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BIOCOMPATIBILITY AND CLINICAL PERFORMANCE OF BIOMATERIALS USED IN DIRECT PULP CAPPING: A COMPREHENSIVE REVIEW

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Abstract

Direct pulp capping is a conservative treatment aimed at preserving the vitality of the dental pulp by applying a biocompatible material directly over the exposed pulp tissue. Over time, calcium hydroxide has been replaced by modern calcium silicate-based biomaterials such as Mineral Trioxide Aggregate (MTA), Biodentine, and TheraCal, which offer superior biological properties and clinical performance. This comprehensive review analyzes the mechanisms underlying pulp healing, including cellular responses, ion release, and dentin bridge formation, while comparing the biocompatibility and long-term outcomes of different biomaterials. Clinical studies consistently demonstrate that MTA and Biodentine achieve higher success rates, promote predictable reparative dentinogenesis, and ensure long-term pulp vitality. Factors such as case selection, immediate treatment, hemorrhage control, and proper isolation significantly affect clinical outcomes. Future perspectives include the integration of bioactive molecules, regenerative endodontic strategies, and advanced biomaterial coatings to further enhance tissue regeneration and treatment predictability.

Keywords: direct pulp capping, biocompatibility, MTA, Biodentine, pulp regeneration

Introduction

Cardiovascular diseases are one of the main causes of morbidity and mortality globally, having a major impact on the health system and on the quality of life of patients [1].

Direct pulp capping is a conservative procedure aimed at preserving the vitality of the dental pulp by applying a biocompatible material directly onto the exposed pulp tissue, to stimulate reparative dentin formation and prevent pulp necrosis [1,2]. Maintaining pulp vitality is crucial for the long-term function of the tooth, as a healthy pulp provides sensory feedback, nutritional support to the surrounding hard tissues, and the ability to respond to external aggression through the deposition of tertiary dentin [3]. In clinical practice, pulp exposures most commonly result from deep caries, trauma, or iatrogenic factors during cavity preparation, and the choice of the capping biomaterial plays a decisive role in determining the outcome of the procedure [4].

Historically, calcium hydroxide has been considered the gold standard for direct pulp capping because of its antibacterial properties and its ability to induce dentin bridge formation. However, it has significant limitations, including high solubility, poor adhesion to dentin, and the

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formation of incomplete or porous dentin bridges that are prone to bacterial microleakage [3,4]. These drawbacks led to the development of advanced calcium silicate-based biomaterials, such as Mineral Trioxide Aggregate (MTA), Biodentine, and, more recently, TheraCal, which demonstrate superior biocompatibility, enhanced stimulation of odontoblastic differentiation, and improved sealing ability [1,5].

The chemical and physical properties of these materials directly influence the biological response of the pulp. TheraCal, a light-curable MTA-like material, has been designed to provide controlled calcium ion release, dimensional stability, and ease of handling, thus improving clinical application and reducing operative time [1]. Calcium silicate cements such as MTA and Biodentine stimulate hydroxyapatite formation at the dentin interface, promoting a stable chemical bond and an optimal biological environment for pulp healing and regeneration [2,5]. In vitro studies have demonstrated that these materials support pulp cell viability and stimulate differentiation of dental pulp stem cells into odontoblast-like cells, thereby enhancing tissue repair and dentin bridge formation [5,6].

Beyond biological properties, the clinical success of direct pulp capping relies on the ability of the material to prevent bacterial microleakage. MTA has been extensively studied and is recognized for its excellent sealing ability, while Biodentine offers a shorter setting time and greater mechanical strength, making it suitable not only for pulp capping but also as a temporary dentin substitute [7,8]. TheraCal, although easy to apply due to its light-curable nature, still requires further long-term clinical evaluation to confirm its effectiveness compared to MTA and Biodentine [1].

Advancements in direct pulp capping techniques have been driven by a deeper understanding of the biological mechanisms underlying pulp healing. When a biocompatible material comes into direct contact with the pulp, it must trigger a controlled inflammatory response that recruits progenitor cells, leading to the deposition of mineralized tissue that protects the pulp [5,6]. Calcium silicate-based materials release calcium and silicon ions, which activate signaling pathways involved in mineralization and angiogenesis, essential processes for pulp tissue regeneration [5].

Long-term clinical studies have demonstrated the superior performance of modern biomaterials compared to calcium hydroxide. Comparative trials show that MTA achieves higher clinical and radiographic success rates, reduces the risk of pulp necrosis, and induces the formation of thicker and more uniform dentin bridges [3,4]. In a follow-up study ranging from 2 to 6 years, Caliskan and Guneri found that MTA was significantly more predictable than calcium hydroxide, especially in cases of carious pulp exposures [4].

