



The Potential of Absorbable Gelatin Sponges as Scaffolds for The Delivery of Platelet-Rich Plasma (PRP) in Peripheral Nerve Regeneration: A Literature Review

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Kata Kunci:	Abstract
Gelatine Sponge; PRP; Nerve Regeneration; Scaffold; Peripheral Nerve Injury	Peripheral nerve injury is a major clinical problem that can cause persistent motor dysfunction, sensory impairment, neuropathic pain, muscle atrophy, and gait abnormalities. Although peripheral nerves possess regenerative capacity, functional recovery is often incomplete because axonal growth is slow and strongly influenced by the microenvironment surrounding the injury. This study aimed to evaluate the potential of absorbable gelatin sponge (AGS) as a scaffold for delivering platelet-rich plasma (PRP) in peripheral nerve regeneration. A literature review was conducted using relevant studies retrieved from PubMed, Google Scholar, and Scopus, focusing on publications from 2016–2026 concerning gelatin-based scaffolds, PRP, peripheral nerve injury, regenerative mechanisms, and functional recovery. The reviewed evidence indicated that AGS possessed favorable porosity, biocompatibility, absorption capacity, and biodegradability, enabling it to retain PRP at the injury site and support the sustained release of neurotrophic growth factors. PRP contributed to Schwann cell activity, angiogenesis, axonal growth, remyelination, and inflammatory regulation. Experimental findings also demonstrated improvements in axon diameter, myelin thickness, nerve morphology, electrophysiological responses, and gait parameters following AGS-mediated PRP application. In conclusion, AGS represents a promising PRP delivery scaffold for peripheral nerve regeneration. However, standardized PRP preparation, scaffold dimensions, dosage, application techniques, and clinical trials are required before routine clinical implementation can be recommended.

INTRODUCTION

Peripheral nerve injury is a complex clinical problem that often leads to permanent motor disability. One of the clinical manifestations that most significantly impairs patient mobility is foot drop, which occurs as a result of injury to the sciatic nerve (nervus ischiadicus). Although peripheral nerves possess intrinsic regenerative capacity, successful functional recovery is highly dependent on the microenvironment at the injury site. Previous research has identified that molecular signaling pathways, such as PI3K, cAMP, and RAS/RAF, play crucial roles in initiating neuronal regeneration (Margiana & Ima, 2019).

The main challenge in peripheral nervous system regeneration therapy is accelerating axonal maturation before irreversible muscle atrophy occurs (Dubin, 2014). PRP has emerged as a promising adjuvant therapy due to its high content of growth factors, including NGF. However, liquid PRP applications have limitations in terms of retention at the injury site.

Therefore, the use of AGS as a carrier scaffold has been proposed to maintain sustained release, which may ultimately stimulate regeneration markers such as GAP-43 (Margiana & Ima, 2019).

Although peripheral nerves possess greater regenerative capacity than the central nervous system, spontaneous recovery is frequently slow and incomplete (Snell & Splittgerber, 2019). Axonal regeneration generally progresses at approximately 1 mm per day, while prolonged denervation progressively reduces Schwann cell responsiveness and promotes irreversible atrophy and fibrosis in target muscles (Kalakoti et al., 2024). This biological mismatch is especially consequential in proximal sciatic nerve injuries, where regenerating axons must travel considerable distances before reaching distal muscles. Failure to restore effective reinnervation may clinically manifest as foot drop, an abnormal gait pattern associated with an inability to dorsiflex the foot (Nori & Das, 2021). Even when microsurgical repair successfully restores anatomical continuity, functional recovery is influenced by injury severity, repair timing, vascularization, neuroinflammation, scar formation, Schwann cell activity, and the biochemical microenvironment surrounding the lesion (Zou et al., 2022). Consequently, surgical reconstruction alone may not provide the trophic and structural support required for optimal nerve regeneration (Zhang et al., 2020).

