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Platelet-Derived Extracellular Vesicle – Rich Plasma Demonstrates Favorable Histological Features Compared With PRP in a Rabbit Skeletal Muscle Injury Model

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ABSTRACT

Platelet-rich plasma (PRP) is commonly used to support skeletal muscle healing, although its efficacy remains variable and concerns persist regarding profibrotic effects. Platelet-derived extracellular vesicles (pEVs) may modulate inflammation, and this study aimed to compare the histological effects of two PRP systems and a pEV-rich plasma preparation in a rabbit muscle injury model.

A standardized partial muscle injury (5 × 5 mm) was created in the biceps femoris of 28 female New Zealand White rabbits. Animals were allocated to four groups: control, Arthrex ACP®, T-LAB PRP®, and platelet-derived extracellular vesicle–rich plasma (Exomine®). Treatments were administered locally on postoperative days 0, 4, and 7. Half of the animals were euthanized at week 3 and the remainder at week 6. Histological evaluation focused on inflammatory infiltration, fibrotic scar formation, and indicators of muscle regeneration.

At week 3, overall group comparisons showed significant differences in acute inflammatory parameters, with the pEV-rich plasma group exhibiting lower neutrophil infiltration and fewer multinucleated giant cells. At week 6, significant differences were observed in chronic inflammation and remodeling, with reduced lymphocyte–macrophage infiltration and fibrosis in the pEV-rich plasma group. Both PRP groups showed histological findings comparable to control.

In this preclinical rabbit model, a platelet-derived extracellular vesicle–rich plasma preparation was associated with more favorable histological features related to inflammation resolution and fibrosis than conventional PRP. These findings are limited to histopathological outcomes and require confirmation with functional studies.

Keywords: Platelet-derived extracellular vesicles, Platelet-rich plasma, Skeletal muscle injury, Biological therapy, Rabbit model.

INTRODUCTION

Muscle injuries are common in athletes and active individuals and often associated with prolonged recovery. Skeletal muscle healing proceeds through overlapping phases of destruction, repair, and remodeling[1,2]. Platelet-rich plasma (PRP) is used as a biological intervention with the potential to accelerate tissue healing by containing high concentrations of growth factors that promote angiogenesis, cell proliferation and extracellular matrix remodeling[3,4]. However, transforming growth factor beta (TGF-β1), which is present in PRP, can increase the risk of fibrosis by triggering excessive collagen production, which may negatively affect functional recovery[5]. Consistent with this concern, randomized clinical trials have demonstrated inconsistent or limited benefits of PRP for muscle injuries, highlighting ongoing uncertainty regarding its overall regenerative effectiveness[6].

Beyond soluble growth factors, increasing evidence suggests that platelet-rich and plasma-based biologics exert part of their biological activity through platelet-derived extracellular vesicles (pEVs). These membrane-bound vesicles, released from activated

platelets and circulating blood cells, carry bioactive proteins, lipids, and nucleic acids that can influence inflammatory signaling and tissue repair processes[7,8]. Platelet-derived extracellular vesicles have been shown to modulate immune responses by attenuating macrophage activation, reducing pro-inflammatory cytokines such as IL-6 and TNF-α, and increasing anti-inflammatory mediators including IL-10, thereby promoting resolution of inflammation[9]. At a mechanistic level, pEVs can counteract macrophage activation, lowering IL-6/TNF-α and increasing IL-10, thereby damping NF-κB–driven inflammation and promoting pro-resolving polarization[8]. Such blood-borne pEVs have shown anti-inflammatory and pro-regenerative properties in preclinical settings[10], and early clinical work with pEVs suggests activation of wound-healing pathways[11].

Despite growing interest in extracellular vesicle–mediated biological effects, comparative data evaluating extracellular vesicle–rich plasma preparations against commercially available PRP systems in standardized muscle injury models remain limited. In particular, it remains unclear whether vesicle-rich plasma formulations provide histological advantages over conventional PRP preparations with respect to inflammation resolution and fibrosis during muscle healing. Therefore, the purpose of this study was to compare the histological effects of two commonly used PRP systems (Arthrex ACP® and T-LAB PRP®) with a platelet-derived extracellular vesicle–rich plasma preparation (Exomine®) in a standardized rabbit skeletal muscle injury model. We hypothesized that extracellular vesicle–rich plasma would be associated with more favorable histological features, characterized by reduced inflammatory cell infiltration and fibrosis, compared with conventional PRP preparations.

MATERIALS (ANIMALS) AND METHODS

This study was conducted with the ethical approval of the Bezmialem University Animal Experiments Local Ethics Committee (approval date: July 22, 2024). Animal handling, housing, and surgical procedures followed the 3Rs principles of replacement, reduction, and refinement to ensure animal welfare. Efforts were made to minimize pain, discomfort, and distress throughout the study. All rabbits were monitored daily for signs of suffering, and no procedures causing prolonged pain or harm were permitted. Anesthesia, analgesia, and postoperative care were administered by trained personnel under veterinary supervision. The study design, sample size, and outcome measures were planned to minimize the number of animals used while maximizing scientific validity, in accordance with ARRIVE reporting guidelines.

