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ZrO_2 and ZnO nanoparticles effect on setting time, microhardness, and compressive strength of calcium-enriched-mixture cement

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Aim: Calcium-enriched mixture (CEM) cement is an endodontic biomaterial; however, enhancing its physical/mechanical properties remains a challenge. This in vitro study investigates the influence of zirconium oxide (ZrO_2) and zinc oxide (ZnO) nanoparticles on the setting time, microhardness, and compressive strength of CEM cement. **Methods:** Four different groups of CEM cement were prepared: a control group without nanoparticles, two groups with ZrO_2 or ZnO, and a group with a combination of nanoparticles. The nanoparticles were added to the powder in predetermined concentrations. The setting time was evaluated using the Gilmore needle method, while microhardness and compressive strength were determined using Vickers hardness and a universal testing machine, respectively. **Results:** The incorporation of ZnO slightly reduced the setting time, while the addition of ZrO_2 significantly prolonged it compared to the control group. Interestingly, the combination of both nanoparticles exhibited a setting time comparable to that of the control group. Regarding the microhardness and compressive strength, both ZrO_2 and ZnO significantly improved these properties compared to the control group. The combination of both nanoparticles showed the highest microhardness and compressive strength values among all groups. **Conclusions:** The addition of nanoparticles to CEM cement effectively modifies its physical and mechanical properties. The optimal combination of these nanoparticles can potentially achieve an improved balance between setting time and enhanced mechanical performance.

Keywords: Calcium-enriched mixture cement. Nanoparticles. Chemical phenomena.

Introduction

Calcium silicate-based cements (CSBCs) have emerged as promising biomaterials for tissue repair in endodontics[1]. Among these, mineral trioxide aggregate (MTA) is considered the gold standard for endodontic regenerative products, demonstrating superior sealing ability compared to amalgam, IRM, and Super-EBA[2]. However, MTA suffers from extended clinical setting time as a disadvantage[3]. To overcome this limitation, researchers have explored the incorporation of various nanoparticles (NPs) and the introduction of new biomaterials such as calcium-enriched mixture (CEM) cement[4,5].

CEM cement, introduced in 2006, is a water-based tooth-colored cement with optimal biocompatibility/bioactivity[5,6]. Calcium-enriched mixture (CEM) cement, a distinguished member of calcium-silicate cements (CSC), boasts a distinctive chemical composition that governs its performance in various clinical applications. Scanning electron microscopy (SEM) and electron probe microanalysis (EPMA) have unveiled that CEM cement primarily consists of calcium oxide (CaO; wt%=51.81), sulfur trioxide (SO_3; wt%=9.48), phosphorous pentoxide (P_2O_5; wt%=8.52), and silicon dioxide (SiO_2; wt%=6.28)[7]. Trace amounts of other elements, including aluminum oxide (Al_2O_3; wt%=0.95), sodium oxide (Na_2O; wt%=0.35), magnesium oxide (MgO; wt%=0.23), and chlorine (Cl; wt%=0.18), contribute to its unique composition[7]. The X-ray diffraction (XRD) results further elucidate the mineralogical content of CEM cement, revealing reflections corresponding to tricalcium silicate (Ca_3SiO_5), dicalcium silicate (Ca_2SiO_4), silicon oxide (SiO_2), and zirconium oxide (ZrO_2); additionally, peaks indicative of calcium hydroxide ($CaOH_2$) and barium sulfate ($BaSO_4$) were observed, providing insights into the crystalline phases present in the material (unpublished data). This detailed characterization aims to enhance our understanding of the intricate composition of CEM cement and its potential interactions with incorporated nanoparticles such as ZrO_2 and ZnO. Compared to MTA, CEM exhibits a smaller particle size distribution, resulting in improved sealing ability, shorter setting time, higher flow, and reduced film thickness[1,7]. An in-depth examination of particle size distribution revealed that CEM cement, while exhibiting no significant differences in mean particle size compared to MTA, displayed variations in particle distribution within the size range of ≤30 µm. Notably, CEM cement showcased a narrower range of particle sizes, with a substantial 62% constituting small particles. These small particles play a pivotal role in enhancing material properties and clinical performance. Their effective penetration into microgaps ensures a thorough seal, influencing optimal setting time for a more efficient setting reaction. Additionally, the film thickness and flow characteristics of CEM cement are positively influenced by the presence of these small particles, resulting in a more compact and adaptable biomaterial[8]. CEM has shown promising results in vital pulp therapy (VPT) modalities[9,10]. However, concerns have been raised regarding its immediate restorative procedure due to potential insufficient compressive strength and microhardness[11]. Achieving a time-efficient treatment session necessitates adequate compressive strength and microhardness to avoid the risks of washout/displacement[12].

