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Review

In vivo effect of platelet gel on human tendon and ligament healing: A narrative review

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ABSTRACT

Tendon and ligament injuries remain a significant challenge for clinicians, despite considerable efforts to develop effective treatment methods. This study reviewed *in vivo* human studies investigating the use of platelet gel, a blood-derived biomaterial that enhances tissue healing, for treating tendon and ligament injuries. Only eight relevant articles were identified, highlighting the limited number of available studies on this topic. Of these eight articles, three reported significant positive treatment effects, two found no significant benefit, and three observed varying degrees of improvement, although not always statistically significant. Overall, six of the eight studies indicated positive effects of platelet gel based on clinical and radiographic outcomes, suggesting its potential as a promising treatment. Further clinical studies are required to confirm its efficacy and establish its role in tendon and ligament healing.

Contents

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1. Introduction

Worldwide, numerous individuals suffer from tendon and ligament injuries annually. These injuries are especially common in older adults, athletes, and active workers, accounting for a large proportion of all musculoskeletal injuries [1–3]. Primary causes of tendon and ligament injuries include overuse, age-related degeneration, and rheumatoid arthritis; however, injuries can also occur acutely due to a single traumatic event that involves extremely high forces [4]. Tendon and ligament injuries can cause symptoms such as pain, instability, and disability, leading to long-term chronic problems. These injuries significantly affect the functional performance of patients in daily life and various activities, including occupational, professional, and recreational pursuits, creating a substantial socioeconomic burden for countries [1,2]. Tendon and ligament injuries are particularly painful for athletes and active workers, resulting in lost time and reduced performance [5,6]. Therefore, these injuries represent a significant public health concern that requires further investigation and attention.

Current conservative treatments for tendon and ligament injuries include physical therapy [7], low-intensity pulsed ultrasound [8], extracorporeal shockwave therapy [9,10], treatment with platelet-rich plasma [11,12], magnetic field therapy [13], and restrictive bracing [14]. Non-steroidal anti-inflammatory drugs and corticosteroid injections offer pain relief but do not promote tendon or ligament healing [14]. Surgical treatment may be necessary for severe tendon and ligament injuries, such as complete ruptures or tears, or when conservative treatments fail [1]. Even in sub-failure injuries, surgical interventions are considered for patients, such as athletes, seeking full restoration of function and strength [14]. Conventional surgical treatment methods for repairing damaged tendons or ligaments include suturing, debridement, and replacement of injured tissues with autografts or allografts to fill large tissue defects [14]. Each of these treatments has limitations, advantages, and applicability. Despite extensive research efforts to develop effective treatments for tendon and ligament injuries, managing these injuries remains a challenge in orthopedics, rehabilitation, physical and occupational therapy, and sports medicine. A large proportion of patients with injured tendons and ligaments heal very slowly and cannot recover completely. Moreover, the healing time and rate remain unsatisfactory, even with novel and advanced conservative treatment methods and surgical techniques [4,15].

In recent years, researchers have shifted their focus to regenerative medicine to explore new and effective strategies for treating tendon and ligament injuries [16,17]. Conventionally, regenerative medicine involves three main areas: cell therapy, tissue engineering, and biomaterials [18]. In the application of cell therapy for tendon and ligament treatment, the most common approach is to inject mesenchymal stem cells along with a carrier (e.g., a collagen-fibrin gel) into the affected site [1]. The ultimate goal of tissue engineering and biomaterials is to develop engineered tendon- and ligament-like tissues that can serve as grafts to repair injured tendons and ligaments [3,4,14,19]. However, most therapeutic approaches based on cell therapy, tissue engineering, and biomaterials for tendon and ligament healing are still under investigation and have not yet been implemented in clinical practice, or their therapeutic effects have not been demonstrated. Although these therapeutic approaches in regenerative medicine are promising, a significant gap remains between laboratory studies and clinical applications.

