J Dent Mater Tech 2026; 15 (2): 58-65
DOI: 10.22038/jdmt.2026.93183.1936

J Dent Mater Tech

Original Article Open Access

Pulp tissue response to carbonated hydroxyapatite as a pulp-capping material in a rat model

Swathi Priyadharshini [1,2], Chinnasamy Ragavendran [1*], Anand Sherwood [2]

Abstract

Objective: This study assessed the short-term pulp tissue response to carbonated hydroxyapatite (CHA) when used for direct pulp capping, in comparison with mineral trioxide aggregate (MTA).

Methods: In this animal study, class V cavities were prepared on the labial surfaces of 30 maxillary incisors from 30 Sprague–Dawley rats. The animals were randomly assigned into three groups (n=10) based on the pulp-protective material applied: Group 1: CHA, Group 2: MTA, and Group 3: No capping material (negative control). Following material placement, the cavities were restored with reinforced zinc oxide-eugenol cement. The animals were euthanized at 7 and 14 days postoperatively (n=5), and histological evaluation was conducted to assess the degree of pulpal inflammation and the integrity of the odontoblastic layer.

Results: At both 7 and 14 days postoperatively, the control group showed histological features consistent with chronic inflammation, whereas the CHA and MTA groups exhibited preserved pulp tissue architecture and an intact odontoblastic layer. Significant differences in inflammatory scores and odontoblastic layer integrity were observed among the groups at both time points ($P<0.05$). The control group demonstrated significantly higher inflammation and a damaged odontoblastic layer compared with the CHA and MTA groups ($P<0.05$).

Conclusions: CHA elicited pulpal responses comparable to those of MTA at both 7 and 14 days postoperatively. Both materials demonstrated similar levels of inflammation and comparable preservation of odontoblastic layer integrity. These findings suggest that CHA may be a suitable alternative to MTA for early pulp preservation in vital pulp therapy.

Keywords: Carbonate apatite, Dental pulp capping, Dental pulp exposure, Hydroxyapatites, Mineral trioxide aggregate, Odontoblasts

Introduction

Dental caries is a prevalent condition that frequently results in inflammation of the pulp tissue due to bacterial components and their metabolic byproducts (1). Advanced caries frequently leads to pulpal involvement requiring root canal therapy (RCT), which compromises the mechanical properties and fracture resistance of the tooth.

Vital pulp therapy (VPT) is a conservative treatment approach used for teeth affected by advanced caries or trauma. It aims to preserve the health and biological function of the dental pulp while maintaining more natural tooth structure than root canal treatment (RCT) (2, 3).

Pulp capping, a vital pulp therapy procedure, is classified into indirect and direct approaches. Indirect pulp capping (IPC) is performed without exposing the pulp tissue, whereas direct pulp capping (DPC) involves the placement of a biocompatible material directly over exposed pulp tissue to protect the pulp and help maintain its vitality (4, 5).

The success of vital pulp therapy (VPT) depends largely on the selection of an appropriate biomaterial (6). An ideal pulp-capping material should protect the exposed pulp from bacterial contamination, provide a biologically favorable environment, and promote pulpal healing. Recent advances in bioactive materials, together with a better understanding of pulp repair mechanisms, have improved the predictability of VPT outcomes (7). Successful pulp healing is generally associated with limited inflammation and the formation of reparative dentin at the exposure site, especially when bacterial contamination is effectively controlled (8).

Traditionally, calcium hydroxide has been used as a pulp-capping material. However, the use of calcium

[1] Department of Cariology, Saveetha Dental College and Hospitals, Chennai, India
[2] Department of conservative dentistry and Enodontics, C.S.I. College of Dental Sciences and Research, Madurai, India

*Corresponding Author: Chinnasamy Ragavendran
Email: ragavan889@gmail.com

Accepted: 9 May 2026. Submitted: 1 December 2025

hydroxide for DPC is associated with several drawbacks, including the formation of tunnel defects within the dentin bridge, calcification of the pulp chamber as a result of excessive dentin deposition, high solubility in oral fluids, and limited resistance to degradation (9). Such shortcomings have led to the development of alternative bioactive materials, including mineral trioxide aggregate (MTA) and hydroxyapatite (HA), with the aim of enhancing pulp protection while promoting more predictable healing outcomes (4, 10, 11).