Efforts have been made to reduce the setting time of CEM, such as the addition of calcium nitrate, which has shown promising results in reducing the setting time[13]. Incorporating specific proportions of propylene glycol into CEM has been found to enhance compressive strength and microhardness[14,15]. Zinc oxide (ZnO) nanoparticles, commonly used as a radiopacifier, have been shown to improve sealing ability, although they may decrease compressive strength[4]. However, the addition of ZnO to MTA does not significantly affect microhardness[16].

Previous studies have explored the use of different radiopacifiers, such as zirconium oxide (ZrO_2) and bismuth oxide (BiO), in MTA, yielding promising results in terms of lower setting time[17], contrary to findings by Silva et al.[18] (2014). Substituting BiO with ZrO_2 in MTA has been reported to increase setting time and decrease compressive strength[18]. Augmented Portland Cement (PC) with ZrO_2-NPs as an inert filler has shown an optimal combination of setting time and compressive strength comparable to ProRoot MTA[19].

The objective of this study is to investigate the effect of ZrO_2 and ZnO nanoparticles on the setting time, microhardness, and compressive strength of CEM. By understanding the impact of these nanoparticles, this research aims to contribute to the development of CEM with improved physical/mechanical properties for enhanced clinical applications in endodontics.

Materials and methods

This study was approved by the Ethical Human Committees of Dental Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran (IR.SBMU.DRC.REC.1401.115). The characteristics of the nanoparticles used in this study are presented in Table 1.

Table 1. The characteristics of nanoparticles used in this study

Nanoparticle	Average particle size (nm)	Specific surface area (m^2/g)	Density (g/cm^3)	Content of nanoparticle (%)	Form
Zirconium oxide	20	30-60	5.89	99.95	powder
Zinc oxide	18	40-70	5.606	99.95	powder

Sample preparation

Four different groups were prepared using CEM mixture: G1 (original CEM cement), G2 (CEM with 10wt.% ZrO_2-NPs), G3 (CEM with 10wt.% ZnO-NPs), and G4 (CEM with 5wt.% ZrO_2-NPs and 5wt.% ZnO-NPs). The liquid and powder components were mixed according to the manufacturer's instructions to achieve a creamy consistency.

Setting time

A total of thirty-two holes (d=10 mm, h=1 mm) were created in eight gypsum molds following ISO 6876:2012. Each group consisted of eight specimens.

To equalize the moisture content of the molds, they were kept in an oven at 100°C for 24 hours. After removal from the oven, the molds were placed at room temperature (23ºC) and a relative humidity of 27%. The holes were filled with the creamy paste, and drainage was performed using a dry cotton pellet at the end of each placement. The setting time was measured using a 113.4 g Gilmore needle test, which was applied to the surface of the specimens for 5 seconds. A sample that was not affected by the Gilmore needle was considered set. The setting time was recorded in minutes.

Microhardness

Stainless steel molds with an internal diameter of 4±1 mm and a height of 6±1 mm were used to prepare 40 specimens (n=10) according to ISO ASTM 384-17. The mixed cements were placed into the molds and compressed using a standard condenser for all samples. Drainage was performed with cotton pellets at the end of placement. After initial setting (~1 hour), the specimens were removed from the molds and incubated at 37ºC and a relative humidity of 95% for 24 hours. After 24 hours, the specimens were soaked in phosphate-buffered saline (PBS). The microhardness test was conducted in two phases. In the first phase (3 days after mixing), the samples were polished for five seconds using wet sandpaper with decreasing particle size (400, 800, 1500, and 2000 grit paper). A load of 50g for 30 seconds was applied for indentation. The surface microhardness was measured using a pyramidal diamond indenter of Vickers Tester (Zwick/Roell, model ZHVμ, England), and the average of three separate indentations on the polished surface was recorded. After the first evaluation, the samples were soaked in PBS and stored for the second phase assessment (7 days after mixing). Vickers microhardness was calculated using the equation: VHN = (2Fsin 136/2)/D2 and HV = 1/854F/D2, where F represents the load in kilogram-force, D represents mean of the two diagonals in mm, and Vickers microhardness value is reported as VHN.