Another key factor is the cytotoxicity profile of the materials. Modern silicate-based cements exhibit low toxicity toward pulp cells and a strong ability to promote osteogenesis and angiogenesis [2,5-7]. Bortoluzzi et al. demonstrated that these biomaterials can be applied not only in direct pulp capping but also in regenerative procedures such as pulp revascularization, thanks to their osteogenic potential and antimicrobial properties [2].

Clinical success is also influenced by procedural factors and operator technique. Cho et al. highlighted that the time elapsed between pulp exposure and material placement significantly affects treatment outcomes, emphasizing the importance of immediate hemorrhage control and effective isolation during the procedure [8-10].

In young permanent teeth, bioactive materials such as Biodentine and MTA show superior outcomes, as they actively promote the maintenance of pulp vitality in cases of carious exposures by stimulating reparative dentinogenesis [11]. Animal studies further support these findings, demonstrating that these materials induce a favorable histological response characterized by the formation of well-organized mineralized pulp tissue [7].

Overall, current evidence shows a clear transition from traditional calcium hydroxide-based pulp capping towards modern calcium silicate-based biomaterials, which offer superior biological and clinical performance. This review aims to comprehensively evaluate the available

data on the biocompatibility and clinical performance of these materials, highlighting their impact on modern vital pulp therapy and evidence-based decision-making in restorative dentistry [1–10].

Biocompatibility and biological properties of biomaterials

The biocompatibility of pulp capping materials is a fundamental requirement for successful vital pulp therapy, as it directly influences the healing response of the pulp tissue and the long-term success of the restoration [1,2]. When a biomaterial is placed in direct contact with exposed pulp tissue, it must provide a non-cytotoxic environment that allows for controlled inflammation, recruitment of progenitor cells, and stimulation of odontoblastic differentiation leading to reparative dentin formation [5,6]. Modern calcium silicate-based materials such as MTA, Biodentine, and TheraCal have been developed to overcome the limitations of calcium hydroxide by providing superior sealing ability, ion release, and bioactivity [1,5,7].

MTA is considered one of the most biocompatible materials available for direct pulp capping. Its composition, which includes tricalcium silicate, dicalcium silicate, and bismuth oxide, promotes the release of calcium ions, which react with tissue fluids to form hydroxyapatite at the interface with dentin [7,8]. This process leads to the creation of a stable biological seal and supports pulp cell survival and differentiation [5,6]. Similarly, Biodentine, which is also based on tricalcium silicate, has been shown to induce the expression of odontogenic markers and to stimulate the formation of a thick and uniform dentin bridge [5,7]. Studies using three-dimensional cultures of dental pulp stem cells have demonstrated that these materials maintain high levels of cell viability and enhance mineralization processes [6].

TheraCal, a newer light-curable MTA-like material, has gained attention for its ease of handling and rapid setting due to its resin-modified composition [1]. Although TheraCal exhibits a controlled release of calcium ions and provides an immediate barrier against bacterial infiltration, concerns have been raised about its polymer content, which may affect its long-term biocompatibility compared to traditional calcium silicate cements [11-17].

The biological effects of these biomaterials have been confirmed through a combination of in vitro, animal, and clinical studies. De Rossi et al. demonstrated in an animal model that both Biodentine and MTA elicit a favorable pulpal response, characterized by minimal inflammatory infiltrate and the presence of newly formed mineralized tissue over the exposed pulp [7]. In clinical settings, randomized controlled trials have provided strong evidence for the high biocompatibility and clinical performance of these materials. For example, Brizuela et al. reported that in young permanent teeth with carious pulp exposures, both Biodentine and MTA outperformed calcium hydroxide, showing higher success rates and better quality of dentin bridge formation [15]. Similarly, Parinyaprom et al. found comparable clinical outcomes between ProRoot MTA and Biodentine in children and adolescents, supporting the use of both materials as reliable options for direct pulp capping [11].

A key indicator of biocompatibility is the reduction of cytotoxic effects on pulp and surrounding tissues. Bortoluzzi et al. evaluated several silicate-based cements and found that they not only had low cytotoxicity but also promoted osteogenic differentiation of mesenchymal stem cells, suggesting a potential role in regenerative procedures beyond pulp capping [2]. Widbiller et al. further confirmed that direct contact between tricalcium silicate cements and pulp stem cells enhances their ability to form mineralized tissue, an essential step in pulp healing [6]. These findings align with clinical observations showing that teeth treated with MTA or Biodentine exhibit stable and predictable outcomes over long-term follow-up periods [3,4,12].

The mechanical properties of pulp capping materials are also crucial for their biological performance. A material must withstand functional loads without degradation, as physical breakdown may compromise the seal and allow bacterial contamination [14]. Biodentine has been highlighted for its superior compressive strength and lower solubility compared to MTA, making it a suitable choice for both temporary restorations and definitive pulp capping [14,15].

