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RESEARCH ARTICLE **OPEN ACCESS**

Evaluation of the Setting Time and pH of Nanohydroxyapatite-Chitosan as a Direct Pulp Capping Material

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Abstract:

Introduction/Objective: Calcium hydroxide (CaOH) and Mineral Trioxide Aggregate (MTA) are the most commonly used materials for Direct Pulp Capping (DPC). However, CaOH is associated with a very high pH and tunnel defects, whereas MTA has a prolonged setting time, potential tooth discoloration, low mechanical strength, and relatively high cost. Since setting time and pH are important physicochemical properties influencing clinical handling and pulp response, biocompatible alternatives are needed. Nanohydroxyapatite–Chitosan (nHA–CH) has shown potential to improve adhesion and promote dentin remineralization. Therefore, this study evaluated the setting time and pH of nHA–CH as a direct pulp capping material.

Methods: An experimental laboratory study with a post-test-only control group design was conducted using nHA–CH, CaOH, and MTA (n = 6 per group). Setting time was measured using a Gillmore apparatus, and pH was measured after 3 and 24 hours using a digital pH meter. Data were analyzed using one-way ANOVA, post hoc LSD, and paired t-tests ($p < 0.05$).

Results: One-way ANOVA showed significant differences in setting time among the three materials ($p < 0.05$). The mean setting times of nHA–CH, CaOH, and MTA were 15.32 ± 0.09, 2.51 ± 0.01, and 17.16 ± 0.03 min, respectively. Paired t-test analysis showed significant changes in pH between 3 and 24 hours for all materials ($p < 0.05$). The pH of nHA–CH (6.90–7.27) remained lower than that of CaOH (10.33–11.51) and MTA (12.01–12.67).

Discussion: The distinct setting and pH characteristics of nHA–CH suggest a potential balance between practical handling and a more pulp-compatible chemical environment, highlighting its potential as an alternative approach to direct pulp capping.

Conclusion: nHA–CH demonstrated favorable gelation characteristics and a near-neutral to slightly alkaline pH; however, further studies are required before clinical application.

Keywords: Chitosan, Direct pulp capping, Nanohydroxyapatite, ph, Setting time, One-way ANOVA.

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1. INTRODUCTION

Pulp exposure caused by caries, trauma, operative errors during tooth preparation, and iatrogenic factors is common in dental practice [1]. It may lead to bacterial infection, inflammation, and dental pain. Vital pulp therapy, including pulp capping, aims to preserve pulp vitality and function [2]. The primary objective of pulp capping is to promote pulp healing while maintaining its vitality and function [3]. This treatment involves the application of a medicament to protect the exposed pulp from bacterial contamination and stimulate reparative dentin formation [2, 4, 5].

Pulp capping is classified into Direct Pulp Capping (DPC) and Indirect Pulp Capping (IPC). IPC is performed when the pulp remains unexposed and presents with mild inflammation, allowing the medicament to be placed without direct contact with the pulp [2]. In contrast, DPC is indicated for pulp exposures smaller than 2 mm, where the medicament is placed directly on the exposed pulp tissue [4]. Therefore, the capping material must exhibit excellent biocompatibility [3].

An ideal DPC material should be biocompatible, capable of controlling infection, preventing microleakage, and promoting reparative dentin formation [2, 6]. he success of DPC is influenced by several factors, including the patient's history of spontaneous pain, bleeding control, complete caries removal, aseptic technique, restoration quality, and age [1, 3]. Histologically, pulp healing begins with inflammation, followed by collagen synthesis and ultimately reparative dentin formation [1, 2].

Reparative dentin forms a protective dentin bridge over the exposed pulp and is considered a hallmark of successful healing [2]. Its formation consists of four phases: the exudative phase (1–5 days), proliferative phase (3–7 days), osteodentin formation phase (5–14 days), and tubular dentin formation phase (>14 days) [2, 4]. Calcium hydroxide (CaOH) and Mineral Trioxide Aggregate (MTA) are among the most commonly used DPC materials [1].

