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Synthetic Biomaterials in Vital Pulp Therapy: A Narrative Review of Conventional and Emerging Approaches

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ABSTRACT

Preservation of pulp vitality is a cornerstone of conservative dentistry and endodontics. The success of vital pulp therapy (VPT) depends heavily on the biomaterials employed, which must provide antimicrobial protection, biocompatibility, sealing ability, and stimulation of reparative dentinogenesis. Calcium hydroxide was historically regarded as the gold standard, but its high solubility, poor sealing, and porous dentin bridge formation limit its long-term success. Mineral trioxide aggregate (MTA) revolutionized VPT by offering superior sealing and bioactivity, though its high cost, difficult handling, and risk of tooth discoloration restrict widespread use. Newer calcium silicate-based materials such as Biodentine and TheraCal LC were developed to overcome these drawbacks, combining improved handling with bioactive potential. In parallel, emerging synthetic biomaterials such as bioactive glasses, enamel matrix derivatives, and dentin matrix hydrogels have demonstrated the ability to stimulate true pulp regeneration through biomimetic mechanisms.

This narrative review consolidates current evidence on conventional and emerging synthetic biomaterials in VPT. Comparative insights highlight their strengths, limitations, and translational challenges. While synthetic agents have advanced clinical outcomes, further innovation and validation are required to achieve predictable pulp preservation and regeneration.

Keywords: *Vital pulp therapy, Calcium hydroxide, Mineral trioxide aggregate, Biodentine, TheraCal LC, Bioactive glass, Bioceramics, Synthetic biomaterials*

1. INTRODUCTION

Preserving the vitality of the dental pulp remains a central goal in conservative dentistry and endodontics. The pulp, a highly specialized connective tissue, plays a critical role in dentinogenesis, immune defense, and sensory function throughout the life of the tooth. Maintaining its health is particularly important in young permanent teeth, where continued root development and apical closure are dependent on pulp vitality. Vital pulp therapy (VPT), which includes direct pulp capping, indirect pulp capping, and pulpotomy, represents a biologically driven alternative to root canal treatment in cases of carious or traumatic exposures where the pulp remains vital [1], [2].

The success of VPT relies heavily on the properties of the pulp capping material used. An ideal material must provide antimicrobial action, biocompatibility, adequate sealing ability, and the capacity to stimulate odontoblastic differentiation, thereby promoting reparative dentinogenesis [3]. Over the last century, significant efforts have been made to identify and refine such materials, leading to the evolution of conventional and synthetic biomaterials for pulp therapy.

Calcium hydroxide, introduced in the 1920s, long served as the gold standard for pulp capping due to its strong antibacterial activity and ability to induce dentin bridge formation. However, its high solubility, poor sealing ability, and the formation of porous dentin bridges with tunnel defects limited long-term success rates [4,5]. In response to these drawbacks, mineral trioxide aggregate (MTA) was developed in the 1990s. MTA demonstrated excellent sealing ability, biocompatibility, and

bioinductive properties, significantly improving clinical outcomes in VPT [6]. Despite these advantages, MTA presents challenges such as prolonged setting time, difficult handling, high cost, and potential for tooth discoloration, which restrict its routine use [7].

To address these issues, newer calcium silicate-based cements such as Biodentine and TheraCal LC have been introduced. Biodentine offers improved handling and shorter setting times, while providing bioactive calcium ion release that supports reparative dentinogenesis. TheraCal LC, a light-curable resin-modified calcium silicate, provides immediate setting and good mechanical strength, though concerns remain about the cytotoxic potential of resin components [8,9]. Collectively, these advances represent important steps in the search for an ideal synthetic pulp capping material, yet none fully meet all the biological and clinical requirements for predictable long-term success.

In parallel with these developments, research has turned toward novel regenerative strategies that move beyond reparative dentin formation to true pulp regeneration. Bioactive glasses, dentin matrix hydrogels, enamel matrix derivatives, and growth factor-loaded scaffolds represent promising innovations, as they aim to mimic the natural extracellular matrix and promote organized dentin-pulp complex regeneration [10,11][12,13]. These experimental approaches demonstrate considerable potential but remain largely confined to laboratory and preclinical settings due to limited clinical data and challenges in translation.

