

ORIGINAL RESEARCH ARTICLE

Innovative dental mineral trioxide aggregate composition based on a nanostructured calcium phosphate biomimetic filler

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Abstract

Mineral trioxide aggregate (MTA)-based dental materials are widely used in endodontic therapy due to their favorable sealing ability, biocompatibility, and bioactivity; however, ongoing research seeks to enhance their functional performance and biological responses by incorporating advanced biomimetic and nanostructured fillers. This study reports the development and comprehensive characterization of a novel MTA-type dental material based on a nanostructured calcium phosphate biomimetic filler. The base MTA was obtained from synthesized dental cement and commercial bismuth oxide, which served as the radiopacifier. To obtain the biomimetic obturating composition (BOC), base MTA was mixed with biomimetic filler consisting of nanostructured calcium-deficient, silicon- and fluorine-substituted hydroxyapatite synthesized using the authors' methodology. Structural-morphological and physicochemical characteristics of all components were investigated using X-ray diffraction, Fourier-transform infrared spectroscopy, and scanning and transmission electron microscopy. In accordance with International Organization for Standardization (ISO) 6876:1986 requirements, key functional properties of BOC samples, such as flowability (20–23 mm), working time (630–660 s), setting time (420–680 s), radiopacity (>3 mmAl), and solubility (1.6–2.1%) were studied. *In vitro* bioactivity of BOC samples was evaluated through calcium ion release in simulated body fluid (SBF) and acetate buffer, as well as apatite-forming ability in SBF. It was found that incorporating the nanostructured biomimetic filler significantly enhanced calcium ion release and promoted the formation of a surface apatite layer, the thickness of which increased with filler content. The results demonstrate that the proposed BOC exhibits improved bioactivity while maintaining acceptable physicochemical and functional characteristics, indicating its potential for dental application.

Keywords: Dental materials; Mineral trioxide aggregate; Biomimetic hydroxyapatite; Calcium phosphate; Sol-gel synthesis; Bioresorbability

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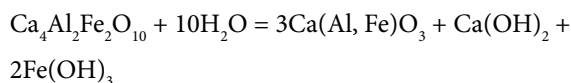
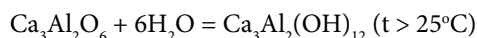
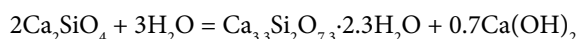
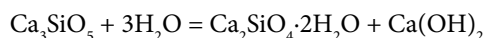
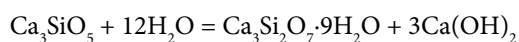
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1. Introduction

Mineral trioxide aggregate (MTA) refers to a class of dental materials that are widely used as obturating materials.^{1,2} The classic (or traditional) MTA composition, developed

at the end of the 20th century, is a mixture of Portland cement and a radiopaque substance, bismuth (III) oxide. The Portland cement used in this composition was mainly represented by phases of the CaO–SiO₂–Al₂O₃ system: alite or tricalcium silicate Ca₃SiO₅ (C3S), belite or dicalcium silicate Ca₂SiO₄ (C2S), and tricalcium aluminate Ca₃Al₂O₆, with impurity amounts of iron and sulfur compounds in the form of aluminoferrite Ca₄Al₂Fe₂O₁₀ and gypsum CaSO₄·2H₂O.^{3–5}

According to previous studies, the hydration of minerals that make up Portland cement proceeds exothermically with the formation of calcium hydroaluminates, calcium hydrosilicates, and calcium hydroxide, following the schemes^{1,6,7}:



The hydration process causes the composition to harden. The Ca(OH)₂ formed as a product determines antibacterial properties of MTA.^{1,4} The classic MTA-type composition has a number of disadvantages^{1,8,9}:

- (i) discoloration of adjacent tooth structure and surrounding tissues to the filling site due to the high content of bismuth (Bi) and iron (Fe) compounds;
- (ii) low plasticity during working time, long setting time, and insufficient mechanical strength for use as a universal filling material; and
- (iii) potential cytotoxicity, insufficient adhesion to tooth tissue, and low bioactivity.