A total of 28 female New Zealand White rabbits were used, with a homogeneous distribution in terms of age (6-8 months) and weight (2.5–3.0 kg). All rabbits were deemed healthy upon veterinary examination, with no pre-existing knee pathologies. The inclusion criteria was a normal hamstring tendon structure, whereas rabbits with any signs of musculoskeletal abnormalities were excluded. A computer-generated sequence with predefined unbalanced allocation was prepared by an investigator not involved in surgeries or assessments; assignments were concealed in opaque, sequentially numbered envelopes. No movement restriction were applied before or after surgery.

All procedures were performed under general anesthesia with intravenous administration of 10 mg/kg xylazine HCl and 35 mg/kg ketamine HCl. Meloxicam (5 mg/kg) was used pre-emptively and continued 24 hours for analgesia. The intravenous administration of 50 mg/kg cefazolin was performed at the initiation of each procedure for infection prophylaxis.

Creation of Hamstring Injury

All procedures were performed in the lateral decubitus position. After the application site was shaved, a 1.5 cm incision was made on the lateral thigh, 5 cm proximal to the knee joint. The skin and subcutaneous tissue were dissected. The femur was palpated and dissection was performed posteriorly to identify the biceps femoris muscle. A standardized partial muscle-injury model, consisting of a 5-mm long and 5-mm deep scalpel-created defect, was established-similar to the model described by Tsai et al.[2] as illustrated in Figure 1.

Study Design

Four rabbits were assigned to the control group and received no treatment. The remaining 24 rabbits were divided equally into three groups (A, B, and C). Group A received Arthrex ACP® injections, Group B received Exomine® injections, and Group C received T-lab PRP® injections on both legs. For all preparations, autologous venous blood was obtained from each rabbit under anesthesia and processed accordingly for ACP-PRP, T-LAB PRP, and pEVs; no allogeneic material was used. Each injection was standardized to 1.5 mL to ensure uniform application. The treatment protocol, including administration on postoperative days 0, 4, and 7, is

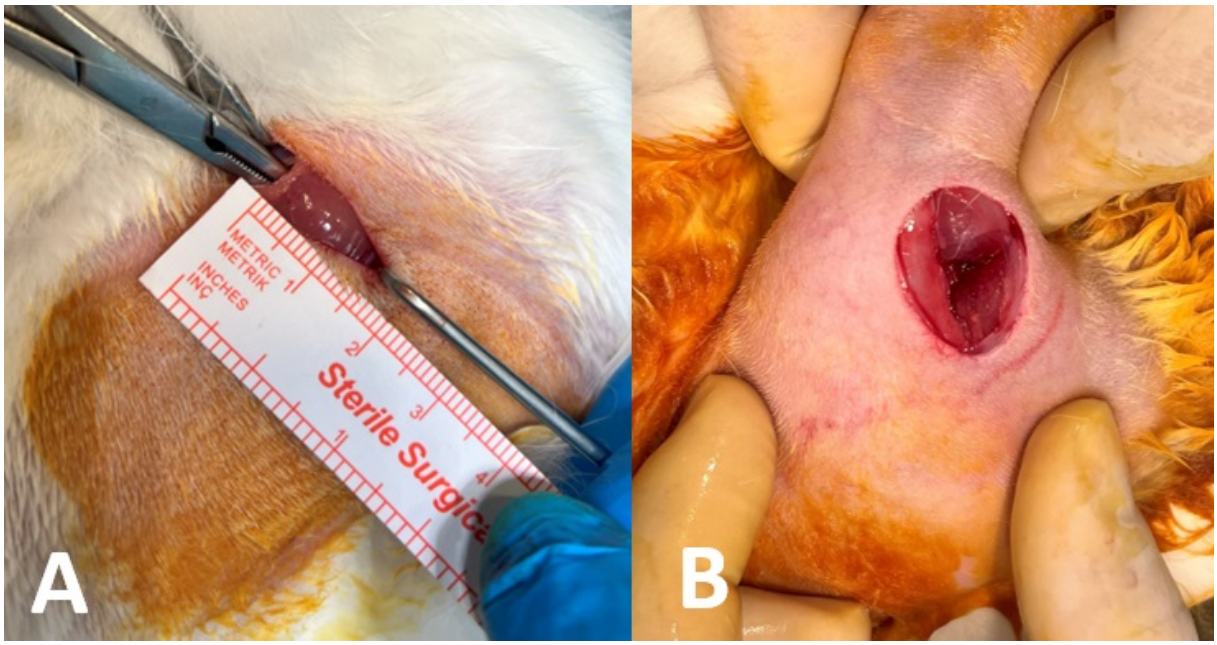

Fig. 1 — Hamstring injury model A. 1.5 cm skin incision and identification of the biceps femoris muscle; B. Creation of a 5 × 5 mm muscle injury using a scalpel.

schematically depicted in Figure 2. Our three-dose schedule aligns with prior preclinical muscle-injury studies that used early repeated intralesional dosing[12]. A complete blood count (CBC) was performed before each injection to measure the platelet concentrations of the two different PRP methods.

