	2.4 $\pm$ 0.547	2 $\pm$ 0
Inflammation	PRP 100 $\mu$ L	2 $\pm$ 0	0.4 $\pm$ 0.547
	PRP 50 $\mu$ L	2 $\pm$ 0	0.8 $\pm$ 0.447
	NaCl 0.9%	2 $\pm$ 0	1.4 $\pm$ 0.547

### Statistical method analysis

A data normality test on bivariate data was conducted using the Shapiro-Wilk test. The data were considered normally distributed if the p-value was greater than 0.05. Normally distributed data were analyzed using the unpaired ANOVA test by comparing each tensile test result and the histological picture of the Achilles tendon with PRP administration. If the data were not normally distributed,

the Kruskal-Wallis test was employed. Should the results of the ANOVA test be significant, the Bonferroni test will be conducted as a post-hoc analysis. For significant results from the Kruskal-Wallis test, the Mann-Whitney test will be performed subsequently. A p-value less than 0.05 is considered significant.

## RESULTS

This research is an experimental study aimed at determining the increase in regeneration and remodeling activity in the histology of the Achilles tendon in Wistar rats that experienced a tear after receiving PRP on the 15th and 30th days, assessed using the Movin score for histological tendon repair scoring and biomechanical function assessment through ultimate tensile strength (UTS) measurement. The Movin score histological scoring evaluates six parameters: fiber arrangement, fiber structure, angiogenesis, nuclear rounding, cell density, and inflammation. The differences in scoring between day 15 and day 30 of observation are presented in Table 1 and Figure 4 until Figure 7. The histopathology scoring tests were presented in Table 2.

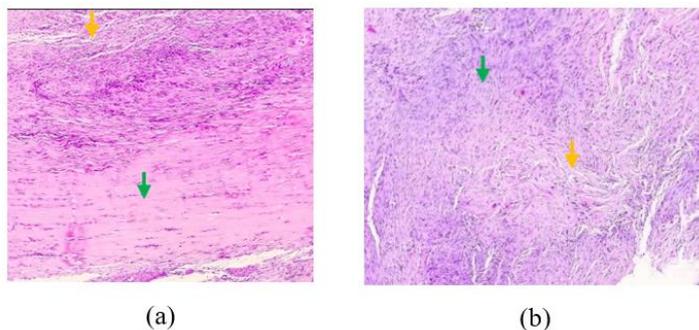


Figure 4. Histological picture of tendon tissue with Movin score (He staining, 100x magnification). (a) Fiber arrangement score 0; (b) Fiber arrangement score 3

In this research, biomechanical function were also carried out using tensile tests to assess ultimate tensile strength (UTS) as seen on Table 2. It is evident that on the 15th day of observation, the group injected with 100  $\mu$ L of PRP achieved the highest histopathological score, at 9.8  $\pm$  0.836 (mean  $\pm$  SD), followed by the group injected with 50  $\mu$ L of PRP (11.4  $\pm$  1.14) and the 0.9% NaCl group (12.6  $\pm$  1.124), with a mean difference of 1.6. Similarly, on day 30, the 100  $\mu$ L PRP injection group also achieved the best histopathological

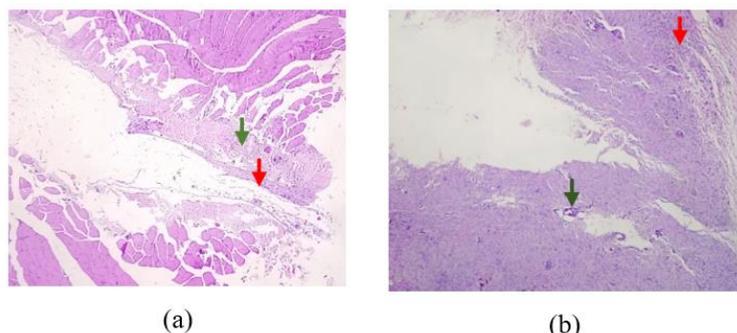


Figure 5. Histological picture of tendon tissue with Movin score (He staining, 40x magnification). (a) Angiogenesis score 0; (b) Angiogenesis score 3

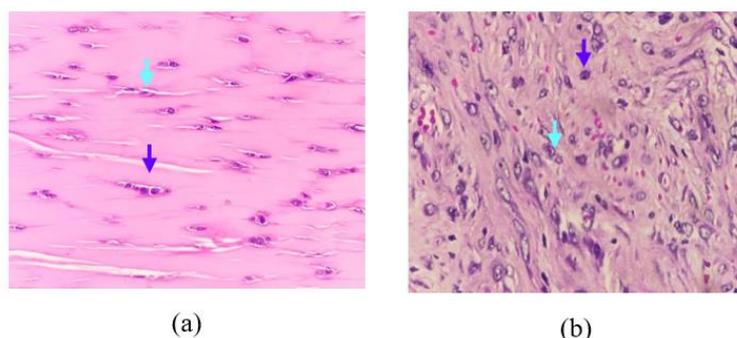


Figure 6. Histological picture of tendon tissue with Movin score (He staining, 400x magnification). (a) Nuclear roundings score 1; (b) Nuclear roundings score 3

