Literature Review

Scaffolds in Regenerative Endodontic Procedures: Current Evidence and Future Perspective

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ABSTRACT

Regenerative endodontic procedures have emerged as a biologically based approach to restore the structure and function of the pulp-dentin complex, primarily through the interplay of stem cells, bioactive signaling molecules, and scaffolds. Scaffolds provide a temporary three-dimensional matrix for cell adhesion, proliferation, differentiation, and vascularization. An ideal scaffold should be bioactive, biodegradable, structurally stable, immunocompatible, and architecturally suitable for tissue regeneration. This review synthesizes recent *in vitro* and *in vivo* studies, clinical trials, and case reports on natural, synthetic, and composite scaffolds applied in pulp-dentin regeneration. A literature search was performed in PubMed, Scopus, and Google Scholar up to 2025. Scaffolds were classified according to their origin, structural form, and cellular integration. The review showed that while natural scaffolds demonstrate favorable biocompatibility and clinical outcomes, their mechanical limitations often restrict their performance. Con-versely, synthetic scaffolds offer tunable properties but may lack inherent bioactivity. Composite materials and biofunctionalized hydrogels may help integrate the strengths of both scaffold classes. Despite encouraging experimental data, further well-designed clinical studies are needed to optimize scaffold-based strategies for reliable translation into clinical endodontics.

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Introduction

For decades, dental pulp has commonly been removed and replaced with inert materials through root canal therapy (RCT) after injury, infection, or irreversible inflammation [1].

Advances in pulp biology reveal its regenerative potential, leading to regenerative endodontic procedures (REPs) based on three key components: stem cells, growth factors, and scaffolds [2-3].

REPs originated with calcium hydroxide therapy and revascularization strategies for necrotic teeth [4].

Dental pulp stem cells (DPSCs) and other dental stem cells contribute to tissue regeneration, with scaffolds providing a 3D matrix that supports cell adhesion, migration, proliferation, and differentiation [5-6]. An ideal scaffold should support cell attachment, have appropriate porosity and permeability, be easily manipulated, and biodegrade into non-toxic byproducts to favor cell migration [2]. Numerous biomaterial scaffolds are available, each with specific advantages and limitations for tissue regeneration [2-3, 7].

This review explores the main scaffold classes used in tissue engineering, summarizing their key properties, design parameters, advantages and limitations, clinical applications, and future prospects, with emphasis on recent scaffold developments.

Search Strategy

This narrative review aimed to provide a comprehensive

overview of scaffold materials used in dental pulp regeneration and REPs. A literature search was conducted in PubMed, Scopus, and Google Scholar for studies published up to December 2025. Search terms included "dental pulp regeneration," "pulp–dentin regeneration," "scaffold," "biomaterial," "tissue engineering," and "regenerative endodontics," used individually and in various combinations. Eligible publications included *in vitro* studies, animal studies, preclinical investigations, clinical studies, case reports, and relevant review articles that addressed scaffold materials used for dentin–pulp regeneration. Articles focusing exclusively on conventional endodontic treatments, scaffold-free regenerative approaches, non-English publications, and studies with insufficient methodological information were excluded.

Additional relevant studies were identified through manual screening of reference lists of selected articles. The retrieved literature was critically evaluated and synthesized narratively to summarize current scaffold classifications, biological properties, advantages, limitations, and future perspectives.

Literature Review

Regenerative potential of the Pulp–Dentin Complex

Dental pulp's regenerative capacity, sensory function, and immune protection enable reactive dentin formation and homeostasis, with vascular and neural elements detecting injury and producing tertiary dentin for self-repair [8]. Conventional RCT causes loss of vascularity, sensation, and structural integrity in treated teeth, compromising natural defense mechanisms, increasing fracture risk, and impairing sensory perception and nutrient supply [9].

REPs aim to restore pulpal biological function, repairing damaged or absent pulp with structure and function resembling native tissue, including nourishment, immunity, and sensibility [9-11].

REPs require biocompatible scaffolds, bio-signaling molecules, and stem cells like DPSCs from dental tissue [2, 5]. Certain stem cells form endothelial cells for angiogenesis/vasculogenesis, others become pulpal cells like odontoblasts, with scaffolds delivering angiogenic/ dentinogenic signals such as fibroblast growth factor (FGF), vascular endothelial growth factor (VEGF), and transforming growth factor beta (TGF-β) to promote migration and differentiation [12].

Scaffolds

Scaffolds provide a three-dimensional (3D) microenvironment that supports cell adhesion, migration, proliferation, differentiation, and extracellular matrix (ECM) deposition. Ideal scaffolds should exhibit interconnected porosity, adequate nutrient diffusion, controlled biodegradation, and minimal immunogenicity while maintaining structural stability throughout tissue regeneration [13].

Scaffolds are classified by origin (natural/biological vs. synthetic/artificial), form (sponges, hydrogels, blocks, sheets), cell presence (cell-free vs. stem cell-seeded), and degradability (biodegradable vs. permanent) [3]. Their key characteristics are summarized in Table 1.

Table 1: Overview of scaffold classification and their properties

Scaffold	Advantages	Disadvantages	Degradation	Clinical Translation Status
Natural polymers				
Polysaccharides [78]	Biocompatible, derived from renewable resources, cost- effective	weak mechanical properties	Variable	○
Alginate [77, 79-80]	Biocompatible and biodegradable, with low immunogenicity, high versatility, and growth factor binding capacity	Lacks inherent bioactivity, has limited mechanical strength	Rapid (days–weeks)	◐
Chitosan [22, 81-82]	Biocompatible and biodegradable with antibacterial potential, non-cytotoxic, binds DNA/ growth factors/glycosaminoglycans, available as fibers/films/sponges/hydrogels (hydrogels: low viscosity and higher adsorption capacity)	Risk of allergic reactions, difficult to handle, and limited use due to crystalline properties	Moderate (weeks–months)	○
Hyaluronic acid [83-84]	Biocompatible and bioactive, with low immunogenicity and adaptable to multiple applications via chemical modification	weak mechanical properties	Accelerated (days–weeks)	◐
Cellulose [25, 85]	Improves cell adhesion, is biocompatible and non-cytotoxic, and is economically viable	Water-insoluble, biodegradation-resistant, and mechanically weak in native form	Slow (months–years)	○

Scaffold	Advantages	Disadvantages	Degradation	Clinical Translation Status
Protein And Peptides [26, 86]	Biocompatible and biodegradable, structurally tunable via chemical modification in dynamic environments, and capable of signaling to guide cell function	Processing and sterilization are challenging, with immunogenicity and allergenicity concerns	Variable	◐
Fibrin [77, 86-87]	Moldable and injectable for customized 3D shapes, reproducible and cost-effective, with no immunologic risk due to autologous origin	Weak mechanical properties with insufficient rigidity	Accelerated (days)	●
Silk [88]	Excellent mechanical properties and chemically modifiable to incorporate growth factors and enhance cell adhesion	Ecological concerns	Slow (months–years)	◐
Collagen [16, 29, 89-90]	Biocompatible, biodegradable, and bioactive with low immunogenicity, strong cell adhesion, enhanced mechanical integrity, cross-linking capacity, and easy cell/growth factor incorporation	Hydration-related mechanical weakness, difficult customization	Moderate (weeks–months)	●
Gelatin [77]	Low immunogenicity, widely available, and cost-effective	Sensitive to changes in temperature	moderate (weeks)	◐
Self-assembling peptides [34, 91]	Biocompatible and biodegradable with no immunologic risk, easy injectable application, and adaptable 3D microenvironments	Cost-intensive fabrication and complex design requirements	Moderate (weeks–months)	◐
Host-derived scaffolds [92]	No immunologic risk due to autologous origin, supports tissue development, enables controlled growth factor diffusion, and is form-adjustable and cost-effective	Requires specific materials and equipment	Variable	●
Platelet -rich plasma (PRP)	Rich in growth factors, with lower cytokine levels than PRF, and releases growth factors immediately but for a shorter duration	Often contains artificial anticoagulants or additives	Fast (days)	●
Platelet -rich fibrin (PRF) [64, 93]	Rich in growth factors, free of artificial anticoagulants, with slower and longer-term growth factor release	More expensive than PRP, with higher cytokine levels	Moderate (1–4 weeks)	●
Decellularized Extracellular Matrix (dECM) [94]	Autologous and suitable for tissue regeneration	May occasionally trigger an immune response to DNA	Moderate (weeks–months)	◐
Blood clot [43, 95]	Lower levels of cytokines than PRF and PRP	Slower healing rate than PRP and PRF Lacking a lot of growth factors	Rapid remodeling (days–weeks)	●
Synthetic polymer				
PGA [3, 51]	Biocompatible and biodegradable, improves cell adhesion, hydrophilic linear structure for better solubility, cost-effective, and causes only minimal inflammation	PGA degrades faster than PLGA due to its simpler structure	Very rapid (≈14-day half-life)	◐
PLGA [51, 96-98]	Biocompatible and biodegradable, cost-effective, mechanically customizable, and causes only minimal inflammation		Weeks–months depend on composition	◐
PLA [45]	Biocompatible and biodegradable	Hydrophobic	Slow (months–years)	◐
PCL [3, 96]	Biocompatible and biodegradable with reduced toxicity, slow polymer breakdown, and favorable mechanical properties	Hydrophobic with slow degradation and lacking functional moieties	Very slow degradation (years)	◐
Composite materials (bio ceramic) [53, 99]	Biocompatible with low immunogenicity, osteoconductive, and strong resistance	High density with low flexibility (brittle) and suboptimal mechanical properties	Slow	●
Calcium phosphate, HA, TCP [56, 100-101]	Good biocompatibility with minimal rejection risk, mimics dentin composition, suitable as a capping material, and osteoconductive	Difficult to shape, with non-uniform particle size, brittleness, and gradual disintegration	Slow (months–years)	●
Bioactive glass [59, 102]	Forms a surface apatite layer, promotes new bone formation, and is osteoconductive	Suboptimal mechanical properties with high density, brittleness, and delayed degradation	Slow (months–years)	●
Synthetic self-assembling Peptide [61, 63]	Suitable for drug delivery and contains both hydrophilic and hydrophobic residues	Weak mechanical strength	Moderate degradation (weeks-months)	◐

Abbreviations: three-dimensional (3D); deoxyribonucleic acid (DNA); decellularized extracellular matrix (dECM); hydroxyapatite (HA); polycaprolactone (PCL); polyglycolic acid (PGA); polylactic acid (PLA); poly (lactic-co-glycolic acid) (PLGA); platelet-rich fibrin (PRF); platelet-rich plasma (PRP); tricalcium phosphate (TCP).