Platelet gel is a blood-derived biomaterial that enhances the healing and regeneration of injured tissues [20,21]. This gel-like material, rich in platelets and growth factors, is produced by mixing fluid-like platelet-rich plasma with activators, such as thrombin and calcium chloride, as illustrated in Fig. 1 [20,22]. Platelet-rich plasma, containing a high concentration of platelets used to produce platelet gel, is obtained by centrifuging autologous whole blood from a patient [23,24]. Mixing platelet-rich plasma with activators induces plasma gelatinization and platelet gel formation while activating platelets to release various growth factors [22,25]. Therefore, platelet gel can be regarded as an activated gel form of platelet-rich plasma with higher concentrations of growth factors. The advantages of platelet gel in tissue healing and regeneration are summarized in Table 1. Since its introduction in the early 1990s, platelet gel has been used in various clinical applications such as orthopedic surgery, soft and hard tissue surgery, oral and maxillofacial surgery, plastic surgery, implantology, wound healing, and treatment of ulcers [26,27]. This study aimed to review *in vivo* human studies on the use of platelet gel to treat tendon and ligament injuries, providing clinical practitioners and researchers with an understanding of its effects on healing. Only studies involving human participants were included, as they offer the most clinically relevant insights that can be directly applied to patient care. Animal studies were excluded from this review.

2. Strategy for literature search

Although this article is a narrative review, a systematic search of electronic databases was conducted to identify relevant literature. *In vivo* studies that applied platelet gel to treat tendon and ligament injuries were searched using three electronic databases: PubMed, Scopus, and Web of Science. Keywords used for the search included “platelet gel,” “platelet-rich plasma gel,” “tendon,” and “ligament.” For each database, the search period spanned from the earliest available date to January 31, 2025.

The inclusion criteria were as follows: (1) original articles and case studies that applied platelet gel (i.e., gel form of platelet-rich plasma after activation) to treat tendon and ligament injuries *in vivo* and (2) studies involving human participants. The exclusion criteria were as follows: (1) articles that did not describe original or case studies; (2) studies that were not *in vivo*; (3) treatment approaches using only platelet-rich plasma instead of platelet gel; (4) studies conducted on animal subjects; and (5) articles published in languages other than English.

Eight original articles met the inclusion criteria. No case studies relevant to this topic were found. Below, reviews of the articles are presented in chronological order of publication. The main results and treatment effects in each article were concisely and comprehensively reviewed and are presented in each paragraph of the review. Treatment effects (positive or negative) are summarized at the beginning of each paragraph. For ease of reading, all the paragraphs are written with similar structures. The treatment strategies and effects of each study are summarized in Table 2.

3. Review of the treatment effect of platelet gel

3.1. Anterior cruciate ligament reconstruction

In 2009, Nin et al. [28] found no significant effect of autologous platelet gel in patients who underwent arthroscopic anterior cruciate ligament reconstruction using patellar tendon allografts. In this study, 100 patients who underwent surgery were equally divided into two groups: one receiving plasma gel (mean age = 26.1 years; age range = 14–57 years) and the other without plasma gel (mean age = 26.6 years; age range = 15–59 years). The average platelet concentration in the platelet-rich plasma for platelet gel formation was 837×10^3 platelets/mm^3. In the platelet gel group, a patellar tendon allograft was covered with platelet gel, sutured over itself with the gel in its interior, and the remaining gel was

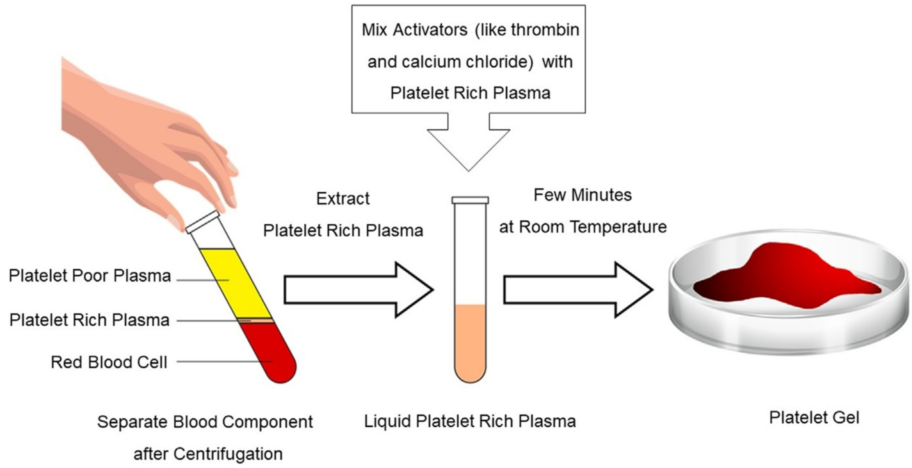

Fig. 1. Illustration of platelet gel, created by combining platelet-rich plasma with activators such as thrombin and calcium chloride.

Table 1
Summary of the advantages of platelet gel in tissue healing and regeneration.