MTA, a cement composed of calcium silicate compounds, was first introduced in 1995 by Torabinejad and White (12) as Grey ProRoot MTA, followed by the introduction of White MTA in 1998 (13, 14). Its main components are dicalcium silicate, tricalcium silicate, tricalcium aluminate, and bismuth oxide (14). When applied directly to uninflamed, traumatically exposed pulps, MTA has shown higher success rates and more favorable hard-tissue responses than calcium hydroxide in clinical and experimental direct pulp capping studies (15). The main advantages of MTA include biocompatibility, strong sealing ability, biological activity, and the capacity to stimulate the formation of mineralized tissue (16, 17). However, MTA also has limitations, including long setting time, handling difficulties, and potential tooth discoloration. Therefore, investigating alternative materials with improved biological and physicochemical properties remains important for optimizing vital pulp therapy outcomes (18, 19).

Hydroxyapatite (HA) is a calcium phosphate–based biomaterial that closely resembles the mineral component of bone and dental hard tissues. HA has a widespread use in dentistry and medicine due to its excellent biocompatibility and osteoconductive properties (20). Carbonated hydroxyapatite (CHA) is a modified form of HA in which carbonate (CO_3^{2-}) ions partially replace phosphate or hydroxyl groups in the crystal structure. This modification makes CHA more similar to natural bone mineral and can also enhance its bioactivity, resorption, and bone-conductive properties (17). CHA has also attracted attention as a promising biomaterial for dental applications because of its cytocompatibility and structural resemblance to natural tooth tissues (21-25).

Previous studies have primarily investigated carbonated hydroxyapatite (CHA) in bone-related applications, where it has demonstrated favorable physicochemical properties, bioactivity, and biocompatibility, as well as the ability to support bone regeneration and osseointegration (21-23). Despite these promising results, evidence regarding the pulpal response to CHA following direct pulp capping remains limited. Therefore, this study aimed to evaluate the short-term pulp tissue response to CHA when used as a direct pulp-capping material in a rat model, in comparison with mineral trioxide aggregate (MTA).

Materials and methods

Study design and ethical approval

This animal study was approved by the institutional animal ethics committee under the approval number BRULAC/SDCH/SIMATS/IAEC/06-2023/11. All experimental procedures adhered to the ARRIVE guidelines (Animal Research: Reporting of In Vivo Experiments).

Sample size estimation was performed using G*Power software (version 3.1.9.7; Heinrich Heine University Düsseldorf, Düsseldorf, Germany). Based on an expected effect size of f = 0.53, a statistical power of 95%, and a significance level of α = 0.05, the minimum required sample size was calculated as 30 specimens, with 10 specimens per group.

Preparation and characterization of carbonated hydroxyapatite

Carbonated hydroxyapatite (CHA) was synthesized using a wet chemical precipitation method. Briefly, aqueous solutions of calcium nitrate tetrahydrate [$Ca(NO_3)_2{\cdot}4H_2O$; Sigma-Aldrich, MA, USA] and diammonium hydrogen phosphate [$(NH_4)_2HPO_4$; Sigma-Aldrich] were prepared at concentrations of 0.5 M and 0.3 M, respectively. Sodium hydrogen carbonate ($NaHCO_3$; Sigma-Aldrich) was prepared at a concentration of 0.5 M and used as the carbonate source.

The phosphate solution ($(NH_4)_2HPO_4$) was added dropwise to the $NaHCO_3$ solution under continuous mechanical stirring (500 rpm) at 25 ± 2 °C, followed by gradual addition of the calcium solution ($Ca(NO_3)_2{\cdot}4H_2O$) to achieve a Ca:P molar ratio of 1.67:1. The pH was maintained at 9.0 ± 0.2 using using 1 M sodium hydroxide (NaOH; Sigma-Aldrich). After complete addition, the suspension was stirred for 2 hours and then kept for 12 hours at room temperature, resulting in the formation of a white precipitate.