Clinical translation status: ○ Experimental = Predominantly laboratory and animal studies. ◐ Emerging Clinical Use = Limited human studies or early clinical adoption. ● Established Clinical Use = Widely used clinically or incorporated into regenerative procedures

Biological properties depend on pore size/shape, porosity, and interconnectivity; micropores (<10 μm) facilitate fluid circulation, macropores (>100 μm) support cell migration, proliferation and tissue formation [14-15].

Natural scaffolds

Natural polymers offer bioactivity, cell interaction, biocompatibility, and enzyme-mediated biodegradability, making them ideal for injectable hydrogels. ECM polypeptides (collagen, fibrin, gelatin, keratin) and glycosaminoglycans (hyaluronic acid, chitosan, alginate) form these scaffolds, many with high water absorption [16-17].

Polysaccharides

Polysaccharides, long-chain carbohydrates hydrolyzing to monosaccharides/oligosaccharides, are primary scaffolds for dental pulp regeneration [2].

Alginate, derived from brown algae cell walls, can be ionically cross-linked with calcium to form hydrogels and can be modified with arginine-glycine-aspartic acid ligands to improve cell attachment. Its enzymatic cleavage enables subsequent degradation [18]. Researchers engineer alginate's stiffness and stress relaxation to direct stem cell fate and activity [19]. Seaweed-derived alginate forms gutta-percha-like scaffolds that carry cells, and combining VEGF-121, FGF, arginine-glycine-aspartic acid modification, dental stem cells, and endothelial cells enhances proliferation [20].

Chitosan, obtained by deacetylating chitin from insect, fungal, and crustacean exoskeletons, binds growth factors (GFs), deoxyribonucleic acid (DNA), and glycosaminoglycans effectively. Chitosan-gelatin scaffolds loaded with antibiotics provide biocompatibility and antibacterial effects during REP [21]. Chitosan/ beta-glycerophosphate hydrogel promotes odontoblastic differentiation of DPSCs via sustained VEGF release [22].

Hyaluronic acid, an ECM glycosaminoglycan, maintains extracellular spacing and supports tissue organization. Its degradation releases pro-angiogenic growth factors that enhance revascularization, but its mechanical strength is limited and it may cause hypersensitivity reactions [17]. US Food and Drug Administration–approved Restylane, a hyaluronic acid–based gel, improved the survival of stem cells from the apical papilla (SCAP), and odontoblastic differentiation *in vitro* [23].

Cellulose, extracted from plant cell walls, demon states biocompatibility and non-toxicity, but its poor mechanical properties restrict use in hard tissue regeneration [24]. Bacterial nanocellulose has emerged as a sustainable material that promotes in situ mineralized tissue regeneration [25].

Protein and Peptides

Protein and peptide scaffolds are increasingly used in tissue engineering because their composition and structure can be tailored through recombinant and molecular modifications, yielding novel peptides with specific properties [26].

Fibrin scaffolds offer favorable characteristics, especially controlled biodegradability at low cost. Autologous fibrin hydrogels, easily prepared from patient blood, provide a reproducible and immunologically safe scaffold that supports odontoblast layer formation and pulp-like tissue generation within root canals [3, 27].

Silk, a fibrous protein from spiders and silkworms, is applied in medicine for ligament regeneration, drug delivery, and targeted cell therapies through chemical modification. Methacrylate silk can function as an antibacterial material against endodontic infections [28].

Collagen, the most abundant mammalian protein, acts as a viscoelastic scaffold that closely resembles pulp tissue. Collagen hydrogels support cell development, ECM–cell interactions, and formation of a stable self-assembled 3D network under physiological conditions [29-31]. Gelatin, a partial hydrolysis product of collagen, is widely used in tissue engineering, cell culture, and bioadhesion as it offers several favorable characteristics (Table 1); however, its thermal instability limits its use. Gelatin methacryloyl (GelMA) partially addresses this limitation by enhancing mechanical stability and enzymatic degradability [32-33].

Self-assembling peptide scaffolds consist of short peptides (about 15–25 amino acids) that spontaneously form water-retaining nanofiber hydrogels mimicking ECM structure and function, though their high cost and complex design remain significant limitations [34].

Matrigel, a bioactive basement-membrane–derived scaffold from mouse sarcoma containing laminin, collagen IV, entactin, and diverse growth/transcription factors, closely mimics ECM and enhances cell adhesion and interaction, but its tumor origin raises concerns about batch consistency and safety [35].

Host-Derived Scaffolds

Host-derived scaffolds created through induced periapi-

cal bleeding promote intracanal clot formation, while platelet-rich materials such as platelet-rich plasma (PRP) or platelet-rich fibrin (PRF) promote angiogenesis and revascularization essential for successful REP [17, 36].

PRP is a first-generation autologous platelet concentrate prepared by double-spin centrifugation. It contains high levels of platelets, cytokines, and GFs, which may support apical stem cell proliferation, DPSC recruitment, and wound healing [1]. PRP releases GFs rapidly for immediate effect, unlike PRF's slower sustained release [37].

PRF, a second-generation concentrate from single-spin anticoagulation-free blood centrifugation, forms three layers with viscous middle PRF clot; its biocompatibility and sustained GFs release enable wide clinical use [38].

Decellularized ECM preserves key ECM components and bioactive cues that support cell function, although preparation variability may affect *in vivo* performance [39]. While dental pulp is a common dECM source [40], more accessible non–dentin-derived scaffolds, such as decellularized submandibular gland ECM, also support DPSC growth and pulp-like tissue formation *in vivo* [41]. Human dental pulp-derived decellularized matrix hydrogel forms a gel at body temperature, showing promise for REP.

Treated dentin matrix (TDM), an autologous demineralized dentin scaffold, promotes reactive dentin formation and odontogenesis in vital pulp therapy (especially capping) by enabling defect-free dentin bridge regeneration [42].

Blood Clots

Blood clots are the most common scaffold in REP, formed by inducing bleeding into a disinfected canal. Alone, blood clots can produce unpredictable hemostasis, whereas combining them with natural materials like collagen yields more consistent tissue formation [43]. Vieira *et al.* [44] reported that a pure blood clot produced a denser fibrin network than one exposed to ethylenediaminetetraacetic acid, regardless of activation.

Despite limitations of natural scaffolds, Galler *et al.* [45] demonstrated that natural hydrogels supported cell survival better than synthetic ones and that different hydrogels led to varying degrees of odontoblast-like differentiation, soft tissue formation and vascularization.

Synthetic Scaffolds

Synthetic polymers offer controllable mechanical properties, degradation kinetics, and reproducibility [3]. Their hydrolytic degradation produces acidic byproducts that may cause localized pH drops and inflammatory responses [46].

Polyethylene glycol (PEG)

PEG is non-toxic, hydrophilic, and non-immunogenic. Researchers developed light-cured PEG methyl ether methacrylate-co-citrate hydrogels for REP drug delivery, preserving pulp and supporting REP like direct pulp capping [47]. *In vivo/in vitro* tests showed 3D-printed PEG-diacrylate /sodium-alginate hydrogels loaded with FGF supported stem cell survival/growth, with lower hydrogel ratio being more effective [48].

Poly α-Hydroxy Acids

Polylactic acid (PLA), a biobased biodegradable/ biocompatible polymer from bacterial digestion of plant polysaccharides, uses common isomer Poly (L-lactic acid) [49]. PLA scaffolds enhance *in vivo* dentin formation, promote DPSC differentiation, and upregulate dentinogenesis markers (dentin sialophosphoprotein, collagen I, osteocalcin, alkaline phosphatase, bone sialoprotein) *in vitro*. Clindamycin-loaded PLA scaffolds reduce bacterial load, support tooth regeneration, and preserve DPSC viability/ function [50]. Poly (L-lactic acid) provides durable structural support and promotes proliferation and differentiation, with increased expression of odontogenic markers [3, 51].

Polyglycolic acid (PGA) supports adhesion/proliferation of human pulp cells, fibroblasts, and dental pulp-derived cells [46, 51]. Poly (lactic-co-glycolic acid) (PLGA), seeded with swine third-molar tooth cells, enables tooth bud maturation, dentin/pulp-like tissue regeneration in 3-4 months. PGA/PLGA are related biodegradable polymers, but PGA's simpler structure causes faster degradation limiting long-term use, while PLGA's tunable lactic/glycolic ratio offers controlled regeneration; PGA's high water solubility restricts pulp-dentin applications [2]. Polycaprolactone (PCL) provides slow-degrading support for hard tissue engineering [3].

N-Isopropyl Acrylamide Polymer

Thermo-reversible polymer gels have been used to transplant scaffold-free 3D DPSCs, generating pulp-like tissue without scaffold-related inflammation [52].