Advantage	Description
Gel-like consistency	Unlike fluid-like platelet-rich plasma, platelet gel is gel-like, allowing it to densely fill defects and remain fixed at the site of injury
High concentration of growth factors	Contains a wide variety and exceptionally high concentration of growth factors essential for tissue healing and regeneration.
Better growth factor retention	Its gelatinous nature enables better retention of growth factors compared to fluid-like platelet-rich plasma.
Natural scaffold for healing	Acts as a natural scaffold, providing an optimal environment for cell and tissue growth, enhancing healing and regeneration.

Table 2
Summary of the number of patients, method of platelet gel application, and treatment effects in each reviewed article.

Study	Patient Number	Method of Platelet Gel Application	Treatment Effect
Nin et al. [28]	100 patients undergoing arthroscopic anterior cruciate ligament reconstruction (50 in platelet gel group, 50 in control group)	Patellar tendon allograft was covered with platelet gel; remaining platelet gel was applied into the tibial tunnel after graft implantation.	No significant effect in clinical and radiographic findings.
Radice et al. [29]	50 patients undergoing anterior cruciate ligament reconstruction (25 in platelet gel group, 25 in control group)	Platelet-rich plasma was mixed with activators and homogeneously sprayed onto the entire graft.	Significant positive effect in radiographic findings.
Vogrin et al. [30]	41 patients undergoing anterior cruciate ligament reconstruction (21 in platelet gel group, 20 in control group)	Platelet-rich plasma was mixed with activators, sprayed onto the graft, and injected into femoral and tibial tunnels.	Significant positive effect in radiographic findings.
Cervellin et al. [31]	40 patients undergoing anterior cruciate ligament reconstruction (20 in platelet gel group, 20 in control group)	Platelet gel was applied to both tendon and bone ends of the donor site and stabilized with a peritenon suture.	Significant positive effect in clinical and radiographic findings.
Azcárate et al. [32]	150 patients undergoing anterior cruciate ligament reconstruction (50 in Group A: platelet gel without leukocytes, 50 in Group B: platelet gel with leukocytes, 50 in control group)	Group A: Activated platelet-rich plasma was injected into the graft before implantation, and biocompatible fibrin was applied into the tibial tunnel at the end of surgery. Group B: Graft was covered with platelet gel, sutured over itself with gel inside, and platelet-poor plasma was activated and applied into the tibial tunnel after graft implantation.	Significant positive effect only in reducing inflammation and swelling shortly after surgery. No significant effect in other clinical and radiographic findings.
Walters et al. [33]	50 patients undergoing anterior cruciate ligament reconstruction (27 in platelet gel group, 23 in control group)	Platelet gel was mixed with autologous cancellous bone chips and placed into the patellar donor site.	No significant effect in clinical and radiographic findings.
Jo et al. [34]	42 patients undergoing arthroscopic rotator cuff repair (19 in platelet gel group, 23 in control group)	Platelet gels were placed at the tendon-bone interface during surgery.	Significant positive effect only in shoulder internal rotation at final follow-up. No significant effect in other clinical and radiographic

Table 2 (*continued*)

Study	Patient Number	Method of Platelet Gel Application	Treatment Effect
			findings. Re-tear rate was lower in the platelet gel group, but not statistically significant despite a higher proportion of severe tears.
Dukan et al. [35]	69 patients undergoing arthroscopic primary rotator cuff repair (32 in platelet gel group, 37 in control group)	Platelet-rich plasma was mixed with activators and injected at the bone–tendon interface near the rotator cuff repair site at the end of surgery.	Significant positive effect only in functional score improvement at 3 months post-surgery. Non-statistically significant trend toward better postoperative outcomes over 24-month follow-up in clinical and radiographic findings.

applied to the tibial tunnel after graft implantation. Follow-up examinations conducted at an average of 24 months showed no significant differences between the two groups regarding inflammatory parameters, pain and functional scores, anterior knee laxity, range of motion, muscle torque, or graft appearance on magnetic resonance imaging and plain radiography.