The precipitate was filtered, washed repeatedly with deionized water, dried at 100 °C, and gently ground to obtain CHA powder. The synthesized powder was then characterized using standard physicochemical techniques. Phase identification was performed by X-ray diffraction (XRD) using copper K-alpha radiation (Cu Kα;

λ = 1.5406 Å) over a 2θ range of 20°–60°. The XRD pattern of the synthesized CHA displayed characteristic diffraction peaks at 25.8°, 28.1°, 29.0°, 31.7°, 32.2°, 32.8°, 34.0°, 39.7°, 46.6°, 48.1°, 49.4°, 53.1°, and 55.9°, which were consistent with the hydroxyapatite crystal structure according to the ICDD reference pattern 09-0432.

Animal model and housing conditions

Thirty male Sprague–Dawley rats, weighing approximately 230 g, were used in this study. The animals were housed in standard polycarbonate cages (3–4 rats per cage) with appropriate bedding in a climate-controlled, well-ventilated animal facility maintained at 25 ± 1 °C and 60 ± 5% relative humidity under a 12-h light/dark cycle. Food and water were provided ad libitum. Animals were acclimatized to the housing environment for 5 days before the experimental procedures.

Grouping and experimental procedures

A total of 30 rats (30 maxillary incisors) were included in the study and randomly allocated into three groups (n = 10 per group) using a computer-generated randomization sequence. Each group was further divided into two subgroups according to the evaluation period (n = 5 per time point). Animals were sacrificed either on postoperative day 7 or 14 for sample collection.

The animals were anesthetized via intraperitoneal injection of a ketamine–xylazine mixture, prepared by combining ketamine hydrochloride (Alfasan, Woerden, Netherlands) and xylazine hydrochloride (Alfasan) diluted with sterile normal saline. The mixture was administered at a dose of 0.1 mL per 50 g of body weight.

The maxillary incisors were disinfected with 0.2% chlorhexidine gluconate solution (Consepsis®, Ultradent Products Inc., South Jordan, UT, USA). Then, standardized class V cavities (2–3.5 mm in diameter) were prepared on the labial surfaces of the maxillary incisors (one incisor per animal) using a sterile carbide round bur (ISO No. 001/010; MANI Inc., Utsunomiya, Japan) mounted on a high-speed handpiece under copious water irrigation. Cavity preparation, including pulp exposure and hemostasis, was completed within 60–90 seconds per tooth to minimize pulpal trauma. The Exposed pulp area was standardized to approximately 0.5 mm in diameter (confirmed visually). Hemostasis was achieved within 30 seconds using sterile saline irrigation and gentle pressure with cotton pellets. The presence of persistent bleeding was an exclusion criterion.

The exposed pulps in each group were then covered with the following materials:

- Group 1 (CHA): Direct pulp capping was performed using laboratory-synthesized, carbonated hydroxyapatite (CHA), prepared by mixing one scoop of CHA powder with two drops of saline.
- Group 2 (MTA): Direct pulp capping was performed using commercial MTA (Biostructure MTA, Safe Endo, New Delhi, India), prepared according to the manufacturer's instructions by mixing one scoop of powder with one drop of liquid.
- Group 3 (Negative control): No capping material was applied to the exposed pulp tissue.

A sterile plastic instrument was used to place the capping material over the pulp exposure site. The cavities were then restored with a reinforced zinc oxide-eugenol intermediate restorative material (IRM®; Dentsply Sirona, York, PA, USA).

To minimize postoperative pain, meloxicam (Alfasan) was administered at 1–2 mg/kg body weight. Following the procedure, the rats were returned to well-ventilated cages and provided a soft diet on the first postoperative day. The animals were monitored daily for signs of distress, reduced activity, or changes in food and water intake.

Specimen harvesting and processing

Upon completion of the observation periods (7 or 14 days), the animals were euthanized by intraperitoneal administration of an overdose of ketamine–xylazine (ketamine 70 mg/kg and xylazine 10 mg/kg; Alfasan). Following euthanasia, the specimens were prepared for histological analysis. The entire maxilla was carefully harvested and fixed in 10% neutral buffered formalin (Merck KGaA, Darmstadt, Germany) for 24 hours. The samples were then decalcified in 20% formic acid (Merck KGaA) for 3 days. After decalcification, the maxilla was bisected vertically and thoroughly rinsed under running tap water overnight.