Preparation of Arthrex ACP®

The preparation of Arthrex ACP® begins with the collection of approximately 10–15 mL of venous blood via the Arthrex ACP® double-syringe system under sterile conditions. This system minimizes the risk of contamination and prevents premature activation of platelets. The collected blood sample is then centrifuged at 1,500 RPM/5 min (approximately 350 g of centrifugal force), separating the PRP from red blood cells and leukocytes. After centrifugation, the PRP is carefully aspirated without disturbing the buffy coat layer to minimize the leukocyte content. The extracted ACP was inspected for clarity and sterility before being transferred into a sterile syringe for immediate use.

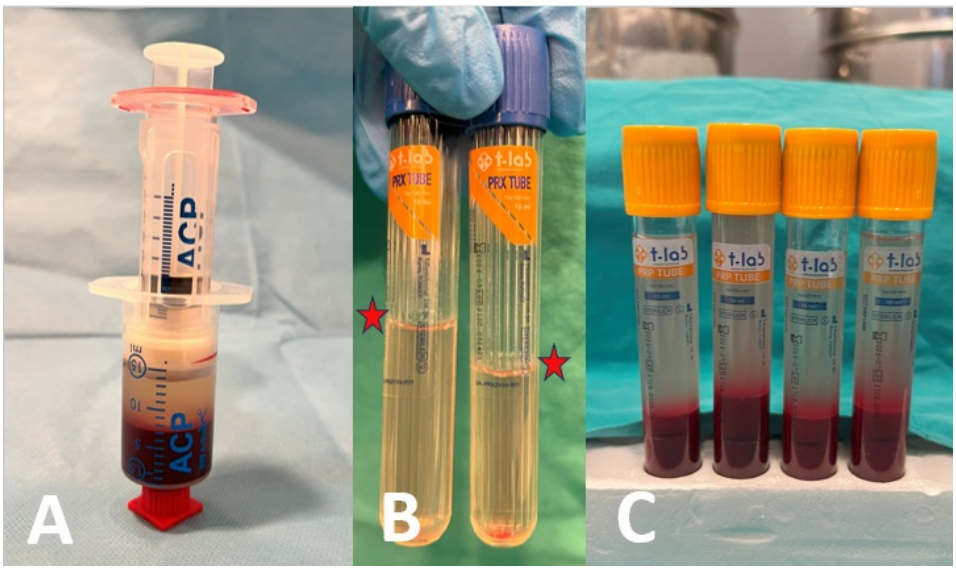

Fig. 2 — Treatment Methods A. Pre-injection form of Arthrex ACP®; B. Injection-ready Exomine® (Star: Vesicle-rich layer); C. T-LAB PRP®.

Preparation of Exomine®

Approximately 20 mL of blood was collected under sterile conditions, and PRP was prepared via the T-LAB PRP Kit (T-Biotechnology Laboratory, Bursa, Turkey). The sample was centrifuged at 2900 RPM/4 min and all the plasma was collected into a 10 mL syringe. The collected plasma was passed through a Microlyzer 600 µm (T-Biotechnology Laboratory, Bursa, Turkey) 51 times. The plasma passed through the 600 µm Microlyzer and was transferred into two Advanced PRX tubes. The Advanced PRX tubes (T-Biotechnology Laboratory, Bursa, Turkey) were centrifuged sequentially at 2000 RPM/3 min, 3500 RPM/4 min, 2000 RPM/3 min, and 4000 RPM/10 min." From the upper layer of each Advanced PRX tube, 2-3 mL of vesicle-rich plasma was collected.

Preparation of T-lab PRP®

Approximately 20 mL of blood was collected under sterile conditions, and PRP was prepared via the T-LAB PRP Kit (T-Biotechnology Laboratory, Bursa, Turkey). The sample was centrifuged at 2900 RPM/4 min and all the plasma was collected for PRP injection.

Histological examination

Half of the rabbits in each group were euthanized in the 3rd week, and the other half were euthanized in the 6th week. After the mice were sacrificed, the previous incision was extended. The injured muscle site was surgically exposed via dissection, as demonstrated in Figure 3. Using the fascia defect as the central reference point, full-thickness muscle samples, each measuring 2x2 cm, were excised.