In addition to material properties, prognostic factors play a role in determining biological success. Cho et al. emphasized that the timing of material placement following pulp exposure significantly influences the healing response, with immediate treatment leading to higher success rates [10]. Proper hemorrhage control and effective isolation are also essential for preventing bacterial infiltration and supporting the regenerative capacity of the pulp [4,10].

Furthermore, comparative studies have demonstrated that modern bioactive materials outperform calcium hydroxide in terms of histological and clinical outcomes. Katge and Patil, in a split-mouth study, confirmed that Biodentine and MTA result in higher quality dentin bridge formation and lower incidence of pulp necrosis compared to calcium hydroxide [12]. These findings reinforce the concept that bioactive ion release and superior sealing ability are key determinants of successful pulp healing [7,11-12,15].

The biocompatibility of direct pulp capping materials is determined by their ability to create a biologically favorable environment that supports pulp survival, controls inflammation, and stimulates dentinogenesis. Evidence from basic science and clinical research indicates that calcium silicate-based biomaterials such as MTA and Biodentine provide optimal conditions for these processes, while TheraCal shows promise but requires further evaluation. The integration of favorable chemical, biological, and mechanical properties has positioned these materials as the standard of care for vital pulp therapy, ensuring predictable long-term outcomes for both pediatric and adult patients (table 1) [12-17].

Table 1. Biocompatibility and biological properties of direct pulp capping biomaterials

Biomaterial	Key biological properties	Cellular / tissue response	Clinical evidence	References
Calcium Hydroxide ($Ca(OH)_2$)	Antibacterial activity promotes initial hard tissue formation, but with high solubility and poor sealing ability.	Induces dentin bridge formation, but bridges are often incomplete and porous, allowing microleakage.	Lower long-term success rates due to incomplete pulp healing and necrosis risk.	[3,4,15,16]
Mineral Trioxide Aggregate (MTA)	Releases calcium ions; forms hydroxyapatite at the dentin interface; excellent sealing ability.	Supports odontoblastic differentiation, angiogenesis, and formation of a thick and uniform dentin bridge.	High clinical success rates in both children and adults; proven long-term stability.	[3,4,7,11,15,16]
Biodentine	Fast setting time; high calcium and silicon ion release; superior compressive strength.	Enhances pulp stem cell viability and mineralization; induces rapid and dense dentin bridge formation.	Comparable to MTA in RCTs; easier handling and favorable for pediatric patients.	[5,6,11,12,15]
TheraCal LC	Resin-modified, light-curable; controlled calcium ion release.	Supports initial pulp healing, but concerns about the potential cytotoxicity of resin components.	Promising early results; requires further long-term studies to confirm efficacy.	[1,17]
Tricalcium Silicate cements (general)	Bioactive ion release (Ca^{2+}, Si^{4+}); promotes hydroxyapatite formation and angiogenesis.	Stimulates proliferation and differentiation of dental pulp stem cells.	Key materials for vital pulp therapy: support tissue regeneration.	[5,6,9]

Table 1 summarizes the main biological and clinical characteristics of biomaterials used in direct pulp capping. Calcium silicate-based materials, such as MTA and Biodentine, demonstrate superior bioactivity and long-term outcomes compared to calcium hydroxide. TheraCal shows promise due to its handling properties, but further studies are needed to confirm its biological safety and clinical reliability.

Clinical performance and prognostic factors

The clinical performance of direct pulp capping materials is closely linked to their biological properties, handling characteristics, and the clinical scenario in which they are used. Several randomized clinical trials and longitudinal studies have compared modern calcium silicate-based biomaterials, such as MTA and Biodentine, with traditional agents like calcium hydroxide, consistently demonstrating superior clinical outcomes for the newer materials [15-19].

Brizuela et al. conducted a randomized clinical trial on young permanent teeth with carious pulp exposures, reporting significantly higher success rates for both MTA and Biodentine compared to calcium hydroxide [15]. These findings were consistent with earlier investigations showing that calcium hydroxide often leads to incomplete or porous dentin bridge formation, which predisposes the pulp to bacterial microleakage and eventual necrosis [3,4,16]. Biodentine, in particular, demonstrated favorable handling characteristics, faster setting time, and the ability to induce a dense and continuous mineralized barrier, which is crucial for long-term pulp vitality preservation [7,15].

The prognostic factors influencing treatment outcomes have been extensively studied. Caliskan and Guneri highlighted the importance of patient age, etiology of pulp exposure, and preoperative pulp status in predicting success rates [4]. Younger patients tend to exhibit better healing responses due to higher cellular activity and regenerative potential [11,15]. Moreover, Cho et al. emphasized the significance of timing, showing that immediate capping following pulp exposure results in significantly better outcomes compared to delayed treatment, as early intervention minimizes bacterial contamination and inflammatory response [10].

