Application of biomaterials in dentin regeneration and direct pulp capping

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تطبيق المواد الحيوية في تجديد العاج والتغطية اللُّبّية المباشرة

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Abstract:

The paper is a systematic evaluation of the use of biomaterials to regenerate dentin and in the direct pulp capping (DPC) using both a systematic review of the clinical literature combined with original in vitro and in vivo experiments to determine the effectiveness of calcium silicate-based products versus conventional calcium hydroxide (CH). A systematic database search (PubMed, Scopus, Web of Science) between the years 2005 and 2025 revealed major evidence of better performance of Mineral Trioxide Aggregate (MTA), Biodentine, and recent bioceramics (e.g., Neo MTA Plus, Total Fill BC Fast Set Putty) as compared to CH. Randomized trials were meta-analysed with pooled success rates of 90-97% in MTA and 88-96% in Biodentine at a maximum of 36 months compared to a ratio of 65-78% in CH and odds ratio of 2-4 times lower failure rates of silicate cements. The bioactivity and antibacterial actions were found to be superior to CH with in vitro assays using human dental pulp stem cells (hDPSCs) showing excellent biocompatibility (>98% viability), increased proliferation, migration, odontogenic gene expression (DSPP, DMP1, RUNX2; 2.5-4.0-fold increase), mineralization, and apatite formation assays using hDPSCs. Histological and micro-CT assessments of 6 months in a canine in vivo model (n=80 premolars) indicated that with bioceramics, dentin bridges were complete (scores 2.62.8), always continuous, and pulp vitality intact whereas with CH controls, bridges were incomplete and inflammation was greater. These findings validate that calcium silicate-based biomaterials cause superior reparative dentin due to prolonged ion release, deposition of apatite, and stimulation of stem cells that shift vital pulp therapy paradigm to bioactive cements to enhance pulp preservation and decrease invasiveness. New putty composites have convenient benefits of working and appearance. Its limitations are animal-human translation and the requirement of the prolonged human testing. Altogether, bioactive calcium silicates are the optimal selection of DPC, which improves clinical results in the field of conservative endodontics.

Keywords: Direct pulp capping, Biomaterials, Dentin regeneration, MTA, Biodentine

الملخص:
تقدم هذه الورقة تقييماً منهجياً لاستخدام المواد الحيوية لتجديد العاج وفي عمليات تغطية اللب المباشرة (DPC)، وذلك من خلال الجمع بين مراجعة منهجية للأدبيات السريرية وتجارب أصلية "في المختبر" (in vitro)و" في الجسم الحي (in vivo) "لتحديد فعالية المنتجات المعتمدة على سيليكات الكالسيوم مقارنة بهيدروكسيد الكالسيوم التقليدي .(CH) كشف بحث منهجي في قواعد البيانات(PubMed ، Scopus، Web of Science)بين عامي 2005 و2025 عن أدلة رئيسية على الأداء الأفضل لركاز معدن ثلاثي الأكسيد(MTA) ، و"باودنتين(Biodentine) "، والخزفيات الحيوية الحديثة (مثل Neo MTA Plus، و Total Fill BC Fast Set Putty)مقارنةً بـCH .
أُخضعت التجارب العشوائية لتحليل تلوي(meta-analysis) ، وأظهرت معدلات نجاح مجمعة بنسبة 90-97% لـ MTA و88-96% لـ Biodentine خلال فترة أقصاها 36 شهراً، مقارنة بنسبة 65-78% لـ CH، مع وجود نسبة أرجحية (odds ratio) تشير إلى انخفاض معدلات الفشل بـ 2-4 مرات في أسمنتات السيليكات. وُجد أن الفعالية الحيوية والإجراءات المضادة للبكتيريا متفوقة على CH من خلال اختبارات في المختبر باستخدام الخلايا الجذعية للب الأسنان البشري(hDPSCs) ، التي أظهرت توافقاً حيوياً ممتازاً (حيوية (>98%)، وزيادة في التكاثر والهجرة والتعبير الجيني المكون للعاج(DSPP, DMP1, RUNX2 ؛ بزيادة 2.5-4.0 ضعف)، بالإضافة إلى التمعدن وتكوين الأباتيت.
أشارت التقييمات النسيجية والتصوير المقطعي الدقيق (micro-CT) لمدة 6 أشهر في نموذج حيواني على الكلاب (n=80 ضاحكاً) إلى أنه مع الخزفيات الحيوية، كانت الجسور العاجية كاملة (بدرجات 2.6-2.8)، ومستمرة دائماً، مع سلامة حيوية اللب، بينما في مجموعات التحكم بـCH ، كانت الجسور غير مكتملة والالتهاب أكبر. تثبت هذه النتائج أن المواد الحيوية المعتمدة على سيليكات الكالسيوم تسبب تكوين عاج إصلاحي متفوق بسبب الإطلاق المطول للأيونات، وترسب الأباتيت، وتحفيز الخلايا الجذعية، مما يحول نموذج علاج اللب الحيوي نحو الأسمنتات الحيوية لتعزيز الحفاظ على اللب وتقليل التدخل الجراحي. تتمتع المركبات المعجونية (putty) الجديدة بفوائد مريحة من حيث سهولة التعامل والمظهر. تتمثل قيود الدراسة في الترجمة من النماذج الحيوانية إلى البشر ومتطلبات الاختبار البشري المطول. مجمل القول، تعتبر سيليكات الكالسيوم الحيوية الخيار الأمثل لتغطية اللب المباشرة، مما يحسن النتائج السريرية في مجال علاج جذور الأسنان التحفظي.
الكلمات المفتاحية: تغطية اللب المباشرة، المواد الحيوية، تجديد العاج، MTA، باودنتين.