New MTA compositions have been developed that better align with modern requirements for dental materials. Such MTAs are characterized by reduced Bi or Fe content (or their absence), improved mechanical strength, and increased biocompatibility. They may contain various radiopaque additives (ZrO₂, BaO, La₂O₃, Ta₂O₅, HfO₂, BaSO₄, SrF₂, BaZrO₃, W, CaWO₄, and Sr compounds), plasticizers, curing agents, strength agents, and other compounds (zinc oxide, propylene glycol, organic polymers, alkali metal salts, chitosan, bioactive glasses, calcium phosphate phases, allotropic modifications of carbon, etc.).^{1,10}

The most energy-intensive process in the production of modern MTA is the thermal synthesis of monophasic calcium silicates, primarily alite C3S. Notably, alite hydrates quickly, ensuring sealing of the filling site,

adhesion of cement to dentin, and the formation of Ca(OH)₂, thereby creating an antimicrobial environment. Currently, the following methods are widely used to obtain bi- and monophasic calcium silicates: high-temperature solid-phase synthesis, sol-gel process, spray pyrolysis, and self-propagating high-temperature synthesis. Higher product quality is achieved using the sol-gel process (or its modification, the Pechini method); however, it is time-consuming and unsuitable for large-scale production.^{4,10} Table 1 presents some commercial MTA-type materials, their composition, and characteristics.

However, for most modern commercial MTAs, bioactivity and osteoinductivity—in terms of their ability to partially regenerate hard tissues, promote osteogenic cell differentiation, and support tooth adhesion—are unsatisfactory. This is due to the insufficient release of calcium ions (Ca²⁺) into the filling area (due to the low solubility of C2S, C3S, CaO, or Ca(OH)₂), as well as the poor apatite-forming ability of the dental material.^{11–21}

A significant improvement in the medical and biological characteristics of dental materials is achieved by introducing calcium phosphate phases, in particular, β-tricalcium phosphate (Ca₃(PO₄)₂) and hydroxyapatite (Ca₁₀(PO₄)₆(OH)₂). A promising area of research and development in recent years has been the synthesis of biomedical hydroxyapatite, which is most similar in chemical composition, structural and morphological characteristics, and surface electrical properties to the bioapatite of the mineral part of the human bone matrix.^{22–24} The advantages of biomimetic hydroxyapatite over calcium-stoichiometric hydroxyapatite are its exceptional ability to remineralize²⁵; high antibacterial properties²⁶, osteoinductivity, and biocompatibility; affinity for bone tissue^{27,28}; and sorption properties.^{29–31}

Bioapatite is calcium-deficient, i.e., it is characterized by a molar ratio of Ca/P less than 1.667, poly-substituted (Table 2), low-crystalline, and nanostructured, and its crystals are represented by thin (1–5 nm) plates with a length, as a rule, not exceeding 40–60 nm.³² It is known that bioapatite contains silicate anions. Their effect on the properties of hydroxyapatite is characterized by increased bioactivity, stimulated by osteoblast activity, leading to accelerated biomineralization. An increase in osteoconductivity and osteoinductivity is also observed, characterized by the highest integration of silicate-substituted hydroxyapatite into biogenic tissue.³³

Along with silicate ions, fluoride anion substitution plays an important role. Their effect on the properties of hydroxyapatite is reflected in increased crystallinity, reduced bioresorbability, and improved chemical and thermal stability. Bioactivity of fluoride-substituted