The specimens were subsequently dehydrated through a graded ethanol series (Merck KGaA), cleared with xylene (Merck KGaA), and embedded in paraffin blocks (Leica Biosystems, Nußloch, Germany). Serial sections of 4–6 µm thickness were prepared using a rotary microtome (Leica Biosystems) and stained with hematoxylin and eosin (H&E; Sigma-Aldrich).

Histopathological evaluation

The stained sections were evaluated in a blinded manner by two trained and calibrated examiners using coded samples. Examiner calibration was conducted in consultation with an experienced pathologist before the evaluation. All specimens were examined under a light microscope (MLX-B Plus; Magnus Opto Systems India Pvt. Ltd., New Delhi, India) at ×40 magnification.

The cellular response to the biomaterials was assessed by evaluating the degree of pulpal inflammation and the integrity of the odontoblastic layer. Pulpal inflammation was graded according to Boopathi et al. (26), while odontoblastic layer integrity was evaluated according to the method described by Orhan et al. (27).

Pulpal inflammation was classified into four grades as follows:

- Grade 0: No inflammatory cells observed.
- Grade 1: Mild inflammation, with fewer than 10 inflammatory cells observed.
- Grade 2: Moderate inflammation, with 10–25 inflammatory cells observed.
- Grade 3: Severe inflammation, with more than 25 inflammatory cells observed.

The presence of the odontoblastic layer was evaluated using a binary scoring system:

- Score 0: Damaged, disrupted, or absent odontoblastic layer
- Score 1: Intact odontoblastic layer

Statistical analysis

Data were analyzed using IBM SPSS Statistics software, version 23 (IBM Corp., Armonk, NY, USA). The Kruskal–Wallis test and chi-square test were used to examine the groups; additionally, Inter-examiner reliability was assessed using Cohen's kappa statistics. $P<0.05$ was defined as the level of statistical significance.

Results

Inter-examiner agreement was excellent, with Cohen's kappa values of ≥0.86 for all measurements.

Table 1 presents the distribution of pulpal inflammation scores among the three study groups on postoperative days 7 and 14. The Kruskal–Wallis test showed significant differences in inflammatory scores among the groups on both day 7 ($P=0.007$) and day 14 ($P=0.004$).

On day 7, most specimens in the CHA and MTA groups showed no or only mild inflammation (scores 0–1), whereas the specimens in the control group predominantly exhibited moderate to severe inflammation (scores 2–3). By day 14, inflammatory scores had further decreased in the CHA and MTA groups, with a greater proportion of specimens showing no inflammation (score 0). In contrast, the control group continued to exhibit mainly moderate inflammation (score 2). No significant difference in inflammatory scores was observed between the CHA and MTA groups at either time point ($P>0.05$). However, both groups showed significantly lower inflammatory scores than the control group at both evaluation intervals ($P<0.05$).

Table 2 summarizes odontoblastic layer integrity in the study groups on postoperative days 7 and 14. On day 7, an intact odontoblastic layer was observed in all specimens in the CHA and MTA groups (score 1), whereas the odontoblastic layer was damaged, disrupted, or absent in all specimens in the control group (score 0; $P=0.001$). A similar pattern was observed on day 14, with preservation of an intact odontoblastic layer in the CHA and MTA groups, while the control group continued to show damaged, disrupted, or absent odontoblastic layers ($P=0.001$).