Compressive strength

Stainless steel molds with an internal diameter of 4±1 mm and a height of 6±1 mm were used, following ISO 9917:2007 for hydraulic cements. A total of 80 samples (20 specimens for each group) were prepared. Forty samples were designated for the first period (3 days after mixing), and another 40 specimens were used for the second phase (7 days after mixing). The molds were lubricated with paraffin wax according to ISO 9917 guidelines. Excess wax was removed from the inner surface of the molds, and they were then filled with the mixed material and compacted using the same condenser. Drainage was performed with dry cotton pellets at the end of placement. After 24 hours, the samples were soaked in PBS. Ten samples from each group were subjected to compressive stress using a Zwick/Roell model Z020 (Germany) testing machine at each time interval. The test was performed at a speed of 0.5 mm/min and a load cell of 2.5 KN until fracture. Compressive strength data were presented as MPa using the formula: $C = 4p / \pi d^2$, where “p” represents the maximum pressure recorded in newton, “d” stands for diameter in millimeters, and compressive strength is denoted as “C” in MPa.

Statistical analysis

Data were analyzed using the Shapiro-Wilk test to assess normality and the Levene test to evaluate the equality of variances. Two-way ANOVA was used to analyze the effects of group and time on microhardness and compressive strength. One-way ANOVA was applied to analyze the setting time. Multiple comparisons were performed using Tukey's Honestly Significant Difference (HSD) test. The significance level was set at α=0.05. Statistical analyses were conducted using SPSS 25.

Results

Setting time

The assessment of initial setting time showed that G1 had the shortest setting time. There was no significant difference in the average setting time between G2, G3, and G4 (Table 2).

Microhardness

At the third day, a significant difference was observed between G1 and the other groups. No statistically significant difference was found between the other groups. The highest microhardness value of 59.43±22.16 VHN was observed in G2, and the lowest value of 26.67±6.88 VHN was observed in G1 during the first stage. At the seventh day, the highest value was observed in G2, while the lowest value was observed in G4. There was no significant difference between the groups (P> 0.05), except for G4, which showed a lower value (Table 2).

Compressive strength

After three days, the highest compressive strength was observed in G3. There was no significant difference between G1, G3, and G4 at the seventh day after mixing, and all of them were higher than G2 (Table 2). The results also showed that the difference in values between the first and second periods was statistically significant in all groups except for G3.

Table 2. The results of three tests: Mean (SD)

Test	Time	G1	G2	G3	G4
Setting time	-	11.25 (2.33) [a]	18 (2.34) [b]	18.87 (1.05) [b]	16.75 (1.19) [b]
Microhardness	3 days	26.67 (6.88) [A,a]	59.43 (22.16) [A,b]	46.32 (17.55) [A,b]	55.03 (22.24) [A,b]
	7 days	49.59 (10.80) [B,a]	71.55 (28.30) [A,a]	61.86 (22.31) [A,a]	29.19 (8.20) [B,b]
Compressive strength	3 days	5.88 (1.07) [A,a]	4.31 (0.39) [A,b]	8.36 (0.55) [A,c]	6.43 (0.75) [A,a]
	7 days	9.25 (0.56) [B,a]	6.04 (0.39) [B,b]	9.06 (0.63) [A,a]	8.8 (0.84) [B,a]

**Similar lower case letters in a row indicate statistical similarity; similar upper case letters in a column in each test indicate statistical similarity*

Discussion

The setting time and mechanical properties of dental cement are crucial for successful restorations, as they impact the ability to complete the procedure in a single session and reduce the risk of washout and infection[1,12]. This study aimed to evaluate the initial setting time, microhardness, and compressive strength of new mixtures of CEM cement by incorporating NPs.

The setting time was determined as the time taken for the mixture to harden from placement in gypsum molds until the discovery of an incomplete circular indentation. The results showed that the addition of ZrO_2-NPs and ZnO-NPs increased the setting time regardless of their proportion. This can be attributed to the slower hydration caused by the incorporation of nanoparticles and the reduction in the proportion of calcium silicate hydrate (C-S-H) powder[20]. This finding is consistent with Silva et al.[18] (2014), Bosso-Martelo et al.[21] (2016) and Nochaiya et al.[22] (2015) but contrary to Tanomaru-Filho et al.'s findings[23] (2012). Bosso-Martelo and Nochaiya describe the greater amount of water used during manipulation of CSBC + ZrO_2 as the main reason for the increased setting time[21,22]. Silva demonstrated a significant increase in the setting time of PC + ZrO_2 compared to PC, attributing it to the lower amount of cement powder in the mixture[18]. On the other hand, Tanomaru-Filho reported a higher setting time for PC than for PC+ ZrO_2[23]. Another study by Li et al.[24] explained that the high surface area of ZrO_2 provides efficient nucleation sites for the precipitation and growth of primary C-S-H hydration products in the first 24 hours but not during the setting time of the CEM. The decrease in MTA proportion resulted in a longer setting time[25], however, Marcinao et al.[26] (2017) observed no statistically significant difference when incorporating ZnO into MTA by decreasing the proportion of MTA. In another study, the combination of ZnO + MTA disrupted cement hydration with an impermeable layer around tricalcium silicate formed by zinc hydroxide[16]. It is worth considering other additives to counterbalance the increased setting time, such as calcium chloride and calcium nitrate, which have been shown to decrease the setting time of CEM[13,27]. Calcium chloride accelerates silicate hydration by penetrating into the pores of CEM, while calcium nitrate increases the formation of calcium hydroxide, reducing the setting time of the cement.