Direct tension-free neurorrhaphy remains the preferred approach when nerve ends can be approximated, whereas autografts, allografts, and nerve guidance conduits are used to bridge larger defects. However, each approach has important limitations. Autografts require the sacrifice of a functional donor nerve and may cause donor-site morbidity, while allografts involve processing requirements and additional costs. Synthetic conduits avoid donor nerve harvesting but may provide inadequate biological support, particularly in long or complex nerve gaps. A meta-analysis of 35 studies involving 1,559 nerve repairs found that meaningful sensory recovery in short gaps reached 81.6% with autografts and 87.1% with allografts, compared with 62.2% with conduits (Lans et al., 2023). Current conduits have consequently demonstrated their clearest clinical utility in short-to-moderate nerve defects, while regeneration across longer gaps remains a technological challenge (Riva et al., 2024). These limitations have encouraged the development of bioactive scaffolds that combine physical guidance with controlled local delivery of regenerative molecules (Ima & Margiana, 2025a).

Platelet-rich plasma (PRP) is a promising biological adjunct because it is obtained from autologous blood and contains concentrated platelets that release multiple bioactive mediators following activation. These mediators include platelet-derived growth factor, vascular endothelial growth factor, transforming growth factor- β , insulin-like growth factor-1, fibroblast growth factor, and nerve growth factor. Collectively, these factors can support angiogenesis, Schwann cell proliferation and migration, extracellular matrix remodeling, axonal growth, and remyelination. PRP may also influence macrophage recruitment and polarization during Wallerian degeneration, thereby helping transform the lesion environment from an inflammatory state into a reparative state. Wang et al. (2022) concluded that PRP has considerable potential to improve peripheral nerve regeneration through its effects on Schwann cells, neurotrophic signaling, and revascularization but emphasized that the number of clinical studies remains limited (Wang et al., 2022). Its autologous origin and relatively accessible preparation further make PRP an attractive candidate for translation into nerve repair procedures.

Despite these advantages, liquid PRP presents an important delivery challenge because it may diffuse away from the repair site, undergo rapid clearance, or release growth factors over a period insufficient for the prolonged process of axonal regeneration. Local injection may also produce uneven concentrations around the epineurium and does not provide mechanical separation between the repaired nerve and surrounding scar-forming tissues. Therefore, the therapeutic effectiveness of PRP depends not only on its platelet and growth-factor composition but also on the delivery system used to retain it at the injury site. An ideal carrier should be biocompatible, biodegradable, porous, surgically manageable, capable of absorbing PRP, and sufficiently stable to support gradual release without compressing the nerve or disrupting microcirculation. This requirement provides the rationale for examining absorbable gelatin sponge (AGS), a collagen-derived porous hemostatic biomaterial that can serve simultaneously as a temporary scaffold and a local reservoir for regenerative agents.

Previous experimental research provides preliminary support for combining PRP with AGS. Küçük et al. applied PRP using a $0.5 \times 0.5 \times 0.1$ cm absorbable gelatin sponge to repaired sciatic nerves in rats. At 12 weeks, the PRP group demonstrated a higher climbing angle than the control group (63.60° versus 38.33°), higher gastrocnemius compound muscle action potential amplitude (14.01 versus 5.78 mV), and a substantially greater mean axon count (1,969.50 versus 879.00; $p = 0.001$) (Küçük et al., 2014). Kokkalas et al. subsequently used AGS to deliver PRP to transected and sutured sciatic nerves in 42 rats and found a significantly higher distal axon count in the PRP group than in the control group ($p = 0.005$), while the distal-to-proximal axon ratio also improved significantly ($p = 0.009$) (Kokkalas et al., 2020). These findings indicate that AGS-supported PRP delivery may improve both histological regeneration and functional recovery.

