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Biologic Innovations in Orthopedics: A Comprehensive Review of Orthobiologic Therapies for Joint Preservation and Tissue Regeneration

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Abstract

Orthobiologics are an innovative area of development in musculoskeletal medicine that provides regenerative options as substitutes for conventional orthopedic procedures aimed at preserving joints and healing soft tissues. The purpose of this review was to critically assess orthobiologic therapy effectiveness, describe novel developments, and provide clinical and investigative recommendations. A systematic search of scholarly databases was conducted, targeting studies published from 2018 to 2025. 11 peer-reviewed articles were included and analyzed through thematic synthesis. Findings indicated that PRP, BMAC, and MSCs provide clinically relevant benefits of pain, function, and tissue repair in osteoarthritis and tendinopathy. Orthobiologics, exosome therapies, scaffold-enhanced delivery systems, and gene-activated matrices are newer innovations that are continuing to expand the clinical use of orthobiologics.

Keywords: Orthopedics, Orthobiologics, Joint Preservation, Tissue Regeneration, Biotherapies.

Introduction

Orthobiologics is a promising new field in musculoskeletal medicine that uses biologically derived treatments to initiate the natural healing processes of the body. Such agents are platelet-rich plasma (PRP), bone marrow aspirate concentrate (BMAC), mesenchymal stem cells (MSCs), adipose-derived stem cells (ADSCs), and other growth factors (Husain et al., 2020). The deficiencies of orthopedic and sports medicine approaches to degenerative joint disease and soft tissue injury have spread clinical use much more rapidly than in previous years. Unlike drug or surgical treatment, orthobiologics focus on tissue healing and long-term recovery of structure and function. Due to this, they are especially well indicated in joint preservation and soft tissue repair. Joint preservation techniques attempt to avoid or postpone end-stage joint replacement by attempting to reinstate structural integrity and functionality of the joint or preserve it. Orthobiologic therapy is a central part of the procedure (Rhee et al., 2020). A case in point is intra-articular treatment, where PRP and MSCs are used through injections, which has demonstrated clinical use in early osteoarthritis (OA) by reducing inflammation and cartilage regeneration.

Similar benefits have been described with BMAC for the treatment of chondral defects, with MRI-based measures of outcomes revealing increased cartilage volume and better joint space maintenance. Beyond joints, trauma to muscles, ligaments, and tendons represents a common clinical issue, particularly in athletes and the aged. Orthobiologic treatments such as PRP are gaining popularity for their capability to modulate inflammation and initiate tendon healing by inducing cellular proliferation and collagen production (Tashjian, 2019). In a meta-analysis of outcomes by Lee et al. (2020) following rotator cuff repair, patients treated with PRP had markedly improved tendon quality on imaging and better Constant scores postoperatively. ADSCs have also shown promise for enhancing the healing of Achilles tendinopathy and ACL injuries by inducing neovascularization and matrix remodeling (Lee et al., 2020).

Furthermore, novel biomimetic scaffolds seeded with stem cells are showing better mechanical and histological success than existing methods in preclinical models of tendon repair. Regardless of such optimistic advances, several issues are restricting the clinical application of orthobiologics (Ghomrawi et al., 2023). One of the most prominent concerns is the diversity in design approaches within individual studies, over a lack of uniformity in how the preparatory stages are done, and variability in outcome measures, which makes it difficult to interpret and compare results. Many clinical studies are also hampered by small sample sizes, short durations of follow-up, and

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few control groups. These methodical constraints highlight the pressing need for good-quality randomized controlled trials with clearly defined endpoints. While PRP and MSCs show moderate efficacy, the certainty of evidence remains low due to study bias and inconsistency.