This narrative review consolidates current evidence on synthetic biomaterials for vital pulp therapy. It begins with an overview of conventional materials such as calcium hydroxide and MTA, followed by newer calcium silicate-based agents including Biodentine and TheraCal LC. It then explores emerging regenerative biomaterials, including bioactive glasses and tissue engineering-based approaches. Comparative insights are presented to highlight the strengths and limitations of each material, as well as the translational challenges that hinder their widespread use. While natural bioactives such as propolis and royal jelly are gaining increasing interest, they are beyond the scope of this review, which is focused exclusively on synthetic and engineered biomaterials.

1.1 Calcium Hydroxide

Calcium hydroxide, introduced in the 1920s, has been historically regarded as the gold standard for direct pulp capping. It is available in various formulations, including aqueous suspensions, oil-based pastes, and as a component of liners and cements. Upon application, its active component, $Ca(OH)_2$, dissociates into calcium and hydroxyl ions in the presence of moisture, which accounts for its therapeutic actions [4].

The biological effects of calcium hydroxide are primarily attributed to its antibacterial activity and its ability to induce reparative dentinogenesis [14]. Its high alkaline pH (~12.5) creates an environment hostile to most oral microorganisms, effectively reducing bacterial contamination at pulp exposure sites. At the same time, hydroxyl ions produce a superficial necrotic layer in the underlying pulp tissue, which triggers a controlled inflammatory response. This stimulates the recruitment and differentiation of pulp progenitor cells into odontoblast-like cells, initiating the formation of reparative dentin [15]. Released calcium ions further contribute to mineralization by promoting hydroxyapatite deposition and mobilizing bioactive molecules such as transforming growth factor-β (TGF-β) from the dentin matrix, which enhances odontoblastic differentiation [16][17]. Experimental studies confirm this mechanism: de Souza Costa et al. (2008) demonstrated that pulp cells capped with $Ca(OH)_2$ expressed higher levels of dentin sialoprotein (DSP), an important marker of odontoblast differentiation.

Despite these advantages, calcium hydroxide is associated with several well-recognized limitations that undermine its long-term effectiveness. Its high solubility in oral fluids leads to material dissolution and gaps at the tooth–restoration interface, which increase susceptibility to bacterial leakage. Moreover, the reparative dentin bridge formed in response to $Ca(OH)_2$ is often porous and irregular, with tunnel defects that compromise sealing and allow reinfection. Ricucci et al. (2023) emphasized this limitation in long-term clinical evaluations, noting that while success rates exceeded 80% at one year, they dropped significantly to 58% after nine years due to microleakage and bridge defects.[5] Additionally, the mechanical properties of calcium hydroxide are weak, providing inadequate support for overlying restorations, and its initial cytotoxic effects, due to superficial necrosis, may delay early healing. Yadav et al. (2025) further observed that direct pulp capping with $Ca(OH)_2$ achieved a 72% success rate after five years, but emphasized that treatment outcomes were strongly dependent on the quality of the coronal seal[18].

In summary, calcium hydroxide has played a pivotal role in the development of vital pulp therapy, owing to its antibacterial effects and capacity to induce dentin bridge formation. However, its long-term performance is compromised by solubility, poor sealing, and the structural weakness of the dentin bridges it produces. These shortcomings have spurred the development of more advanced biomaterials such as mineral trioxide aggregate and newer calcium silicate cements, which aim to address the deficiencies of calcium hydroxide while maintaining its biological advantages.

1.2 Mineral Trioxide Aggregate (MTA)

Mineral trioxide aggregate (MTA), developed by Torabinejad in the 1990s, represents a major milestone in vital pulp therapy. It is a calcium silicate-based material derived from Portland cement and consists primarily of tricalcium silicate, dicalcium

silicate, tricalcium aluminate, tetracalcium aluminoferrite, and bismuth oxide, which provides radiopacity. Two variants are commercially available: grey and white MTA, the latter formulated with reduced iron content to minimize tooth discoloration [7,19].