Calcium hydroxide (CaOH) has long been regarded as the gold standard for pulp capping and has been used since the 1930s [3]. Its high pH provides antibacterial and anticariogenic effects. However, excessive alkalinity may induce superficial pulp necrosis and inflammation following pulp capping. In addition, CaOH is highly soluble, degrades over time, has low mechanical strength, and may cause tunnel defects within the dentin bridge, thereby facilitating bacterial penetration and subsequent pulp irritation [7-9]. To overcome these limitations, newer biomaterials such as Mineral Trioxide Aggregate (MTA) have been developed [10]. MTA promotes reparative dentin formation, and its high alkalinity contributes to antibacterial activity and pulp healing [11, 12]. Nevertheless, MTA also has several disadvantages, including a prolonged setting time, tooth discoloration, poor mechanical properties, limited adhesion to tooth structure, and relatively high cost [1, 10, 12].

Despite their clinical effectiveness, both CaOH and MTA have limitations related to reparative dentin formation, adhesion, and physicochemical properties. Important physicochemical properties of DPC materials include ion release, solubility, setting time, and pH. Setting time influences clinical handling and the practicality of material placement, particularly under moist oral conditions [13]. Likewise, pH plays an essential role in determining pulp tissue response [13-15]. An acidic pH may impair protein synthesis and pulp cell proliferation [14, 16]. Therefore, alternative DPC materials with improved physicochemical and biological properties are required [17]. One promising candidate is a combination of Hydroxyapatite (HA) and Chitosan (CH) [18-20].

Hydroxyapatite (HA) is one of the most extensively studied biomaterials in dentistry because of its excellent biocompatibility and its role as the primary mineral component of bone and teeth [21]. HA serves as an effective source of calcium and phosphate ions, making it suitable for remineralizing early carious lesions [22]. In recent decades, nanosized biomaterials, particularly Nanohydroxyapatite (nHA), have gained considerable attention in dentistry. nHA has a high surface area that allows proper adhesion and remineralization [19, 20]. nHA has a high surface area, which enhances adhesion and remineralization. It also promotes the proliferation and differentiation of dental pulp fibroblasts and odontogenic stem cells, thereby supporting reparative dentin formation [2, 17]. However, nHA exhibits limited antibacterial activity and may induce inflammatory responses [22, 23]. Therefore, combining nHA with another biomaterial may help overcome these limitations. Chitosan (CH) has been reported to reduce inflammation and promote tissue healing [24].

CH is a natural polysaccharide originating from crustaceans. It is biocompatible and has excellent antibacterial properties [25]. This natural polysaccharide derived from chitin is non-toxic, biodegradable, biocompatible, and has osteoinductive properties. CH also has antibacterial properties and is suitable for regenerative purposes in dentistry [21, 24]. The combination of nHA and CH has shown potential as an alternative DPC material by optimizing pulp tissue healing [17]. When combined with nHA, which has osteoconductive properties, this can provide material effectiveness, improved mechanical properties, and the ability to support pulp tissue healing due to the antibacterial properties of CH [17, 23]. This plays an important role in preventing infection while the pulp is healing [17, 19, 21].

Given the limited evidence regarding the use of nHA–CH as a direct pulp-capping material, further investigation of its physicochemical properties, particularly its setting time and pH, is warranted. Therefore, this study aimed to evaluate the setting time and pH of nHA–CH as a potential direct pulp capping material, providing preliminary evidence for the future development of alternative pulp capping biomaterials.

2. MATERIAL AND METHODS

This study was an experimental laboratory study with a post-test-only control group design conducted at the Central Laboratory, Andalas University. The experimental material was nanohydroxyapatite–chitosan (nHA–CH), while calcium hydroxide (CaOH) and Mineral Trioxide Aggregate (MTA) were used as the control materials. A total of 18 cylindrical specimens (2 mm in thickness and 10 mm in diameter) according to ISO 6876:2012 [26]. The specimens were equally allocated to three experimental groups (n = 6): group 1 CaOH, group 2 MTA, and group 3 nHA–CH. The pH was measured after 3 and 24 hours of incubation. The normality of the data was assessed using the Shapiro–Wilk test, and homogeneity of variance was evaluated using Levene's test. Differences in setting time among the three groups were analyzed using one-way ANOVA followed by the post hoc LSD test. Changes in pH values between 3 and 24 hours within each group were analyzed using the paired t-test ($p < 0.05$).