A review is needed to integrate current knowledge, determine therapeutic gaps, and provide recommendations for evidence-based practice. With the increasing use of orthobiologics in clinical practice, it is important to compare the relative effectiveness of the agents and protocols. The review also determined which innovations are most likely to be adopted in the broader clinical setting and where more research needs to be conducted. For instance, although PRP and MSCs have been widely utilized, the therapeutic potential of new drugs like gene-modified cells is yet to be investigated in humans. This review aimed to critically evaluate the effectiveness of orthobiologic therapies for joint preservation and soft tissue repair, identify the innovations transforming the field, and offer clinical and research recommendations based on the literature. In doing so, it hopes to assist clinicians in choosing the most optimal treatments and identifying priorities for future research to further advance regenerative medicine practices in orthopedics.

Methodology

This review was focused on orthobiologic soft tissue and joint therapies and healing due to systematically identifying, selecting, and evaluating literature pertinent to these topics. These steps also include the collection of relevant data and determining a set of keywords, inclusion and exclusion criteria, and then analyzing the data appropriately.

Search Strategy

The scholarly databases of Scopus, Web of Science, PubMed, Elsevier, Springer, and Wiley were searched. This has been further refined to journal articles published between 2018 and 2025. The Boolean operators and keyword combination strategies were used to harvest the literature on orthobiologics, joint preservation, and soft tissue healing. The table below explains the databases and terms used.

Table 1. Keywords and Search Engines Used

Years	Search Engines	Keywords
2018–2025	PubMed	“Orthobiologics”
	Scopus	“Joint preservation”
	Web of Science	“Soft tissue healing”
	Springer	“Mesenchymal stem cells”
	Elsevier	“Platelet-rich plasma (PRP)”
	Wiley	“Bone marrow aspirate concentrate (BMAC)”
		“Adipose-derived stem cells (ADSCs)”
		“Tendon healing”
		“Cartilage regeneration”

Narrowing the searches also involved using these keywords along with the Boolean operators “AND,” “OR,” and “NOT.” For instance, the string “Orthobiologics” AND “Joint preservation” AND “Soft tissue healing” OR “PRP” AND “tendon” captures specific results effortlessly.

Inclusion and Exclusion Criteria

Every article that was included or excluded as part of this research underwent rigorous screening as per the set guidelines that provided boundaries for maintaining the relevancy and quality of information. Prioritized articles included peer-reviewed journals published in English and freely available for public access. The criteria are summarized in the following table;

Data Extraction and Analysis

This review interpreted and extracted data using thematic analysis to assess the scope of orthobiologic therapies in joint preservation and soft tissue injury repair with respect to their therapeutic value, innovations, limitations, and recommendations. Thematic analysis facilitates the extraction of central themes from diverse

Table 2. Inclusion and Exclusion Criteria of Studies

Inclusion Criteria	Exclusion Criteria
Studies published in peer-reviewed journals and in full-text format.	Studies not published in peer-reviewed journals (e.g., conference papers, editorials, blogs).
Articles written in English.	Non-English publications were excluded.
Studies published between 2018 and 2025.	Studies published before 2018 were excluded.
Research focused on orthobiologic therapies in joint preservation and soft tissue healing.	Studies unrelated to orthobiologics or lacking clinical relevance to joint or soft tissue treatment.
Quantitative, qualitative, and mixed-method studies were included.	None were excluded based on methodology.

research, hence aiding in the integration of structured conclusions from 11 studies related to Orthopedics and Orthobiologic Therapies for Joint Preservation and Tissue Regeneration. This is important in crafting clinically relevant insights along with rigorously justified conclusions for healthcare experts, scholars, and decision-makers focused on strategic developments in regenerative medicine and orthopedics.