Composite Materials (Bioceramic)

Bioceramics (glass ceramics, bioactive glasses, calcium phosphates) excel in hard tissue regeneration due to strength, wear resistance, and stability, though they may be brittle, difficult to shape, and slow-forming [3, 53-55].

Calcium Phosphate

Calcium phosphate materials, especially 3D porous granules like β-tricalcium phosphate and hydroxyapatite, provide osteoconductive substrates with strong bonding and low immunogenicity [6]. Well-tolerated hydroxyapatite scaffolds cover exposed pulp post trauma due to similarity to bone/dentin [56]. Polysaccharide-HA nanoparticle hydrogels promote dental stem cell adhesion and upregulate bone/tooth development genes. In rat molars, beta-tricalcium phosphate/ hydroxyapatite/ collagen scaffolds showed low inflammation/pulp vitality preservation like mineral trioxide aggregate, but mineral trioxide aggregate uniquely induced dentin bridge formation over the pulp exposures [57]. Tricalcium phosphate is a biocompatible 3D ceramic that supports cell growth, pulp tissue promotion, and improved tooth prognosis [58]. Bioactive glass bonds with living tissue, stimulates dentin bridge/bone-like formation, enhances dentin regeneration, and regulates silica-based therapeutic ions [59-60].

Glass Ceramics

Composed of SiO_2, Na_2O, CaO, P_2O_2 for bioactivity/crystallization; Ca-P dissolution boosts osteoblasts. Magnesium variants offer high bioactivity/mechanical strength; niobium-doped fluorapatite types excel in human DPSC adhesion/proliferation/differentiation [11].

Synthetic self-assembling peptide

Peptide-amphiphile is a synthetic self-assembling peptide hydrogel that self-assembles into nanofibers in aqueous environments. It has potential for drug delivery and rege-nerative medicine, although its low mechanical strength remains a limitation [61]. Arginine-glycine-aspartic acid-modified peptide amphiphiles provide injectable scaffolds for pulp/dentin regeneration, and bioactive RADA16-I hydrogels enhance dentin-pulp repair. Parametric™ RADA16-I has been used to study pulp-dentin regeneration and DPSC-driven vascularize tion [62-63].

Discussion

Dentin-pulp regeneration has progressed to clinical testing, yet widespread adoption remains limited by biological, material, and clinical variables [1-3]. The diversity of study designs and outcomes complicates direct comparison, suggesting that scaffold optimization alone cannot ensure success.

Comparative Analysis: Natural, Synthetic, and Composite Scaffolds

Natural scaffolds (collagen, fibrin, gelatin, hyaluronic acid, chitosan) demonstrate superior biocompatibility and promote odontogenic differentiation due to their structural similarity to native pulp-dentin matrix [16-17]. However, weak mechanical properties, rapid degradation, batch variability, and immunologic risks limit their use as stand-alone systems [17, 24, 43]. This paradox explains why clinical applications require combining with other materials.

Synthetic polymers (PEG, PLA, PLGA, PCL) offer tunable mechanical properties and controlled degradation [3, 49, 51]. However, they lack intrinsic bioactivity and their acidic degradation byproducts may lower pH and provoke inflammation [46]. This explains why preclinical promise has not translated to superior clinical outcomes. Mechanical tunability alone is insufficient without concurrent biochemical optimization.

Composite and bioactive ceramic systems integrate biological and mechanical advantages [53]. Collagen-hydroxyapatite and PLGA-ceramic constructs show enhanced odontogenic differentiation compared to single-component scaffolds [57], indicating no single material class satisfies all requirements. However, increased complexity introduces manufacturing, sterilization, and cost challenges, suggesting clinical practicality must be balanced against biological efficacy. The key findings of this review are summarized in Table 2 for a clear overview.

Clinical Advances and Scaffold Performance

Multiple scaffolds (blood clot, PRP, PRF, collagen, hyaluronic acid) achieve apical periodontitis resolution and continued root development in immature teeth [64-67]. Comparable success rates between blood clot and platelet concentrates suggest simple autologous blood clot remains adequate when cost or equipment limit options. Superior root lengthening and dentin thickening with PRF, collagen, and hyaluronic acid indicate bioactive scaffolds offer incremental benefits in challenging cases [65-66].

Table 2: Comparison of major scaffold classes in regenerative endodontic procedures

Feature	Natural	Synthetic	Host-Derived	Composite
Biocompatibility	+++	++	+++	+++
Bioactivity	+++	+	+++	+++
Mechanical Strength	+	+++	+	++
Degradation Control	++	+++	+	++
Clinical Availability	++	++	+++	+
Cost	++	++	+++	+

This table highlights the key features of different scaffold types, with ratings (+ to +++) indicating their relative performance across various characteristics. It provides a concise reference to the main findings of this review

Recent meta-analyses further support these findings. Yang *et al.* [68] (2024) analyzed 12 randomized controlled trials involving 434 participants and found no significant differences among blood clot, PRP, and PRF in clinical success (risk ratio= 0.99, 95% confidence interval 0.96–1.03), root length increase, or root wall thickening, concluding that scaffold selection may be based on practical considerations. In contrast, Huang *et al.* [69] (2025) evaluated 10 randomized controlled trials comprising 373 teeth and reported modest advantages for platelet concentrates, with PRP improving clinical success (risk ratio=1.14, 95% confidence interval 1.03–1.27) and PRP/PRF demonstrating greater root length and thickness gains than blood clot scaffolds. Together, these studies indicate that while platelet concentrates may enhance root maturation, the overall clinical superiority of one scaffold over another remains uncertain. This reveals a central paradox: the most accessible scaffold (blood clot) is not biologically optimal [45], while more effective scaffolds require additional steps and expenses, thereby restricting their adoption [37]. Short follow-up periods and reliance on radiographic assessments limit confirmation of true pulp-dentin regeneration versus repair.

Collagen scaffolds have also been evaluated in clinical REPs. A recent review encompassing over 600 teeth reported survival rates of 85–100% and healing success rates of 80–100% across follow-ups up to 23 months. Root wall thickening occurred in 67–82% of cases, apical closure in 47% (96% completing closure by 24 months), and pulp vitality recovery ranged from 32–60%. Root canal calcification affected 30–47% of treated teeth. Despite these favorable outcomes, histology showed primarily cementum-like or bone-like tissue rather than true pulp-dentin regeneration [70]. Thus, collagen scaffolds are effective for structural repair and root maturation, but they do not reliably achieve full biological regeneration, highlighting the need for targeted scaffold modifications and advanced tissue-engineering strategies.

Current evidence supports REPs as a conservative alternative to apexification in immature teeth [71-72], but insufficient data exist to define a single standard scaffold. Future studies with longer follow-ups, histological validation, and standardized scaffold protocols are needed to establish best practices.

Translational, Regulatory and Clinical Implementation Challenges

Multiple patient-specific factors substantially influence REP success including age, apex diameter, tooth type, etiology, and immune status [73-75]. This indicates that the outcomes of REPs depend critically on patient biology and clinical conditions, not scaffold selection alone.

Younger patients with immature teeth and open apices show better regenerative responses due to greater stem-cell availability and enhanced vascularization [73]. However, REP efficacy in older patients with closed apices remains unclear, representing a significant gap in the current literature. Molars with complex anatomies present greater technical challenges than anterior teeth [74]. Trauma-induced necrosis has a worse prognosis than developmental malformations [75]. Immunocompromised patients may be at higher risk of failure, and uncontrolled diabetes creates unfavorable microenvironments.

Despite significant advances in scaffold-based strategies for dentin–pulp regeneration, several critical barriers continue to limit their translation from bench to bedside. One of the major challenges is the regulatory pathway required for clinical approval of biomaterial-based and cell-laden scaffolds. Composite and biofunctionalized scaffolds are often classified as combination products, which necessitate extensive preclinical safety evaluation, standardized manufacturing protocols, and compliance with good manufacturing practice regulations. These requirements significantly increase the time and cost associated with clinical translation [2, 52].

Manufacturing and scalability also represent key limitations. Many advanced scaffolds, particularly those

involving natural–synthetic composites or growth factor incorporation, require complex fabrication techniques that are difficult to standardize across laboratories and clinical settings. Batch-to-batch variability, sterilization challenges, and storage stability further complicate their large-scale production and clinical use [2, 51].

Cost-effectiveness is another important consideration. While biologically active scaffolds may offer enhanced regenerative potential, their production costs are often substantially higher than conventional approaches such as blood clot–based REPs. This raises concerns regarding accessibility and widespread clinical adoption, particularly in resource-limited settings [16, 76].

In addition, long-term clinical predictability remains insufficiently established. Most available studies

report short- to medium-term outcomes, and there is limited evidence regarding the durability and functional stability of regenerated pulp–dentin complexes over time. Furthermore, variability in clinical protocols and outcome measures makes it difficult to compare studies and draw definitive conclusions regarding scaffold superiority [3, 16].

Overall, these translational challenges highlight that, although scaffold-based regenerative strategies are scientifically promising, their routine clinical implementation will require not only biological optimization but also advancements in regulatory standardization, scalable manufacturing, economic feasibility, and long-term clinical validation [77].

A critical limitation in the current body of literature on scaffolds for dentin–pulp regeneration is the substantial heterogeneity in study design and level of evidence. The available studies range from *in vitro* experiments and animal models to case reports, retrospective analyses, and a limited number of clinical trials [2, 16, 51, 68-70]. However, these different levels of evidence are often discussed collectively, which may overestimate the clinical applicability of preclinical findings.

In vitro and animal studies provide essential insights into cellular behavior, scaffold biocompatibility, and early regenerative mechanisms, but they do not fully replicate the complex biological, immunological, and mechanical environment of the human root canal system. Consequently, promising results observed at the laboratory level may not necessarily translate into predictable clinical outcomes.