The nHA paste was prepared by gradually dispersing 0.3 grams of nHA powder (nanoparticles <200 nm; Code 677418, Sigma Aldrich, USA) into 1–2 mL of 0.9% saline solution, followed by stirring with a magnetic stirrer. HPMC (Type 100, Green Pharmacy) 2% was then added until a paste consistency was obtained. The 3% CH paste was prepared by dissolving 0.3 grams of chitosan powder (Code: 448869, Sigma-Aldrich, USA) in 10 mL of 1% acetic acid solution and stirring the mixture with a magnetic stirrer for 30–60 minutes until homogeneous. The solution was gradually neutralized with 1 N NaOH while maintaining the pH at 6.8–7.2. Finally, 1 mL of 0.9% saline solution and 2% HPMC were added until a paste consistency was obtained.

The nHA–CH paste was prepared by mixing the nHA and CH pastes in a sterile mortar until homogeneous. Subsequently, 1 mL of 0.9% saline solution and HPMC were added to obtain the desired paste consistency. The paste was transferred into a 3-mL syringe wrapped with aluminum foil. The paste was then placed into a stainless-steel mold.

The control materials were CaOH (Dycal®, Dentsply Tulsa Dental, USA) and MTA (Biostructure MTA, SafeEndo Dental, India). Each material was placed into a stainless-steel mold. Setting time was measured using a Gillmore apparatus. After mixing, each specimen was placed into the mold, and a Gillmore indenter (2 mm in diameter and 100 grams in weight) was positioned at the center of the specimen. The setting time was recorded as the time from the completion of mixing until the indenter no longer produced a visible indentation on the specimen surface. For the pH measurement, the set specimens were immersed in conical tubes containing distilled water and incubated at 37°C. The pH was measured after 3 and 24 hours using a digital pH meter (MW160 Max, Milwaukee, Hungary) [13].

3. RESULT

This study evaluated the setting time and pH of nanohydroxyapatite–chitosan (nHA–CH) compared with calcium hydroxide (CaOH) and Mineral Trioxide Aggregate (MTA) as direct pulp capping materials. The mean setting time of each experimental group is presented in Table **1**.

As shown in Table **1**, CaOH exhibited the shortest mean setting time (2.51 ± 0.01 min), whereas MTA exhibited the longest (17.16 ± 0.03 min). The nHA–CH group formed a semi-solid gel with a mean gelation time of 15.32 ± 0.09 min.

The data were statistically analyzed to determine differences in setting time among the experimental groups. The normality test using the Shapiro–Wilk test showed $p > 0.05$, indicating that the data were normally distributed. Levene's test also showed $p > 0.05$, indicating homogeneity of variance; therefore, a parametric one-way ANOVA was performed.

As shown in Table **2**, one-way ANOVA demonstrated a statistically significant difference in setting time among the three groups ($p < 0.01$). Therefore, Post Hoc LSD analysis was performed for pairwise comparisons.

Based on Table **3**, the results of the Post Hoc LSD analysis showed a significant difference in setting time among all treatment groups, with $p < 0.05$.

The pH values were measured using a pH meter at 3-hour and 24-hour intervals to evaluate the pH levels of each treatment group. The measurement results are presented in Table **4**.

As shown in Table **4**, all materials exhibited increased pH values after 24 hours of incubation. CaOH and MTA maintained highly alkaline pH values, whereas nHA–CH showed a near-neutral to slightly alkaline pH. The lowest mean pH value was observed in the nHA–CH group after 3 hours, at 6.90 ± 0.01, followed by 7.27 ± 0.01 after 24 hours. The highest mean pH value was observed in the

MTA group after 3 hours, at 12.01±0.19, increasing to 12.67±0.14 after 24 hours. The pH data were statistically analyzed to determine differences between the 3-hour and 24-hour measurements within each treatment group. The normality test (Shapiro–Wilk) and the homogeneity test (Levene's) both showed p>0.05, indicating that the data were normally distributed and homogeneous. Therefore, a parametric paired t-test ($p < 0.05$) was performed.

Based on Table 5, paired t-test analysis demonstrated significant differences in pH between 3 and 24 h for all experimental groups ($p < 0.05$).

Table 1. Mean setting time of DPC materials.

Materials	n	Mean±SD (Minute)	Min	Max
CaOH	6	2.51 ±0.01	2.50	2.55
MTA	6	17.16 ±0.03	17.13	17.21
nHA-CH	6	15.32 ±0.09	15.21	15.45

Table 2. Results of the One-Way ANOVA Test of DPC materials.