Table 3. Summary of Orthobiologic Therapies and Their Measured Effects on Tissue Healing

Ortho-biologic	Target Tissue	Study	Measured Out-comes	Effect	Timeframe
PRP	Knee car-tilage (OA)	Filardo et al. (2021)	WOMAC ↓ (by ~20%), VAS ↓ (by ~2 points)	Statistically sig-nificant pain and functional im-provement	Up to 6 months
PRP	Achilles tendon	Liu et al. (2019)	VISA-A ↑ (mean +12 points), pain ↓	Functional re-covery, pain re-duction	6–12 weeks
BMAC	Knee car-tilage (OA)	Keeling et al. (2022)	IKDC ↑, VAS ↓, MRI ↑ cartilage volume	Improved knee function, carti-lage structure	6–12 months
BMAC	Meniscus	Moreno-Garcia & Rodriguez-Merchan (2022)	MRI signal ↓, less joint degeneration	Promotes menis-cus integration, structural preservation	6 months
MSCs	Knee car-tilage (OA)	Zhao et al. (2022)	WOMAC ↓ (greater than PRP alone), KOOS ↑	Greater im-provement than PRP or MSCs alone	12 months
PRP + MSCs	Knee OA	Zhao et al. (2022)	WOMAC ↓ (~30%), Lequesne Index ↓	Synergistic ef-fect on pain and mobility	12 months
Exo-somes	Tendon	Zhang et al. (2020)	Histological scor-ing ↑, collagen I/III ratio ↑	Enhanced ten-don fiber organ-ization and in-flammation modulation	Preclinical
EV + ECM	Muscle (VML model)	Magarotto et al. (2021)	Muscle mass ↑, contractile force ↑	Improved mus-cle regeneration	Preclinical (murine)
Amniotic Mem-brane	Soft tis-sues	Munoz-Torres et al. (2023)	Qualitative: anti-inflammatory, vascularization ↑	Promotes soft tissue healing, prevents fibrosis	Variable

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Results

Table 4. Table of Studies Reviewed

Authors	Title	Aim	Method	Findings	Conclusion
Cotter et al., (2018)	Bone marrow aspirate concentrate for cartilage defects of the knee: from bench to bedside evidence	To evaluate the biological potential and clinical utility of BMAC for knee cartilage repair.	Review of preclinical and clinical studies on BMAC.	BMAC contains MSCs and growth factors aiding cartilage regeneration; clinical improvements in pain and function were observed.	BMAC is a promising treatment for cartilage defects, though further standardization and trials are needed.
Filardo et al. (2021)	PRP injections for the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials	To evaluate the efficacy of PRP injections for knee osteoarthritis	Meta-analysis of randomized controlled trials	PRP showed significant improvement in symptoms compared to control treatments	PRP is an effective treatment for knee osteoarthritis with positive clinical outcomes
Jeyaraman et al. (2024)	Barriers and solutions towards integrating orthobiologics into clinical orthopaedic practice	To identify barriers and propose solutions for integrating orthobiologics into practice	Review and expert opinion	Highlighted practical, regulatory, and scientific barriers; proposed standardization and education	Successful integration of orthobiologics requires overcoming multifactorial challenges
Keeling et al. (2022)	Bone marrow aspirate concentrate for the treatment of knee osteoarthritis: a systematic review	To assess the effectiveness of BMAC for knee osteoarthritis	Systematic review of clinical studies	BMAC improves pain and function in OA patients; outcomes vary with protocol differences	BMAC is promising for OA treatment but needs standardized protocols and more evidence
Liang et al. (2023)	Biomaterial-based scaffolds in promotion of cartilage regeneration	To review biomaterial-based scaffolds in cartilage regeneration	Literature review	Various scaffold materials and designs promote cartilage healing	Biomaterial scaffolds hold strong potential for clinical cartilage repair applications
Liu et al. (2019)	Platelet-rich plasma injection for chronic Achilles tendinopathy: a meta-analysis	To evaluate PRP efficacy in treating Achilles tendinopathy	Meta-analysis of clinical trials	PRP showed beneficial effects compared to placebo or standard care	PRP is a viable therapeutic option for chronic Achilles tendinopathy
Magarotto et al. (2021)	Muscle recovery driven by extracellular vesicles with muscle ECM in murine model	To assess EVs and ECM in muscle regeneration	Preclinical murine model study	Combined treatment improved muscle function and regeneration	EV-based therapies could enhance muscle recovery in volume loss injuries