The samples were fixed in 10% buffered formalin. 4-µm thick sections were prepared from paraffin-embedded tissues and stained with hematoxylin and eosin. Following the four-level grading approach described by Delos et al.[13], semiquantitative assessment was performed by a pathologist blinded to the treatment, who analyzed ten randomly chosen fields per sample at 100× magnification under a light microscope (Nikon microscope, model eclpise Ci-S). Digital images were acquired, and staining was evaluated using the following criteria: grade 0 (absence of positive staining), grade 1 (scattered positive cells), grade 2 (moderate positivity involving less than half of the total cells), and grade 3 (intense staining observed in the majority of cells). In all cases, the general morphology due to injury (cellular swelling, interstitial edema, loss of striation, necrosis, dystrophic calcification, neutrophil infiltration, lymphocyte-macrophage infiltration, giant cells, vascular proliferation, fibroblastic proliferation, and scar tissue) and the number of centronucleated fibers, which are considered indicators of muscle regeneration, were evaluated, as in Sarıtaş et al.[14] , using semi-quantitative scoring parameters.

Statistical analysis

All the statistical analyses were performed via SPSS Version 27.0 (IBM, Armonk, NY, USA). Histological healing variables (e.g., neutrophil infiltration, multinucleated giant cells, edema, fibrosis) were treated as ordinal scores (0–3: none, mild, moderate, severe) and summarized as median (min–max). Group comparisons for ordinal outcomes used the Kruskal–Wallis test, followed—when appropriate—by pairwise Mann–Whitney U tests with Holm–Bonferroni correction. A

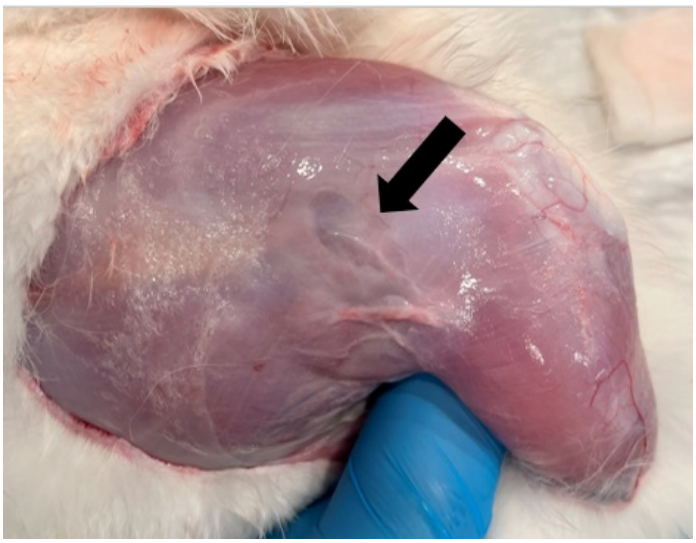

Fig. 3 — Fascial defect indicating the injured area. (Black arrow: Fascia defect).

p-value < 0.05 was considered statistically significant. Because injuries were created bilaterally, observations from the two limbs of the same animal cannot be considered statistically independent; therefore, the individual animal was defined as the experimental unit, and histological scores from both limbs were averaged per animal prior to analysis.

For the platelet concentration analysis, the data were tested for normality via the Shapiro-Wilk test. As the data followed a normal distribution, differences in the mean platelet concentrations between Arthrex ACP®, T-LAB PRP®, and whole blood were analyzed via one-way analysis of variance (ANOVA). Post- hoc comparisons were performed via Tukey's honestly significant difference (HSD) test to identify specific group differences. The platelet concentrations are presented as the means ± standard deviations (SDs).

A formal a priori power analysis was not performed. The sample size was set a priori based on group sizes reported in comparable muscle-injury studies using PRP with histologic assessment[15,16] and constrained by the maximum number of rabbits approved by the institutional ethics committee (3R principles).

RESULTS

Macroscopically, muscle healing was observed in all rabbits at both the 3rd and the 6th week. All animals completed the study according to the predefined protocol, and no animal loss occurred during the experimental period. No wound-related complications, infections, or adverse local reactions were observed at the surgical or injection sites.

3rd Week Histological Findings

At the third-week histological assessment, overall group comparisons demonstrated significant differences in key inflammatory parameters. Specifically, neutrophil infiltration differed significantly among groups (Kruskal–Wallis test, p = 0.0186). Post-hoc pairwise analyses using the Mann–Whitney U test indicated lower neutrophil infiltration scores in the Exomine® group compared with the other treatment and control groups, with unadjusted p values ranging between approximately 0.02 and 0.03. However, these pairwise differences did not remain statistically significant after Holm–Bonferroni correction, likely reflecting the small animal-level sample size.

Similarly, overall group differences were observed for multinucleated giant cells, a marker of acute inflammation (Kruskal–Wallis test, p = 0.0200). (Figure 4) Post-hoc comparisons suggested reduced multinucleated giant cell scores in the Exomine® group relative to the other groups (unadjusted p ≈ 0.02–0.03), although these differences did not persist following correction for multiple comparisons.