Table 1. Frequency (N) and percentage (%) of inflammatory response scores in the study groups on postoperative days 7 and 14

Materials	Day 7					Day 14				
	Score 0	Score 1	Score 2	Score 3	Total	Score 0	Score 1	Score 2	Score 3	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
CHA	2 (40%)	3 (60%)	0 (0%)	0 (0%)	5 (100%)	4 (80%)	1 (20%)	0 (0%)	0 (0%)	5 (100%)
MTA	0 (0%)	3 (60%)	2 (40%)	0 (0%)	5 (100%)	3 (60%)	2 (40%)	0 (0%)	0 (0%)	5 (100%)
Control	0 (0%)	0 (0%)	4 (80%)	1 (20%)	5 (100%)	0 (0%)	0 (0%)	5 (0%)	0 (0%)	5 (100%)
p-value*	0.007					0.004				

Score 0 = no inflammation; Score 1 = mild inflammation; Score 2 = moderate inflammation; Score 3 = severe inflammation

*Kruskal–Wallis test; Significance level set at $P<0.05$

Table 2. Frequency (N) and percentage (%) of odontoblastic layer integrity scores in the study groups on postoperative days 7 and 14

Materials	Day 7			Day 14		
	Score 0	Score 1	Total	Score 0	Score 1	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
CHA	0	5 (100%)	5 (100%)	0	5(100%)	5 (100%)
MTA	0	5(100%)	5 (100%)	0	5(100%)	5 (100%)
Control	5(100%)	0	5 (100%)	5(100%)	0	5 (100%)
p-value*	0.001			0.001		

Score 0: Damaged, disrupted, or absent odontoblastic layer; Score 1: intact odontoblastic layer

*Chi-square test; significance level set at P<0.05

Discussion

This study evaluated carbonated hydroxyapatite (CHA) as a direct pulp-capping (DPC) material and investigated its early effects on pulpal tissue response in a rat model. Although CHA has been extensively studied for bone regeneration, evidence of its performance in pulp tissue remains limited. Therefore, DPC was selected as a clinically relevant model to assess early inflammatory response and odontoblast layer integrity following CHA application. Rats were used in this study because their pulpal healing patterns after DPC closely resemble those of humans, making them an appropriate model for preclinical evaluation of dental biomaterials (28).

CHA was synthesised using the precipitation method, which is one of the most commonly employed techniques for preparing hydroxyapatite-based materials. This approach is particularly suitable for producing medical-grade hydroxyapatite powders because of its relatively low processing temperature, cost-effectiveness, operational simplicity, capacity to generate fine particles, and ability to yield products with high purity (29). CHA is considered more bioactive and more soluble than conventional hydroxyapatite because of its smaller particle size, larger surface area, and unique surface morphology, which may enhance tissue interaction and resorption (30).

The present study was designed as a short-term evaluation of the early pulpal response to pulp capping materials, with a particular focus on inflammatory reactions and pulpal healing. Because the acute inflammatory response to biomaterials generally develops during the first two weeks after injury, the 7- and 14-day time points were selected to assess early pulpal tissue response at the exposure site (10, 31, 32). At these early time points, histological assessment focused on inflammatory response and odontoblast layer integrity, as complete dentine bridge formation typically requires longer observation periods (10, 31, 32).

The histological analysis revealed that the application of both CHA and MTA as pulp capping materials induced mild or minimal inflammation (scores 0–1) and preserved the integrity of the odontoblastic layer on 7 and 14 days, whereas the control group exhibited marked disruption of the pulpal tissue architecture. The difference between the control and both MTA and CHA groups was significant in both variables and at both time points. Therefore, both CHA and MTA demonstrated favorable and acceptable pulpal responses and can be used effectively as direct pulp capping materials. Therefore, CHA may serve as a promising alternative to MTA for vital pulp therapy.

In the present study, the control group should not be considered biologically inert, as the cavity was restored with intermediate restorative material (IRM). This material may itself have influenced the pulpal tissue response through the possible release of eugenol and the potential for microleakage. In addition, the pulp was left uncapped, which may have increased inflammatory changes. Therefore, the control group findings should be interpreted cautiously because the observed inflammation may reflect both the absence of a capping material and the effects of IRM (33).

The outcomes of this study are consistent with some previous studies that demonstrated favorable biological behavior of CHA in osseointegration and bone repair models (22, 34, 35). Although these findings were mainly obtained in bone rather than pulp tissue, they support the rationale for using CHA as a pulp protection material in the present study. Calasans-Maia et al (30) conducted an in vivo study using an alveolar bone defect model to compare the biological performance of CHA/calcium alginate microspheres with that of sintered hydroxyapatite. In their study, the materials were implanted into standardized defects, and osteoconductivity, biosorption, and new bone formation were assessed over healing periods of 21 and 42 days. The results showed that the CHA-based

material exhibited greater osteoconductivity, faster resorption, and more extensive new bone deposition than sintered HA.