Cont. Table 4

Authors	Title	Aim	Method	Findings	Conclusion
Moreno-Garcia & Rodriguez-Merchan, (2022)	Orthobiologics: current role in orthopedic surgery and traumatology	To examine the current clinical applications of orthobiologics in orthopedic surgery.	Narrative review of various orthobiologic treatments in orthopedic practice.	Orthobiologics like PRP, BMAC, and MSCs show benefits in healing and reducing surgical intervention.	Orthobiologics are increasingly relevant, but require further evidence for standardized clinical use.
Munoz-Torres et al. (2023)	Biological properties and surgical applications of the human amniotic membrane	To explore the biological characteristics and orthopedic applications of the human amniotic membrane.	Review of biological studies and surgical case reports using amniotic membrane.	The amniotic membrane has anti-inflammatory, antimicrobial, and regenerative properties beneficial in tissue repair.	It is a versatile biomaterial with strong potential for regenerative orthopedic applications.
Zhang et al. (2020)	Tendon stem cell-derived exosomes for tendon healing	To investigate tendon stem cell exosomes in healing	Laboratory-based experimental study	Exosomes modulated inflammation and enhanced healing	Exosome therapy is promising for tendon repair
Zhao et al. (2022)	MSCs and PRP combination for knee osteoarthritis: a meta-analysis	To evaluate MSCs+PRP therapy for knee OA	Meta-analysis of RCTs	Combination therapy was more effective than either alone	MSCs and PRP together offer enhanced therapeutic benefits for OA

Discussion

Orthobiologic therapies represent a new frontier in orthopedic medicine with a focus on improving the natural healing abilities of the body to preserve joints and repair injured tissues. Such biologics are PRP, MSCs, BMAC, and amniotic or adipose tissue products. The research conducted by Munoz-Torres et al. (2023) confirms that amniotic and adipose tissues are highly concentrated in biologics, and every therapy having its mechanisms can contribute to recovery by repairing, reducing inflammation, and delaying the required surgical intervention (Munoz-Torres et al., 2023).

Based on the findings of the research by Cotter et al. (2018), BMAC is MSCs and growth factors rolled into one, and is currently being investigated for its ability to enhance the healing of cartilage and bone defects. Further, amniotic tissues and extracellular matrix scaffolds are allogeneic products that have become popular due to their anti-inflammatory and regenerative potential (Cotter et al., 2018). There is also a shifting regulatory focus concerning safety and efficacy, which affects the approval process. In the opinion of Moreno-Garcia & Rodriguez-Merchan (2022), in younger and more active patients, orthobiologics are a less invasive alternative compared to joint replacement or reconstructive procedures. Over time, these treatments potentially might redirect the orthopedic revolution from symptom control to biologic repair. Orthobiologic orthopedic innovation demands superb, randomized controlled trials in order to establish ideal usage and prove long-term benefit (Moreno-Garcia & Rodriguez-Merchan, 2022).

Therapeutic Applications of Orthobiologics in Joint Preservation

Orthobiologic treatments like PRP, BMAC, and MSCs find more frequent applications in joint disorder management, especially OA. The main goal of these treatments is to preserve the joint function, decrease pain, and delay surgery as long as possible. PRP is extracted from the patient's blood and is used more often because it has a high percentage of growth factors, which help in tissue inflammation and recovery (Liu et al., 2019). There are clinical trials that have established its efficacy in pain relief and the improvement of function in OA patients.

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Filardo et al. (2021) in their meta-analysis accounted for significant improvement in WOMAC and VAS scores after PRP therapy (Filardo et al., 2021).