The clinical effectiveness of MTA is largely attributable to its biological mechanisms. Upon hydration, MTA forms calcium hydroxide and calcium silicate hydrate. These products contribute to excellent sealing ability, as the material undergoes slight expansion during setting, improving marginal adaptation and reducing microleakage. Released calcium ions interact with phosphate in tissue fluids to precipitate hydroxyapatite, creating a biologically compatible interface with dentin and pulp tissue. Furthermore, MTA exerts bioinductive effects, promoting odontoblastic differentiation and upregulating dentin matrix proteins such as dentin sialophosphoprotein (DSPP) and dentin matrix protein-1 (DMP-1), both essential for reparative dentinogenesis [20][21][22].

Clinical evidence strongly supports the superior outcomes of MTA compared to calcium hydroxide. In a randomized clinical trial, Brizuela et al. (2017) reported significantly higher quality dentin bridges with MTA, characterized by greater thickness and fewer tunnel defects [23]. Uyar and Alacam (2021) evaluated immature permanent molars treated with MTA pulpotomy and found reduced pulpal inflammation and improved reparative dentinogenesis compared to calcium hydroxide [24]. Similarly, Koc Vural et al. (2017) observed higher long-term success rates for indirect pulp capping with MTA than with $Ca(OH)_2$, underscoring its superior sealing and regenerative potential [25].

Despite these advantages, MTA is not without limitations. One of its chief drawbacks is its extended setting time, approximately 2–3 hours for ProRoot MTA, though newer formulations such as Angelus MTA reduce this to around 15 minutes. Its handling properties are also challenging; the material has a sandy consistency and is sensitive to moisture, complicating placement. Additionally, the high cost of MTA limits its widespread adoption in routine practice, especially in resource-limited settings. Finally, tooth discoloration remains a concern, particularly with grey formulations, which can compromise esthetic outcomes in anterior teeth [7].

In summary, MTA has significantly advanced vital pulp therapy by combining superior sealing ability, biocompatibility, and bioinductive properties with favorable clinical success rates. However, its extended setting time, handling difficulties, high cost, and potential for discoloration prevent it from being the ideal pulp capping material. These limitations have driven the development of newer calcium silicate-based biomaterials such as Biodentine and TheraCal LC, which aim to retain the biological advantages of MTA while offering greater clinical practicality.

1.3 Newer Calcium Silicate-Based Materials

The clinical limitations of mineral trioxide aggregate (MTA), particularly its long setting time, handling difficulties, and cost, have prompted the development of newer calcium silicate-based biomaterials designed to combine biological efficacy with improved practicality. Among these, Biodentine and TheraCal LC are the most widely investigated in vital pulp therapy.

Biodentine is a bioactive dentin substitute composed of tricalcium silicate, dicalcium silicate, calcium carbonate, zirconium oxide (as a radiopacifier), and calcium chloride, which acts as a setting accelerator. Unlike MTA, which can take hours to set, Biodentine has a clinically acceptable setting time of 12–15 minutes, making it more convenient for single-visit procedures [7]. In addition to faster setting, it demonstrates high compressive strength and excellent sealing properties, reducing the risk of microleakage. Biodentine releases bioactive calcium ions, which stimulate pulp cells to differentiate into odontoblast-like cells and promote tertiary dentin formation [26]. Gandolfi et al. (2011) showed that Biodentine induces early fluorapatite deposition and favorable pulp healing, while Drukteinis and Camilleri (2020) highlighted its shorter setting time and high biocompatibility, establishing it as a promising alternative to MTA [8,27]. Clinical trials have also reinforced its value: Mangat et al. (2025) reported that Biodentine achieved outcomes comparable to or superior to MTA in pulpotomy and pulp capping, with less discoloration and easier manipulation [28].

TheraCal LC represents another innovation: a light-curable resin-modified calcium silicate cement. It provides immediate setting upon light activation, simple handling, and good mechanical properties. These advantages make it attractive for use as a liner or pulp capping material in routine restorative procedures. However, concerns have been raised regarding its resin components. Studies indicate that incomplete polymerization in deep cavities may lead to residual monomers, which could exert cytotoxic effects on pulp cells [7]. While TheraCal LC has shown acceptable clinical outcomes in short-term studies, long-term evidence remains limited, and its role in vital pulp therapy requires further investigation.

Taken together, Biodentine and TheraCal LC represent the next step in the evolution of calcium silicate cements. Biodentine, with its bioactivity, favorable handling, and shorter setting time, appears particularly well-suited for vital pulp therapy and has gained increasing clinical acceptance. TheraCal LC, while convenient, still requires further validation regarding its biological safety in deep pulp exposures.