Materials	n	*Mean* ± SD (menit)	*p*
CaOH	6	2.51 ±0.01	<0.01*
MTA	6	17.16 ±0.03	
nHA-CH	6	15.32 ±0.09	

Note: * denotes significantly different comparisons at the $p < 0.05$ confidence level.

Table 3. Post hoc LSD test analysis.

Materials	CaOH	MTA	nHA-CH
CaOH	-	<0.01*	<0.01*
MTA	-	-	<0.01*
nHA-CH	-	-	-

Note: * denotes significantly different comparisons at the $p < 0.05$ confidence level.

Table 4. Mean pH values of DPC materials.

Materials	n	pH after 3 hours			pH after 24 hours		
		Mean±SD	Min	Max	Mean±SD	Min	Max
CaOH	6	10.33±0,64	10.23	10.40	11.51±0.01	11.46	11.58
MTA	6	12.01±0.19	11.77	12.24	12.67±0.14	12.51	12.85
nHA-CH	6	6,90 ±0.01	6.88	6.92	7.27±0.01	7.25	7.30

Table 5. Results of the paired t-Test for pH values of samples after 3 and 24 hours.

Materials	pH Measurement	Mean	P
CaOH	pH after 3 hours	10.33±0,64	<0.01*
	pH after 24 hours	11.51±0.01	
MTA	pH after 3 hours	12.01±0.19	<0.01*
	pH after 24 hours	12.67±0.14	
nHA-CH	pH after 3 hours	6,90 ±0.01	<0.01*
	pH after 24 hours	7.27±0.01	

Note: * denotes significantly different comparisons at the $p < 0.05$ confidence level.

4. DISCUSSION

In the present study, nHA–CH exhibited a shorter gelation time than MTA but a longer setting time than CaOH. The shorter gelation time observed in nHA–CH compared with MTA may be attributed to the interaction between chitosan and hydroxyapatite particles, which may facilitate faster gel formation. A shorter setting time is clinically advantageous because it reduces the risk of material displacement during placement under moist oral conditions. The nHA–CH material combination does not undergo complete hardening, as seen in CaOH and MTA, but instead forms a semi-solid gel phase after mixing [27, 28]. CH serves as a high-viscosity organic matrix, slowing the diffusion of water and ionic reactions during the hardening phase [29, 30].

This study is in alignment with studies conducted by Zhao *et al*. (2025), Manasi *et al*. (2024) and Cai *et al*. (2022), which state that the gelation process of the nHA–CH material combination is caused by electrostatic interactions between the positively charged amino groups of chitosan and the phosphate groups of nanohydroxyapatite, forming a viscoelastic, stable polymer structure [29, 31, 32]. The mechanical properties of chitosan–nHA gel can be improved by adding a cross-linking agent or increasing the nHA fraction; however, without these modifications, the material only exhibits semi-solid hydrogel properties [32-34].

In contrast to nHA-CH, CaOH hardens via solvent evaporation and the formation of CaOH crystals, whereas MTA undergoes calcium silicate hydration, yielding calcium silicate hydrate and calcium hydroxide as the final products [5, 12, 35, 36]. Although the combination of nHA–CH is at gelation time, the use of materials with nano-sized particles (<200 nm) of nanohydroxyapatite combined with chitosan (nHA-CH) has been reported to improve adaptation due to its high surface area, which allows for good adhesion and remineralization, thus reducing particle deformation [19, 20, 37]. nHA is also shown to increase the proliferation and differentiation of dental pulp fibroblasts and odontogenic stem cells, which contribute to the formation of reparative dentin [2, 17].

The results of this study also showed that MTA has a longer setting time compared to CaOH. This is in alignment with studies conducted by Zhu *et al*. (2015), Poggio *et al*. (2015) and Back *et al*. (2022), which state that MTA has a setting mechanism based on calcium silicate cement hydration, which progresses slowly due to the forming of calcium silicate hydrate (C–S–H) and calcium hydroxide phases [7, 13, 35]. In contrast, CaOH sets very quickly because it involves only a simple dissolution reaction without polymerization or further hydration [13].