Other parameters, including cellular swelling, interstitial edema, lymphocyte–macrophage infil-

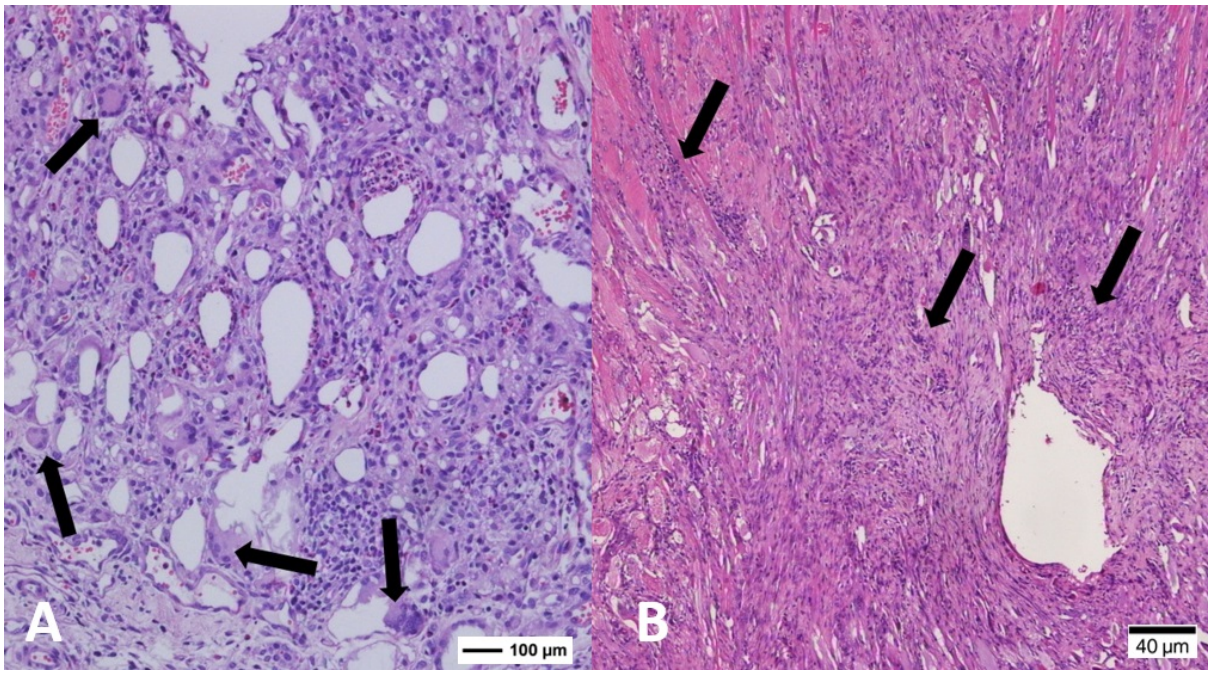

Fig. 4 — Histological findings at the 3rd week of sacrifice A. Multinucleated giant cells in a sample from the Arthrex ACP® group (H&E staining, 100x magnification); B. Mononuclear cell infiltration in a sample from the T-LAB PRP® group (H&E staining, 40x magnification).

tration, and fibrotic tissue formation, did not significantly differ between the groups (all $p > 0.05$). However, descriptive analysis still revealed a trend toward lower inflammatory and fibrotic activity in the Exomine® group (Table I).

6th Week Histological Findings

At the sixth-week evaluation, significant overall group differences were identified in parameters related to chronic inflammation and tissue remodeling. Lymphocyte–macrophage infiltration differed significantly among groups (Kruskal–Wallis test, $p = 0.0152$). Post-hoc pairwise analyses demonstrated lower lymphocyte–macrophage infiltration scores in the Exomine® group compared with the other treatment and control groups, with unadjusted p values in the range of approximately 0.02–0.03; however, these differences did not remain significant after Holm–Bonferroni adjustment.

Likewise, fibrotic scar tissue formation showed significant overall group differences at the sixth week (Kruskal–Wallis test, $p = 0.0310$) (Figure 5). Post-hoc analyses again indicated lower fibrosis scores in the Exomine® group relative to the other groups (unadjusted $p \approx 0.02–0.03$), although statistical significance was not retained following correction for multiple testing.

The other parameters did not significantly differ among the groups at this time point ($p > 0.05$). However, the Exomine® group continued to have lower descriptive scores across multiple histological indicators, maintaining a favorable profile in both inflammation resolution and fibrosis prevention (Table II).

Platelet Concentration Comparisons

In addition to histological evaluations, the platelet concentrations of Arthrex ACP® and T-LAB PRP® were compared with each other and with those of whole blood. Statistical analysis revealed that both products presented significantly higher mean platelet concentrations than did whole blood (Arthrex ACP®: 1,000,000 ± 60,000/µL; T-LAB PRP®: 1,050,000 ± 70,000/µL; whole blood: 400,000 ± 40,000/µL; $p < 0.05$ for both comparisons). The results confirm that both systems effectively achieved platelet enrichment at approximately 2.5–3 times the baseline blood level, as shown in Figure 6.