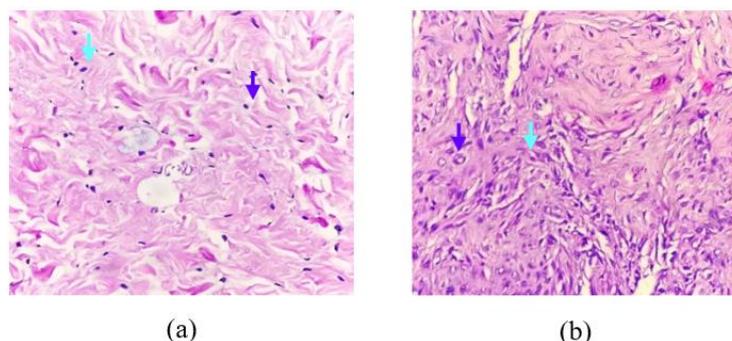


Figure 7. Histological picture of tendon tissue with Movin score (He staining, 400x magnification). (a) Cell density score 1; (b) Cell density score 3

score, at  $5.4 \pm 0.547$ , followed by the 50  $\mu\text{L}$  PRP injection group ( $6.6 \pm 1.14$ ) and the 0.9% NaCl group ( $7.8 \pm 0.836$ ), with a mean difference of 1.2. This indicates that both 100  $\mu\text{L}$  and 50  $\mu\text{L}$  doses of PRP accelerate tendon healing with a histological profile approaching that of a normal tendon (score of 0 on the Movin Score) compared to controls.

Based on the mean differences, it is apparent that the 100  $\mu\text{L}$  PRP dose was significantly more effective on the 15th day of observation, while by the 30th day, both doses yielded nearly identical results, suggesting that administering 100  $\mu\text{L}$  of PRP had a greater impact in the early phase of histological tendon healing. The results of the ANOVA test analysis indicated a significant difference between PRP administration and a reduction in histopathological scoring approaching normal tendon levels on both the 15th day ( $p\text{-value} = 0.004$ ) and the 30th day ( $p\text{-value} = 0.004$ ) of observation.

It is evident that on the 15th day of observation, the group injected with 100  $\mu\text{L}$  of PRP achieved the highest UTS value, at  $19,998 \pm 3,337$  (mean  $\pm$  SD), followed by the group injected with 50  $\mu\text{L}$  of PRP ( $18,361 \pm 1,115$ ) and the 0.9% NaCl group ( $14,638 \pm 1,124$ ), with a mean difference of 1,637. Similarly, on day 30, the 100  $\mu\text{L}$  PRP injection group also achieved the highest UTS value, at  $27,272 \pm 3,144$ , followed by the 50  $\mu\text{L}$  PRP injection group ( $23,786 \pm 1,494$ ) and the 0.9% NaCl group ( $21,133 \pm 0.653$ ), with a mean difference of 3,486. This indicates that both 100  $\mu\text{L}$  and 50  $\mu\text{L}$  doses of PRP

accelerate tendon healing with an increase in UTS values compared to controls. Based on the mean differences, it is apparent that the 100  $\mu\text{L}$  PRP dose was significantly more effective on the 30th day of observation, while on the 15th day, both doses yielded nearly identical results. Thus, administering the 100  $\mu\text{L}$  dose of PRP had a greater impact in the later phase of biomechanical tendon healing. The results of the ANOVA test analysis indicated a significant difference between PRP administration and the increase in UTS values on both the 15th day ( $p\text{-value} = 0.005$ ) and the 30th day ( $p\text{-value} = 0.002$ ) of observation.

Table 2. Histopathology scoring and ultimate tensile strength

Group	Histopathology Scoring (Mean $\pm$ SD)	Mean difference	p-value	Ultimate Tensile Strength (Mean $\pm$ SD)	Mean difference	p-value
Day-15						
PRP 100 $\mu\text{L}$	$9.8 \pm 0.836$			$19,998 \pm 3,337$		
PRP 50 $\mu\text{L}$	$11.4 \pm 1.14$			$18,361 \pm 1,115$		
NaCl 0.9%	$12.6 \pm 1.124$	1.6	0.004	$14,638 \pm 1,124$	1.637	0.005
Day-30						
PRP 100 $\mu\text{L}$	$5.4 \pm 0.547$			$27,272 \pm 3,144$		
PRP 50 $\mu\text{L}$	$6.6 \pm 1.14$			$23,786 \pm 1,494$		
NaCl 0.9%	$7.8 \pm 0.836$	1.2	0.004	$21,133 \pm 0.653$	3.486	0.002