In the present study, nHA–CH exhibited a near-neutral to slightly alkaline pH (6.90–7.27), which was lower than that of CaOH and MTA. A near-neutral to slightly alkaline pH may provide a more favorable environment for pulp cell survival while maintaining the potential to support mineralization. Previous studies have reported high pH levels in CaOH and MTA, indicating that the release of hydroxyl ions (OH^-) plays a role in antibacterial and odontoblast differentiation stimulation activities [2, 4]. MTA produces a higher pH because the hydration process of calcium silicate compounds produces calcium hydroxide as a side product, which increases the concentration of OH^- for 24 hours [5]. In contrast, nHA–CH has a lower pH but increases from neutral to slightly alkaline after 24 hours. This is due to chitosan having a pKa of approximately 6.3, resulting in it initially being weakly acidic and able to neutralize some of the base ions released by hydroxyapatite [21]. Over time, nanohydroxyapatite particles undergo superficial dissolution, releasing Ca^{2+} and PO_4^{3-} ions, and creating an alkaline microenvironment surrounding the material [32]. CaOH and MTA act by creating an extremely alkaline environment, in contrast to nHA–CH, which has a pH value that is more pulp-friendly while still possessing antibacterial properties [7, 24]. Consequently, nHA–CH is not only more biocompatible, but it also provides a stable healing environment without dependence on extreme pH [21, 24].

The results of this study are in alignment with several previous studies. Poggio *et al*. (2015) have reported that MTA and CaOH have an alkaline pH (>11), while chitosan-based materials exhibit a lower pH and still support dentin regeneration [13]. Studies by Uswatta *et al*. (2016) and Harsas *et al*. (2025) also demonstrate that the combination of HA and CH produces a material with high chemical stability, neutral pH, and excellent bioactivity, thereby supporting dentin remineralization and odontoblast cell adhesion [34, 38]. Moreover, Busrha *et al*. (2023) reported that hydroxyapatite plays a role in peritubular dentin remineralization due to the diffusion of calcium and phosphate ions, where CH serves to improve the cohesion and adhesion to dentin [21]. Neutral to slightly alkaline pH stability offers biological advantages as it does not cause tissue irritation and supports pulp cell viability [21, 25].

This study has several limitations. First, only two physicochemical properties (setting time and pH) were evaluated, whereas other clinically relevant properties such as compressive strength, solubility, sealing ability, calcium ion release, and long-term bioactivity were not investigated. Second, this was an *in vitro* laboratory study; therefore, the biological performance of nHA–CH in the pulp tissue environment could not be confirmed. Finally, only one formulation of the nHA–CH composite was evaluated. Future studies should investigate different material compositions along with comprehensive physicochemical, biological, and *in vivo* evaluations before clinical application. Another limitation of this study is the relatively small sample size (n = 6 per group; 18 cylindrical specimens in total). Although this sample size is comparable to those used in previous laboratory studies evaluating the physicochemical properties of dental biomaterials, a larger number of specimens would provide greater statistical power and improve the precision and generalizability of the findings. Therefore, future studies with larger sample sizes are recommended to further validate these results.

CONCLUSION

This study demonstrated that nHA–CH exhibited a gelation time of 15.32 ± 0.09 min, which was shorter than that of MTA (17.16 ± 0.03 min) but longer than that of CaOH (2.51 ± 0.01 min). The pH of nHA–CH increased from 6.90 ± 0.01 after 3 hours to 7.27 ± 0.01 after 24 hours, remaining lower than CaOH and MTA. These findings indicate that nHA–CH possesses favorable gelation characteristics and a near-neutral to slightly alkaline pH. However, further investigations evaluating additional physicochemical, biological, and in vivo properties are required before its clinical application as a direct pulp capping material.

AUTHORS' CONTRIBUTIONS

The authors confirm their contributions to the paper as follows: A.F, S.S, R.R and A.E Study conception and design; A.F and R.N Data collection; A.F and H.F.A: Analysis and interpretation of results; A.F and H.F.A.: Draft manuscript. All authors reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

CaOH	=	Calcium Hydroxide
DPC	=	Direct Pulp Capping
MTA	=	Mineral Trioxide Aggregate
nHA-CH	=	Nanohydroxyapatite–Chitosan

ETHICAL APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

The data of this study are available from the corresponding author [A.E.] upon reasonable request.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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