Table 1. Commercial dental mineral trioxide aggregate-type materials

Material (product [company])	Declared composition ^a	Declared advantages ^a
ProRoot (Dentsply)	Ca ₃ SiO ₅ , Ca ₂ SiO ₄ , Ca ₃ Al ₂ O ₆ , Ca ₄ Al ₂ Fe ₂ O ₁₀ , CaSO ₄ ·2H ₂ O, CaO, Bi ₂ O ₃	High biocompatibility and bioactivity; good antibacterial activity.
MTA Angelus (Angelus)	Ca ₃ SiO ₅ , Ca ₂ SiO ₄ , Ca ₃ Al ₂ O ₆ , CaO, Bi ₂ O ₃ , and others	Stimulates the formation of a dentin bridge; good antibacterial activity.
Biodentine (Septodont)	Ca ₃ SiO ₅ , Ca ₂ SiO ₄ , CaCO ₃ , CaO, Fe ₂ O ₃ , ZrO ₂	Wide range of applications; osteoinductivity and high adhesion to dentin; minimal tissue staining; rapid setting (<15 min).
Endocem MTA (Maruchi)	Calcium-alumosilicate cement, radiopaque filler	Rapid setting (~4 min); minimal tissue staining; excellent antibacterial properties and biocompatibility.
DiaRoot (DiaDent)	Calcium silicate, ZrO ₂ , citric acid, silamine, hydroxypropyl methylcellulose	Biocompatible and bioactive material; high antibacterial activity; good adhesion to dentin.
Retro MTA (BioMTA)	CaCO ₃ , SiO ₂ , Al ₂ O ₃ , calcium-zirconium complex	Minimal tissue staining; rapid setting; affordability.
Rootdent (TehnoDent)	Calcium-alumosilicate cement, ZrO ₂	Rapid setting; minimal tissue staining; high antibacterial activity; high durability.
Endocem Zr (Maruchi)	Calcium-alumosilicate cement, ZrO ₂	Minimal tissue staining; good radiopacity; rapid setting (~4 min).
Bioaggregate (Innovative Bioceramix)	Calcium silicate, Ca(OH) ₂ , hydroxyapatite, Ta ₂ O ₅ , amorphous SiO ₂	Aluminum-free; bioactive and biocompatible material; minimal tissue staining.
Trioxident (VladMiVa)	Calcium-alumosilicate cement, radiopaque filler, Cu(OH) ₂ , Ca(OH) ₂	Rapid setting (<15 min); stimulates dentin bridge formation; high antibacterial activity.
PD MTA White (PD)	Ca ₃ SiO ₅ , Ca ₂ SiO ₄ , Ca ₃ Al ₂ O ₆ , CaO, CaWO ₄	Minimal tissue staining; rapid setting (<15 min).

Note: ^a According to the manufacturer.

Table 2. Effect of certain ion substitutions on the properties of hydroxyapatite

Ion	Effect
Na ⁺ , K ⁺	Increase in thermal stability; improvement in protein adsorption and cell adhesion
Sr ²⁺	Decrease in thermal stability; inhibition of bone resorption; increase in mechanical strength, osteoinductivity, and antibacterial activity
SiO ₄ ⁴⁻	Reduction in thermal stability; improvement in bioactivity; increase in bioresorbability
CO ₃ ²⁻	Decrease in thermal stability; increase in bioresorbability
F ⁻	Improvement in mechanical strength; increase in thermal stability, osteoinductivity, and antibacterial activity
Cl ⁻	Increase in thermal stability, bioactivity, and acidity; improvement in bioresorbability and osteoconductivity

hydroxyapatite remains largely unchanged compared to unsubstituted hydroxyapatite. Introduction of fluoride anions provides increased resistance of hydroxyapatite in acidic environments, including biological ones.³³

Previously, our research group developed a method for obtaining nanostructured biomimetic hydroxyapatite substituted with SiO₄⁴⁻ and F⁻ ions and studied its bioresorbability. It was shown that the stability of nanostructured biomimetic hydroxyapatite in simulated body fluid (SBF) increases with increasing fluoride substitution. Furthermore, the novelty of the proposed

biomimetic hydroxyapatite and its production method is evidenced by a patent.³⁴

A number of published studies have investigated the influence of calcium phosphate phases on the properties of dental MTA compositions.^{35–42} However, limited studies have examined the role of biomimetic hydroxyapatite in dental materials.

Taking these aspects into account, this work aims to develop an MTA-type dental composition based on a nanostructured calcium phosphate biomimetic filler and to establish its effect on the physicochemical and biomedical

characteristics of dental materials.