In 2010, Radice et al. [29] found a positive effect of treatment on radiographic findings in athletes who underwent anterior cruciate ligament reconstruction using autologous platelet gel. Fifty athletes undergoing anterior cruciate ligament reconstruction due to isolated anterior cruciate ligament tears were recruited and equally divided into two groups: one receiving platelet gel (mean age = 30 years; age range = 18–33 years) and the other without platelet gel (mean age = 32 years; age range = 18–35 years). Platelet concentration in the platelet-rich plasma for platelet gel formation was not mentioned. Patellar tendon autografts were used for rugby and soccer players, whereas hamstring autografts were used for skiing, hockey, taekwondo, and volleyball players. In the platelet gel group, activated platelet-rich plasma was homogeneously sprayed onto the entire graft and then gelatinized with the graft after a few minutes. Magnetic resonance imaging revealed that the graft became homogeneously visible at a mean of 177 days in the platelet gel group and 369 days in the control group, implying that platelet gel significantly shortened the healing time of the anterior cruciate ligament graft after reconstruction.

In 2010, Vogrin et al. [30] reported that autologous platelet gel benefited patients who underwent anterior cruciate ligament reconstruction for knee instability caused by anterior cruciate ligament rupture. The study included 21 patients in the platelet gel group (mean age, 37.2 ± 8.4 years) and 20 in the control group (mean age, 32.6 ± 12.3 years). The average platelet concentration used for platelet gel formation was 978×10^6 platelets/L. All the patients received double-looped semitendinosus and gracilis tendon autografts. In the platelet gel group, platelet-rich plasma was mixed with activators, sprayed onto the entire graft, and injected into the femoral and tibial tunnels, where it formed a gel around the graft and within the tunnels under approximately 2 min. Magnetic resonance imaging revealed significantly greater vascularization in the platelet gel group than in the control group at the osteoligamentous interface of the tibial tunnel (the interface zone between the graft and tunnel) at 4–6 weeks postoperatively. However, between 10 and 12 weeks, vascularization in the platelet gel group decreased to a level comparable to that in the control group, while vascularization in the control group remained stable throughout both follow-up periods. No evidence of revascularization was observed in the intra-articular portion of the graft in either group at any time point. The authors concluded that platelet gel could enhance early revascularization and graft healing at the osteoligamentous interface after anterior cruciate ligament reconstruction.

In 2012, Cervellin et al. [31] found that autologous platelet gel enhanced healing after patellar tendon autograft harvesting for anterior cruciate ligament reconstruction based on clinical and radiographic findings. Forty patients undergoing anterior cruciate ligament reconstruction using patellar tendon autograft were recruited and equally divided into platelet gel (mean age = 22.9 ± 4.3 years; age range = 18–29 years) and control (mean age = 22.7 ± 3.5 years; age range = 19–27 years) groups. Platelet concentration in the platelet-rich plasma for platelet gel formation was not mentioned. In the platelet gel group, the gel was applied to both the tendon and bone ends of the donor site at the end of surgery and stabilized using peritenon sutures. Twelve months postoperatively, questionnaire-based evaluations of functionality and pain showed significantly better outcomes in the platelet gel group than in the control group. Magnetic resonance imaging revealed satisfactory healing of bone defects at the donor site in 85 % of patients in the platelet gel group compared with 60 % in the control group.

In 2014, Azcárate et al. [32] found no significant effect on postoperative outcomes from using platelet gel during anterior cruciate ligament reconstruction. A total of 150 patients who underwent arthroscopic anterior cruciate ligament reconstruction using a patellar tendon allograft were recruited and equally divided into three groups. Group A used platelet gel without leukocytes (mean age = 27.4 years; age range = 16–50 years), group B used platelet gel with leukocytes (mean age = 26.1 years; age range = 14–57 years), and the control group did not use platelet gel (mean age = 26.1 years; age range = 15–59 years). The average platelet concentration in the platelet-rich plasma for platelet gel formation was 504×10^6 and 837×10^6 platelets/mL in groups A and B, respectively. In group A, activated platelet-rich plasma was injected into the graft before implantation, and biocompatible fibrin was applied to the tibial tunnel at the end of surgery. In group B, the graft was covered with platelet gel, sutured over itself with the gel in its interior, and supplemented with activated platelet-poor plasma applied to the tibial tunnel after graft implantation. At 24 h postoperatively, group A showed significantly greater improvement in swelling and inflammatory parameters than the other two groups. However, at all follow-up time points, no significant differences were observed among the three groups in other outcomes, including knee range of motion, muscle torque, arthrometer score, functional score, pain score, and graft structural integrity, as assessed using magnetic resonance imaging. Although the only observed benefit of platelet gel (without added leukocytes) was a reduction in inflammation and swelling shortly after surgery with no significant advantages in clinical outcomes or graft structural integrity, it is noteworthy that the addition of leukocytes provided no significant benefit.

