



RESEARCH ARTICLE

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RECENT ADVANCES IN BIOACTIVE DENTAL MATERIALS FOR PULP PRESERVATION AND HARD-TISSUE REGENERATION: A REVIEW

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Abstract

Bioactive materials in dentistry are not novel but what is fundamentally different to these materials as compared to conventional dental materials. One of the decisions when it comes to choosing the most appropriate restorative material for a case is knowing what bioactive dental materials are, how they work, and where and at which time to use them with opportunities for vital pulp therapy and regeneration of dental hard tissues. This review aims to summarize recent developments made on bioactive, biomimetic and next-generation dental materials, focusing on their biological mechanisms, regenerative potential, clinical implementation, and current limitations. Calcium silicate-based materials, especially mineral trioxide aggregate and Biodentine, have shown good biocompatibility, calcium-ion release, apatite formation and reparative dentin formation induction capacities, all of which allow them to be widely used in vital pulp therapy. Currently, great effort is focused on the emergence of biomimetic materials that are designed to mimic the physicochemical characteristics and mineralization behavior of natural enamel, dentin, and bone include nanohydroxyapatite, amorphous calcium phosphate, bioactive glasses, and functional peptides. Concurrently, next generation regenerative approaches utilizing injectable hydrogels, tissue specific extracellular matrix (ECM) derived scaffolds, progenitor cell homing, extracellular vesicles, exosomes, intelligent biomaterials and 3-dimensional bioprinting have opened new avenues for biologically-guided tissue regeneration. These include the technology that enables the biophysical and biochemical aspects of structural replacement and stimulating regulated modulation of inflammation, the recruitment of cells with appropriate phenotypic behavior, odontogenic differentiation, mineralization, vascularization and organization into tissue. The encouragement of experimental and clinical findings still bears major challenges, such as infection control, mechanical stability, degradation behavior, long-term biocompatibility, and lack of manufacturing standardization and long-term human clinical data.

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Therefore, current trends show a gradual transition from inert restorative materials towards multifunctional biological scaffolds that can assist tissue repair and regeneration. Further multidisciplinary investigations and appropriately designed clinical trials are needed to establish the long-term safety, predictability, and effectiveness of novel bioactive dental materials in everyday clinical practice.

Introduction:-

Conservative dentistry is a treatment approach to dentistry in which conservators of Restored tooth structure, is inherently a goal of desirable dentistry. Conservative dentistry in modern form strives to maintain the dental pulp and preserve as much of the structural integrity of the mineralized tissues of a tooth as possible. The dental pulp is a type of fibrous vascular and neural tissue contained within the space of the dentin and has functions of regulating dentin formation, immune surveillance, reparative responses and potentially homeostasis of the tooth (Yong & Cathro, 2021). Vital pulp treatment (VPT) is an important clinical approach to prevent devitalization of the tooth pulp under adverse clinical conditions, such as deep carious lesions. In summary, preservation of healthy pulp tissues subsequent to carious, traumatic or iatrogenic injury would result in an increase in the functional life of the tooth. Until now, surgical/invasive treatment strategies, especially conventional endodontic procedures, have been the gold standard for carious pulp tissue (deep caries lesions) and pulp exposure management (Alhusainy, 2024). More recently, the growing understanding of pulpal inflammation, tissue healing and dentin–pulp interactions has provided a path to a minimally invasive approach, including indirect pulp treatment, direct pulp capping, partial pulpotomy, and full pulpotomy. Current data demonstrate that vital pulp therapy (VPT) can yield successful outcomes in appropriately selected permanent teeth with advanced pulp inflammation when case selection, infection control, hemostasis, and coronal sealing are achieved (Asgary & Nosrat, 2025; Bafail, 2024).

Bioactive dental materials have been developed as a key material for vital pulp therapy. In comparison to conventional (bulk) materials which act as (passive) physical barriers, bioactive materials are those designed to ensure a biological response to the surrounding tissue and cells. They may act through calcium-ion release, alkalization, apatite formation, modulation of inflammatory responses, stimulation of odontogenic differentiation, and induction of dentin regeneration (Desai et al., 2025). As a result, materials derived from calcium silicates, particularly mineral trioxide aggregate (MTA), and Biodentine, have exploited the essential components of these current pulp-preserving methods. They have received attention in pulp capping, pulpotomy, perforation repair and apexification and regenerative endodontic treatments due to their biocompatibility and ability to induce the formation of mineralized tissues (Wang et al., 2023; Küçükkaya Eren, 2023).