More recent research has expanded the evidence by examining PRP administration routes and wrapping techniques. Maulina et al. reported that a gelatin sponge moistened with 0.2 mL of PRP improved fiber diameter, axon diameter, axon count, and myelin sheath thickness following sciatic nerve axonotmesis. The combined local and systemic PRP group achieved a mean fiber diameter of 4.20 ± 0.22 μm , compared with 2.22 ± 0.15 μm in the saline group, while the corresponding axon counts were 71.53 ± 4.16 and 47.07 ± 5.89 fibers/ mm^2 , respectively (Maulina et al., 2024). Mukai et al. further demonstrated that PRP-gel wrapping increased myelinated axon density, approximately doubled the pain withdrawal threshold relative to untreated animals, and reduced sciatic nerve expression of tumor necrosis factor- α and interleukin-6 by approximately half on postoperative days 7 and 14 (Mukai et al., 2025). Together, these studies suggest that maintaining PRP around the injured nerve may support structural repair while also moderating neuroinflammation and neuropathic pain.

Nevertheless, a clear research gap remains. Existing studies vary substantially in injury models, PRP preparation protocols, platelet concentrations, activation methods, delivered volumes, scaffold dimensions, administration routes, treatment timing, and follow-up periods. Several studies treat gelatin sponge merely as an application medium and do not separately evaluate how its porosity, biodegradation, fluid absorption, and mechanical properties affect PRP retention and growth-factor release. Evidence also remains predominantly preclinical, and the relationship between molecular markers, such as nerve growth factor and growth-associated protein 43, and meaningful functional indicators, including axon diameter, compound muscle action potential, sciatic functional index, and toe-out angle, has not been consistently

synthesized. Moreover, questions concerning circumferential versus unilateral application, the risk of compression of the vasa nervorum, degradation kinetics, sterile preparation, and optimal PRP dosage remain unresolved. These inconsistencies currently prevent the formulation of standardized protocols and limit clinical translation.

A focused review is therefore warranted because successful nerve regeneration requires the simultaneous provision of biological signals, spatial guidance, vascular support, and protection from excessive inflammation and fibrosis. The novelty of the present research lies in positioning AGS not simply as a passive hemostatic material but as a bioactive delivery platform whose physical characteristics may determine the localization, duration, and effectiveness of PRP-mediated regenerative signaling. The review integrates three dimensions that have often been considered separately: the molecular effects of PRP on Schwann cells and axonal growth; the structural and biodegradation properties of gelatin-based scaffolds; and the histological, electrophysiological, and locomotor outcomes used to evaluate peripheral nerve recovery. It also critically considers circumferential wrapping as a potential strategy for achieving more uniform growth-factor exposure while recognizing the need to control scaffold thickness and mechanical pressure.

Accordingly, this research aims to critically examine the potential of absorbable gelatin sponges as scaffolds for PRP delivery in peripheral nerve regeneration. Its specific objectives are to describe the biological mechanisms through which PRP supports nerve repair; evaluate the biocompatibility, porosity, absorption capacity, degradation characteristics, and mechanical limitations of AGS; synthesize previous evidence concerning axonal regeneration, remyelination, nerve conduction, pain reduction, and motor recovery; compare AGS with alternative scaffold materials; and identify methodological and translational challenges that should guide future research. Academically, this review contributes an integrated framework connecting scaffold design, growth-factor delivery, molecular responses, and functional recovery. Clinically, it may support the development of more effective and standardized adjunctive strategies for peripheral nerve repair. Its broader benefit is to provide researchers and clinicians with an evidence-based foundation for designing preclinical experiments and eventual human trials of localized AGS–PRP therapy.

METHOD

This literature review was conducted by analyzing previous research studies retrieved from PubMed, Google Scholar, and Scopus databases. The literature search used keywords including “gelatin sponge,” “PRP,” “nerve regeneration,” “peripheral nerve injury,” and “gait analysis.” Articles published between 2016 and 2026 were selected to ensure the relevance and currency of the reviewed evidence. This review focused on the growth-factor release mechanism from the gelatin matrix, the biocompatibility of AGS in peripheral nerve applications, and the synthesis of functional recovery outcomes reported in previous studies, including toe-out angle (TOA) parameters and axon diameter measurements.