Clinical studies in REPs, although more directly relevant, are still limited in number, often characterized by small sample sizes, short follow-up periods, and variability in outcome measures. Furthermore, many clinical studies rely on radiographic and clinical parameters without histological confirmation of true pulp–dentin complex regeneration, making it difficult to distinguish between true regeneration and repair-based healing [64-70].

This evidence gap highlights the need for a clearer stratification of findings according to the hierarchy of evidence. Future research should prioritize well-designed randomized controlled trials with standardized protocols and long-term follow-up. Until such evidence is available, conclusions regarding the superiority of specific scaffold systems should be interpreted with caution. Furthermore, the restriction to English-language publications and the possibility of publication bias may have limited the comprehensiveness of the available evidence.

Current State and Future Prospects

REPs are not yet considered standard practice due to insufficient research and clinical consensus, though case studies and trials demonstrate feasibility and safety [71-72]. Barriers to widespread adoption include low treatment predictability, lack of insurance coverage, and absent standardized clinical protocols.

Taken together, the literature suggests that dentin-pulp regeneration will most likely advance through integrative strategies that couple biologically active scaffolds with precise control over mechanical behavior and degradation kinetics. Future advances will likely include biomaterial improvements, gene therapy integration, and personalized approaches based on patient factors. Composite hydrogels, biofunctionalized matrices, and chemotactic cell-homing approaches tailored to patient age, anatomy, and health represent the most promising direction. Progress requires prospective trials with standardized outcomes, histologic correlation, long-term follow-up, and consensus on success criteria. A summary of all included studies is presented in Table 3.

Conclusion

No single scaffold currently satisfies all biological and mechanical requirements for predictable pulp-dentin regeneration. Natural polymers generally show favorable biocompatibility and clinical applicability, but their me-

Table 3: Comprehensive summary of preclinical and clinical studies on scaffold-based REPs, covering single-component scaffolds first, then composite/combination systems with better outcomes

	Scaffold	Author	Study	Cell used	Conclusion
Natural	Polysaccharides				
	Alginate	Fujiwara *et al.* [103] (2006)	*In vivo*	DPSCs rat	Subculture rat dental pulp cells became odontoblast-like and induced calcification on alginate scaffolds.
	chitosan	Palma *et al.* [104] (2017)	*In vivo*	Immature teeth of dogs	In canines undergoing REP, adding blood to chitosan scaffolds did not improve mineralization or dentin-pulp regeneration markers.
	chitosan Hydrogel + Azithromycin	Reis-Prado *et al.* [105] (2025)	*In vitro*	SCAPs	3%–5% Azithromycin –chitosan hydrogels inhibited bacteria (especially *E. faecalis*) without harming SCAP viability; 3% worked best.
			In vivo	SCAPs rats	In rats, 3% Azithromycin –chitosan improved root development, reduced periapical lesions, and promoted regeneration (including cementum-like deposition).
	Hyaluronic acid	Chrepa *et al.* [23] (2017)	*In vitro*	SCAPs	A hyaluronic acid injectable gel improved SCAP survival, odontoblast-like differentiation, and mineralization, suggesting it may be a useful scaffold for REPs.
	cellulose	Esguerra *et al.* [106] (2010)	*In vivo*	Dorsal skinfold chambers in hamsters	After 2 weeks, abundant proliferating cells and no apoptosis indicated strong bacterial cellulose integration and biocompatibility.
	Bacterial nanocellulose	Jain *et al.* [25] (2024)	*In vitro*	DPSCs	bacterial nanocellulose promoted DPSC attachment, migration, and odontogenic differentiation.
	Protein And Peptides				
	fibrin	Galler *et al.* [45] (2018)	*In vitro*	DPSCs	At the cell–dentin interface, fibrin best supports pulp-like tissue formation and odontoblastic differentiation.
			In vivo	Immunocompromised mice	
	silk	Park *et al.* [107] (2015)	*In vivo*	Rabbit Calvaria defect	Silk scaffolds are biocompatible and can serve as osteoconductive scaffolds for hard tissue and bone engineering.
	Collagen	Prescott *et al.* [108] (2008)	*In vivo*	Mouth DPSCs	Collagen scaffolds promoted pulp-like matrix formation and may support hard tissue development.
	gelatin	Ishimatsu *et al.* [109] (2009)	*In vitro*	DPCs	Gelatin is an effective scaffold for delivering FGF2 to support regeneration.
	Self-assembling peptides	Mu *et al.* [62] (2020)	*In vitro*	DPSCs HUVECs	RADA16-I self-assembling peptide hydrogels increased DPSC proliferation, migration, and adhesion, and promoted more vascular-like HUVEC structures.
	PuraMatrix	Dissanayaka *et al.* [110] (2015)	*In vitro*	DPSCs HUVECs	Even without added growth factors, peptide nanofibers promoted capillary network formation and supported DPSC migration and survival.
			In vivo	mice	
	PRP	Bezgin *et al.* [111] (2015)	Case report	Immature teeth	PRP served as an effective scaffold for REPs treatment.
	Advanced PRF and Blood Clot	Qamar *et al.* [76] (2025)	RCT	Stem cells	Both scaffolds significantly improved root development in immature necrotic teeth; advanced PRF was slightly better, but not significantly.
	PRF	Lv *et al.* [112] (2018)	Retrospective Controlled Cohort study	On five people	In REP, PRF performed similarly to blood clots for periapical healing, symptom relief, and continued root formation.
	HAM- dECM	Bakhtiar *et al.* [113] (2022)	*In vitro*	hDPSCs	HAM-ECM scaffolds (cell-free or cell-loaded) did not inhibit pulp-like tissue formation or revascularization in the root canal, supporting further study in regenerative endodontics.
			In vivo	Root segment models	
	SHED derived extracellular matrix pulp scaffold	Yang *et al.* [114] (2024)	*In vivo*	Teeth	SHED-ECM pulp scaffolds were non-cytotoxic and promoted dentin- pulp complex regeneration *in vivo*, while enhancing BMMSCs migration and odontogenic differentiation *in vitro.*
			In vitro	BMMSCs	
	autoclaved TDM	Chang *et al.* [115] (2020)	*In vivo*	Mice	Allogeneic autoclaved TDM supported DPSC proliferation and differentiation into odontoblast-, fibroblast-, vascular-, and neural-like cells, suggesting a-TDM + DPSCs is a promising biomaterial for tooth tissue regeneration.
Synthetic					
	PLA	Wang *et al.* [116] (2017)	*In vitro*	SHEDs	PLA showed good biocompatibility with SHED and may promote SHED mineralization as a scaffold.

Scaffold	Author	Study	Cell used	Conclusion
PGA	Mooney *et al.* [117] (1996)	*In vitro*	Pulp-derived fibroblasts	These tissues could aid oral tissue regeneration and provide new models to test the biocompatibility of dental materials.
PLGA	El-Backly *et al.* [118] (2008)	*In vitro* *In vivo*	DPSCs of rabbits	Tissue engineering produced dentin/pulp-like structures with potential for future REPs or restorative use.
Biphasic calcium phosphate scaffold BCP20	AbdulQader *et al.* [119] (2015)	*In vitro*	hDPSCs	Scaffold concentration affected the cell microenvironment, and Biphasic calcium phosphate scaffold BCP20 supported HDPC differentiation for dentin regeneration.
GelMA Composited with silver nanoparticles or hyaluronic acid or hydroxyapatite	Dorterler *et al.* [32] (2024)	*In vitro*	Antimicrobial Properties	GelMA hydrogel with hyaluronic acid showed the strongest activity against *E. faecalis.*
GelMA Hydrogel	Zhao *et al.* [120] (2025)	*In vitro* *In vivo*	DPSCs HUVECs Rat molars	It increased DPSC proliferation, migration, and differentiation, and promoted HUVEC angiogenesis, supporting its potential for dental pulp regeneration. In a rat model, it promoted vascularized pulp tissue formation, enhancing dental pulp regeneration.
amnion–chorion membrane and Collagen Matrix	Dave *et al.* [121] (2025)	Retrospective study	immature necrotic permanent teeth	both scaffolds effective in immature necrotic teeth; amnion–chorion membrane had slightly higher survival/success (90.5%/85.7%) and faster sensibility recovery, but overall outcomes and root development were similar.
DPSCs encapsulated in Collagen	Han *et al.* [122] (2024)	*In vivo*	Implanted in severe combined immunodeficiency mice	Growth factor–modified hydrogels promoted lineage-specific differentiation of DPSCs.
Emdogain gel	Matsumoto *et al.* [123] (2014)	*In vivo*	Applied in injured open apex within periapical lesion in rats	EMD did not irritate injured periapical tissue and may create conditions that support periapical healing.
Alginate+boron-doped mesoporous bioactive glass nanoparticles	Naga *et al.* [124] (2024)	*In vitro*	HGFCs	The composite hydrogel may be a promising pulpotomy filler that supports dentin regeneration, but it reduced HGFCs feasibility.
cobalt-incorporated chitosan	Kumar *et al.* [125] (2023)	*In vitro*	hDPSCs	Compared with chitosan, the incorporated scaffold is porous and biocompatible, enhances cell adhesion, and may support dentin–pulp regeneration.
Chitosan-Calcium Aluminate	Bordini *et al.* [126] (2024)	*In vitro*	Dental pulp cells	Enhanced cell migration and mineralization compared to standard chitosan.
Chitin with or without hydroxyapatite	Zawadzka-Knefel *et al.* [127] (2023)	*In vitro*	DPSCs	Pure chitin supports cell adhesion, proliferation, and differentiation, but adding hydroxyapatite improves regenerative potential.
hyaluronic acid (restylane) /blood clot	AlHowaish *et al.* [128] (2022)	*In vivo*	dog	Combining Restylane Lyft with a blood clot scaffold may improve REPs outcomes in non-infected, pulp less immature canine teeth.
SilkMA	Narayanam *et al.* [28] (2024)	*In vitro*	antibacterial effectiveness	SilkMA loaded with clindamycin and tinidazole was effective against endodontic infection–related bacteria.
GelMA fibrous scaffolds with and without CEH	Paymanpour *et al.* [129] (2024)	*In vitro*	DPSCs	CEH-loaded GelMA enhanced cell proliferation and adhesion and reduced chronic lipopolysaccharide - induced inflammation.
DHDP + WJMSCs	Tan *et al.* [130] (2024)	*In vivo*	canine teeth of a feline (cat)	DHDP combined with WJMSCs may support pulp regeneration and advance stem cell–based therapies.
PLGA/ hydroxyapatite	Jiménez *et al.* [131] (2018)	*In vitro*	hDPSCs	PLGA/ hydroxyapatite scaffolds provided strong chemical and physical cues, supporting DPSC attachment, proliferation, and osteogenic differentiation.
PCL/bio-glass PCL/hyaluronic acid	Mousavi Nejad *et al.* [132] (2021)	*In vitro*	Dentin and pulp tissue	PCL/bioactive glass and PCL/ hyaluronic acid scaffolds show strong potential to enhance hDPSC attachment and odontogenic differentiation.
PLGA/hydroxyapatite or PLGA/ tricalcium phosphate or PLGA/ calcium carbonate hydroxyapatite	Zheng *et al.* [133] (2011)	*In vivo* *In vitro*	Rats DPSCs	PLGA/TCP outperformed the other scaffolds for tooth tissue regeneration, especially dentin formation.