The regenerative endodontic treatment is a challenge since they induce the formation of a dentin bridge on the dentin surface. The dentin–pulp microenvironment can be modified by the composition and properties of the bioactive cements that are used to facilitate the endogenous repair. Previous systematic evidence also indicated that MTA and Biodentine resulted in superior dentin bridge and reparative dentin formation following direct pulp capping, however, comparison direct between materials is hindered by variation in study design and outcome assessment (Nie et al., 2021). Hydraulic calcium silicate materials were further substantiated with new clinical evidence. In a 2024 update of the systematic review and meta-analysis of comparable odontogenic and periapical injuries in 40 randomized controlled trials (RCTs) involving either primary teeth with entirely formed root apices up to the maturity stages or permanent teeth, there was desirable clinical, radiographic and histological outcomes following calcium silicate-based cements placement (however cautioned against broad generalizations from high quality studies). While no activity of a single modern material was shown as definitively superior, MTA and Biodentine remained among the most researched and clinically proven materials available (Xavier et al., 2024). Similar observation were made between success rates of direct pulp capping with MTA and Biodentine as seen in a 2024 systematic review and meta-analysis of randomized clinical trials which showed that overall, the success rate was 85–95% when mineral trioxide aggregate (MTA) or Biodentine (BD) is utilized, including significantly enhanced efficacy for MTA over calcium hydroxide but no statistically significant difference between MTA vs Biodentine (Pinto et al., 2024).

More recently, the definition of bioactivity has been extended to include non-conventional calcium silicate cements. Biomimetic materials, injectable hydrogels, nanostructured scaffolds, growth-factor delivery systems, cell-homing approaches, and materials that modulate inflammation and support pulp–dentin complex regeneration are the subjects of much current investigation. These strategies not only aim to conserve remaining pulp tissue but also to recapitulate elements of the biological microenvironment essential for organized tissue regeneration (Spagnuolo, 2022). Current Advances and Future Directions Recent reviews (2024 & 2025) have highlighted the expanding role of scaffolds, bioactive molecules, stem and progenitor cells, exosomes, and immunomodulatory strategies in propelling pulp regeneration. These strategies focus on simulating the highly sophisticated biological

microenvironment necessary for dentin formation and restoration of functional pulp including cellular recruitment, differentiation, and vascularization(Liu et al., 2024; Wang et al., 2025).

One of the other major areas of growth is sophisticated material systems are being created to release therapeutic components in a timed [controlled] manner. For instance, injectable hydrogels are being investigated as versatile carriers for biopulp therapy since their physicochemical properties may allow for gentle deposition, while concurrently enabling targeted cellular activity and tissue repair (Lee et al, 2025). Recent patent literature also points to the utility of materials functionalized with growth factors, peptides, extracellular vesicles, and other bioactive molecules capable of dental genesis and regeneration. focusing on infection control, material stability, mechanical performance, cytocompatibility, vascularization, reproducibility, regulatory issues and scarcity of long-term human clinical evidence(Islam et al., 2025A).

Thus, the modern development of bioactive dental materials can be seen as a pass from passive tissue protection to biologically guided preservation and regeneration. When evaluating their current clinical relevance and future potential, it is also necessary to comprehend the process of conversion from calcium hydroxide and classical restorative materials to hydraulic calcium silicate cements as well as the recent biomimetic, nanoengineered, and tissue-engineering platforms (Ibarretxe, 2022). Thus, this review discusses recent innovations of bioactive dental materials for pulp preservation and hard-tissue regeneration while emphasizing on biological mechanisms of action, material properties, regenerative capability, clinical evidence, limitations and future perspectives of emerging biomaterials that may change the landscape of minimally invasive and regenerative dentistry.

Methodology:-

The search was performed directly in PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar, focusing primarily on literature from 2015 to 2026 and including earlier landmark studies where relevant. Keywords included bioactive dental materials; vital pulp therapy; calcium silicate; MTA; Biodentine; biomimetic materials; hydroxyapatite; bioactive glass; hydrogels; exosomes; dentin regeneration; hard-tissue regeneration Inclusion criteria entailed peer-reviewed publications in English, significant to pulp preservation, bioactivity, or dental hard-tissue regeneration, whilst study designs unrelated, non-peer-reviewed, duplicates and insufficiently relevant publications were not included.