RESULTS AND DISCUSSION

Biomaterial Characteristics: Advantages of Gelatin Sponge

AGS is a natural polymer derived from collagen hydrolysis. In nerve regeneration, the selection of biomaterials greatly determines the success of Schwann cell migration. The pore

structure of AGS (50–200 μm) is ideal for cellular infiltration. (Joko Sriwidodo & M.S. Tumanggor, 2024), gelatin-based biomaterials are able to maintain their structural integrity during the critical phase of regeneration (the first 7–14 days) before being fully absorbed by the body through enzymatic processes. (Wang et al., 2023) This is crucial so that the release of growth factors occurs gradually, providing a consistent stimulus to the regenerating axons.

Comparison of Absorbable Gelatine Sponge (AGS) with Other Scaffolds

To understand the effectiveness of AGS, here is a comparison table with other frequently used scaffolding materials:

Table 1. Comparison of Scaffold Biomaterial Characteristics

Type of scaffold	Advantages	Disadvantages	Clinical Relevance	References
 Fibrin Glue	Strong adhesion, low cost	Degradation too quickly (< 7 days)	Less stable to withstand long-term PRP	Sánchez et al. (2018)
 Scaffold Sintetik polycaprolactone (PCL) / polylactic co-glycolic acid (PLGA)	High mechanical strength	The result of degradation is acidic, triggering inflammation	May inhibit the growth of axon diameter	(Bhang et al., 2017)
 Collagen Conduit	Highly biocompatible	High price, high density inhibits nutrients	Difficult to modify for local wrapping	(Pan, 2019)
 Absorbable Gelatine Sponge	High porosity, optimal absorption, biocompatible	Medium mechanical strength	Ideal for PRP carriers and enveloping clamp areas	(Everts, 2020); Bhang et al. (2017)

Based on a comparative review of various biomaterials scaffold in Table 1, Absorbable Gelatine Sponge (AGS) exhibits significant advantages in terms of porosity and biocompatibility over synthetic scaffold PCL & PLGA, collagen conduit, and fibrin glue (Sánchez, 2018)."

AGS-PRP molecular synergy

In previous studies, AGS has been used by local application of 0.2 ml PRP, with a precision dimension of 0.5 x 0.5 x 0.1 cm into the injured nervus ischiadicus to ensure that growth factors remain concentrated in the epineural area. This dimension provides one-sided coverage of the injury area without causing compressive ischemia (Kokkalas et al., 2020). The released NGF will slowly bind to receptors at the axon ends, activating a signaling pathway that stimulates the transcription of the GAP-43 protein (Eckles et al., 2014). This regenerative effect is not only local, but also prevents broader systemic impacts, given that peripheral nerve injury can induce a response up to the adult brain (Ima & Margiana, 2025b).

Macroscopic Response and Functional Recovery

Macroscopically, nerve clamp trauma using hemostatic forceps causes the condition of axonotmesis which can be seen in figure 1B below. A comparison of nerve diameter recovery in the control group (sham surgery), sciatica without PRP, and sciatica with PRP can be visually seen in figure 1 below (Riva & al., 2024).

Figure 1. Experimental Procedures and Macroscopic Comparison of Sciatic Nerve Regeneration Following Platelet-Rich Plasma Treatment