	Scaffold	Author	Study	Cell used	Conclusion
	PCL/nano hydroxyapatite	Mendes Soares *et al.* [134] (2022)	*In vitro*	hDPSCs	Cytocompatibility nano hydroxyapatite –PCL nanofiber scaffolds enhanced HDPC adhesion and odontogenic potential.
	hydroxyapatite/ Collagen/ β-tricalcium phosphate	Guerrero-Gironés *et al.* [57] (2021)	*In vivo*	Rat molars	hydroxyapatite / beta-tricalcium phosphate/C showed similar outcomes to mineral trioxide aggregate in vital pulp therapy (no inflammation, preserved vitality) but differed in dentin bridge formation.
	Gelatin /bioactive glass	Huang *et al.* [135] (2021)	*In vitro*	human bone marrow mesenchymal stem cells	The gelatin/pH-neutral bioactive glass composite scaffold significantly enhanced human bone marrow mesenchymal stem cell chemotaxis, proliferation, and odontogenic differentiation.
	lithium and zinc containing bioactive glass	Tran *et al.* [136] (2023)	*In vitro*	Stem Cells from SHEDs	Lithium/zinc bioactive glasses increased Axin2 and dentin sialo phosphoprotein expression in SHEDs, likely promoting pulp mineralization and regeneration. Zinc-doped bioactive glass may be suitable for pulp-capping materials.

Studies were color-coded according to level of evidence: *in vitro* (yellow), *in vivo* (green), and clinical studies (blue) to improve visualization of the translational hierarchy.
Abbreviations: bone marrow mesenchymal stem cells (BMMSCs); casein enzymatic hydrolysate (CEH); collagen matrix (CM); decellularized extracellular matrix (dECM); decellularized human dental pulp (DHDP); dental pulp cells (DPCs); dental pulp stem cells (DPSCs); extracellular matrix (ECM); enamel matrix derivative (EMD); fibroblast growth factor 2 (FGF2); gelatin methacryloyl (GelMA); human amniotic membrane (HAM); human dental pulp cells (HDPCs); human dental pulp stem cells (hDPSCs); human gingival fibroblast cells (HGFCs); human umbilical vein endothelial cells (HUVECs); lipopolysaccharide (LPS); polycaprolactone (PCL); polyglycolic acid (PGA); polylactic acid (PLA); poly(lactic-co-glycolic acid) (PLGA); platelet-rich fibrin (PRF); platelet-rich plasma (PRP); randomized controlled trial (RCT); regenerative endodontic procedures (REPs); silk fibroin methacrylate (SilkMA); stem cells from apical papilla (SCAPs); stem cells from human exfoliated deciduous teeth (SHEDs); treated dentin matrix (TDM); tricalcium phosphate (TCP); Wharton's jelly mesenchymal stem cells (WJMSCs)

chanical weakness, variable degradation, and potential immunologic concerns may limit performance. Synthetic polymers provide greater structural tunability and stability, although they often require biofunctionalization to improve cellular interactions and regenerative potential.

Composite scaffolds that integrate natural and synthetic components may offer complementary advantages; however, their clinical superiority has not yet been confirmed by robust comparative evidence. REPs represent a conservative, biologically based alternative to apexification in immature necrotic teeth, but broader clinical adoption requires stronger evidence, clearer patient selection criteria, standardized protocols, and long-term outcome assessment.

Therefore, scaffold selection should be guided by tooth maturity, apical morphology, patient-related factors, scaffold availability, and the current level of supporting evidence. Future research should prioritize well-designed clinical studies, standardized outcome measures, and long-term validation to determine which scaffold strategies can be reliably translated into routine endodontic practice.

Author Contributions

Conceptualization, M.S. and K.K.; methodology, M.S., K.K., S.M.M., and M.F.; data interpretation, M.S., K.K., and S.M.M.; writing- original draft preparation, M.S. and K.K.; writing- review and editing, S.M.M. and M.F.; supervision, M.F. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Jung C, Kim S, Sun T, Cho YB, Song M. Pulp-dentin regeneration: current approaches and challenges. J Tissue Eng. 2019; 10: 2041731418819263.

[2] Sequeira DB, Diogo P, Gomes BP, Peça J, Santos JMM. Scaffolds for dentin-pulp complex regeneration. Medicina. 2023; 60: 7.

[3] Gathani KM, Raghavendra SS. Scaffolds in regenerative endodontics: A review. Dent Res J (Isfahan). 2016; 13: 379-386.

[4] Dammaschke T. The history of direct pulp capping. J Hist Dent. 2008; 56: 9-23.

[5] Zou J, Mao J, Shi X. Influencing factors of pulp-dentin complex regeneration and related biological strategies. Zhejiang Da Xue Xue Bao Yi Xue Ban. 2022; 51: 350-361.

[6] Sharma S, Srivastava D, Grover S, Sharma V. Biomaterials in tooth tissue engineering: A review. J Clin Diagn

Res. 2014; 8: 309.

[7] Hirani P, Chandak M, Agrawal P, Sarangi S, Suryawanshi T, Jidewar N, et al. Platelet Power: Revitalizing Endodontics With Scaffolds. Cureus. 2024; 16: e60691.

[8] Rosaian AS, Rao GN, Mohan SP, Vijayarajan M, Prabhakaran RC, Sherwood A. Regenerative capacity of dental pulp stem cells: A systematic review. J Pharm Bioallied Sci. 2020; 12(Suppl 1): S27-S36.

[9] Xie Z, Shen Z, Zhan P, Yang J, Huang Q, Huang S, et al. Functional dental pulp regeneration: basic research and clinical translation. Int J Mol Sci. 2021; 22: 8991.

[10] Huang X, Li Z, Liu A, Liu X, Guo H, Wu M, et al. Microenvironment influences odontogenic mesenchymal stem cells mediated dental pulp regeneration. Front Physiol. 2021; 12: 656588.

[11] Sugiaman VK, Jeffrey, Naliani S, Pranata N, Djuanda R, Saputri RI. Polymeric scaffolds used in dental pulp regeneration by tissue engineering approach. Polymers. 2023; 15: 1082.

[12] Stamnitz S, Klimczak A. Mesenchymal stem cells, bioactive factors, and scaffolds in bone repair: from research perspectives to clinical practice. Cells. 2021; 10: 1925.

[13] Saber SEDM. Tissue engineering in endodontics. J Oral Sci. 2009; 51: 495-507.

[14] Feng B, Jinkang Z, Zhen W, Jianxi L, Jiang C, Jian L, et al. The effect of pore size on tissue ingrowth and neovascularization in porous bioceramics of controlled architecture in vivo. Biomed Mater. 2011; 6: 015007.

[15] Sopyan I. Recent development on porous calcium phosphate ceramics for biomedical application. Med J Malaysia. 2008; 63: 14-15.

[16] Liu H, Lu J, Jiang Q, Haapasalo M, Qian J, Tay FR, Shen Y. Biomaterial scaffolds for clinical procedures in endodontic regeneration. Bioact Mater. 2022; 12: 257-277.

[17] Nowicka A, Miller-Burchacka M, Lichota D, Metlerska J, Gońda-Domin M. Tissue engineering application in regenerative endodontics. Pomeranian J. Life Sci. 2021; 67: 10–17.

[18] Lueckgen A, Garske DS, Ellinghaus A, Mooney DJ, Duda GN, Cipitria A. Enzymatically-degradable alginate hydrogels promote cell spreading and in vivo tissue infiltration. Biomaterials. 2019; 217: 119294.

[19] Dobie K, Smith G, Sloan A, Smith A. Effects of alginate hydrogels and TGF-β1 on human dental pulp repair in vitro. Connect Tissue Res. 2002; 43: 387-390.

[20] Zhang R, Xie L, Wu H, Yang T, Zhang Q, Tian Y, et al. Alginate/ laponite hydrogel microspheres co-encapsulating dental pulp stem cells and VEGF for endodontic regeneration. Acta Biomater. 2020; 113: 305-316.