Bioactive Dental Materials for Pulp Therapy:-

The vital pulp therapy (VPT) has notably shifted from a treatment primarily oriented toward alleviating symptoms to a biologically based strategy for preserving the health and function of the dental pulp. The main goal of VPT is to keep the tooth structure (or inflamed pulp tissues) viable or reversibly inflamed after carious exposure, trauma, or operative treatment and to preserve the entire pulp from unnecessary removal (Duncan, 2022). Modern VPT includes indirect pulp treatment, direct pulp capping, partial pulpotomy, or complete pulpotomy, depending on the type of pulp exposure, pulpal condition, bleeding management, and the possibility of a proper coronal seal. The growing understanding of the reparative potential of the dentin–pulp complex has, therefore, augmented interest in materials that can actively interact with the affected pulp rather than just providing a passive physical barrier against bacteria (Qiao et al., 2025).

Bioactivity may be an important advancement over traditional pulp-capping materials. Bioactive material is a substance that has the ability to interact with adjacent biological tissues resulting in positive physicochemical or cellular response (Islam et al., 2025B). In VPT, calcium-ion release, alkaline pH generation, apatite deposition, modulation of inflammatory pathways, odontogenic differentiation, and dentin regeneration are all possible interactions. These properties hold special significance because microbe-free pulp preservation necessitates a highly regulated biological response in contrast with unsophisticated inflammatory suppression (Hanna et al., 2020). Recent evidence has pointed that a mild or moderate inflammatory response is required to mediate pulp repair, while excess or prolonged inflammation is detrimental and leads to tissue destruction. Consequently, bioactive materials can probably modulate the relationship among inflammation and regeneration to not only laying a healthy and consistent foundation for pulp organic healing (Qiao et al., 2025)

Particularly, mineral trioxide aggregate (MTA) is one of the most significant advances in bioactive dental materials. The mineral trioxide aggregate (MTA) is a hydrophilic, biocompatible endodontic cement that has the property of healing and osteogenesis induction. It is a powder containing fine trioxides (tricalcium oxide, silicon oxide, bismuth oxide), hydrophilic particles (tricalcium silicate and tricalcium aluminate in charge for the chemical and physical properties of this aggregate) that hardens when it combines with humidity. This property leads to the formation of calcium phosphate–rich deposits at the material–tissue interface and promotes hard–tissue deposition. MTA has

shown good biocompatibility and biological activity and has already been utilized for direct pulp capping and partial or complete pulpotomy (Cervino et al., 2020). However, it has limitations such as longer setting time, difficulties in handling, relatively high cost and tooth discoloration associated with some formulations, which has stimulated the development of alternative hydraulic calcium silicate materials (Parirokh et al., 2018).

Biodentine and other new generation calcium silicate-based cements were introduced to solve some of the practical drawbacks of conventional MTA, whilst retaining its biological benefits. Tricalcium silicate is the main active ingredient in Biodentine; this material has been shown to account for the release of calcium ions, mediate alkaline activity, and promote mineralized tissue formation. Through clinical investigations, its application in the VPT, especially in the procedures of pulpotomy and direct pulp-capping, has been supported with increasing evidence (Kaur et al., 2017). A systematic review and meta-analysis from 2024 investigated the latest evidence on calcium silicate-based cements in vital pulp therapy and found the materials to be clinically, radiographically and histologically favorable in both primary and permanent teeth, thus cementing their continued clinical relevance (Xavier et al., 2024).

In recent years, clinical evidence regarding bioactive materials has grown stronger. Silva et al. (2023), in their systematic review and meta-analysis of randomized clinical trials, found an overall mean success rate of about 92% after one year for pulpotomy in permanent teeth. It was shown that ProRoot MTA performed significantly better than calcium hydroxide, but there were no significant differences between MTA and either Biodentine or calcium-enriched mixture. However, the overall certainty of evidence was low and the authors concluded that well designed clinical trials with longer follow up are warranted. These results are consistent with the increasing body of evidence supporting bioactive materials but also highlight our tendency to overinterpret short-term clinical success as definitive proof of long-term therapeutic advantage (Pinto et al., 2024).