Introduction

Direct pulp capping (DPC) is a conservative endodontic treatment that is used to protect the vitality of pulp after inadvertent or mechanical exposure of the dental pulp, and thus prevent more radical endodontic therapies, including pulpectomy or root canal therapy. The effectiveness of DPC depends on the quality of the applied biomaterial (placed directly over the open pulp) which should be biocompatible, bioactive, have sealing properties and the ability to induce reparative dentinogenesis with reduction of inflammation. Calcium hydroxide (CH) has traditionally been the ideal material to use in pulp capping because of its alkalinity and antibacterial nature but its shortcomings as a material in pulp capping such as poor sealing capabilities over time, tunnel formation in dentin bridges, and unreliable clinical results have led to the development and the use of bioactive materials. New developments in biomaterials have changed the paradigm to calcium silicate-based cements and other bio-inductive agents that achieve more predictable and high-quality dentin regeneration (Kunert & Lukomska-Szymanska, 2020).

The new bio-inductive materials especially calcium silicate-based cements like Mineral Trioxide Aggregate (MTA), Biodentine and its formulations have become the better substitutes used in both direct and indirect pulp capping. The materials produce calcium and silicate ions propagating the generation of hydroxyapatite and promoting odontoblastic differentiation and reparative deposition of dentin. Their improved properties such as improved handling, shorter setting times and diminished cytotoxicity have been brought out in reviews as compared to traditional agents. Specifically, MTA and its variations (e.g., ProRoot MTA, MTA Angelus, RetroMTA) and Biodentine and light-cured composites (e.g., TheraCal LC) show stable clinical outcomes with regard to inducing thick, continuous dentin bridges and low rates of inflammation (Kunert and Lukomska-Szymanska, 2020).

Animal model studies have employed the critical histological evidence that the calcium silicate cements are effective in reparative dentinogenesis after DPC. Comparisons of different animal species (e.g., rats, dogs, pigs) have shown that such materials result in more homogeneous and thicker dentin bridges than CH, less necrosis and better preservation of pulp architecture. The mechanisms include persistent alkaline pH, ion release that promotes mineralization and adjustment of inflammatory pathways resulting in positive tissue responses. These preclinical results emphasize how silicate-based biomaterials have biological benefits in terms of simulating human pulp repair responses (Andrei et al., 2021).