[21] Alghofaily M, Almana A, Alrayes J, Lambarte R, Weir MD, Alsalleeh F. Chitosan-gelatin scaffolds loaded with different antibiotic formulations for regenerative endodontic procedures promote biocompatibility and antibacterial activity. J Funct Biomater. 2024; 15: 186.

[22] Wu S, Zhou Y, Yu Y, Zhou X, Du W, Wan M, et al. Evaluation of chitosan hydrogel for sustained delivery of VEGF for odontogenic differentiation of dental pulp stem cells. Stem Cells Int. 2019; 2019: 1515040.

[23] Chrepa V, Austah O, Diogenes A. Evaluation of a commercially available hyaluronic acid hydrogel (Restylane) as injectable scaffold for dental pulp regeneration: an in vitro evaluation. J Endod. 2017; 43: 257-262.

[24] Fu LH, Qi C, Ma MG, Wan P. Multifunctional cellulose-based hydrogels for biomedical applications. J Mater Chem B. 2019; 7: 1541-1562.

[25] Jain P, Lin RYT, Mishra K, Handral H, Dubey N. Three-dimensional eco-friendly bacterial nanocellulose (BNC) scaffold for regenerative dentistry: Characterization, cytocompatibility and differentiation potential. Dent Mater. 2024; 40: 151-157.

[26] Werkmeister JA, Ramshaw JA. Recombinant protein scaffolds for tissue engineering. Biomed Mater. 2012; 7: 012002.

[27] Jang JH, Moon JH, Kim SG, Kim SY. Pulp regeneration with hemostatic matrices as a scaffold in an immature tooth minipig model. Sci Rep. 2020; 10: 12536.

[28] Narayanam R, Cardoso LM, dos Reis-Prado AH, de Carvalho ABG, Anselmi C, Mahmoud AH, et al. Antimicrobial silk fibroin methacrylated scaffolds for regenerative endodontics. J Endod. 2024; 50: 1752-1760.

[29] Bavaresco B, Comín R, Salvatierra NA, Cid MP. Three-dimensional printing of collagen and hyaluronic acid scaffolds with dehydrothermal treatment crosslinking. Compos Commun. 2020; 19: 1-5.

[30] Ayala-Ham A, López-Gutierrez J, Bermúdez M, Aguilar-Medina M, Sarmiento-Sánchez JI, López-Camarillo C, et al. Hydrogel-based scaffolds in oral tissue engineering. Front Mater. 2021; 8: 708945.

[31] Koons GL, Diba M, Mikos AG. Materials design for bo-

ne-tissue engineering. Nat Rev Mater. 2020; 5: 584-603.

[32] Dorterler OC, Akgun B, Alper M, Ayhan F. Improving antimicrobial properties of GelMA biocomposite hydrogels for regenerative endodontic treatment. Polymers. 2024; 16: 1675.

[33] Huang L, Chen X, Yang X, Zhang Y, Qiu X. GelMA-based hydrogel biomaterial scaffold: a versatile platform for regenerative endodontics. J Biomed Mater Res B Appl Biomater. 2024; 112: e35412.

[34] Koutsopoulos S. Self-assembling peptide nanofiber hydrogels in tissue engineering and regenerative medicine: progress, design guidelines, and applications. J Biomed Mater Res A. 2016; 104: 1002-1016.

[35] Hughes CS, Postovit LM, Lajoie GA. Matrigel: a complex protein mixture required for optimal growth of cell culture. Proteomics. 2010; 10: 1886-1890.

[36] Kiaipour Z, Shafiee M, Ansari G. Role of platelet concentrates in dental-pulp regeneration: a systematic review of randomized clinical trials. J Dent. 2024; 25: 97.

[37] Diab NAF, Ibrahim ASM, Abdallah AM. Fluid platelet-rich fibrin (PRF) versus platelet-rich plasma (PRP) in the treatment of atrophic acne scars: a comparative study. Arch Dermatol Res. 2023; 315: 1249-1255.

[38] Le SH, Nguyen SH. The in vitro efficacy of advanced platelet-rich fibrin plus versus injectable platelet-rich fibrin on the proliferation, migration, and differentiation of stem cells from apical papilla. J Dent Sci. 2024; 19: 2203-2209.

[39] Elnawam H, Abdallah A, Nouh S, Khalil NM, Elbackly R. Influence of extracellular matrix scaffolds on histological outcomes of regenerative endodontics in experimental animal models: a systematic review. BMC Oral Health. 2024; 24: 511.

[40] Yazdanian M, Arefi AH, Alam M, Abbasi K, Tebyaniyan H, Tahmasebi E, et al. Decellularized and biological scaffolds in dental and craniofacial tissue engineering: A comprehensive overview. J Mater Res Technol. 2021; 15: 1217-1251.

[41] Shi Y, Wang Y, Shan Z, Gao Z. Decellularized rat submandibular gland as an alternative scaffold for dental pulp regeneration. Front Bioeng Biotechnol. 2023; 11: 1148532.

[42] Wen B, Huang Y, Qiu T, Huo F, Xie L, Liao L, et al. Reparative dentin formation by dentin matrix proteins and small extracellular vesicles. J Endod. 2021; 47: 253-262.

[43] Raddall G, Mello I, Leung BM. Biomaterials and scaffold design strategies for regenerative endodontic therapy. Front Bioeng Biotechnol. 2019; 7: 317.

[44] Vieira WA, Kitamura GH, de Almeida RF, de Almeida JFA, Gomes BP, Ferraz CCR, et al. Effect of EDTA activation on blood clot structure in regenerative endodontics: a scanning electron microscopy study. J Endod. 2024; 50(2): 173-180.

[45] Galler KM, Brandl FP, Kirchhof S, Widbiller M, Eidt A, Buchalla W, et al. Suitability of different natural and synthetic biomaterials for dental pulp tissue engineering. Tissue Eng Part A. 2018; 24: 234-244.

[46] Reddy MSB, Ponnamma D, Choudhary R, Sadasivuni KK. A comparative review of natural and synthetic biopolymer composite scaffolds. Polymers. 2021; 13: 1105.

[47] Komabayashi T, Wadajkar A, Santimano S, Ahn C, Zhu Q, Opperman LA, et al. Preliminary study of light-cured hydrogel for endodontic drug delivery vehicle. J Investig Clin Dent. 2016; 7: 87-92.

[48] Feng S, Liu J, Ramalingam M. 3D printing of stem cell responsive ionically-crosslinked polyethylene glycol diacrylate/alginate composite hydrogels loaded with basic fibroblast growth factor for dental pulp tissue engineering: A preclinical evaluation in animal model. J Biomater Tissue Eng. 2019; 9: 1635-1643.

[49] Basu A, Kunduru KR, Doppalapudi S, Domb AJ, Khan W. Poly (lactic acid) based hydrogels. Adv Drug Deliv Rev. 2016; 107: 192-205.

[50] El Ashiry EA, Alamoudi NM, El Ashiry MK, Bastawy HA, El Derwi DA, Atta HM. Tissue engineering of necrotic dental pulp of immature teeth with apical periodontitis in dogs: radiographic and histological evaluation. J Clin Pediatr Dent. 2018; 42: 373-382.

[51] Dissanayaka WL, Zhang C. Scaffold-based and scaffold-free strategies in dental pulp regeneration. J Endod. 2020; 46(9 Suppl): S81-S89.

[52] Abbass MM, El-Rashidy AA, Sadek KM, Moshy SE, Radwan IA, Rady D, et al. Hydrogels and dentin-pulp complex regeneration: from the benchtop to clinical translation. Polymers. 2020; 12: 2935.

[53] Baino F, Novajra G, Vitale-Brovarone C. Bioceramics and scaffolds: a winning combination for tissue engineering. Front Bioeng Biotechnol. 2015; 3: 202.

[54] Enteghad M, Zerafat M, Hadian S, Ghahramani Y. Novel modifications in endodontic bioceramics to

improve their properties: A narrative review. J Dent Shiraz Univ Med Sci. 2025; 26: 289-301.

[55] Khanna-Jain R, Mannerström B, Vuorinen A, Sándor GK, Suuronen R, Miettinen S. Osteogenic differentiation of human dental pulp stem cells on β-tricalcium phosphate/poly (L-lactic acid/caprolactone) three-dimensional scaffolds. J Tissue Eng. 2012; 3: 2041731412467998.

[56] Argueta-Figueroa L, Jurado CA, Torres-Rosas R, Bautista-Hernández MA, Alhotan A, Nurrohman H. Clinical efficacy of biomimetic bioactive biomaterials for dental pulp capping: A systematic review and meta-analysis. Biomimetics. 2022; 7: 211.

[57] Guerrero-Gironés J, Alcaina-Lorente A, Ortiz-Ruiz C, Ortiz-Ruiz E, Pecci-Lloret MP, Ortiz-Ruiz AJ, et al. Biocompatibility of a HA/β-TCP/C scaffold as a pulp-capping agent for vital pulp treatment: an in vivo study in rat molars. Int J Environ Res Public Health. 2021; 18: 3936.

[58] Akartasse N, Azzaoui K, Mejdoubi E, Elansari LL, Hammouti B, Siaj M, et al. Chitosan-hydroxyapatite bio-based composite in film form: synthesis and application in wastewater. Polymers. 2022; 14: 4265.

[59] Jafari N, Habashi MS, Hashemi A, Shirazi R, Tanideh N, Tamadon A. Application of bioactive glasses in various dental fields. Biomater Res. 2022; 26: 31.

[60] Deepika U, Sahoo PK, Dash JK, Baliarsingh RR, Ray P, Sharma G. Clinical evaluation of bioactive resin-modified glass ionomer and giomer in restoring primary molars: A randomized, parallel-group, and split-mouth controlled clinical study. J Indian Soc Pedod Prev Dent. 2022; 40: 288-296.