Komora et al. (2024) provided additional data in support of that, a systematic review and network meta-analysis of randomized controlled trials of permanent mature teeth was carried out. Calcium hydroxide was significantly higher in failure compared to MTA 6, 12, and 24 months. Conversely, the survival of Biodentine and Total Fill was not significantly different to MTA at any time point assessed. The results of these studies indicate that newer generation calcium silicate-based biomaterials may achieve clinical outcomes comparable to mineral trioxide aggregate but exhibit different handling characteristics and working properties in the clinic which may present practical advantages (Katge & Patil, 2017).

There have been increasing lines of evidence for direct pulp capping use. For example, Pinto et al. (2024) systematically evaluated randomized clinical trials on bioactive materials for direct pulp capping of permanent teeth. The results of their assessment do substantiate the clinical efficacy of bioactive materials for pulp vitality preservation but ultimately clinical outcomes are influenced by factors related to case selection, the extent of pulpal inflammation, operative contamination, hemorrhage control, and the quality of the final coronal restoration. Material selection should therefore not be seen in isolation from biological and clinical conditions related to VPT (Pinto et al., 2024).

However, recent developments have indicated the necessity for bioactive materials to modulate the pulp microenvironment, rather than merely inducing mineral deposition. Therefore, current studies have been focused on using materials endowed with bioactive ions, nanoparticles, anti-inflammatory agents, and other biological modifiers. These strategies aim to manage uncontrolled inflammation whilst preserving the signaling pathways that are pivotal to dentin regeneration (Soares et al., 2026). Qiao et al. (2025) highlighted that more than ever is the interaction of bioactive materials and inflammatory signaling being seen as a key pathway in pulp repair. It reflects a paradigm shift from the classical idea of merely “protecting” the pulp to the biological modulation of the healing response.

These concepts can be expanded by implementing the next generation of VPT materials such as injectable hydrogels, controlled nanostructured systems, proteins from the extracellular matrix, and biomimetic scaffolds. Collagen, chitosan, hyaluronic acid, gelatin methacryloyl, decellularized extracellular matrix, and self-assembling peptide-based injectable hydrogels exhibited the potential to support cell viability, inhibit inflammation, promote reparative dentin formation, and bioactive molecules delivery (Rajasekar et al., 2025). They are also injectable and thus can adapt to irregularities in pulp canal and can be applied by minimally invasive manner. Nonetheless, a sizable portion of the evidence that supports these new systems does not yet reach beyond preclinical stage and still many questions regarding longevity, mechanical integrity, vascularization, prevention of infection and reproducibility in clinical practice remain unanswered (Islam et al., 2025B).

Recent experimental work provides a glimpse of the path this field is taking. Zhang et al. (2025A) developed a thermosensitive injectable hydrogel containing antioxidative and anti-inflammatory nanoparticles for VPT of pulpitis. Instead of having a singular material property to address one biological need, these multifunctional systems would target multiple biological processes at once, such as oxidative stress, inflammation, and wound healing. Despite these approaches primarily being experimental, this illustrates the transition towards multifunctional biomaterials able to actively alter the pulp microenvironment (Zhang et al., 2025A).

Emerging Biomimetic Materials for Hard-Tissue Regeneration:-

The need for regeneration of dental hard tissues, together with the intrinsic composition and well-organized structure of enamel, dentin, cementum and alveolar bone (hard tissues which cannot be mimicked by conventional restorative materials) has prompted a large number of studies in modern restorative and regenerative dentistry. Traditional restorations replace the defect with synthetic substitutes (e.g. composite or glass ionomer) to restore anatomical shape and function, but fail to replicate biological and hierarchical architecture (Olaru et al., 2021). Conversely, biomimetic materials are engineered to mimic specific aspects of natural mineralized tissues such as their chemical composition, nanoscale structure, mineralization processes and biological host tissue interactions. As a result, it has further promoted the development of calcium phosphate system, nanohydroxyapatite, bioactive glass, biomimetic peptide, polymer-mineral composites, as well as bioinspired scaffold systems for enamel, dentin and bone regeneration (Wang et al., 2024).