2. Materials and methods

2.1. Materials

To obtain the components of the biomimetic obturating composition (BOC), calcium nitrate ($\text{Ca}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, chemically pure, NevaReaktiv LLC, Russia), ammonium hydroorthophosphate ($(\text{NH}_4)_2\text{HPO}_4$, analytical grade, NevaReaktiv LLC), sodium carbonate (Na_2CO_3 , analytical grade, NevaReaktiv LLC), calcium chloride (CaCl_2 , analytical grade, NevaReaktiv LLC), ammonium fluoride (NH_4F , analytical grade, NevaReaktiv LLC), aluminum nitrate ($\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$, analytical grade, NevaReaktiv LLC), bismuth (III) oxide (Bi_2O_3 , analytical grade, NevaReaktiv LLC), and tetraethoxysilane ($\text{Si}(\text{C}_2\text{H}_5\text{O})_4$ or TEOS, analytical grade, EKOS-1 JSC, Russia) were used. Citric acid ($\text{C}_6\text{H}_8\text{O}_7 \cdot \text{H}_2\text{O}$, chemically pure, NevaReaktiv LLC) was used as an agent for regulating the structural and morphological characteristics of the calcium phosphate biomimetic filler.³⁴

To prepare precursor solutions, double-distilled water obtained by distillation in the presence of potassium permanganate was used. The pH of the reaction systems during synthesis was controlled by adding 25 wt.% ammonia solution (NH_4OH , analytical grade, NevaReaktiv LLC).

The following reagents were used to prepare the model SBF: sodium chloride (NaCl , chemically pure, NevaReaktiv LLC), sodium bicarbonate (NaHCO_3 , analytical grade, NevaReaktiv LLC), potassium chloride (KCl , chemically pure, NevaReaktiv LLC), potassium hydroorthophosphate ($\text{K}_2\text{HPO}_4 \cdot 3\text{H}_2\text{O}$, analytical grade, NevaReaktiv LLC),

magnesium chloride ($\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$, chemically pure, NevaReaktiv LLC), calcium chloride, sodium sulfate ($\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$, chemically pure, NevaReaktiv LLC), and tris-hydroxymethyl aminomethane ($(\text{HOCH}_2)_3\text{CNH}_2$, cultural purity, CDH Ltd., Hong Kong).⁴³

2.2. Synthesis of components and the preparation of mineral trioxide aggregate and biomimetic obturating composition

In this study, dental cement powder and a calcium phosphate biomimetic filler, both synthesized at the preliminary stage, were used as components of MTA and BOC.

2.2.1. Preparation of dental cement for mineral trioxide aggregate

Calcium carbonate, TEOS, and aluminum nitrate were used as precursors to prepare dental cement for MTA.³⁹ Calcium carbonate was precipitated from a solution containing Ca^{2+} and carbonate (CO_3^{2-}) ions, according to the scheme shown in Figure 1. The equipment used for the synthesis included a beaker and an HS-100D WiseStir overhead rotary stirrer (DAIHAN Scientific Co., Ltd., South Korea). In brief, 1 M solutions of Na_2CO_3 and CaCl_2 were combined in a beaker in a 1:1 volume ratio and stirred at 1,000 rpm for 5 min. The resulting calcium carbonate precipitate was separated by filtration, washed with distilled water, and dried at 70 °C to a constant weight. The product was ground using a porcelain mortar and pestle.

The synthesis of clinker minerals as the basis for dental cement in MTA was carried out according to the following scheme (Figure 2). Distilled water (1,000 mL) was transferred into a beaker equipped with an overhead