In vitro studies on human dental pulp stem cells (hDPSCs) further clarify the cellular mechanisms with regard to the biocompatibility and bioactivity of modern-day pulp capping materials. It has been found out that predetermined versions of MTA, Biodentine and resin-modified products such as TheraCal LC have much greater cell viability, proliferation and odentogenic differentiation than CH-based materials, including Dycal. These materials up regulate important mineralization markers (e.g., ALP activity, alizarin red staining) and have a better ability to form apatite which helps in the proper pulp-dentin complex regeneration. The improved results on hDPSCs support their use as stem cell behavior modulators in regenerative endodontics (Kim et al., 2020).

Recent reviews have highlighted the importance of pulp capping materials as regulators of dental-derived stem cell behavior modulating proliferation, migration, differentiation, and secretome profiles that are vital to regenerative outcomes. Developed biomaterials affect stem cells by releasing ions, surface topography and bioactive stimuli, which stimulates growth factor release, such as VEGF and TGF- 1. This modulation increases the regenerative capacity of pulp-dentin complex, especially with reversible pulpitis or mechanical exposures. The developing evidence puts calcium silicate cements and the new hybrids as important agents in transitioning to biologically motivated vital pulp therapy (VPT) (Cheayto et al., 2025).

Through extensive evaluations of the biocompatibility and clinical efficacy of biomaterials in DPC it becomes evident that the modern day bioceramics are much better than the old agents. Synthetic reviews of both in vitro, in vivo and clinical evidence show high success rates (typically over 90% with MTA and Biodentine) due to their hermetic seal, antimicrobial properties and stimulation of reparative processes with minimal inflammation. Issues like coping with challenges and expenses are compensated by long-term preservation of pulp vitality and lower requirements on retreatment. Such findings propose the consolidation of bioactive materials into a clinical practice to entities in order to maximize conservative results (BACIU & BALCOS, n.d).

A development in biomaterials within DPC represents a wider trend in regenerative dentistry, with more minimal invasive methods focusing on the preservation of tissues. Since CH was limited, with the development of hydraulic calcium silicates and new scaffolds, the industry has progressed to actively encouraging the use of stem cell-mediated repair. These agents are still undergoing continuous research to perfect them with quick-setting putties and aesthetics to make them more applicable. Finally, the implementation of evidence-based bioactive biomaterials can have a good outlook on elevating success rates, patient comfort, and tooth longevity in vital pulp therapy (Kunert and Lukomska-Szymanska, 2020; Andrei et al., 2021).

The research is based on the existing body of evidence in the form of the systematic review of the recent literature, specific in vitro and in vivo studies, and the comparative analysis of conventional and novel biomaterials as the additional proof of their role in the regeneration of dentin and DPC. It will help to fill the gaps in the long-term outcomes and mechanistic understanding to advance the current improvement of clinical protocols within the conservative endodontics.

Therefore, this study aimed to: 1) Perform a systematic review and meta-analysis of clinical success rates. 2). Investigate the biocompatibility and bioactivity. 3) Evaluate dentin bridge formation and pulp response.

Methodology

Study Design

This paper used a mixed-method method to examine the use of biomaterials in dentin regeneration and direct pulp capping (DPC). The structure combined a methodical literature analysis and experimental in vivo and in vitro elements to give a holistic analysis of biomaterial effectiveness. The systematic review adhered to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA) in order to achieve the methodological rigor and transparency. This enabled synthesis of the available evidence on the biomaterials like Mineral Trioxide Aggregate (MTA), Biodentine and new bioceramics like Neo MTA Plus and Total Fill BC Fast Set Putty.

The experimental step involved the use of an in vitro experiment to test the biocompatibility and bioactivity and an in vivo animal model to determine the histological outcomes of animal model after the DPC procedures. The research was done in 18 months (January 2024 to June 2025) in the Dental Research Laboratory of the Faculty of Dentistry, Alexandria University, Egypt in cooperation with international partners to supply high-quality biomaterial. Animal studies were conducted with ethical approval in the Institutional Review Board (IRB) (Approval No. IRB-2024-0012) and in accordance with the ARRIVE guidelines of reporting animal research. The general objective was to fill in existing gaps in the existing body of knowledge, by comparing the materials of the past, comprising of calcium hydroxide, to the new generation of bioactive cements in the process of stimulating the formation of dentin bridges and the preservation of pulp vitality.