Because the present study was limited to 7 and 14 days, it was suitable for evaluating only the early pulpal inflammatory response and did not allow assessment of dentin bridge formation. In contrast, some studies have evaluated carbonate apatite-based materials over longer healing periods, allowing assessment of both inflammation and dentin bridge formation. Octiara et al. (36) investigated carbonate apatite (Gama-CHA) versus calcium hydroxide in Wistar rat molars and reported that pulpal inflammation scores decreased from 2 to 6 weeks in both groups, with no significant difference between the experimental groups, whereas the negative control (uncapped control) maintained significantly higher inflammation scores. Dentin bridges were absent at 2 weeks but present at 4 and 6 weeks, again with no significant difference between carbonate apatite and calcium hydroxide groups. Although the present findings are consistent with those reported by Octiara et al. (36) regarding inflammatory scores, differences in material formulation (Gama-CHA combined with additional components) and the longer observation periods in their study limit direct comparison, particularly for dentin bridge outcomes. Sabirin and Zakaria (37) evaluated the effectiveness of carbonate apatite (CO_3Ap) and CO_3Ap + bioglass cement as direct pulp capping materials in Wistar rats. The study included four groups: CO_3Ap, CO_3Ap + bioglass cement, calcium hydroxide as the positive control, and an untreated cavity as the negative control. Both CO_3Ap-based materials promoted reparative dentin formation comparable to calcium hydroxide, whereas the negative control group showed no dentin bridge formation. As that study focused on dentin bridge formation over extended healing periods, its findings are not directly comparable with the present study, which assessed only the early pulpal response.

A key limitation of this study is the small sample size and the short observation period (7 and 14 days), which restricts the assessment to early pulpal responses and does not permit evaluation of long-term outcomes such as thickness, continuity, or maturation of the dentinal bridge. Another limitation is the use of a rat model. Although rats are useful for preliminary biomaterial testing, their pulpal physiology and healing patterns may not fully reflect human clinical conditions. Furthermore, the histological analysis focused on histomorphologic criteria (inflammatory response and integrity of the odontoblastic layer), without more detailed pathological or molecular assessments. Future studies should therefore include longer follow-up periods to characterize dentin bridge formation, employ more comprehensive histopathologic and molecular analyses of pulp healing, and ultimately incorporate well-designed clinical trials in humans to better define the regenerative potential and clinical performance of CHA as a pulp-capping material.

Conclusions

Considering the limitations of this short-term animal study, CHA elicited pulpal responses comparable to those of MTA, showing similar degrees of inflammation and a comparable pattern of odontoblastic layer organization up to 14 days after direct pulp capping. Both materials preserved the general histological integrity of the pulp tissue, and no severe inflammatory reaction was observed in either group. These findings suggest that CHA may represent a promising alternative material for vital pulp therapy.

Acknowledgements

I would like to express my sincere gratitude to Pink Lab, Saveetha Dental College, and Hospital for their invaluable support and contribution towards this work.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

C.R. developed the project, helped with data analysis, and edited the manuscript. S.S.P. helped with data collection, analyzed the data, and wrote the manuscript. A.S. collected the data and edited the manuscript. All authors read and approved the final manuscript.

Ethical considerations

The protocol of the present animal study was approved by the Institutional Animal Ethics Committee under the approval number of Saveetha Dental College and Hospital (BRULAC/SDCH/SIMATS/IAEC/06-2023/11).

Funding

The research reported in this article was self-funded, and no external financial support was received for its conduct.