Hemorrhage control at the exposure site is another critical determinant of success. A well-controlled pulpal bleeding, managed with sterile saline or sodium hypochlorite, provides a clean environment for material placement, while uncontrolled bleeding may interfere with the sealing ability of the biomaterial and compromise the healing process [4,10,15]. Effective isolation, typically achieved using a rubber dam, is equally essential to prevent salivary contamination and bacterial ingress [8,10].

Comparative clinical studies have provided valuable insights into the relative performance of different bioactive materials. Katge and Patil, in a split-mouth design study, found no statistically significant differences in clinical success between MTA and Biodentine, although Biodentine offered easier handling and faster setting, making it advantageous in pediatric cases where chairside time must be minimized [12,15]. Similarly, Paula et al. demonstrated in a retrospective study that both MTA and Biodentine were associated with high survival rates of capped teeth, outperforming traditional calcium hydroxide-based therapies [13,15].

From a histological perspective, these clinical outcomes are supported by evidence showing that MTA and Biodentine induce the formation of thicker and more homogenous dentin bridges compared to calcium hydroxide [7,15,16]. The biocompatibility of these materials, characterized by low cytotoxicity and the ability to stimulate odontoblastic differentiation, plays a central role in their superior performance [2,5,6,18]. Additionally, the release of calcium and silicon ions contributes to pulp healing and angiogenesis, further promoting long-term pulp vitality [5,18-20].

Mechanical stability is another factor influencing clinical outcomes. Nielsen et al. demonstrated that Biodentine possesses superior mechanical properties compared to MTA, particularly regarding compressive strength and resistance to solubilization, making it better suited for use in stress-bearing areas [14,15]. These characteristics ensure the durability of the restoration and reduce the risk of material breakdown, which could otherwise lead to microleakage and treatment failure [14].

Recent studies have also explored the interaction of calcium silicate-based cements with surrounding tissues. Seo et al. reported that these materials exhibit excellent mineralization

potential and low cytotoxicity compared to conventional resin-based sealers, confirming their compatibility with pulp and periapical tissues [18]. Lee et al. further demonstrated that these biomaterials promote the differentiation of gingiva-derived stem cells, which may contribute to enhanced tissue regeneration and healing following direct pulp capping [19].

Clinical evidence strongly supports the use of MTA and Biodentine as first-choice materials for direct pulp capping due to their superior sealing ability, bioactivity, and mechanical stability. Prognostic factors such as patient age, etiology of pulp exposure, immediate treatment, hemorrhage control, and proper isolation significantly influence success rates. These materials not only provide predictable clinical outcomes but also promote biological regeneration, offering a comprehensive solution for maintaining pulp vitality and preventing tooth loss [17-21].

Future perspectives

The future of direct pulp capping lies in the integration of biomaterials science with regenerative endodontic strategies. Next-generation capping agents are expected to combine robust mechanical performance with advanced bioactivity, including the controlled release of signaling molecules and growth factors to actively guide pulp tissue regeneration [5,6,18]. Personalized approaches, potentially involving patient-specific stem cell therapies and biomimetic scaffolds, may further enhance healing outcomes and broaden the indications for vital pulp therapy [2,9,19].

Moreover, innovations in surface coatings and nanostructured biomaterials offer opportunities to enhance the biological interaction between capping agents and pulp tissue, improving both osteogenic and angiogenic responses. These advancements aim not only to preserve pulp vitality but also to restore the natural structure and function of the dentin-pulp complex. Recent experimental research highlights the potential of these strategies, demonstrating enhanced regenerative effects through the use of bioactive coatings and osteogenic stimulators in combination with calcium silicate-based biomaterials [21].

Conclusion

The development of advanced bioactive materials has significantly improved the outcomes of direct pulp capping, moving the focus from passive protection to active biological regeneration. Modern calcium silicate-based materials such as MTA and Biodentine have demonstrated superior biocompatibility compared to traditional calcium hydroxide, promoting odontoblastic differentiation, reparative dentin formation, and effective bacterial sealing. Clinical studies consistently report higher success rates and more uniform dentin bridges when these materials are used, particularly in young permanent teeth where regenerative capacity is greater.

Their favorable physical and mechanical properties, including dimensional stability and resistance to solubilization, further contribute to predictable long-term outcomes by preventing microleakage and structural degradation. Despite these advantages, challenges remain with newer materials like TheraCal, which, while offering handling benefits and light-curing convenience, require further investigation to fully establish their long-term safety and effectiveness due to their resin-modified composition. Furthermore, clinical success is highly dependent on proper case selection and technique, with factors such as isolation, hemorrhage control, and immediate treatment following exposure being critical for optimal pulp healing.

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