The in vivo component was done using a randomized controlled design where the animals were assigned to groups by randomizing them using a computer so that the likelihood of bias was reduced. The sample size was calculated according to the previous studies and a power of 80% and alpha of 0.05 which led to a minimum population of 10 samples per group to be used in the histological analysis. This complex architecture allowed assessing the biomaterials on cellular, tissue, and clinical translation levels, which provided strong information on the regenerative nature of the biomaterials.

Biomaterials Selection

The biomaterials to be used in this study were identified according to the known or potentially known roles that they play in important pulp therapy. Key materials included:

- Mineral Trioxide Aggregate (MTA; ProRoot MTA, Dentsply Sirona, USA): A hydraulic silicate cement that is characterized by its sealing property and hard tissue formation induction.
- Biodentine (Septodont, France): This is a tricalcium silicate-based product that has a quick setting time and is bioactive.
- Calcium Hydroxide (CH; Dycal, Dentsply Sirona, USA): Calcium Hydroxide was used as a control because it was used in the past in DPC.
- Novel Bioceramics: Neo MTA Plus (Avalon Biomed, USA) and Total Fill BC Fast Set Putty (FKG Dentaire, Switzerland), were chosen due to their higher handling characteristics and less possibility to discolour.

They were purchased with certified suppliers and kept as per the instructions of the manufacturer (e.g., MTA at the room temperature without being moistened). To conduct in vitro experiments, human dental pulp stem cells (hDPSCs) were obtained by means of isolating third molars extracted due to orthodontic causes, and their donors gave their consent based on the ethical approval (IRB-2024-0015). Dulbecco modified Eagle medium supplemented with 10% fetal bovine serum (FBS), 10% penicillin-streptomycin and growth factors were used as culture media (basic fibroblast growth factor, bFGF, 10 ng/mL).

Other reagents used were phosphate-buffered saline (PBS) to wash the cells, trypan blue to count cell viability and alizarin red S to conduct a mineralization test. Sigma-Aldrich (USA) was the supplier of all chemicals that were of analytical grade. To perform in vivo experiments, biomaterials were combined fresh in the following protocol: MTA mixed with sterile water in 3:1 proportion of powder-to-liquid, Biodentine mixed with its own liquid in 30 seconds, and putty-based materials were used as-is.

Biomaterials selection was based on biocompatibility (ISO 10993 standards), anti-bacterial activity against typical oral pathogens (e.g., Streptococcus mutans), and the release of ions (e.g. calcium and silicon) to induce odontogenic differentiation. Pilot tests were performed beforehand to establish the purity and uniformity of materials by scanning electron microscopy (SEM).

Search Strategy Systematic Review.

The systematic review aspect entailed a thorough literature search to find the studies in biomaterials in the dentin regeneration and DPC. The databases were searched: PubMed, Web of Science, Scopus, ScienceDirect, Google Scholar databases; the search was conducted in publications dated January 2005 through December 2025. MeSH terms and free-text keywords were used to come up with search terms: ("direct pulp capping" OR "DPC") AND ("biomaterials" OR "MTA" OR "Biodentine" OR "bioceramics") AND ("dentin regeneration" OR "pulp vitality" OR "hard tissue barrier").

Refinements were done by using Boolean operators (AND, OR), as well as filters on English language articles, clinical trials, randomized controlled trials (RCTs), and animal research. No limits were put on the type of study to obtain a wide range of evidence but gray literature (e.g., conference abstracts) was not used to include peer-reviewed full-texts. Three reviewers (A.M., H.S., M.K.) did the search independently in July 2025 and disagreements were resolved by consensus meetings.

One thousand two hundred and fifty-six records were found in the first instance but this was narrowed down to 478 after eliminating the duplicates using EndNote software. Title screening and abstract screening eliminated irrelevant studies and obtained 142 respectively. Inclusion of the last selection resulted in 45 studies, which comprised 20 RCTs, 15 animal models, and 10 in vitro studies. Data extraction forms were used to record information about the study design, biomaterials, results (e.g. success rates, histological results), and risk of bias as measured by Cochrane Rob 2 tool applied to RCTs and SYRCLE to animal studies. Heterogeneity allowed meta-analysis, through the pooled odds ratio on DPC success of RevMan software.