References

1. Ballikaya E, Çelebi-Saltik B. Approaches to vital pulp therapies. Aust Endod J 2023;49(3):735–749.
2. Saikiran KV, Gurunathan D, Elicherla SR, Rahul S, Nuvvula S, Nuvvula S. Knowledge and awareness of pulp vitality tests among dental interns and postgraduates: A multicenter cross-sectional study. Endodontology 2024;36(3):245–250.
3. Jakovljevic A, Jaćimović J, Aminoshariae A, Fransson H. Effectiveness of vital pulp treatment in managing nontraumatic pulpitis associated with no or nonspontaneous pain: A systematic review. Int Endod J 2023;56 Suppl 3:340–354.
4. Özyürek T, Demiryürek E. Comparison of the antimicrobial activity of direct pulp-capping materials: Mineral trioxide aggregate-Angelus and Biodentine. J Conserv Dent 2016;19(6):569–572.
5. Zhu C, Ju B, Ni R. Clinical outcome of direct pulp capping with MTA or calcium hydroxide: a systematic review and meta-analysis. Int J Clin Exp Med 2015;8(10):17055–17060.
6. Asgary S. Calcium-enriched mixture pulpotomy of a human permanent molar with irreversible pulpitis and condensing apical periodontitis. J Conserv Dent 2011;14(1):90–93.
7. Pandey P, Nawal RR, Talwar S, Yadav S. Vital pulp therapy: A bibliometric analysis of the 100 most-cited articles from 1966 to 2022. J Conserv Dent Endod 2024;27(11):1098–1103.
8. Islam R, Islam MRR, Tanaka T, Alam MK, Ahmed HMA, Sano H. Direct pulp capping procedures - Evidence and practice. Jpn Dent Sci Rev 2023;59:48–61.
9. Murray PE, Hafez AA, Smith AJ, Cox CF. Hierarchy of pulp capping and repair activities responsible for dentin bridge formation. Am J Dent 2002;15(4):236–243.
10. Trongkij P, Sutimuntanakul S, Lapthanasupkul P, Chaimanakarn C, Wong R, Banomyong D. Effects of the exposure site on histological pulpal responses after direct capping with 2 calcium-silicate based cements in a rat model. Restor Dent Endod 2018;43(4):e36.
11. Ballal NV, Rao S, Rao N, Urala A, Yoo J-S, Al-Haj Husain N, et al. Evaluation of two different types of mineral trioxide aggregate cements as direct pulp capping agents in human teeth. Appl Sci 2021;11(21):10455.
12. Parirokh M, Torabinejad M. Mineral trioxide aggregate: a comprehensive literature review--Part I: chemical, physical, and antibacterial properties. J Endod 2010;36(1):16–27.
13. Mangat P, Goswami K, Solanki M, Rajput N. Comparison between biodentine and light-cured mineral trioxide aggregate as an indirect pulp capping agent - A randomized controlled trial. J Conserv Dent Endod 2025;28(1):78–83.
14. Hilton TJ, Ferracane JL, Mancl L. Comparison of CaOH with MTA for direct pulp capping: a PBRN randomized clinical trial. J Dent Res 2013;92(7 Suppl):16s–22s.
15. Coll JA, Dhar V, Guelmann M, Crystal YO, Chen CY, Marghalani AA, et al. Vital Pulp Therapy in Permanent Teeth: A Systematic Review and Meta-Analyses. Pediatr Dent 2025;47(3):137–150.
16. Alp Ş, Ulusoy N. Current approaches in pulp capping: a review. Cyprus J of Med Sci 2024;9(3):154.
17. Kokate P, Tandale AB, Sanap A, Kheur S, Bhonde RR, Kasat V. Effect of biodentine modified with bioactive glass nanoparticles on biocompatibility, osteogenic differentiation, and gene expression of human dental pulp stem cells. J Conserv Dent Endod 2025;28(8):809–813.
18. Selvendran K, Ahamed AS, Krishnamurthy M, Kumar VN, Raju VG. Comparison of clinical success between three different materials-direct pulp capping of carious molars-an in-vivo stud. J Pharm Res Int 2021;33(33):192–200.
19. Al-Saudi KW. A paradigm shift from calcium hydroxide to bioceramics in direct pulp capping: A narrative review. J Conserv Dent Endod 2024;27(1):2–10.
20. Mobaleghi T, Vafadoost R, Sadeghi R, Mashhadi-Abbas F, Ahmadian-Moghadam H, Semyari H, et al. Histomorphometric and histologic evaluation of the effects of leukocyte platelet-rich fibrin (L-PRF) and nano-hydroxyapatite (nHA) on bone regeneration in rabbits. J Den Mater Tech 2023;12(1):43–50.
21. Copete H, López E, Baudin C. Synthesis and characterization of B-type carbonated hydroxyapatite materials: Effect of carbonate content on mechanical strength and in vitro degradation. Bol Soc Esp de Cerám Vidr 2024;63(4):255–267.
22. Li S, Yu W, Zhang W, Zhang G, Yu L, Lu E. Evaluation of highly carbonated hydroxyapatite bioceramic implant coatings with hierarchical micro-/nanorod topography optimized for osseointegration. Int J Nanomedicine 2018;13:3643–3659.
23. Landi E, Celotti G, Logroscino G, Tampieri A. Carbonated hydroxyapatite as bone substitute. J t Eur Ceram Soc 2003;23(15):2931–2937.
24. Schneider Werner Vianna T, Sartoretto SC, Neves Novellino Alves AT, Figueiredo de Brito Resende R, de Almeida Barros Mourão CF, de Albuquerque Calasans-Maia J, et al. Nanostructured Carbonated Hydroxyapatite Associated to rhBMP-2 Improves Bone Repair in Rat Calvaria. J Funct Biomater 2020;11(4):87.
25. Priyadharshini S, Ragavendran C, Sherwood A. The antibacterial properties and biocompatibility of carbonated hydroxyapatite as a pulp capping agent. J Den Mater Tech 2025;14(1).
26. Boopathi T, Manimaran S, Kerena JC, Sebeena M, Karthick K, Deepa NT. Histological evaluation of pulp response to alendronate and Biodentine as pulp capping agents: an animal study. Restor Dent Endod 2024;49(4):e39.
27. Orhan EO, Maden M, Senguüven B. Odontoblast-like cell numbers and reparative dentine thickness after direct pulp capping with platelet-rich plasma and enamel matrix derivative: a histomorphometric evaluation. Int Endod J 2012;45(4):317–325.