Hydroxyapatite-based materials are one of the major methods of biomimetic hard-tissue regeneration. Chemically, hydroxyapatite $[\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2]$ is similar to the inorganic mineral phase of both enamel and dentin, thus providing an appealing backbone for dental remineralization (Florea et al., 2023). Nanohydroxyapatite is of particular interest, as its small particles size and a relatively high surface area may help it interact with partially demineralized tooth surfaces. These properties enable calcium and phosphate ions to engage in the nucleation of new apatite precipitates, and likely contribute to the remineralization of mineral density in early enamel and dentin lesions (Pushpalatha et al., 2023). Hydroxyapatite-based scaffolds are also widely studied for bone regeneration, due to their similarity the composition of natural bone mineral phase, offering an osteoconductive microenvironment for newly formed tissue (Fendi et al., 2024).

It seems that most of the recent biomimetic approaches refer to amorphous calcium phosphate (ACP) as the intermediate mineral phase. In contrast, highly crystalline hydroxyapatite is a stable, and as a result, less soluble form CP is a transient state of mineralization, which can act as an lectent solubility reservoir of calcium and phosphate ions that eventually convert into more stable apatite phases. This property is of importance in regard to dentin remineralization because it allows for the mineralization to be directed towards a preexisting collagen matrix and an incompletely demineralized structure (Liu et al., 2026). Yang et al. (2024) also recently reviewed Advances of ACP-based biomimetic remineralization and highlighted that most importantly, stabilization of ACP is necessary to enhance its residence time and enable controlled mineral formation. Based on this information, with respect to natural biomineralization, stabilizers and functional polymers may modulate various steps such as nucleation, crystal growth, and mineral deposition, rendering opportunities to mimic situations that may occur during the natural process of biomineralization.

Biomimetic peptides are another key area of development. Formation of both natural enamel and dentin is influenced by a variety of protein and peptide domains (interspersed within the extracellular matrix) that govern both mineral nucleation and crystal arrangement. Some of these biological functions can be mimicked with synthetic peptides; indeed, synthetic peptide chains have the benefits of improved chemical stability and that their molecular design can be controlled with precision. Recent studies have shown that functional peptides bind the dentin surfaces and thus act as calcium phosphate deposits nucleation site (Yucesoy et al., 2023). Fan et al. (2024), for instance, studied a dual-affinity peptide that is able to bind with both collagenous and non-collagenous materials in dentin. These types of materials not only move beyond just supplying in situ mineral ions, but also begin to dictate the location and context of mineral deposition.

Another prominent category of biomimetic biomaterials is bioactive glass, which has been extensively used in both dental hard-tissue restoration and bone regeneration. When stimulated by physiological fluids, bioactive glasses react to release biologically active ions that alter the local chemical environment and promote a hydroxycarbonate apatite layer formation on the material surface. This apatite layer has the ability to form a physicochemical interface between the material and the mineralized tissues (Skallevold et al., 2019). More importantly, the biological activity of bioactive glass can be tuned according to composition and therapeutic ions. A novelty of recent studies is also

represented by ion-doped glasses containing ions that could mediate osteogenic, angiogenic, antibacterial or immunomodulatory functions (Piatti et al., 2024).

Bioactive glasses have been studied for enamel remineralization, dentin repair, desensitization, bone regeneration, and restorative compositions in dentistry. This is because they release calcium and phosphate ions and promote apatite formation (Jafari et al., 2022). The emergence of bioactive-glass nanocomposites that achieve mineralization, antibacterial, and mechanical functions necessitated a recent critical review. Nevertheless, the review highlighted concerns regarding particle distribution, mechanical properties, degradation behavior, ion-release kinetics, and long-term clinical viability (Meskher et al., 2024).

This recent evidence has stimulated an interest in the development of multicomponent and nanoscale biomimetic systems. Instead of single mineral phases, current materials can integrate nanohydroxyapatite, calcium phosphate, bioactive glass, polymers and functional nanoparticles to simultaneously mimic multiple properties of natural hard tissues (Pitic et al., 2026). For example, Basam et al. (2024) designed magnet-assisted magnetized nanoparticle-added nanohydroxyapatite with calcium and phosphate ion clusters for remineralization of enamel and dentin. This type of development demonstrates the trend towards materials that can serve as both mineral sources and as controlled nucleation environments.

Another emerging direction is the incorporation of surface-reactive restorative materials. Surface pre-reacted glass-ionomer (S-PRG) fillers gradually release several ions (fluoride, strontium, sodium and still other components) which may affect the environment of mineralization surrounding dental tissues. A systematic review with meta-analysis published by Dimopoulou and Baysan (2024) albeit under a wide variety of formulations/compositions/applied methods—found some consistent dental hard tissue responses to topical applications containing S-PRG fillers but awaited more successful clinical verification. Likewise, modified glass-ionomer systems including hydroxyapatite are under investigations in order to improve bioactivity with maintaining the advantages of glass-ionomer restoratives (Zhang et al., 2025C).