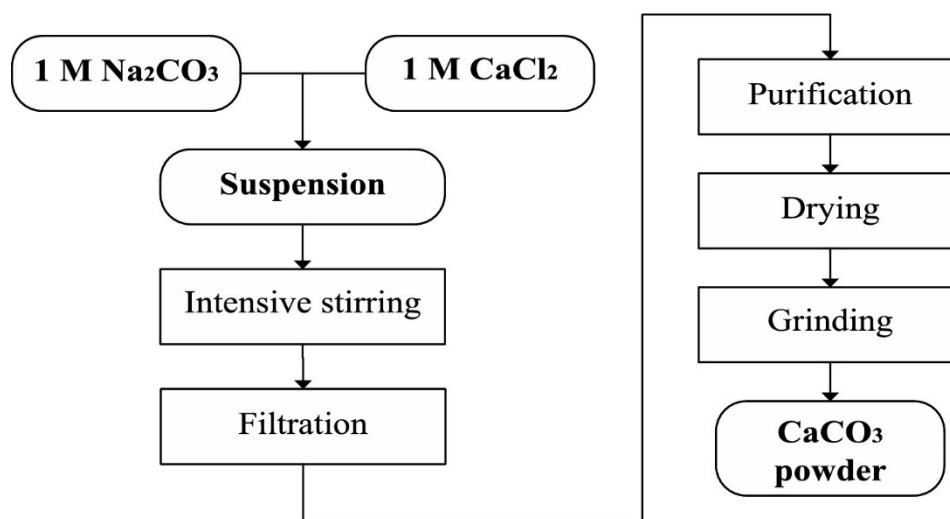


Figure 1. Scheme of the synthesis process of calcium carbonate powder

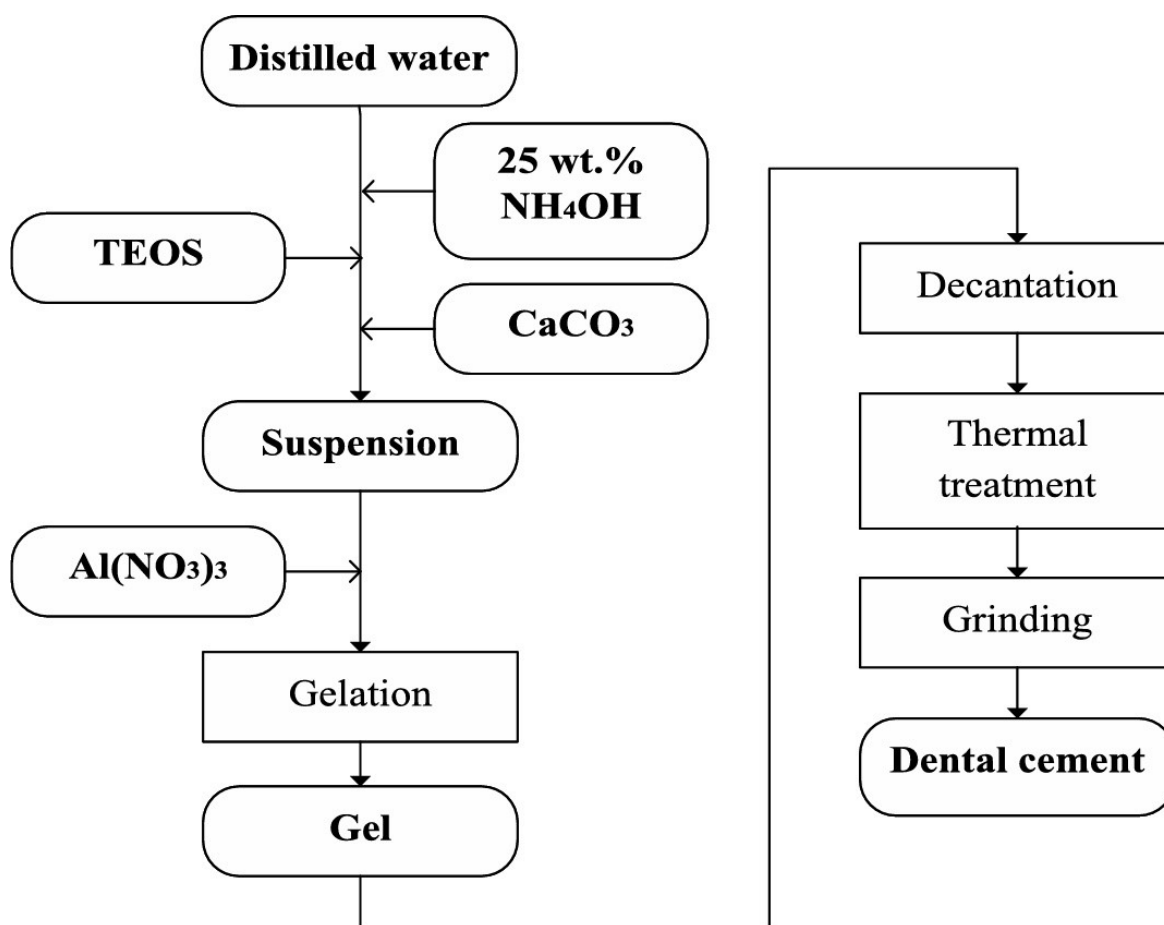


Figure 2. Scheme of the preparation process of dental cement for mineral trioxide aggregate
Abbreviation: TEOS: Tetraethoxysilane.

rotary stirrer, and 1 mL of a 25 wt.% ammonia solution was added. Stirring was carried out for 15 min at 500 rpm. In the resulting solution, TEOS and synthesized CaCO_3 were added in a molar ratio of 0.093:0.300. The mixture was then homogenized for 30 min. Then, aluminum nitrate (0.010 mol) was added, the system was heated to 60 °C using an electric stove, and the mixture was gelatinized for 12 h. The resulting precipitate was separated from the mother liquor by filtration, washed with distilled water, then dried at a temperature not exceeding 120 °C and thermally treated at 1,000 °C in a SKV 12/16 muffle electric furnace (Termopech, Russia) for 1 h (heating rate: 10 °C/min). Dental cement was obtained by grinding the calcination products using a porcelain mortar and pestle to a fine powder.³⁹

2.2.2. Preparation of mineral trioxide aggregate

The base MTA was obtained by mixing synthesized dental cement and Bi_2O_3 powders at a mass ratio of 82:18 to obtain a homogeneous mixture using a porcelain mortar

and pestle. The designed chemical composition of MTA is presented in Table 3.

2.2.3. Synthesis of nanostructured calcium phosphate biomimetic filler

Nanostructured calcium phosphate biomimetic filler was synthesized by precipitation from a solution containing Ca^{2+} , PO_4^{3-} , F^- , and SiO_4^{4-} ions.³⁴ The designed molar ratio of Ca/(P+Si) for the filler was 1.550. The synthesis scheme is shown in Figure 3.