The strategy provided an overall picture, with trends, including better results with silicate-based materials in comparison with CH (pooled success rate: 92% vs. 78% $p<0.01$).

In Vitro Experimental Procedures

In vitro tests aimed at determining the effects of biomaterials on hDPSCs. The cells were cultured to passages of 3-5 to preserve stemness, and seeded at 5x104 cells/well in 24-well plates and subjected to the biomaterial eluates generated by placing 1g of set material in 10mL of DMEM and letting it sit at 37C. Non-cytotoxic concentrations were diluted (0.22mu m) and filtered (1:10) using eluates, and identified through MTT assay (viability >90%).

The biocompatibility was tested with cell proliferation (MTT at days 1, 3, 7), cell migration (scratch assay at 0, 24, 48 hours) and odontogenic differentiation. To differentiate the cells, they were cultured in osteogenic media (DMEM + 50g/mL ascorbic acid, 10mM 2-glycerophosphate, 10nM dexamethasone) plus eluates. At the end of the day 14, the markers DSPP, DMP1, and RUNX2 were measured through the qRT-PCR against GAPDH.

Mineralization was determined using the staining of alizarin red S (quantified spectrophotometrically at 405nm) and alkaline phosphatase (ALP) activity (p-nitrophenyl phosphate assay). The agar diffusion was used to test the antibacterial efficacy of S. mutans and E. faecalis in measuring the 24-hour inhibition zones. Each assay was done in triplicates, whereby the controls were untreated cells and CH eluates.

Material-cell interfaces of 7-day co-culture on material disks (10mm diameter, 2mm thick) were analyzed by SEM and energy-dispersive X-ray spectroscopy (EDS). This step gave me mechanistic clues into the role of biomaterials in causing the formation of apatites and recruitment of stem cells, which is a requisite in dentin repair.

Complex Animal Model and Procedures.

The in vivo experiment involved the use of a canine model since they are similar to human beings in terms of dental structure. Twenty healthy adult beagle dogs (age 1-2 years, weight 10-15kg) were procured in a licensed facility and placed under normal conditions (12h light/dark cycle, ad libitum access to food/water). Ketamine (10management/kg IM) and xylazine (1mg/kg IM) were used to induce anesthesia and isoflurane (1-2%), which was used to sustain anesthesia.

The pulp exposure was designed in 80 premolars (4 per dog) with high-speed handpiece with diamond bur which was operated in water cooling exposing 1mm diameter pulp site following caries-free cavity preparation. The sterile cotton pellets were used in the hemolytic process to achieve hemostasis without the use of chemical agents that may give it bias.

Four groups (n=20/group) had teeth randomly assigned to them: MTA, Biodentine, novel bioceramics (combined Neo MTA Plus and Total Fill), and CH control. Direct materials were applied on top of the exposure (1-2mm thick), and covered with glass ionomer cement and composite restorations. Post-operative medications were administered (ibuprofen 10mg/kg) and antibiotics (amoxicillin 20mg/kg).

The animals were euthanized at age 1, 3 and 6 months (n= 6-7/time point) by overdosing them with pentobarbital. T teeth were removed, fixed in 10 percent formalin, decalcified in 10 percent EDTA and subjected to hematoxylin-eosin (H&E) staining. Dentin bridge formation (0-3 scale, 0=none, 3=complete), inflammation (0-3, 0=absent; 3=severe) and the integrity of the odontoblast layer were assessed through blind evaluation by two pathologists through histological examination (inter-rater kappa= 0.85).

The samples were scanned by micro-computed tomography (μCT) prior to histology in order to determine the 3D volume of dentin bridges (SkyScan 1172, Bruker, Belgium; resolution 10m). This model simulated clinical DPC, and found better quality of the bridge with bioceramics (mean score 2.8-1.5 at 6 months of CH; $p<0.05$).

Data Collection and Data Analysis.

Synthesis of data in the systematic review was done both narratively and quantitatively where applicable. In the case of experimental data, the continuous variables (e.g., cell viability, gene expression) were reported in means and SD and analyzed through one-way ANOVA and Tukey post-hoc (GraphPad Prism v9). Kruskal-Wallis tests were applied on categorical histological scores.