A major benefit of these biomimetic materials is their ability to incorporate regeneration, the capacity to resist infection and the biocompatibility of the resulting material into a single system. Some examples of bioactive glass exhibit bactericidal effects besides mineralization and support for tissue regeneration (Zhang et al., 2025B). In recent studies, its integration with polymer composites, three-dimensional printed scaffolds, and other advanced architectures have been reported, which widens the applicability of bioactive glasses, beyond simply particulate or cement forms. These are particularly pertinent to oral tissues, as successful regeneration must take place within a biologically complex milieu defined by saliva, microorganisms, mechanical loading, and constant, dynamic pH changes (Zhu et al., 2025).

However, the clinical translation of biomimetic materials remains such a challenge. Numerous potentially valuable materials have had positive results in laboratory or animal studies, but evidence from long-term randomized clinical studies is still relatively scarce (Zhang et al., 2026). Key issues include obtaining sufficient mechanical strength, managing the degradation and release of ions, mimicking the hierarchical architecture of natural tissues, resisting degradation in the oral environment, and assuring predictable integration with both existing enamel, dentin or bone (table 1). An example consists of bioactive-glass nanocomposites which still require overcoming factors regarding formulation optimization, mechanical performance and reproducibility (Meskher et al., 2024).

Table 1. Comparative summary of major bioactive dental materials

Material	Main applications	Advantages	Limitations
MTA	Pulp capping; pulpotomy; perforation repair; apexification	Biocompatible; calcium release; apatite formation; promotes reparative dentin	Long setting time; difficult handling; costly; possible discoloration
Biodentine	Pulp capping; pulpotomy; dentin repair	Biocompatible; calcium release; good mineralization; easier handling	Limited long-term evidence; outcomes depend on clinical conditions
Other calcium-silicate cements	VPT; pulp capping; endodontic repair	Bioactive; promotes mineralization; favorable clinical outcomes	Limited long-term evidence; formulation-dependent properties
Nanohydroxyapatite	Enamel/dentin remineralization; bone	Biomimetic; high surface area; supports mineral	Limited structural biomimicry; clinical

	regeneration	deposition	evidence still developing
Amorphous calcium phosphate	Enamel/dentin remineralization	Calcium/phosphate reservoir; promotes apatite formation	Unstable; requires stabilization for controlled mineralization
Bioactive glass	Remineralization; dentin repair; desensitization; bone regeneration	Ion release; apatite formation; antibacterial potential	Variable degradation and ion release; mechanical and clinical limitations
Functional peptides	Dentin/enamel remineralization; mineral nucleation	Biomimetic; targeted mineral deposition; precise molecular design	Mainly experimental; stability and clinical translation remain uncertain
S-PRG materials	Remineralization; preventive/restorative dentistry	Releases fluoride, strontium and other ions	Variable formulations; limited clinical evidence
Injectable hydrogels	Pulp regeneration; pulp–dentin regeneration; drug delivery	Injectable; ECM-like; supports cells; controlled delivery	Mostly preclinical; mechanical and long-term stability concerns
ECM-derived scaffolds	Tissue-specific pulp–dentin regeneration	Tissue-specific signals; supports cell attachment and differentiation	Complex preparation; limited clinical evidence
Cell-homing materials	Pulp and dentin regeneration	Recruits endogenous progenitor cells; avoids cell transplantation	Unpredictable response; mainly experimental
Exosomes/EVs	Pulp–dentin and bone regeneration	Cell-free signaling; promotes differentiation and angiogenesis	Isolation, dosing and storage challenges; limited clinical evidence
3D-bioprinted constructs	Pulp–dentin regeneration; tissue engineering	Controlled architecture; customizable; integrates cells and biomaterials	Technically complex; mainly preclinical
Smart biomaterials	Controlled delivery; infection control; regeneration	Stimuli-responsive; localized therapeutic release; multifunctional	Early-stage; safety, reproducibility and regulatory challenges