In 2018, Walters et al. [33] reported that platelet gel had no significant effect on patients who underwent anterior cruciate ligament reconstruction with a patellar tendon autograft. The study included 50 patients, of whom 27 received platelet gel during surgery and 23 served as controls. Platelet concentrations used for platelet gel formation were not determined. In the platelet gel group, platelet gel was mixed with autologous cancellous bone chips and placed into the patellar donor site. In the control group, the bone chips were placed without platelet gel. Follow-up evaluations at 12 weeks and 6, 12, and 24 months postoperatively showed no significant differences between the two groups in terms of kneeling pain, pain during daily activities, knee function scores, or magnetic resonance imaging findings of bone and tendon healing at the donor site. However, these measures significantly improved over time in both groups.

3.2. Rotator cuff tendon repair

In 2011, Jo et al. [34] found no significant effect of platelet gel in patients who underwent arthroscopic rotator cuff repair for full-thickness rotator cuff tears based on clinical and radiographic findings. The study enrolled 42 patients, with 19 assigned to a platelet gel group (mean age = 61.8 ± 8.86 years) and 23 to a control group (mean age = 59.8 ± 8.84 years). The average platelet concentration in platelet-rich plasma used for platelet gel formation was $900.86 \pm 78.06 \times 10^3$ platelets/mL. During the surgery, several pieces of platelet gel were placed at the tendon-bone interface at the repair site in the platelet gel group. Follow-up evaluations conducted immediately after surgery and at 3, 6, 12, and an average of 19.7 months postoperatively showed no significant differences in range of motion, strength, pain, overall satisfaction, or functional scores between the two groups. Postoperative magnetic resonance imaging also revealed no significant difference in the structural integrity of the repaired tendons between the groups. The only significant finding in the platelet gel group was an improvement in shoulder internal rotation at the final follow-up. Although the re-tear rate was lower in the platelet gel group (26.7 %) than in the control group (41.2 %), the difference was not statistically significant. Notably, a higher proportion of patients in the platelet gel group had more severe tears (57.9 %) than those in the control group (26.1 %).

In 2019, Dukan et al. [35] reported that the use of platelet gel showed a non-statistically significant trend toward better postoperative outcomes over a 24-month follow-up period in patients (mean age = 56 ± 7.8 years) who underwent arthroscopic primary rotator cuff repair using knotless tape bridging. The study included 69 patients, of whom 32 received platelet gel during surgery and 37 served as controls. Platelet concentrations used for platelet gel formation were not determined. In the platelet gel group, platelet-rich plasma was mixed with activators and injected at the bone–tendon interface near the rotator cuff repair site at the end of surgery. Magnetic resonance imaging at 24 months postoperatively showed that tendon healing was achieved in 90 % of patients in the platelet gel group and 86 % in the control group, with three and five re-tear cases, respectively. However, these differences were not statistically significant. Functional assessments indicated that scores for pain, muscle strength, flexion angle, and upper limb disabilities were consistently higher in the platelet gel group at all follow-up time points (3, 6, 12, and 24 months). However, the only statistically significant difference was observed at the three-month follow-up.

4. Discussion

Based on the article search criteria of the present study, only eight articles regarding the application of platelet gel to tendon and ligament healing were found, indicating that the number of studies on this topic is relatively small. This is an unexpected finding, considering the long history of applying platelet gel to various clinical applications since its introduction in the early 1990s and the prevalence of tendon and ligament injuries worldwide.

Given the limited number of studies, it is difficult to draw definitive conclusions regarding the effectiveness of platelet gel in tendon and ligament healing. Of the eight reviewed studies, three found significant positive effects [29,30,34], two reported no significant benefits [28,33], and three showed mixed or marginally positive findings [32,34,35]. Jo et al. [34] observed an improvement in shoulder internal rotation, Azcárate et al. [32] noted reduced inflammation and swelling, and Dukan et al. [35] reported a significant improvement in functional scores at three months. Overall, six studies indicated potential benefits, suggesting that platelet gel may accelerate healing, although further studies are needed to confirm its clinical efficacy.