When Arthrex ACP® and T-LAB PRP® were compared, no statistically significant difference was detected in the mean platelet concentration ($p > 0.05$). The similar levels of enrichment achieved by the two systems highlight their comparable efficacy in preparing PRP with increased platelet concentrations. These results underscore the utility of both products in applications requiring concentrated platelets for therapeutic purposes.

DISCUSSION

In this study, we compared the histological effects of different PRP systems (Arthrex ACP®, T-LAB PRP®) and platelet-derived extracellular vesicle–rich plasma preparation (Exomine®) on skeletal muscle healing in a standardized rabbit muscle-injury model at two biologically relevant time points. At week 3 the Exomine® group showed fewer multinucleated giant cells and lower neutrophil infiltration, and at week 6 it

Table I. — Histologic outcomes at week 3 by treatment group [median (Q1–Q3)].

Variable	Arthrex ACP®	Exomine®	T-LAB PRP®	Control
Cellular swelling	2 (2-3)	2 (2-2)	2 (2-3)	2.5 (2-3)
Interstitial edema	2 (2–3)	2 (2–2)	2 (2–3)	2.5 (2–3)
Neutrophil infiltration *	3 (2.5-3)	2 (1.5-2)	3 (2-3)	3 (3-3)
Lymphocyte–macrophage infiltration	2.5 (2-3)	2 (2-2.5)	2 (2-2)	2.5 (2-3)
Scar tissue	0.5 (0-1)	0.5 (0-1)	1 (1-1)	0.5 (0-1)
Multinucleated giant cells *	3 (3-3)	2 (1.5-2)	3 (2.5-3)	3 (3-3)
Centrally nucleated fibers	3 (2–3)	3 (2–3)	3 (2–3)	2.5 (2–3)
Eosinophil infiltration	0 (0–0.5)	0.5 (0–1)	0 (0–0.5)	0.5 (0–1)
Loss of striations	3 (2.5–3)	2.5 (2–3)	2.5 (2–3)	3 (2.5–3)
Necrosis	0 (0–0)	0 (0–0.5)	0 (0–0)	0 (0–0.5)
Dystrophic calcification	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Vascular proliferation	2 (1.5–2)	2 (1.5–2.5)	2 (2–2)	2 (1.5–2.5)
Decreased interfascicular spacing	1 (0.5–1)	1 (0–1)	0.5 (0–1)	0.5 (0–1)
Fibroblastic proliferation	2 (1.5–2)	2 (1–2.5)	2 (1.5–2.5)	2 (2–2.5)
Lymphoid follicle	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Satellite cells	1.5 (1–2)	1 (1–2)	1 (1–2)	1 (1–1.5)
* Indicates a statistically significant difference ($p<0.05$).				

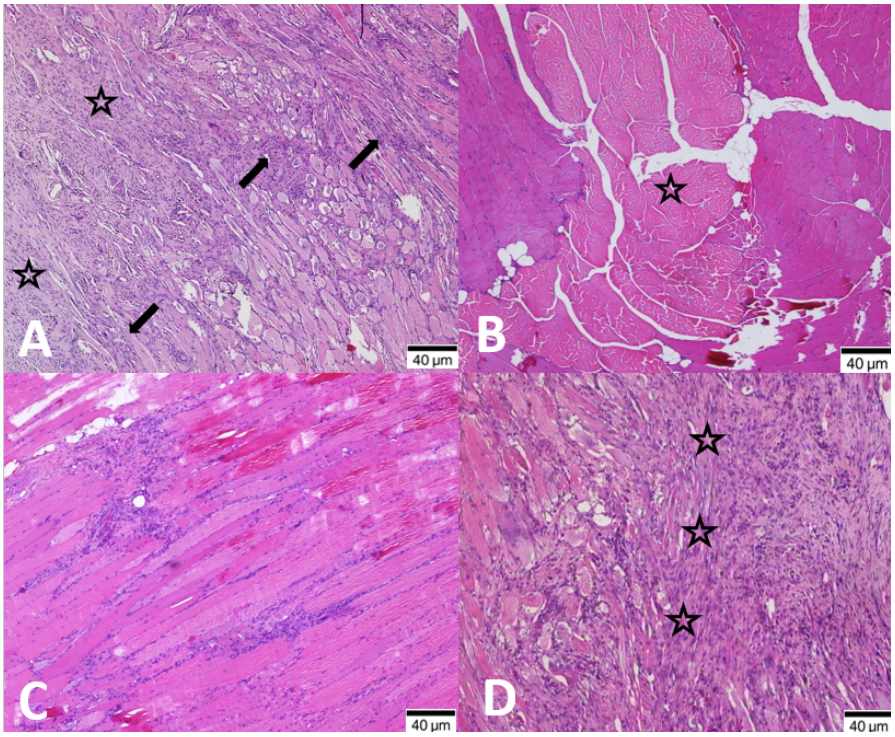

Fig. 5 — Histological findings at the 6th week of sacrifice A. Sample from the Arthrex ACP® group (H&E staining, 40x magnification, Star: Fibrous area, Black arrow: Mononuclear cell infiltration) B. Sample from control group (H&E staining, 40x magnification, Star: Scar area) C. Healed muscle area without fibrosis and with minimal inflammation in a sample from the Exomine® group (H&E staining, 40x magnification) D. Sample from T-LAB PRP® group (H&E staining, 40x magnification, Star: Scar area)

Table II. — Histologic outcomes at week 6 by treatment group [median (Q1–Q3)].