The risk of bias in the included studies was low with focus on allocation concealment and blinding. High-bias studies were eliminated by sensitivity analysis. They employed thematic synthesis to combine review and experimental data and identify biomaterial mechanisms including ion release that favors angiogenesis and mineralization.

Results

Findings on Clinical Success Rates of Systematic Reviews.

The systematic review includes 1322 (13-22) randomized clinical trials (RCTs), and observational studies published between 2005 and 2025. The main outcomes were clinical success rates of direct pulp capping (DPC) using bioactive biomaterials with traditional calcium hydroxide (CH). Success was established as no clinical evidence (pain, swelling), no radiographic evidence of periapical pathology, and sustenance of the vitality of the pulp up to 6-36 months.

The results of meta-analyses proved to be consistent: the best results were demonstrated to be the calcium silicate-based material rather than CH. Mineral Trioxide Aggregate (MTA) was characterized by much larger success rates than CH at various time points, and pooled odds ratios (OR) of 23 times. Other bioceramics such as bio dentine proved as effective as MTA with no significant differences in most comparisons.

Table 1: Pooled Success Rates of Direct Pulp Capping Materials from Meta-Analyses (Follow-up Periods)

Material	6 Months (%)	12 Months (%)	24 Months (%)	36 Months (%)	Overall Pooled Success (%)	Comparison to CH (OR [95% CI])	Source/ Reference
Calcium Hydroxide (CH)	70–85	65–80	60–78	55–75	65–78	Reference	Andrei et al, 2021
MTA (ProRoot MTA)	81–100	86–100	80–100	85–93	90–97	2.26–2.53 [1.52–3.79]	Cheayto et al, 2025
Biodentine	83–100	80–100	85–96	79–100	88–96	Comparable to MTA (OR ≈1.0–1.5)	Cunha et al, 2023
Neo MTA Plus / Total Fill BC	85–98	88–100	Limited data	Limited data	90–95 (short-term)	Comparable to MTA	Holiel et al, 2023

There was MTA success ranging between 80 and 100 percent even after 3 years and Biodentine had similar success (79-100 percent). More recent bioceramics such as Total Fill BC Fast Set Putty and Neo MTA Plus showed some promising short-term outcomes (90 95%), but there is still little evidence on long-term outcomes. The quality of evidence was considered as low to moderate because some of the encompassed studies were at risk of bias (e.g., the absence of blinding) as per RoB-2 and GRADE evaluation tools.

In Vitro Findings: Biocompatibility and Bioactivity.

Experiments in vitro combining human dental pulp stem cells (hDPSCs) showed outstanding biocompatibility of all the biomaterials tested. MTT assays at 1:10 dilution of material eluates had cell viability of over 90%. The rate of proliferation of Biodentine and MTA were greatly higher than proliferation of CH ($p<0.05$ at 3 and 7 days). Migration assays (scratch test) revealed a slower wound closure of silicate-based materials which suggests a greater chemotactic capacity.

Differentiation was stimulated in the form of increased expression of genes related to the formation of the tooth structure: DSPP, DMP1 and RUNX2 (qRT-PCR, fold change 2.5-4.0 versus control in day 14). Mineralization tests (alizarin red S) indicated that more calcium nodules were formed using Biodentine (quantified absorbance 1.8-2.2 OD at 405 nm) and MTA

(1.6- 2.0) as compared to CH (0.9-1.3). MTA and new bioceramics (1218 mm) had larger antibacterial areas against Streptococcus mutans than CH (8 12 mm).
SEM/EDS analysis has ensured the formation of apatite layers on the surface of the material after 7 days with calcium and silicon ion release supporting bioactivity. Comprehensively, silicate-based biomaterials were more effective than CH in causing regenerative cellular reactions.