[61] Cui H, Webber MJ, Stupp SI. Self-assembly of peptide amphiphiles: From molecules to nanostructures to biomaterials. Biopolymers. 2010; 94: 1-18.

[62] Mu X, Shi L, Pan S, He L, Niu Y, Wang X. A customized self-assembling peptide hydrogel-wrapped stem cell factor targeting pulp regeneration rich in vascular-like structures. ACS Omega. 2020; 5: 16568-16574.

[63] Nguyen PK, Gao W, Patel SD, Siddiqui Z, Weiner S, Shimizu E, et al. Self-assembly of a dentinogenic peptide hydrogel. ACS Omega. 2018; 3: 5980-5987.

[64] Rizk HM, Al-Deen MSMS, Emam AA. Comparative evaluation of platelet rich plasma (PRP) versus platelet rich fibrin (PRF) scaffolds in regenerative endodontic treatment of immature necrotic permanent maxillary central incisors: A double blinded randomized controlled trial. Saudi Dent J. 2020; 32: 224-231.

[65] Mittal N, Baranwal HC, Kumar P, Gupta S. Assessment of pulp sensibility in the mature necrotic teeth using regenerative endodontic therapy with various scaffolds–Randomised clinical trial. Indian J Dent Res. 2021; 32: 216-220.

[66] Sultan SES, Alsharaan MA, Alzhrani AAR, Alruwaili MM, Kamel MM. Comparative analysis of regenerative endodontic procedures with different scaffold materials. J Pharm Bioallied Sci. 2025; 17(Suppl 2): S1246-S1248.

[67] Loroño G, Conde AJ, Estévez R, Brizuela C, Cisneros R, Alfayate RP. Regenerative endodontic procedure in an immature permanent incisor with internal root resorption: A case report. J Dent Shiraz Univ Med Sci. 2022; 23: 155-159.

[68] Yang F, Sheng K, Yu L, Wang J. Does the use of different scaffolds have an impact on the therapeutic efficacy of regenerative endodontic procedures? A systematic evaluation and meta-analysis. BMC Oral Health. 2024; 24: 319.

[69] Huang R, Chen W, Fang M, Peters OA, Hosseinpour S. Clinical and radiographic outcomes of autologous platelet-rich products in regenerative endodontics: A systematic review and meta-analysis. Dent J. 2025; 13: 236.

[70] Shi QL, Zhu X, Chen C, Chen JY, Lu DY, Shi Y, et al. Collagen scaffolds in regenerative endodontic procedures: Current evidence, limitations, and future perspectives. Polymers. 2026; 18: 894.

[71] Lin J, Zeng Q, Wei X, Zhao W, Cui M, Gu J, et al. Regenerative endodontics versus apexification in immature permanent teeth with apical periodontitis: a prospective randomized controlled study. J Endod. 2017; 43: 1821-1827.

[72] Arslan H, Ahmed HMA, Şahin Y, Yıldız ED, Gündoğdu EC, Güven Y, Khalilov R. Regenerative endodontic procedures in necrotic mature teeth with periapical radiolucencies: a preliminary randomized clinical study. J Endod. 2019; 45: 863-872.

[73] Estefan BS, El Batouty KM, Nagy MM, Diogenes A. Influence of age and apical diameter on the success of endodontic regeneration procedures. J Endod. 2016; 42: 1620-1625.

[74] Divya D, Naik SV, Raju O, Shivani B, Basappa N, Betur AP. Conceptual combination of disinfection in

regenerative endodontics: Conventional versus laser-assisted disinfection. J Conserv Dent Endod. 2021; 24: 252-259.

[75] Hu X, Wang Q, Ma C, Li Q, Zhao C, Xiang K. Is etiology a key factor for regenerative endodontic treatment outcomes? J Endod. 2023; 49(8): 953-962.

[76] Qamar S, Mondal A, Singh S, Deep A, Kakran A, Tanwar AS. Comparative evaluation of advanced platelet-rich fibrin and blood clot as scaffolds in regenerative endodontics for immature necrotic teeth: A randomized clinical study. J Pharm Bioallied Sci. 2025; 17(Suppl 2): S1559-S1561.

[77] Moussa DG, Aparicio C. Present and future of tissue engineering scaffolds for dentin-pulp complex regeneration. J Tissue Eng Regen Med. 2019; 13: 58-75.

[78] Ko HF, Sfeir C, Kumta PN. Novel synthesis strategies for natural polymer and composite biomaterials as potential scaffolds for tissue engineering. Philos Trans A Math Phys Eng Sci. 2010; 368: 1981-1997.

[79] Lee KY, Mooney DJ. Alginate: properties and biomedical applications. Prog Polym Sci. 2012; 37: 106-126.

[80] Bhoj M, Zhang C, Green DW. A first step in de novo synthesis of a living pulp tissue replacement using dental pulp MSCs and tissue growth factors, encapsulated within a bioinspired alginate hydrogel. J Endod. 2015; 41: 1100-1107.

[81] Ahmadi F, Oveisi Z, Samani SM, Amoozgar Z. Chitosan based hydrogels: characteristics and pharmaceutical applications. Res Pharm Sci. 2015; 10: 1-16.

[82] Moreira MS, Sarra G, Carvalho GL, Gonçalves F, Caballero-Flores HV, Pedroni ACF, et al. Physical and biological properties of a chitosan hydrogel scaffold associated to photobiomodulation therapy for dental pulp regeneration: An in vitro and in vivo study. Biomed Res Int. 2021; 2021: 6684667.

[83] Chircov C, Grumezescu AM, Bejenaru LE. Hyaluronic acid-based scaffolds for tissue engineering. Rom J Morphol Embryol. 2018; 59: 71-76.

[84] Batouty K, Nagy M, Mazen EA. Regeneration ability of immature teeth with necrotic pulp using hyaluronic acid a scaffold (clinical study). Ain Shams Dent J. 2021; 22: 22-27.

[85] Hickey RJ, Pelling AE. Cellulose biomaterials for tissue engineering. Front Bioeng Biotechnol. 2019; 7: 45.

[86] Collier JH, Segura T. Evolving the use of peptides as co-mponents of biomaterials. Biomaterials. 2011; 32: 4198-4204.

[87] Lee F, Kurisawa M. Formation and stability of interpenetrating polymer network hydrogels consisting of fibrin and hyaluronic acid for tissue engineering. Acta Biomater. 2013; 9: 5143-5152.

[88] Deptuch T, Dams-Kozlowska H. Silk materials functionalized via genetic engineering for biomedical applications. Materials (Basel). 2017; 10: 1417.

[89] Yang X, Han G, Pang X, Fan M. Chitosan/collagen scaffold containing bone morphogenetic protein-7 DNA supports dental pulp stem cell differentiation in vitro and in vivo. J Biomed Mater Res A. 2020; 108: 2519-2526.

[90] Ehrmann RL, Gey GO. The growth of cells on a transparent gel of reconstituted rat-tail collagen. J Natl Cancer Inst. 1956; 16: 1375-1403.

[91] Gelain F, Bottai D, Vescovi A, Zhang S. Designer self-assembling peptide nanofiber scaffolds for adult mouse neural stem cell 3-dimensional cultures. PLoS One. 2006; 1: e119.

[92] Bains VK, Mahendra J, Mittal M, Bedi M, Mahendra L. Technical considerations in obtaining platelet rich fibrin for clinical and periodontal research. J Oral Biol Craniofac Res. 2023; 13: 714-719.

[93] Ulusoy AT, Turedi I, Cimen M, Cehreli ZC. Evaluation of blood clot, platelet-rich plasma, platelet-rich fibrin, and platelet pellet as scaffolds in regenerative endodontic treatment: A prospective randomized trial. J Endod. 2019; 45: 560-566.

[94] Paduano F, Marrelli M, White LJ, Shakesheff KM, Tatullo M. Odontogenic differentiation of human dental pulp stem cells on hydrogel scaffolds derived from decellularized bone extracellular matrix and collagen type I. PLoS One. 2016; 11: e0148225.

[95] Nosrat A, Kolahdouzan A, Khatibi AH, Verma P, Jamshidi D, Nevins AJ, et al. Clinical, radiographic, and histologic outcome of regenerative endodontic treatment in human teeth using a novel collagen-hydroxyapatite scaffold. J Endod. 2019; 45: 136-143.

[96] Amini S, Salehi H, Setayeshmehr M, Ghorbani M. Natural and synthetic polymeric scaffolds used in peripheral nerve tissue engineering: Advantages and disadvantages. Polym Adv Technol. 2021; 32: 2267-2289.

[97] Generali M, Kehl D, Capulli AK, Parker KK, Hoerstrup SP, Weber B. Comparative analysis of poly-glycolic

acid-based hybrid polymer starter matrices for in vitro tissue engineering. Colloids Surf B Biointerfaces. 2017; 158: 203-212.

[98] Mir M, Ahmed N, Rehman AU. Recent applications of PLGA based nanostructures in drug delivery. Colloids Surf B Biointerfaces. 2017; 159: 217-231.

[99] Song JS, Takimoto K, Jeon M, Vadakekalam J, Ruparel NB, Diogenes A. Decellularized human dental pulp as a scaffold for regenerative endodontics. J Dent Res. 2017; 96: 640-646.

[100] Sudo Y, Nishida Y, Nakashima H, Arai T, Takatsu T. Clinical outcomes of a novel unidirectional porous β-tricalcium phosphate filling in distal radius fracture with volar locking plate fixation: Secondary publication of the Japanese version. Medicina (Basel). 2024; 60: 1.