Variable	Arthrex ACP®	Exomine®	T-LAB PRP®	Control
Cellular swelling	1.5 (1–2)	1.5 (1–2)	1.5 (1–2)	1.5 (1–2)
Interstitial edema	1.5 (1–2)	1.5 (1–2)	1.5 (1–2)	1.5 (1–2)
Neutrophil infiltration	1.5 (1-2)	1.5 (1-2)	2 (1-2)	2 (2-2)
Lymphocyte–macrophage infiltration *	2 (2-2)	1 (1-2)	2 (2-2.5)	3 (2.5-3)
Scar tissue *	3 (2-3)	1 (0.5-2)	3 (2-3)	2.5 (2-3)
Multinucleated giant cells	2 (1-2)	1.5 (1-2)	1.5 (1-2)	1 (1-1.5)
Centrally nucleated fibers	1 (0.5–1)	1 (0.5–1)	1 (0–1)	0.5 (0–1)
Eosinophil infiltration	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Loss of striations	1 (0–1)	0 (0–1)	1 (0–1)	0.5 (0–1)
Necrosis	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Dystrophic calcification	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Vascular proliferation	1 (0–1)	0.5 (0–1)	1 (0–1)	1 (0.5–1)
Decreased interfascicular spacing	2 (2–2)	2 (2–3)	2.5 (2–3)	2 (2–2)
Fibroblastic proliferation	1 (0–1)	1 (0.5–1)	1 (0–1)	0.5 (0–1)
Lymphoid follicle	0 (0–0)	0 (0–0)	0 (0–0)	0 (0–0)
Satellite cells	0 (0–0.5)	0 (0–0)	0 (0–0)	0 (0–0.5)
* Indicates a statistically significant difference ($p<0.05$).				

showed reduced lymphocyte–macrophage infiltration with less scar tissue. In contrast, both PRP groups showed histological findings comparable to those of the control group at both time points. Importantly, these observations remained consistent when analyses were performed at the animal level, supporting the robustness of the overall histological trends.

The principal insight of the present study is therefore biological rather than purely statistical. The pEV-rich plasma preparation was associated with a pattern suggestive of earlier inflammatory resolution and a more favorable tissue-remodeling profile,

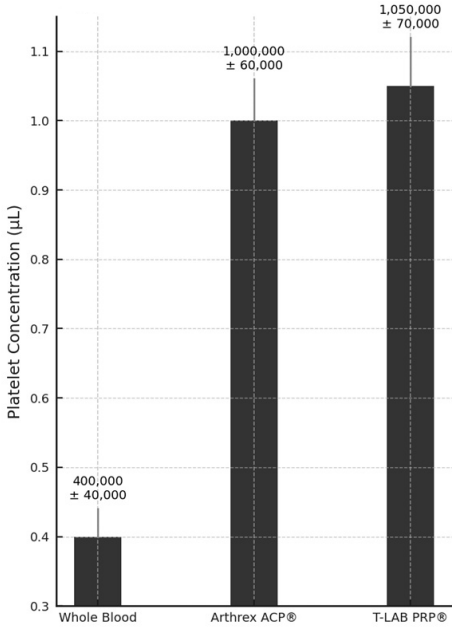

Fig. 6 — Platelet concentrations of different PRP products.

whereas conventional PRP preparations did not confer a clear histological advantage over no treatment under the conditions tested. Notably, markers of chronic inflammation and fibrosis were lower in the pEV-rich plasma group at the later time point, indicating a potential influence on the remodeling phase of muscle healing. However, given the exploratory nature of this preclinical study and the modest animal-level sample size, these findings should be interpreted cautiously

The healing process of skeletal muscle follows a three-phase overlapping process of destruction, repair, and remodeling[1]. PRP has been widely used to accelerate tissue healing because of its high concentrations of growth factors such as PDGF, IGF-1, and VEGF[2,13]. These factors play critical roles in promoting angiogenesis, cell proliferation, and extracellular matrix remodeling[17]. However, there is concern that the presence of transforming growth factor beta (TGF-β1) in PRP may promote excessive collagen deposition, thereby increasing fibrosis and negatively affecting functional recovery. Consistent with this concern, clinical trials evaluating PRP for muscle injuries have reported heterogeneous and often limited benefits[5,18,19].