Table 3. Chemical composition of the base mineral trioxide aggregate

Component	Content (wt.%)
CaO	60
SiO_2	20
Al_2O_3	2
Bi_2O_3	18

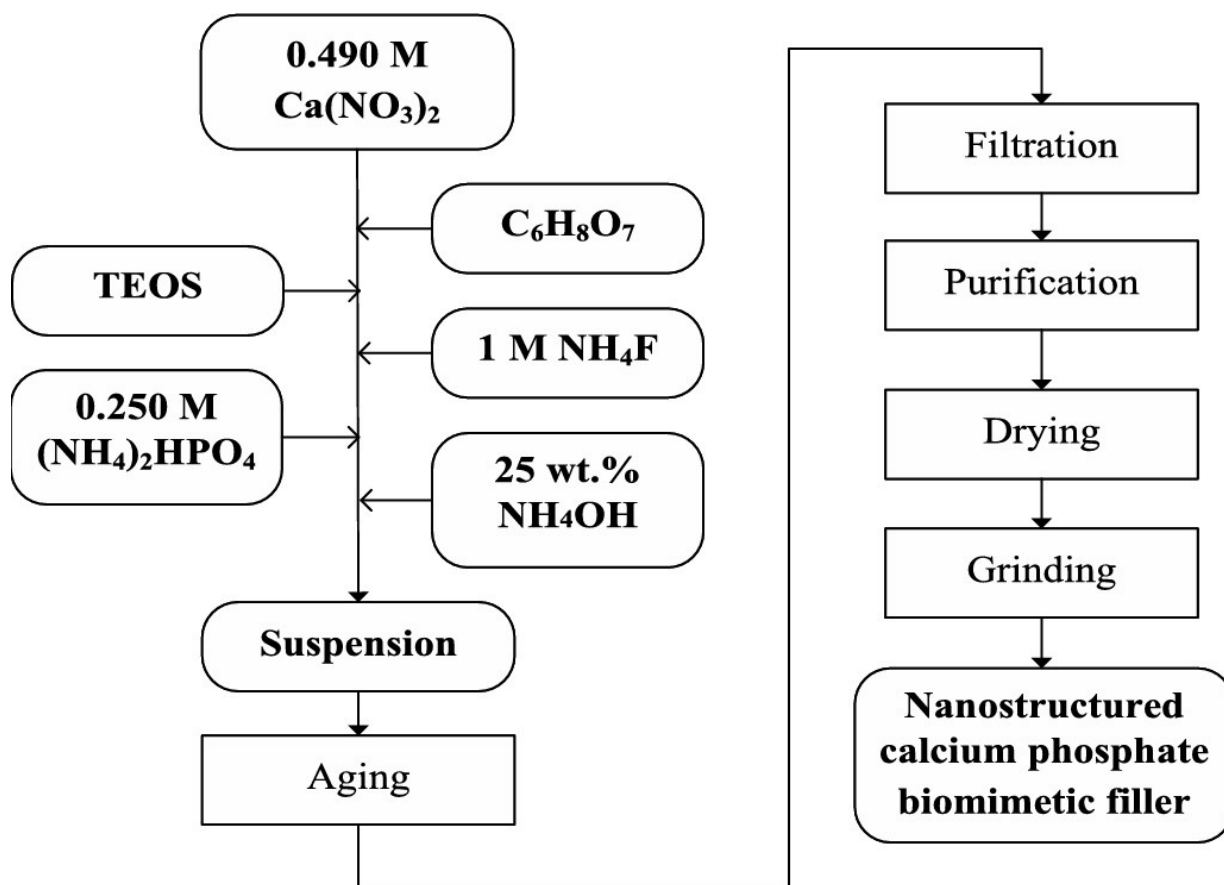


Figure 3. Scheme of the synthesis process of nanostructured calcium phosphate biomimetic filler
Abbreviation: TEOS: Tetraethoxysilane.

The sample was synthesized as follows. A freshly prepared 0.490M $\text{Ca}(\text{NO}_3)_2$ solution was transferred into a beaker equipped with an overhead rotary stirrer, a heating element, and a pH-150MI pH meter (Izmeritel'naya Tekhnika, Russia) using a combined electrode ESK-10303 (Izmeritel'naya Tekhnika). The contents of the beaker were stirred at 500 rpm, and the medium temperature was maintained at $40 \pm 5^\circ\text{C}$. The mass fraction of citric acid in the solution was 0.48%. Meanwhile, a 25 wt.% NH_4OH solution was used to maintain a pH of 10–11 in the reaction system. TEOS and a 1M NH_4F solution were added to the resulting solution in amounts necessary to obtain a calcium phosphate biomimetic filler with silicon and fluorine contents of 2.88% and 1.95% by mass, respectively, and the mixture was stirred for 10 min. Next, using a separating funnel, a 0.250 M solution of $(\text{NH}_4)_2\text{HPO}_4$ was added dropwise at a constant rate of 8–10 mL/min. The system was then stirred for 20 min and aged under isothermal conditions for 12 h to complete phase formation. The resulting precipitate was separated from the mother liquor by filtration, washed with distilled water until the filtrate

was neutral, and dried at 110°C to a constant weight. The dried calcium phosphate biomimetic filler was ground using a porcelain mortar and pestle to a powdery state.³⁴

2.2.4. Preparation of biomimetic obturating composition

A series of BOC samples was prepared by mixing the base MTA with varying amounts of nanostructured calcium phosphate biomimetic filler. BOC compositions and their codes are presented in Table 4.

Table 4. Material composition of biomimetic obturating composition (BOC) samples

Composition code	Component mass ratio (g)	
	Base MTA	Biomimetic filler
BOC-0 (control)	10.00 ± 0.01	None
BOC-10	10.00 ± 0.01	1.00 ± 0.01
BOC-20	10.00 ± 0.01	2.00 ± 0.01

Abbreviation: MTA: Mineral trioxide aggregate.