## DISCUSSION

This study found that the 100 µL PRP injection group had the best histopathological scores on day 15 and day 30, followed by the 50 µL PRP group and the 0.9% NaCl group. This shows that PRP at doses of 100 µL and 50 µL accelerates tendon healing with a histological picture that is close to normal compared to controls. The Movin Score is used for analysis with six variables: fiber structure, fiber arrangement, rounding of the nuclei, inflammation (area infiltrated by inflammatory cells), increased vascularity, and cell density. Each variable is given a score of 0-3, with a total score of 0-18.<sup>14</sup>

Aspenberg and Virchenko<sup>15</sup> found in mice that PRP injection showed no real effect on day 11, but on day 21, a homogeneous mass of fibrous callus formation with few fat cells was seen in the PRP group. Another study by Xu et al.<sup>16</sup> found relatively normal tendon tissue within 3 weeks after transplantation of stem cells derived from collagen tendons with PRP into ruptured rat Achilles tendons. Zhang et al.<sup>17</sup> studied the effects of thrombin-activated PRP, PAR1, or PAR4 on rat patellar tendon rupture and found better tissue repair in the PRP group. Another study reported that PRP improved fibroblast orientation, collagen matrix, and reduced cell apoptosis on days 5 and 10 after injection.<sup>18</sup>

This research also shows that administration of PRP at doses of 100 µL and 50 µL accelerates tendon healing with improved biomechanical function that approaches normal tendons when compared to controls. PRP has been shown to positively treat tendinopathy and promote tendon healing in in vivo animal studies. Intratendinous injections of PRP have been studied to treat tendinopathy in rat patellas and Achilles tendons, increasing joint mobilization and improving tendon fiber organization 25 days after treatment.<sup>19</sup> Another study compared the effects of PRP and normal saline on an in vivo rat tendon healing model and found that at 14 days after treatment, ultimate tensile load and UTS were significantly increased in rats given PRP compared to those given normal saline.<sup>20</sup>

The results of histological examination also showed more elongated cells indicating the presence of tenocytes and the absence of chondrocytes in the group given PRP, thus confirming the safety of using PRP in vivo.<sup>21</sup> Lyras et al.<sup>9</sup> observed the effects of PRP gel on the early phase of patellar tendon healing and found that after 2 weeks, PRP treatment increased UTS values by 72.2%, ultimate tension by 39.1%, and stiffness levels by 53.1% compared with untreated controls. PRP treatment also induces better cell orientation and tissue maturation. These results show that PRP can speed up the healing process of tendon wounds. After a longer healing period, other studies report fewer new vessels in tendons after PRP treatment. PRP was also found to increase growth factor (IGF-I) expression in healing tendons.<sup>19</sup>

Our study should be seen in light of a few limitations. Firstly, our study involved animal models and therefore had limited sample sizes due to ethical considerations, cost, and resource constraints. This can affect the statistical power and generalizability of the results. Furthermore, the duration of follow-up in our experimental study may be shorter than needed to observe the long-term effects of PRP treatment on tendon healing. Our study also does not capture all outcome measures of tendon healing, such as growth factors involved in the healing process.

## CONCLUSION

This study found that PRP administration had a significant effect on histological tendon healing on the 15th and 30th, with the best improvement at a PRP dose of 100 µL, especially in the early phase of healing. PRP also had a significant effect on tendon healing in terms of biomechanical function on the 15th and 30th days, with the best improvement at a PRP dose of 100 µL, especially in the final phase of healing. This study provides detailed biomechanical and histological insights into the tendon healing process, which may be challenging to obtain in human studies due to ethical and logistical constraints.

## REFERENCES

1. Kaux JF, Drion P, Libertaux V, Colige A, Hoffmann A, Nusgens B, et al. Eccentric training improves tendon biomechanical properties: A rat model. *J Orthop Res.* 2013 Jan;31(1):119–24.
2. Çirci E, Akman YE, Sükür E, Bozkurt ER, Tüzüner T, Öztürkmen Y. Impact of platelet-rich plasma injection timing on healing of Achilles tendon injury in a rat model. *Acta Orthop Traumatol Turc.* 2016;50(3):366–72.
3. Yüksel S, Adanir O, Gültekin MZ, Çağlar A, Küçükıldırım BO, Güleç MA, et al. Effect of platelet-rich plasma for treatment of Achilles tendons in free-moving rats after surgical incision and treatment. *Acta Orthop Traumatol Turc.* 2015;49(5):544–51.
4. Parafioriti A, Armiraglio E, Del Bianco S, Tibalt E, Oliva F, Berardi AC. Single injection of platelet-rich plasma in a rat Achilles tendon tear model. *Muscles Ligaments Tendons J.* 2011;1(2):41–7.
5. Huegel J, Boorman-Padgett JF, Nuss CA, Minnig MCC, Chan PY, Kuntz AF, et al. Quantitative comparison of three rat models