Beyond soluble growth factors, increasing evidence indicates that plasma-based biologics may exert part of their biological activity through platelet-derived extracellular vesicles[20], which are membrane-bound structures released from activated platelets and circulating blood cells[21]. These vesicles carry bioactive proteins, lipids, and nucleic acids capable of modulating inflammatory signaling and tissue responses[9]. Experimental studies have demonstrated that plasma-derived extracellular vesicles can attenuate macrophage activation and shift the inflammatory milieu toward a more pro-resolving profile, potentially facilitating tissue repair[8,10]. In this context, the earlier reduction in acute inflammatory markers observed in the pEV-rich plasma group in the present study may reflect such immunomodulatory effects. Nevertheless, because extracellular vesicle characterization was not performed, mechanistic inferences remain speculative.

Fibrosis is a major concern during the muscle recovery process. Studies have shown that PRP can accelerate muscle recovery but can also lead to fibrosis because the TGF-β1 in PRP promotes scar tissue formation[6]. However, some studies have indicated that combining PRP with anti-fibrotic agents may reduce the development of fibrosis[22]. Agents such as suramin, decorin and losartan in particular have been shown to support tissue repair by blocking the fibrotic effects of TGF-β1[5]. It has also been shown that neutralization of TGF-β1 increases the effectiveness of PRP[23]. In contrast, plasma-derived extracellular vesicles have been proposed to influence fibroblast activity and extracellular matrix deposition in a manner that may limit excessive fibrosis. In the present study, fibrotic scar tissue was lower in the Exomine® group than in the other groups. These finding suggests that pEVs may direct tissue repair by regulating fibroblast activity although definitive conclusions regarding underlying cellular mechanisms cannot be drawn.

The absence of a significant histological advantage of PRP over control in our study aligns with several clinical investigations reporting limited or no benefit of PRP for muscle injuries. Hamilton et al.[24] reported in their randomized controlled study that PRP applied together with an exercise program in hamstring injuries did not accelerate the healing process compared with the placebo group and did significantly differ. Hamid et al.[25] compared groups that received PRP injection and those that received follow-up without injection and reported that PRP did not significantly contribute to the healing process. Similarly, Reurink et al.[6] reported that PRP did not shorten the functional recovery period. However, some studies have reported that PRP can accelerate muscle recovery and promote tissue regeneration[3,26]. One of the most important reasons for these contradictory results is the lack of standardization of the PRP[22]. During the preparation process of PRP, variables such as different centrifugation speeds, blood collection techniques, activation methods and platelet concentrations cause different results. In the literature, PRP concentrations generally vary between 4 and 10-fold[3]. Studies conducted with different commercial PRP systems have shown that these systems cause changes in platelet concentration. Castillo et al.[27] reported that the platelet concentration differed in three among different PRP systems and that this may have a direct effect on biological activity. In our study, no significant difference was observed between the PRP groups and the control group. This suggests that the platelet concentration of the PRP used may not be in the optimal range; therefore, its biological activity may have been limited. Clinically, functional outcomes after PRP remain variable, reflecting heterogeneity in formulations and protocols; recent reviews likewise underscore the lack of consensus for routine use[28].

The lack of a statistically significant difference between the PRP and control groups may be related to the injury model used. The literature has shown that the effectiveness of PRP varies depending on the type and severity of the injury. PRP can have significant healing effects, especially in severe muscle tears or volumetric muscle defects, but this effect is limited in milder injuries[1,13]. The 10 mm partial muscle injury model used in our study can be considered mild-moderate muscle injury, which may be one of the possible reasons why PRP did not provide a significant advantage. Similarly, some studies have shown that PRP suppresses inflammation and accelerates healing in severe muscle injuries, but does not significantly differ from placebo in milder injuries such as contusions[2,24].

Limitations

Several limitations of this study should be acknowledged. First, the findings derived from a rabbit model may not be directly generalizable to human muscle biology and clinical outcomes. Second, biochemical characterization of PRP and the pEV-rich plasma preparation—such as growth-factor content, leukocyte composition, and extracellular vesicle profiling—was not performed, limiting mechanistic interpretation and cross-study comparability. Third, outcome assessment was restricted to histopathological evaluation; functional and biomechanical properties of the healed muscle were not assessed. Additionally, no formal a priori power analysis was conducted, and the study may be underpowered to detect small between-group differences at the animal level. Finally, only a single dosing schedule was evaluated, and alternative dosing strategies or timing of administration were not explored.

CONCLUSION

In this preclinical rabbit model,a platelet-derived extracellular vesicle–rich plasma was associated with more favorable histologic features at defined time points, whereas ACP-PRP and T-LAB PRP did not differ from control under the present conditions. These findings are limited to histopathologic outcomes and do not permit conclusions about athletes or humans. Future studies should evaluate dosing and timing, characterize the cytokine profile of PRP and pEVs rich plasma, and incorporate functional/biomechanical assessments to determine translational relevance.

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Conflict of Interest: The authors declare no conflicts of interest. The authors had no financial or personal relationships with any of the manufacturers of the products used in this study.

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