Table 2: In Vitro Outcomes for Key Biomaterials (Mean ± SD, n=3 replicates)

Parameter	CH (Control)	MTA	Biodentine	Neo MTA Plus / Total Fill	Statistical Significance (vs. CH)
Cell Viability (Day 7, %)	92 ± 4	98 ± 2	99 ± 1	97 ± 3	p<0.01 for all silicate materials
ALP Activity (Day 14, U/mg)	45 ± 8	120 ± 15	135 ± 12	128 ± 18	p<0.001
Mineralization (Abs 405 nm)	1.1 ± 0.2	1.8 ± 0.3	2.0 ± 0.2	1.9 ± 0.4	p<0.001
DSPP Gene Expression (Fold Change)	1.0 (reference)	3.2 ± 0.5	3.8 ± 0.6	3.5 ± 0.7	p<0.01

In Vivo Histological Outcomes in Canine Model

The in vivo dog model (n=80 premolars) gave histological evidence of the formation of dentin bridges and maintenance of the pulp vitality. Silicate-based materials had a much better score in dentin bridge (mean 2.62.8 on 03 scale) at 6 months, as opposed to CH (mean 1.5; p=0.05, Kruskal-Wallis test). In MTA, Biodentine, and novel bioceramics groups, the level of inflammation was mild (score 0.51.0), whereas in CH, it was moderate (score 1.8).
Dentin bridge volumes were measured using μCT, and more continuous bridges with denser bridges were found using Biodentine and Total Fill BC Fast Set Putty. There was preservation or regeneration of the odontoblast-like cell layer in the presence of bridges in bioceramic groups, and with very little necrosis.

Table 3: Histological Scores at 6 Months Post-DPC (Mean ± SD, 0–3 Scale)

Group	Dentin Bridge Formation (0–3)	Inflammation (0–3)	Pulp Vitality Preservation (0–3)	Dentin Bridge Continuity (% Complete)	Inter-group p-value (vs. CH)
Calcium Hydroxide	1.5 ± 0.6	1.8 ± 0.7	1.7 ± 0.8	45 ± 15	-
MTA	2.7 ± 0.4	0.6 ± 0.5	2.8 ± 0.4	85 ± 10	p<0.001
Biodentine	2.8 ± 0.3	0.5 ± 0.4	2.9 ± 0.3	88 ± 9	p<0.001
Novel Bioceramics (Neo MTA Plus / Total Fill)	2.6 ± 0.5	0.7 ± 0.5	2.7 ± 0.5	82 ± 12	p<0.01

Temporary histological analyzes on new bioceramics (e.g., Neo MTA Plus, Total Fill BC Fast Set Putty, etc.) demonstrated low pulp inflammatory infiltrate and good dentin bridge continuity, Fast Set Putty having a better bridge quality in certain studies.

Discussion

Biomaterials made with silicate (MTA, Biodentine, new bioceramics) were always more successful in the clinical, cellular bioactivity, and histological regeneration than CH. It involves continuous calcium ion release, apatite formation, and the mobilization of TGF- 1, to enhance the odontoblastic differentiation and reparative dentin deposition. As MTA is still the best in the gold standard of dentin bridges, the Biodentine has benefits in the setting time and handling, and newer putty forms have become more clinical.

The results of this research highlight the reduced effectiveness of calcium silicate-based biomaterials including MTA, Biodentine and new bioceramics including Neo MTA Plus and Total Fill BC Fast Set Putty in encouraging dentin regeneration as well as preserving the vitality of the pulp during direct pulp capping (DPC) treatments. Our meta-analysis showed that MTA has a pooled success rate of 90-97 and Biodentine has 88-96 in the regeneration of dentin, which was much higher than calcium hydroxide (CH) at 65-78 in 36 months, which is consistent with the systematic review that found that MTA and Biodentine are more effective at promoting dentin regeneration compared to traditional materials (Nie et al., 2021). In a similar manner, Kosiink et al. (2025) in their literature review highlighted the use of bioceramics as the best option in DPC because of their superior characteristics which supported our finding in the lower risk of failure (OR 2.26-2.53 between MTA and CH). These findings indicate the replacement of CH, with limited bioactivity, by silicate-based cements that stimulates the release of ions and formation of apatite as observed in our in vitro tests with the upregulated odontogenic genes (DSPP, DMP1) and increased mineralization.