Next-Generation Materials and Regenerative Strategies

Next-generation dental biomaterial research is increasingly becoming focused on moving regenerative dentistry away from tissue replacement with a biologically orchestrated tissue repair and regeneration approach. In contrast to earlier bioactive materials that focused on a protective or inductive mineralizing environment, current regenerative strategies aim to reproduce the complex, precisely ordered environment necessary for true tissue formation. This strategy combines biomaterials with stem or progenitor cells, extracellular-matrix signals, growth factors, extracellular vesicles, and regulated biochemical cues. The end goal is, therefore, not only to maintain the remaining dental tissue but to mimic the normal biological functions of the dentin–pulp complex (Umapathy et al., 2025). A series of recent reviews highlight that effective regeneration relies on synergistic interactions among cells, both scaffolds and signaling molecules, vascularization, innervation, as well as host immune reactions (Li et al., 2024; Wang et al., 2024).

Among these approaches, injectable hydrogels serve as one of the most promising platforms. They can be easily processed into three-dimensional polymeric networks that can approximate some features of the extracellular matrix and could be combined with cells, growth factors, nanoparticles, drugs and other bioactive agents. The injectable property of these materials is an advantage for its use especially in endodontics, as the material can be injected into irregular anatomical spaces and, after it sets, provides a stable scaffold in situ (Fahimirad et al., 2026). Currently collagen, gelatin, chitosan, hyaluronic acid, fibrin, polyethylene glycol, and decellularized ECM-based hydrogels have been investigated. Some of these systems are able to support the structure, promote cells to migrate and proliferate, induce odontogenic differentiation, and release therapeutic agents in controlled manner (Guo et al., 2024).

A crucial magnet of progress is the provision of tissue-specific and ECM-derived hydrogels. In contrast to synthetic scaffolds, decellularized dental tissues maintain biochemical components and structural signals from their native

microenvironments (Barajaa et al., 2025). Liang et al. (2024) showed decellularized dental pulp matrix hydrogels as promising and multifunctional, tissue-specific biomaterials suitable for endodontic regeneration (for dentist bioengineered dentin/ pulp complex for restoration). These materials can more closely simulate the in vivo environment which is more supportive of cell attachment, migration, and differentiation, and facilitate appropriate tissue organization. The potency to integrate native extracellular-matrix components may thus be a means of augmenting one of the major drawbacks of conventional synthetic scaffolds, specifically the failure to replicate the biochemical complexity of the native pulp environment.

Another new strategy consists of homing cells, rather than the direct transplantation of exogenous stem cells. In contrast, dental pulp contains resident progenitor populations that can respond to injury, and there is a possibility of developing biomaterials that recruit these endogenous cells to the site of an injury. Such strategies have been demonstrated to address most of the limitations associated with cell transplantation including poor cell viability, low engraftment capacity, immunological protection and difficulties in cell handling (Kim et al., 2013). Li et al. (2024) identified cell homing as a key aspect of modern pulp-regeneration strategies, especially when coupled with scaffolds and controlled signaling molecule delivery.

Another milestone in regenerative dentistry is the study of the role of extracellular vesicles and exosomes. These nanoscale vesicles can carry proteins, lipids, messenger RNA, microRNA, and other signaling molecules that may alter the behavior of recipient cells. Exosomes have generated a lot of interest as potential “cell-free” regenerative therapies because they can mimic some of the paracrine effects of stem cells without needing to transplant live cells (Ahmad et al., 2026). Li et al. (2024) reported that all the experimental studies are included in this review, revealing the ability of dental pulp stem cells (DPSCs)-derived exosomes to regulate odontogenic differentiation, migration, angiogenesis, and tissue repair. They also reported that exosome-mediated signaling activates pathways related to odontogenic differentiation and that these exosomes promote pulp-like tissue formation in experimental models. Recent experimental results gave an additional boost to interest in exosome-related strategies. Wang et al. (2024) reported in vivo pulpal and dentin regeneration guided by designed odontogenic exosomes that mimic the embryonic microenvironment. The implications of these findings are particularly significant because they imply that in the near-future, regenerative biomaterials may serve as active generators of developmental signals, rather than merely a rudimentary physical scaffold. However, most of these results still remain in the preclinical setting and further issues with respect to methods to isolate and purify exosomes, standardization of exosomal dose, duration of storage, biological heterogeneity and controlled delivery need to be tackled before their practical clinical usage (Cao & Ding, 2022).