Vicker's microhardness test was conducted to assess the material's ability to resist plastic deformation. In the immediate placement of coronal restorations on CEM cement, the setting reaction of the restorative material may interfere with the hardening process of the underlying layer[28], however, according to Bolhari et al.'s study[29] (2021) immediate placement of restorative materials does not affect the microhardness of the restoration and it can improve the sealing ability of the restoration. Previous studies have explored the addition of various nanoparticles to CSBC to enhance microhardness. Sobhnamayan et al.[15] (2017) incorporated propylene glycol into CEM, which initially resulted in lower microhardness values after 4 days but showed a peak in microhardness at 21 days. The lower microhardness in the initial period was attributed to the lower water content in the liquid phase. Bolhari et al.[16] (2020) investigated the addition of ZnO to MTA and found no significant difference in microhardness, suggesting that the microhardness of zinc is

similar to that of calcium, silicon, and phosphorus. In our study, the incorporation of ZrO_2 or ZnO in G2, G3, and G4 accelerated the degree of hydration, leading to improved surface microhardness within 3 days. However, this enhancement was not sustained until the seventh day, as the mixture reached a similar microhardness level as the control group in G2 and G3, and even a lower value was observed in G4.

Higher compressive strength is desirable to withstand occlusal forces and ensure immediate restoration placement. Various studies have investigated the incorporation of different nanoparticles to improve compressive strength[19]. In this study, ZnO and ZrO_2 were added. The addition of ZrO_2-NPs had an adverse effect on compressive strength in both time periods, suggesting interference with the silicate structure. On the other hand, the addition of ZnO-NPs initially improved compressive strength on the third day but did not cause any significant change compared to the control group on the seventh day. All groups exhibited an increasing trend in compressive strength from the first to the second stage. Contrary to previous studies in calcium silicate cements[16,17,22,30], the addition of ZnO to CEM not only did not decrease compressive strength but also resulted in a significant increase in the value in the first period. Nochaiya et al.[22] (2015) described a decreased value at 3 days but an increased value at 7 days after mixing. Differences in composition, experimental setups, time intervals, and maintenance protocols used in these studies could account for the discrepancy. For example, in a study by Eskandarinezhad et al.[31] (2020) that incorporated hydroxyapatite and ZnO-NPs with MTA, no significant difference in compressive strength was found compared to white MTA. The author suggested that cracks caused by the reaction between ZnO and MTA may have contributed to the decrease in compressive strength. In our study, the reduction in compressive strength in addition of ZrO_2 contradicted Kamali et al.'s study[32] (2017) but aligned with findings from others[17,18,30,33], confirming the interference of ZrO_2-NPs with the CEM structure. No significant difference was observed between CEM + ZnO and CEM in the second period. Moreover, CEM + ZnO + ZrO_2 showed no statistically significant difference from CEM in both time intervals.

In conclusion, the addition of nanoparticles (NPs) to CEM cement did not have a favorable effect on the setting time. The incorporation of NPs increased the Vickers hardness number (VHN) on the third day but eventually reached a similar level as the control group on the seventh day. There were no significant changes in VHN and compressive strength values of the new mixtures after seven days.

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Competing Interests

The authors have no conflict of interests to disclose.

Data availability

Datasets related to this article will be available upon request to the corresponding author.

Author Contribution

Faezeh Sadat Razavi: Substantial contributions to the conception or design of the work, laboratory practices.

Fatemeh Mahmoudi Afsah: Substantial contributions to the conception or design of the work, drafting the work.

Alireza Akbarzadeh Baghban: Analysis, or interpretation of data, final approval of the version to be published.

Hasan Torabzade: Analysis, or interpretation of data, reviewing the work critically for important intellectual content, supervising the aboratory practices.

Saeed Asgary: Analysis, or interpretation of data, reviewing the final draft critically for important intellectual content, final approval of the version to be published.

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