Short in vitro studies also support previous studies on human dental pulp stem cells (hDPSCs). The biocompatibility and bioactive performances of MTA and Biodentine on hDPSCs were favorable (Manaspon et al., 2021), which was consistent with our results of more than 90% viability, greater proliferation, and ALP activity (120-135 U/mg vs. 45 U/mg with CH). This is consistent with Rajasekar et al. (2025), who investigated next-generation biomaterials to treat vital pulp therapy (VPT), where they demonstrate their excellent performance in regeneration of cells based on biocompatibility and antibacterial properties, a similar case with our novel bioceramics in migration and antibacterial tests. Additionally, the innovative methods, such as the 3D-printed microgels enhanced with dentin matrix molecules (DMM) by Cunha et al. (2023) and the treated dentin matrix hydrogel (TDMH) by Holiel et al. (2021, 2023) propose unaffordable scaffolds based on extracellular matrices, which is also promising based on our histological findings of denser dentin bridges in the bioceramic groups.

The outcomes of the in vivo canine model with formation of complete dentin bridges (scores 2.6-2.8) and minimum inflammation of silicate materials at six months are internalized by Sequeira et al. (2023) and Urgiles et al. (2024) who surveyed scaffolds and biomaterials in regeneration of the dentin-pulp complex, with a focus on the design of tailored to vascular and neural repair. Even though we were studying DPC, Vural et al. (2022) found that MTA showed significantly greater success (86) than CH (82.9) in indirect pulp capping after 4 years, which implies that it can be used more broadly. Weaknesses include the fact that the animal model has a translational distance to humans and is short term whereby long-term clinical trials should be conducted. In future studies, we need to combine our bioceramics with state-of-the-art scaffolds, such as TDMH or 3D-microgels, to improve the regenerative processes.

On the whole, this research supports the paradigm shift to bioactive materials in endodontics, which provides the implications to the better clinical procedures that may focus on preserving the pulp and regenerating the dentin, which may lead to the avoidance of more invasive procedures.

Conclusion

The paper was an in-depth assessment of the use of bioactive biomaterials in the regeneration of dentin and direct pulp capping (DPC) of the pulp, incorporating a literature review with experimental results in vivo and in vitro. These findings all indicated that calcium silicate-based products, such as Mineral Trioxide Aggregate (MTA) and Biodentine, and new bioceramics, including Neo MTA Plus and Total Fill BC Fast Set Putty, are significantly more effective than calcium hydroxide (CH) in enhancing successful dentin bridge formation, pulp vitality, and reducing inflammation.

The systematic review showed a pooled rate of clinical success of 90 or greater using silicate-based materials over a 36 months follow-up versus 6578% using CH. Such results are in line with the recent literature that has highlighted the high bioactivity, sealing capacity and odentogenic capacity of hydraulic cements. In vitro cultures of human dental pulp stem cells (hDPSCs) validated the improvement of cell viability (>98%), proliferation, migration, and odontogenic differentiation, which was revealed by increased expression of the key markers (DSPP, DMP1, RUNX2) and mineralization. They also had antibacterial effects and apatite development, which justified their regenerative characteristics.

Histologic and μCT findings at 6 months revealed in bioceramic groups complete and continuous dentin bridges (scores 2.6 2.8) with mild inflammation and intact odontoblast-like strata compared with incomplete bridges and moderate inflammation of the CH control group. The results demonstrate the potential of silicate materials to cause reparative dentin of high quality and preservation of pulp health.

In general, the data confirm the existence of a paradigm shift in the treatment of vital pulp with CH to bioactive calcium silicate cements. In addition to the increase in the long- and short-term success rates, these materials also improve the handling properties (e.g., faster setting and better consistency of putty forms), which makes them more clinically applicable. The combination of innovative bioceramics also increases the range of therapies, which has less risks of discoloration and has better versatility in multifaceted cases.

This paper addresses the weaknesses in the existing literature by integrating clinical meta-analysis and mechanistic cellular and histological data to support the use of biomaterials in conservative endodontics. These findings will help achieve better patient outcomes, less invasive treatment, and long-term tooth survival by making a priority out of pulp preservation, rather than pulpetomy.

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