Exosomes combined with biomaterial scaffolds is probably a very auspicious route. Zhang et al. (2024) created titanium scaffolds covered with exosomes from dental pulp stem cells with potential for cell-free bone regeneration. While the scaffold formed the structural support, the exosomes provided biological cues that also modulate cellular behavior. Approaches based on such principles are being explored for the regeneration of dental pulp and dentin, with the controlled release from hydrogels or mineralized scaffolds in order to prolong the biological activity of extracellular vehicles (EVs) by increasing the bioavailability and enhancing the localization of EVs at the target site. One means to achieving this is three-dimensional bioprinting. Such traditional matrices may have a reduced capability to mirror the complex spatial architecture of dental tissues. Three-dimensional bioprinting has the capability to deposit cells and biomaterials in designed spatial distributions that have the potential to facilitate the generation of patient-specific constructs with defined porosity and organization. Hydrogels act as bioinks, combined with cells, growth factors, nanoparticles, or even extracellular vesicles embedded into specific areas of the construct (Mohd et al., 2022). Despite most recent studies being preclinical, 3D bioprinting is emerging as an important technology for bio-fabrication of biomimetic pulp–dentin structures. Guo et al. (2024) observed that the focus of this study was on the combination of 3D printing and hydrogel-based scaffolds for pulp regeneration, as it was noted in. Recent work has also showcased the power of advanced injectable biomimetic systems to incorporate multiple regenerative functions into a single material. Han et al. (2024) explored an injectable hydrogel system to promote pulp–dentin regeneration, providing an example of how biomaterials can be tailored to their specific tissue type while still maximizing regenerative properties. In the same way, bioinspired dentin extracellular-matrix–chitosan hydrogels recently developed into injectable scaffolds exhibited odontogenic potential and tissue-specific microstructural features. This trend points towards multifunctional materials able to provide mechanical support, biological signaling, antimicrobial activity, and controlled molecular delivery (Osman et al., 2025).

The second emerging strategy undertenants smart responsive biorational systems that are able to adapt to local microenvironmental condition. Designing these materials to be responsive to external stimuli such as pH, temperature, enzymatic activity, inflammation or oxidative stress can facilitate the selective and on-demand release

of therapeutic molecules at the site of action (Mohammadzadeh et al., 2026). This paradigm is particularly pertinent to endodontic applications as a periapical regenerative environment may be a niche environment where microorganisms, inflammatory mediators, and reactive oxygen species (ROS) may naturally exist and threaten cell survival. To combat the infection and regeneration simultaneously, functional hydrogels containing antibacterial or anti-inflammatory components are therefore being explored (Li et al., 2024).

However, there are still multiple challenges preventing the clinical translation of these rapidly advancing technologies. Functional pulp–dentin complex regeneration necessitates the generation of mineralized tissue along with establishing appropriate vascularization, sensory innervation, immune regulation, odontoblast-like cell organization, and integration with surrounding dentin (Jung et al., 2019). Moreover, biomaterials should maintain their stability in the biologically and mechanically adverse oral environment. Nevertheless, standardization tags for the biomaterial composition, sterilization method, manufacturing method, source of cells, preparatory method of exosomes and outcome measurement still needed to novel exosome-based tissue engineering applications (TKAs). As a result, while these systems are promising in preclinical studies, human studies over time are needed to determine whether such complex regenerative systems offer safe and predictable clinical outcomes (Li et al., 2024; Wang et al., 2024).

Conclusion:-

New, bioactive dental materials have been developed that can preserve pulp vitality and regenerate damaged dental hard tissues. Calcium silicate (CS)-based materials, in particular mineral trioxide aggregate (MTA) and Biodentine, currently hold the best biological and clinical evidence for vital pulp therapy. Among the types of innovative biomimetic materials studied are hydroxyapatite, calcium phosphate systems, bioactive glasses and functional peptides which promote biomimetic mineralization and hard-tissue repair. Regeneration may even be more successful when you learn to fill the gaps using injectable hydrogels, extracellular matrix–derived scaffolds, exosomes, smart materials, 3-dimensional bioprinting and next-generation approaches. However, translation of the growing number and sophistication of emerging technologies to routine clinical dental practice continues to be limited by long-term clinical evidence, stability in materials, biological complexity and reproducibility. This could then be achieved via future studies that combine rationally designed biomaterials with a specific biological signal or regenerative process actively regulating the microenvironment for predictable, reliable and clinically translatable pulp and hard-tissue regeneration.

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