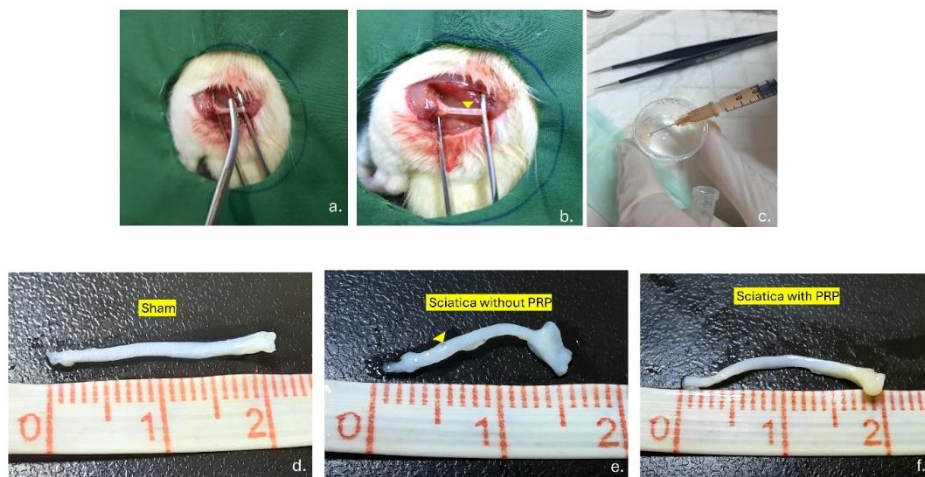


Figure 1. Documentation of procedures and macroscopic observations of the nervus ischiadicus in previous studies. (A) Induction of nerve injury using clamping of hemostatic forceps for 3 minutes; (B) Visualization of the clamping results that cause the condition of axonotmesis but still leave the epineural structure intact (yellow arrow); (C) Preparation of Absorbable Gelatine Sponge (AGS) media with 0.2 ml PRP before local application. On day 42; (D) The Sham Surgery Group showed normal neurological morphology; (E) The Sciatica group without PRP showed areas of atrophy and scarring (yellow arrow); (F) The Sciatica group with PRP showed a restoration of nerve diameter that resembled control, signaling an effective axonal regeneration process.

The success of this structural regeneration is validated by the improvement of gait. The use of the TOA parameter provides objective data on motor control ability. The improvement in TOA values on day 42 showed that the acceleration of axonal regeneration by PRP-AGS had reached the target organ functionally to correct the condition of the drop foot (Ima & Margiana, 2022; Margiana, 2021).

Future Outlook and Clinical Challenges

Although the combination of AGS and PRP shows very promising results in experimental animal models, the transition to clinical application in humans still faces some challenges. One of the future research focuses is the standardization of personalized PRP doses based on the severity of a patient's nerve injury. In addition, the development of gelatin scaffolds combined with 3D printing techniques (3D Bioprinting) with full wrapping techniques (enveloping nerves 360 degrees) has the potential to create more precise scaffolding according to the diameter of individual nerves. The use of AGS as a delivery system also opens up opportunities for fusion with stem cells to provide a more synergistic regenerative effect in cases of severe chronic nerve injury (Song et al., 2025).

CONCLUSION

The integration of AGS as a carrier scaffold for PRP represents a potential strategy for improving clinical outcomes in cases of peripheral nerve injury. Current findings emphasize that regenerative effectiveness is largely determined by the application method of biomaterials. The use of AGS with a full wrapping technique (enveloping the nerve circumferentially by 360 degrees) is predicted to provide superior structural and biochemical protection compared with unilateral applications. This system not only functions as a reservoir for NGF but also serves as a physical scaffold that separates nerves from surrounding connective tissue, thereby reducing scar tissue formation and maintaining neurotrophic factor concentrations across the epineurial surface.

However, the implementation of this 360-degree technique presents technical challenges that require rigorous surgical procedures. First, mechanical stability must be considered because the fragile nature of hydrated AGS requires precise microhandling to prevent damage to the pore structure during scaffold formation. Second, fixation methods require attention; the use of fibrin glue as a biological adhesive may help secure the sponge ends while avoiding excessive microsuturing that could damage the internal scaffold structure or compress the nerve. Third, space management is essential because the thickness of AGS must be precisely calibrated to prevent secondary stress on nerve microcirculation, including the vasa nervorum, due to the space-occupying effect within narrow anatomical regions.

By addressing these challenges, optimization of AGS into circumferential conduit structures has the potential to accelerate improvements in axon diameter and distal motor recovery. Therefore, these considerations may serve as a direction for developing future standardized approaches that move beyond partial or unilateral applications.

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