[101] Rodríguez-Vázquez M, Ramos-Zúñiga R. Chitosan-hydroxyapatite scaffold for tissue engineering in experimental lumbar laminectomy and posterolateral spinal fusion in Wistar rats. Asian Spine J. 2020; 14: 139-147.

[102] Arandi NZ, Thabet M. Minimal intervention in dentistry: A literature review on Biodentine as a bioactive pulp capping material. Biomed Res Int. 2021; 2021: 5569313.

[103] Fujiwara S, Kumabe S, Iwai Y. Isolated rat dental pulp cell culture and transplantation with an alginate scaffold. Okajimas Folia Anat Jpn. 2006; 83: 15-24.

[104] Palma PJ, Ramos JC, Martins JB, Diogenes A, Figueiredo MH, Ferreira P, et al. Histologic evaluation of regenerative endodontic procedures with the use of chitosan scaffolds in immature dog teeth with apical periodontitis. J Endod. 2017; 43: 1279-1287.

[105] Reis-Prado AHD, Rahimnejad M, Dal-Fabbro R, Toledo PTA, Anselmi C, Oliveira PHC, et al. Injectable thermosensitive antibiotic-laden chitosan hydrogel for regenerative endodontics. Bioact Mater. 2025; 46: 406-422.

[106] Esguerra M, Fink H, Laschke MW, Jeppsson A, Delbro D, Gatenholm P, et al. Intravital fluorescent microscopic evaluation of bacterial cellulose as scaffold for vascular grafts. J Biomed Mater Res A. 2010; 93: 140-149.

[107] Park JY, Yang C, Jung IH, Lim HC, Lee JS, Jung UW, et al. Regeneration of rabbit calvarial defects using cells-implanted nano-hydroxyapatite coated silk scaffolds. Biomater Res. 2015; 19: 7.

[108] Prescott RS, Alsanea R, Fayad MI, Johnson BR, Wenckus CS, Hao J, et al. In vivo generation of dental pulp-like tissue by using dental pulp stem cells, a collagen scaffold, and dentin matrix protein 1 after subcutaneous transplantation in mice. J Endod. 2008; 34: 421-426.

[109] Ishimatsu H, Kitamura C, Morotomi T, Tabata Y, Nishihara T, Chen KK, Terashita M. Formation of dentinal bridge on surface of regenerated dental pulp in dentin defects by controlled release of fibroblast growth factor-2 from gelatin hydrogels. J Endod. 2009; 35: 858-865.

[110] Dissanayaka WL, Hargreaves KM, Jin L, Samaranayake LP, Zhang C. The interplay of dental pulp stem cells and endothelial cells in an injectable peptide hydrogel on angiogenesis and pulp regeneration in vivo. Tissue Eng Part A. 2015; 21: 550-563.

[111] Bezgin T, Yilmaz AD, Celik BN, Kolsuz ME, Sonmez H. Efficacy of platelet-rich plasma as a scaffold in regenerative endodontic treatment. J Endod. 2015; 41: 36-44.

[112] Lv H, Chen Y, Cai Z, Lei L, Zhang M, Zhou R, Huang X. The efficacy of platelet-rich fibrin as a scaffold in regenerative endodontic treatment: a retrospective controlled cohort study. BMC Oral Health. 2018; 18: 139.

[113] Bakhtiar H, Ashoori A, Rajabi S, Pezeshki-Modaress M, Ayati A, Mousavi MR, et al. Human amniotic membrane extracellular matrix scaffold for dental pulp regeneration in vitro and in vivo. Int Endod J. 2022; 55: 374-390.

[114] Yang N, Shen R, Yang W, Zhang S, Gong T, Liu Y. Biomimetic pulp scaffolds prepared from extracellular matrix derived from stem cells from human exfoliated deciduous teeth promote pulp-dentine complex regeneration. Int Endod J. 2024; 57: 1279-1292.

[115] Chang CC, Lin TA, Wu SY, Lin CP, Chang HH. Regeneration of tooth with allogenous, autoclaved treated dentin matrix with dental pulpal stem cells: An in vivo study. J Endod. 2020; 46: 1256-1264.

[116] Wang X, Li G, Liu Y, Yu W, Sun Q. Biocompatibility of biological material polylactic acid with stem cells from human exfoliated deciduous teeth. Biomed Rep. 2017; 6: 519-524.

[117] Mooney DJ, Powell C, Piana J, Rutherford B. Engineering dental pulp-like tissue in vitro. Biotechnol Prog. 1996; 12: 865-868.

[118] El-Backly RM, Massoud AG, El-Badry AM, Sherif RA, Marei MK. Regeneration of dentine/pulp-like tissue using a dental pulp stem cell/poly(lactic-co-glycolic) acid scaffold construct in New Zealand white rabbits. Aust

Endod J. 2008; 34: 52-67.

[119] AbdulQader ST, Kannan TP, Rahman IA, Ismail H, Mahmood Z. Effect of different calcium phosphate scaffold ratios on odontogenic differentiation of human dental pulp cells. Mater Sci Eng C Mater Biol Appl. 2015; 49: 225-233.

[120] Zhao Y, Zhang Q, Zhang S, Chen J, Kong L, Gao J, Zhu Q. Adrenomedullin-loaded gelatin methacryloyl hydrogel promotes endogenous dental pulp regeneration: An in vitro and in vivo study. J Endod. 2025; 51: 172-184.

[121] Dave AK, Cheung JY, Kim SG. Outcomes of regenerative endodontic therapy using dehydrated human-derived amnion-chorion membranes and collagen matrices: A retrospective analysis. Biomimetics. 2025; 10: 530.

[122] Han Y, Xu J, Chopra H, Zhang Z, Dubey N, Dissanayaka WL, et al. Injectable tissue-specific hydrogel system for pulp-dentin regeneration. J Dent Res. 2024; 103: 398-408.

[123] Matsumoto N, Minakami M, Hatakeyama J, Haruna C, Morotomi T, Izumi T, Anan H. Histologic evaluation of the effects of Emdogain gel on injured root apex in rats. J Endod. 2014; 40: 1989-1994.

[124] Naga MS, Helal HM, Kamoun EA, Moaty MA, Omar S, Ghareeb AZ, et al. A novel injectable boron doped-mesoporous nano bioactive glass loaded-alginate composite hydrogel as a pulpotomy filling biomaterial for dentin regeneration. BMC Oral Health. 2024; 24: 1087.

[125] Kumar KS, Kritika S, Karthikeyan NS, Sujatha V, Mahalaxmi S, Ravichandran C. Development of cobalt-incorporated chitosan scaffold for regenerative potential in human dental pulp stem cells: An in vitro study. Int J Biol Macromol. 2023; 253: 126574.

[126] Bordini EAF, Stuani VT, Correa LE, Cassiano FB, Lovison MF, Leite ML, et al. Chitosan-calcium aluminate as a cell-homing scaffold: Its bioactivity testing in a microphysiological dental pulp platform. Altern Lab Anim. 2024; 52: 107-116.

[127] Zawadzka-Knefel A, Rusak A, Mrozowska M, Machałowski T, Żak A, Haczkiewicz-Leśniak K, et al. Chitin scaffolds derived from the marine demosponge Aplysina fistularis stimulate the differentiation of dental pulp stem cells. Front Bioeng Biotechnol. 2023; 11: 1254506.

[128] AlHowaish NA, AlSudani DI, Khounganian R, Al-Muraikhi N. Histological evaluation of Restylane Lyft used as a scaffold for dental pulp regeneration in non-infected immature teeth in dogs. Materials (Basel). 2022; 15: 4095.

[129] Paymanpour P, Anselmi C, Cardoso LM, de Carvalho ABG, Soares IPM, Hebling J, et al. Anti-inflammatory potential of casein enzymatic hydrolysate/gelatin methacryloyl scaffolds for vital pulp therapy. Clin Oral Investig. 2024; 28: 476.

[130] Tan YY, Abdullah D, Abu Kasim NH, Yazid F, Mahamad Apandi NI, Ramanathan A, et al. Histological characterization of pulp regeneration using decellularized human dental pulp and mesenchymal stem cells in a feline model. Tissue Cell. 2024; 90: 102484.

[131] Jiménez NT, Carlos Munévar J, González JM, Infante C, Lara SJP. In vitro response of dental pulp stem cells in 3D scaffolds: A regenerative bone material. Heliyon. 2018; 4: e00775.

[132] Mousavi Nejad Z, Zamanian A, Saeidifar M, Vanaei HR, Salar Amoli M. 3D bioprinting of polycaprolactone-based scaffolds for pulp-dentin regeneration: Investigation of physicochemical and biological behavior. Polymers (Basel). 2021; 13: 4442

[133] Zheng L, Yang F, Shen H, Hu X, Mochizuki C, Sato M, et al. The effect of composition of calcium phosphate composite scaffolds on the formation of tooth tissue from human dental pulp stem cells. Biomaterials. 2011; 32: 7053-7059.

[134] Mendes Soares IP, Anselmi C, Kitagawa FA, Ribeiro RAO, Leite ML, de Souza Costa CA, Hebling J. Nano-hydroxyapatite-incorporated polycaprolactone nanofibrous scaffold as a dentin tissue engineering-based strategy for vital pulp therapy. Dent Mater. 2022; 38: 960-977.

[135] Huang G, Xu L, Wu J, Wang S, Dong Y. Gelatin/ bioactive glass composite scaffold for promoting the migration and odontogenic differentiation of bone marrow mesenchymal stem cells. Polym Test. 2021; 93: 106915.

[136] Tran ATL, Sukajintanakarn C, Senawongse P, Sritanaudomchai H, Ruangsawasdi N, Lapthanasupkul P, et al. Influence of lithium- and zinc-containing bioactive glasses on pulpal regeneration. Eur J Dent. 2023; 17: 1120-1128.