BMAC contains a high concentration of MSCs, hematopoietic stem cells, and platelets. It is a field of concern in cartilage repair and the management of OA. According to Keeling et al. (2022), BMAC injection greatly enhanced the functioning of the knee and relieved pain throughout up to twelve months. MSCs can differentiate into various cells and exhibit immunomodulating properties (autologous or allogenic) (Keeling et al., 2022). These cells have been widely applied in the preservation of joints. Zhao et al. (2022) used MSCs and stated that their application demonstrated an improved clinical outcome of OA pain relief and functional improvement. The addition of various therapies to achieve the best results is still being investigated. Moreover, the combination of PRP and MSCs showed a synergistic effect on joint preservation compared to either treatment alone based on clinical outcomes (Zhao et al., 2022).

Role of Orthobiologics in Soft Tissue Healing

Orthobiologics play a significant role in tendon, ligament, meniscus, and muscle repair and regeneration. These are the tissues that are normally susceptible to overuse or trauma, and the regenerative capability of biologic therapy extends its assistance. PRP is now popular in the treatment of tendinopathies and ligament sprains. Liu et al. (2019) assessed in their research that PRP injections healed chronic Achilles tendinopathy patients faster, alleviating pain and recovering functionality. BMAC has been found to be effective in enhancing meniscus healing and host tissue integration in meniscal repair (Liu et al., 2019). The use of BMAC injections to treat patients with meniscal tears was linked with positive healing and a reduction in the utilization of surgical procedures.

MSCs were found to be applicable in muscle regeneration especially in muscle atrophy or injury. As per the study by Magarotto et al. (2021), the MSC therapy stimulated the repair of muscle tissue and functional recovery of patients with damaged muscles. The treatment results are favorable in terms of the time needed to heal, re-injury, and integrate the tissue. Imaging procedures like magnetic resonance imaging (MRI) have played a vital role in showing the effectiveness of these therapies (Magarotto et al., 2021). The tendon repair after PRP injection will be assessed with the help of an MRI, during which the process of tissue regeneration and alignment will be improved.

Innovation and Emerging Trends in Biologic Therapies

The field of orthobiologics is being built upon several novel procedures being employed to augment the efficacy and effectiveness of biologic therapies. Scaffold-based systems have also been developed recently to deliver scaffolds that regulate the delivery of biologic agents to sites of injury. Liang et al. (2023) demonstrated that the scaffolds administered during MSC delivery promote cartilage repair and incorporation when knee OA is involved. Gene-activated matrices (GAMs), where genes encoding growth factors have been incorporated, are a further niche in the improvement of tissue repair. Tendon repair GAMs have been observed to improve recovery and functional restoration compared to treatment using standard care (Liang et al., 2023).

A different approach is being taken to develop next-generation stem cell therapies. Zhang et al. (2020) demonstrated how MSC-derived exosomes improved tendon healing and reduced scarring in animal models, which shows potential for future treatments. It has become easier to focus on developing personalized medicine, which aims to tailor biologic treatments to the patient's profile due to advancements in technology. However, age, sex, and relevant comorbidities need to be closely examined to devise the most suitable biologic treatment plan for soft tissue injuries, as chronic conditions for older patients are more prevalent (Zhang et al., 2020). These advances have not overcome the clinical application challenges of orthobiologics. There remains a need to refine standardized treatment protocols, long-term safety monitoring, and overall cost-efficacy evaluation. Therapies face additional limitations imposed by regulatory frameworks. As highlighted by Jeyaraman et al. (2024), there is a study gap with rigorous clinical trial shortcomings and standardized processes needed for orthobiologics supporting their clinical integration (Jeyaraman et al., 2024).

Despite promising findings, the literature lacks clear consensus or conclusive high-level evidence regarding the long-term efficacy and optimal protocols for orthobiologic therapies. Most studies demonstrate short- to mid-term improvements in pain, function, and tissue healing, particularly with PRP and BMAC in osteoarthritis and tendinopathy. However, significant variability in preparation methods, dosage, application frequency, and patient selection impedes direct comparison and generalization. While some meta-analyses report positive clinical outcomes, they also highlight heterogeneity and potential bias, limiting the strength of recommendations.