1.4 Comparative Summary

The progression from calcium hydroxide to MTA and then to newer calcium silicate-based materials reflects a continuous effort to overcome the limitations of earlier agents. Calcium hydroxide remains valued for its strong antibacterial activity

and proven ability to induce dentin bridge formation, but its solubility, poor sealing capacity, and the porous nature of the bridges it produces have reduced its long-term reliability. MTA addressed many of these issues by offering excellent sealing ability, biocompatibility, and bioinductive properties, resulting in higher success rates and more predictable pulp healing. Nevertheless, its long setting time, handling challenges, high cost, and discoloration limit its widespread use. Biodentine and TheraCal LC represent attempts to combine the biological benefits of MTA with improved handling and practicality. Biodentine, in particular, has gained clinical traction due to its shorter setting time, strong sealing ability, and favorable biological performance, while TheraCal LC provides immediate setting but requires further validation due to concerns regarding resin cytotoxicity.

Table 1. Comparative properties of conventional pulp capping agents

Feature	Calcium Hydroxide ($Ca(OH)_2$)	Mineral Trioxide Aggregate (MTA)	Biodentine	TheraCal LC
Antibacterial effect	Strong (high alkaline pH)	Moderate (Ca^{2+} release)	Moderate–High	Moderate
Dentin bridge quality	Porous, with tunnel defects	Dense, continuous	Dense, uniform, tubular	Acceptable but variable
Sealing ability	Poor; prone to microleakage	Excellent	Excellent	Good
Biocompatibility	Moderate (initial necrosis)	High	High	Moderate (resin-related concerns)
Setting time	Immediate (mix-dependent)	2–3 h (ProRoot); ~15 min (Angelus)	12–15 min	Immediate (light-cured)
Handling	Easy to manipulate	Difficult (sandy, moisture-sensitive)	User-friendly	Very easy
Cost	Low	High	Moderate	Moderate
Discoloration risk	None	Present (grey MTA)	Minimal	Minimal
Clinical evidence	Extensive, but declining long-term success	Extensive, high long-term success	Increasing, favorable	Limited, emerging

Overall, synthetic materials have progressively improved outcomes in vital pulp therapy, with MTA and Biodentine representing significant advancements over calcium hydroxide. However, no single material fully satisfies the criteria for the "ideal" pulp capping agent. Challenges such as solubility, handling, cost, and biological variability persist, underscoring the need for continued innovation in biomaterial design. These limitations have fueled interest not only in newer synthetic approaches but also in natural bioactive alternatives, which may provide complementary or superior biological advantages in pulp preservation

2. EMERGING REGENERATIVE SYNTHETIC BIOMATERIALS

While conventional biomaterials such as calcium hydroxide, MTA, and Biodentine have improved outcomes in vital pulp therapy (VPT), they are largely reparative in nature. Their primary role is to induce dentin bridge formation and provide antimicrobial protection rather than to regenerate the pulp–dentin complex. Recent research has therefore shifted toward regenerative synthetic biomaterials that aim to mimic the natural extracellular matrix, stimulate odontoblast differentiation, and promote organized tissue regeneration.

2.1 Bioactive Glasses

Bioactive glasses are silica-based materials that release calcium, sodium, and phosphate ions when in contact with physiological fluids, leading to the formation of a hydroxyapatite-like surface layer. This bioactivity allows for chemical bonding to dentin and stimulates reparative processes. Hanada et al. (2019) demonstrated that bioactive glass-based cements promoted odontoblast-like cell differentiation and induced the formation of thick, homogeneous dentin bridges in animal models [10]. In addition, their ion release contributes to antimicrobial effects by increasing local pH, creating an unfavorable environment for cariogenic and endodontic pathogens. Compared to calcium hydroxide, which often produces porous bridges, bioactive glasses have shown the ability to generate more uniform and structurally sound reparative dentin.

2.2 Dentin Matrix Hydrogels

Hydrogel-based scaffolds derived from demineralized dentin matrix (DDM) are designed to closely replicate the composition of native dentin [29]. These injectable hydrogels contain bioactive molecules such as transforming growth factor-beta (TGF-β) and bone morphogenetic proteins (BMPs), which are critical for odontogenic differentiation. Holiel et al. (2021) reported that dentin matrix hydrogels promoted organized odontoblast alignment and homogeneous dentin bridge formation in pulp capping models, with favorable long-term tissue responses [11]. Their injectability and adaptability to irregular pulp exposure sites make them particularly attractive for minimally invasive regenerative procedures.