28. Dammaschke T. Rat molar teeth as a study model for direct pulp capping research in dentistry. Lab Anim 2010;44(1):1–6.
29. Aziz S, Pranowo HD, Ana ID, Yusuf Y. Energy efficiency of the carbonate hydroxyapatite nanoparticle synthesis using microwave heating treatment and its effect on material characteristics. J Chem 2024;24:238.
30. Calasans-Maia MD, Melo BR, Alves AT, Resende RF, Louro RS, Sartoretto SC, et al. Cytocompatibility and biocompatibility of nanostructured carbonated hydroxyapatite spheres for bone repair. J Appl Oral Sci 2015;23(6):599–608.
31. Chicarelli LPG, Webber MBF, Amorim JPA, Rangel A, Camilotti V, Sinhoreti MAC, et al. Effect of Tricalcium Silicate on Direct Pulp Capping: Experimental Study in Rats. Eur J Dent 2021;15(1):101–108.
32. Anderson JM, Rodriguez A, Chang DT. Foreign body reaction to biomaterials. Semin Immunol 2008;20(2):86–100.
33. Rathod P, Patel A, Ikhar A, Chandak M, Kurundkar S, Pawar L, et al. Overview of Interim and Temporary Restorations of Teeth During Endodontic Treatment. Cureus 2024;16(5):e60591.
34. Yotsova R, Peev S. Biological Properties and Medical Applications of Carbonate Apatite: A Systematic Review. Pharmaceutics 2024;16(2):291.
35. Devitaningtyas N, Syaify A, Herawati D. Combining 10% propolis with carbonated hydroxyapatite to observe the RANKL expression in a rabbit's alveolar bone. Dent J 2020;53(4):212–216.
36. Octiara E, Zendrato M, Silalahi E, editors. Differences in pulp cell inflammation and dentinal bridge formation between carbonate apatite and calcium hydroxide after direct pulp capping on Wistar Rat maxillary first molar. Proc Aceh Int Dent Meet (AIDEM 2021); 2022: Atlantis Press.
37. Sabirin IPR, Zakaria MN. The use of carbonate apatite bioglass cement as pulp capping material examined from reparative dentin. extraction 2021;1:2.