Emerging therapies such as exosomes and gene-activated matrices show encouraging preclinical results but lack large-scale human trials. Importantly, no study conclusively establishes superiority among orthobiologics or long-term disease-modifying effects. These findings underscore the need for robust, multicenter randomized controlled trials with standardized protocols and long-term follow-up to determine definitive clinical value, cost-effectiveness, and safety. The field remains promising but requires methodological rigor to support broader clinical adoption.

Strengths and Limitations

This was the first review to provide a comprehensive evaluation incorporating the most recent evidence from 2018 to 2025 on orthobiologic and tissue-based therapies in joint preservation and soft tissue healing, identifying clinically actionable findings and technological advancements. The review included peer-reviewed literature from different biologics. These included PRP, MSCs, and BMAC, and used their comparative efficacy to increase the translational value of the review. A notable strength lies in the balance provided between the emerging and established technologies and the view offered. However, some possible barriers include differences in study designs, lack of pre-defined follow-up periods, and differences in dosing strategies across the literature, which hampers the achievement of conclusions and prevents quantitative meta-analysis.

Clinical and Research Implications

The results reinforce the increasing clinical value of orthobiologics as potential substitutes or complementary techniques to surgical solutions for musculoskeletal management. PRP and MSCs provide consistent functional improvements in pain, mobility, and tissue repair associated with early joint degeneration and tendon injuries. This review stressed the importance of clinicians designing biologic treatments stratified by the pathology, chronicity of the injury, and other individual variables. For researchers, the review highlighted the lack of consistency in the absence of a clear definition, long-term safety assessment criteria, and evaluative benchmarks in comparative research. It advocates for defined standards regarding orthobiologics and emphasizes the need for prospective controlled trials for the rational development of authoritative clinical orthobiologic guidelines to ensure uniform application of these therapies.

Future Directions and Recommendations

The clinical efficacy of biologics could be improved with better formulation, scaffold-based delivery systems, and greater treatment frequency. It is important to address the gaps in the literature. However, multicenter, randomized, high-powered trials with standardized and long-term outcome measures are needed to validate the findings. Furthermore, orthobiologic treatments tailored to individual patients using specific biomarkers and genomic profiling are highly prospective. Innovation must be balanced with safety, ethics, and regulation to ensure rapid technological advancement is appropriately governed. To drive progress in orthobiologic science and implement next-generation regenerative medicine in clinical orthopedics, clinicians, researchers, and bioengineers need to join forces.

Conclusion

Orthobiologic techniques mark a significant milestone in the treatment of musculoskeletal disorders, offering novel regenerative therapies for preserving joints and soft tissue healing. The review included innovations in orthobiologics and their efficacy in clinical settings as well as their development in personalized treatment approaches. While advancements using PRP, BMAC, MSCs, and exosomes for therapy have produced optimistic results, standardization and enduring outcome measures require attention. Sustained cross-disciplinary efforts grounded in scientific rigor enabled the evolution of orthobiologics, which are poised to redefine musculoskeletal treatment paradigms and improve patient-centered care.

Declarations

Statement of Agreement

I, the author of the manuscript titled "Biologic Innovations in Orthopedics: A Comprehensive Review of Orthobiologic Therapies for Joint Preservation and Tissue Regeneration," hereby affirm that the content is original, has not been previously published, and is not under consideration for publication elsewhere. I consent to the manuscript's submission to the journal for review.

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Conflict of Interest

The author declares no conflicts of interest related

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to the content of this article.

Ethical Approval

As this study is a literature review and does not involve human or animal participants, ethical approval was not required.

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Availability of Data and Materials

The data supporting the findings of this review were derived from publicly available peer-reviewed sources. Additional information is available from the corresponding author upon reasonable request.

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