2.3 Enamel Matrix Derivatives (EMD)

Enamel matrix derivatives, composed mainly of amelogenins, have been extensively used in periodontal regeneration and more recently applied to pulp therapy. These proteins stimulate odontoblast differentiation, extracellular matrix production, and dentinogenesis, while also exerting anti-inflammatory effects. Singer et al. (2023) demonstrated that EMD reduced pulpal inflammation and induced the deposition of tubular dentin when used as a pulp capping material [13]. Although clinical evidence is still limited, the potential of EMD lies in its ability to activate signaling pathways similar to those involved in natural tooth development.

2.4 Growth Factor- and Scaffold-Based Approaches

Tissue engineering approaches in endodontics increasingly focus on scaffolds loaded with growth factors or stem cells. Hydrogels and biopolymers incorporating growth factors such as BMP-2, VEGF, or PDGF have shown the ability to accelerate angiogenesis, odontoblastic differentiation, and reparative dentinogenesis [30]. Rajasekar et al. (2025) demonstrated that scaffold-based systems seeded with dental pulp stem cells supported the formation of organized dentin–pulp-like tissue, representing a step toward true pulp regeneration rather than mere reparative dentin formation [31].

2.5 Adjunctive Strategies: Nitric Oxide Donors and Antimicrobial Nanoparticles

Adjunctive innovations have also been explored to enhance pulp healing. Nitric oxide donors such as NOC-18 have been reported to stimulate odontoblast activity and tubular dentin deposition, potentially accelerating dentin bridge formation [32]. Similarly, incorporating silver nanoparticles into pulp capping systems provides targeted antibacterial activity against resistant pathogens such as *Enterococcus faecalis* without compromising material properties [33].

Summary

Emerging regenerative biomaterials aim to move beyond reparative approaches by creating a biomimetic microenvironment that promotes true tissue regeneration. While promising results have been reported in preclinical studies, these materials are still in early stages of development, with limited clinical translation. Cost, complexity of formulation, and lack of long-term trials remain significant barriers to their widespread adoption.

3. DISCUSSION

The trajectory of vital pulp therapy materials reflects the constant effort to balance antimicrobial action, biocompatibility, and regenerative potential. Calcium hydroxide, while antibacterial and dentinogenic, suffers from poor sealing and long-term instability. MTA, despite being a breakthrough with superior sealing and bioinduction, is limited by cost, difficult handling, and discoloration. Biodentine addresses some of these concerns with improved handling and shorter setting times, though long-term evidence is still emerging. TheraCal LC offers immediate setting but raises safety concerns due to resin components.

Emerging synthetic materials such as bioactive glasses, dentin matrix hydrogels, and enamel matrix derivatives show

considerable potential to advance pulp preservation toward true regeneration. However, they remain largely experimental, with minimal clinical validation. Comparative studies highlight that while MTA and Biodentine currently offer the most predictable clinical outcomes, novel biomaterials may eventually surpass them if issues of standardization, cost, and long-term performance are addressed.

A key challenge across all synthetic materials is the gap between promising in vitro and animal results versus real-world clinical outcomes. This underlines the need for well-designed randomized clinical trials that assess not only immediate success but also long-term pulp vitality and dentin bridge quality.

4. FUTURE PERSPECTIVES

The future lies in nano-enhanced calcium silicates, hybrid materials combining mechanical stability with bioactive additives, and biomimetic scaffolds. Clinical translation will depend on cost-effectiveness, regulatory approval, and large-scale randomized trials. Achieving true pulp regeneration remains the ultimate goal.

5. CONCLUSION

Synthetic biomaterials have transformed vital pulp therapy by improving pulp preservation outcomes. Calcium hydroxide laid the foundation, while MTA and Biodentine advanced bioactivity and sealing. Yet challenges remain, particularly in cost, handling, and long-term predictability. Emerging regenerative materials offer exciting possibilities but require further validation. Innovation at the intersection of material science and biology will be essential to develop the ideal pulp capping agent.

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