- of Achilles tendon injury: A multidisciplinary approach. *J Biomech.* 2019 May;88:194–200.
6. Lemme NJ, Li NY, DeFroda SF, Kleiner J, Owens BD. Epidemiology of Achilles Tendon Ruptures in the United States: Athletic and Nonathletic Injuries From 2012 to 2016. *Orthop J Sport Med.* 2018 Nov 1;6(11).
  7. Yu TY, Pang JHS, Lin LP, Cheng JW, Liu SJ, Tsai WC. Platelet-Rich Plasma Releasate Promotes Early Healing in Tendon After Acute Injury. *Orthop J Sport Med.* 2021;9(4).
  8. De Mos M, Van El B, Degroot J, Jahr H, Van Schie HTM, Van Arkel ER, et al. Achilles tendinosis: Changes in biochemical composition and collagen turnover rate. *Am J Sports Med.* 2007 Sep;35(9):1549–56.
  9. Lyras DN, Kazakos K, Verettas D, Polychronidis A, Tryfonidis M, Botaitis S, et al. The influence of platelet-rich plasma on angiogenesis during the early phase of tendon healing. *Foot Ankle Int.* 2009 Nov;30(11):1101–6.
  10. De Carli A, Lanzetti RM, Ciompi A, Lupariello D, Vadalà A, Argento G, et al. Can platelet-rich plasma have a role in Achilles tendon surgical repair? Vol. 24, *Knee Surgery, Sports Traumatology, Arthroscopy.* Knee Surg Sports Traumatol Arthrosc; 2016. p. 2231–7.
  11. Schepull T, Kvist J, Norrman H, Trinks M, Berlin G, Aspenberg P. Autologous platelets have no effect on the healing of human Achilles tendon ruptures: A randomized single-blind study. *Am J Sports Med.* 2011 Jan;39(1):38–47.
  12. Kaux JF, Le Goff C, Seidel L, Péters P, Gothot A, Albert A, et al. Étude comparative de cinq techniques de préparation plaquettaire (platelet-rich plasma). *Pathol Biol.* 2011 Jun;59(3):157–60.
  13. Black DA, Lindley S, Tucci M, Lawyer T, Benghuzzi H. A new model for repair of the Achilles tendon in the rat. *J Investig Surg.* 2011 Aug;24(5):217–21.
  14. Genç E, Beytemur O, Yuksel S, Eren Y, Çağlar A, Küçükıldırım BO, et al. Investigation of the biomechanical and histopathological effects of autologous conditioned serum on healing of Achilles tendon. *Acta Orthop Traumatol Turc.* 2018 May;52(3):226–31.
  15. Aspenberg P, Virchenko O. Platelet concentrate injection improves Achilles tendon repair in rats. *Acta Orthop Scand.* 2004;75(1):93–9.
  16. Xu K, Al-ani MK, Sun Y, Xu W, Pan L, Song Y, et al. Platelet-rich plasma activates tendon-derived stem cells to promote regeneration of Achilles tendon rupture in rats. *J Tissue Eng Regen Med.* 2017 Apr;11(4):1173–84.
  17. Zhang J, Nie D, Williamson K, Rocha JL, Hogan M V, Wang JHC. Selectively activated PRP exerts differential effects on tendon stem/progenitor cells and tendon healing. *J Tissue Eng.* 2019;10.
  18. Cao Y, Zhu X, Zhou R, He Y, Wu Z, Chen Y. A narrative review of the research progress and clinical application of platelet-rich plasma. *Ann Palliat Med.* 2021 Apr;10(4):4823–9.
  19. Zhou Y, Wang JHC. PRP Treatment Efficacy for Tendinopathy: A Review of Basic Science Studies. Vol. 2016, *BioMed Research International.* Wiley; 2016.
  20. Kaux JF, Drion P V., Colige A, Pascon F, Libertiaux V, Hoffmann A, et al. Effects of platelet-rich plasma (PRP) on the healing of Achilles tendons of rats. *Wound Repair Regen.* 2012 Sep;20(5):748–56.
  21. Spang C, Chen J, Backman LJ. The tenocyte phenotype of human primary tendon cells in vitro is reduced by glucocorticoids. *BMC Musculoskelet Disord.* 2016 Dec 10;17(1):467.