Platelet gel is theoretically effective in promoting the healing of injured tendons and ligaments because of its high platelet concentration, which releases various growth factors. The lack of significant findings in certain studies does not necessarily imply that platelet gel is ineffective. Variations in study design may play a crucial role in the interpretation of results and obscure the true effects of platelet gel. Several authors of the included studies raised similar concerns [30,31,33–35]. For example, differences in statistical methods, outcome measures, or follow-up time points could hinder the detection of a treatment effect, even if it exists. If platelet gel exerts a short-term effect, it may go unnoticed if follow-up is conducted after a long time postoperatively. Additionally, the lack of standardized preparation and application protocols for platelet gel has been identified as a factor contributing to inconsistent findings across studies [28,31–35]. To properly assess the therapeutic effects of platelet gel, rigorous study design and methodology are necessary. Ultrasound imaging combined with artificial intelligence [36] may provide an objective means of evaluating the treatment effect throughout the follow-up period.

The reviewed articles showed considerable variability in the average platelet concentration in platelet-rich plasma for platelet gel formation, with four studies not reporting this information. Platelet concentration plays a key role in determining the quality and therapeutic potential of platelet gel. For example, Jo et al. [34] suggested that the lack of significant treatment effects in their study might be due to suboptimal platelet concentration ($900.86 \pm 78.06 \times 10^3$ platelets/mL), which was approximately 10 % lower than the clinically meaningful threshold of 1000×10^3 platelets/mL. However, as only four studies reported platelet concentrations, this review could not quantitatively assess whether the efficacy of platelet gel is linked to platelet concentration. Furthermore, none of the studies specified the types and concentrations of growth factors in platelet gels. Ensuring high concentrations of platelets and growth factors is critical for optimal healing. Additionally, accurate application of platelet gel to a target site is crucial [28,32,35]. Patient age also affects treatment response, with younger patients generally showing better results owing to their more robust cellular activity [32]. Furthermore, age and sex influence growth factor concentrations and cytokine content, potentially affecting treatment outcomes [37,38]. Although most of the reviewed studies involved relatively young patients, the small sample sizes prevented a thorough analysis of whether age influenced the observed treatment effects.

Several factors may affect the therapeutic efficacy of platelet gel, including patient-specific variables, such as self-healing capacity and overall health status, as well as injury type and severity. Additionally, methodological factors in platelet gel preparation, such as platelet-rich plasma processing techniques, platelet concentration, activator type and concentration, and gel composition, can affect platelet and growth factor levels as well as activation efficiency [39–42]. Other considerations include the number of treatment sessions [29] and the standardization and reproducibility of the preparation methods. Future studies should systematically investigate these variables to refine the application of platelet gel in tendon and ligament healing. Establishing an optimized and standardized preparation protocol is essential for enhancing clinical efficacy.

In the eight reviewed studies, platelet gel was used in surgical procedures, specifically in anterior cruciate ligament reconstruction and rotator cuff repair. To the best of our knowledge, no studies have explored the non-invasive application of platelet gel via injection, where platelet-rich plasma is mixed with activators and directly injected into the target site for treating common tendon and ligament injuries such as tendinopathy and ligament sprains. Although numerous studies have examined platelet-rich plasma for such conditions [11,43,44], the potential of platelet gel in non-surgical management remains unexplored. Given the high prevalence of these musculoskeletal injuries, future studies should investigate the feasibility and efficacy of non-invasive platelet gel application.

This narrative review had some limitations. First, no quantitative analysis was conducted to compare the results or explore potential explanations for the discrepancies among the reviewed studies because the limited number of articles precluded such an analysis. Second, this review did not address fundamental topics, such as the mechanisms by which platelet gel facilitates tendon and ligament healing, as its primary focus was to summarize current clinical findings on its therapeutic effects. Additionally, although several studies have examined the effects of platelet gel in laboratory-controlled animal models [45–47], these were not included in this review because of physiological and biomechanical differences that may limit the direct applicability of their findings to clinical practice. This study aimed to provide a clearer understanding of the clinical efficacy of platelet gel by exclusively reviewing *in vivo* human studies.

5. Conclusions

This review identified only eight studies on the application of platelet gel for tendon and ligament healing, highlighting the limited research on this topic. Among these studies, three reported significant positive effects, two reported no benefits, and three reported mixed or inconclusive results. Overall, six studies demonstrated some degree of positive clinical or radiographic outcomes, suggesting that platelet gel is a promising treatment for tendon and ligament injuries. Although all reviewed studies applied platelet gel during surgery (anterior cruciate ligament reconstruction or rotator cuff repair), none explored its non-invasive use via injection for conditions such as tendinopathy or ligament sprains. Further clinical studies are required to validate the efficacy of platelet gel use and expand its potential applications.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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