2.3. Analysis of synthesized products and biomimetic obturating composition components

Powder samples of synthesized CaCO_3 and dental cement were studied using Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), and scanning electron microscopy (SEM). Sample preparation for FTIR analysis was carried out by pressing the sample powder with potassium bromide (KBr, infrared [IR] spectroscopy grade, NevaReaktiv LLC). IR spectra were recorded in the range of $400\text{--}4000\text{ cm}^{-1}$ using a FSM 2202 IR-spectrometer (Infraspek LLC, Russia). XRD was performed using quartz cuvettes on a Rigaku Ultima IV diffractometer (Rigaku, Japan) using $\text{CuK}\alpha$ radiation ($\lambda = 1.54178\text{ \AA}$) with the following parameters: accelerating voltage of 40 kV, tube current of 250 mA, 2θ scanning range of $5\text{--}80^\circ$, step of $0.02^\circ 2\theta$, and spectra recording speed of $5^\circ/\text{min}$. Microscopic studies of powders' morphology in scanning mode were performed on a SU1510 electron microscope (Hitachi, Japan).

The structural and morphological characteristics of particles in calcium phosphate biomimetic filler suspensions at the end of the aging process were studied using a JEM-2100 transmission electron microscope (TEM; JEOL Ltd., Japan). Biomimetic filler powder was analyzed using SEM, XRD, and FTIR methods. The initial and hydrated samples of varying BOC compositions were studied using SEM.

2.4. Determination of functional characteristics of biomimetic obturating composition

To test BOC compositions for compliance with the requirements for dental filling materials, the following functional characteristics were studied: flowability, working time, setting time, radiopacity, and solubility in distilled water. These characteristics were determined in accordance with the methods set out in International Organization for Standardization (ISO) 6876:1986, "Dental root canal sealing materials."

To determine flowability, 0.075 mL of BOC mixed with distilled water at a mass ratio of 1:3 was placed on a glass plate using a graduated pipette. After $180 \pm 5\text{ s}$ from the start of mixing, another glass plate was placed in the center of the BOC sample, and a load of 2.5 kg was applied using a loading device. After 10 min from the start of mixing, the load was removed, and the largest and smallest diameters of the disc were measured, with their average calculated. The flowability of each BOC composition was measured three times; the average value was calculated and recorded with an accuracy of 1 mm as the experimental flowability.

To determine working time, 0.075 mL of BOC mixed with distilled water at a mass ratio of 1:3 was placed on a

glass plate using a graduated pipette. After $210 \pm 5\text{ s}$ from the start of mixing, another plate was placed in the center of the BOC sample, and a load of 2.5 kg was applied using a loading device. The load was held for 7 min, then removed, and the largest and smallest diameters of the resulting BOC disc were measured, with their average calculated. The test was repeated with a newly mixed portion of BOC, applying the load at increasing intervals from the start of mixing until the diameter of the resulting BOC disc decreased by 10% relative to the experimental flowability value. The working time of each BOC sample was determined three times; the average value was calculated and recorded with an accuracy of 30 s as the experimental working time.

To determine setting time, a ring mold (height $[h] = 2\text{ mm}$; diameter $[d] = 10\text{ mm}$) was placed on a 1-mm-thick glass plate and filled to the top with a BOC sample mixed with distilled water at a mass ratio of 1:3. After $120 \pm 10\text{ s}$ from the start of mixing, the mold with a portion of BOC, mounted on a metal block with a temperature of $37 \pm 1^\circ\text{C}$, was placed in a thermostat ($37 \pm 1^\circ\text{C}$). Periodically, a Gilmore needle was lowered perpendicular to the horizontal surface of the BOC sample until the needle stopped leaving a mark on the material. Then, the time from the start of mixing was recorded. The test was performed three times for each BOC sample, and the average value was calculated and recorded as the experimental setting time.

To determine radiopacity, a portion of BOC mixed with distilled water at a mass ratio of 1:3 was placed in a ring mold ($h = 1\text{ mm}$; $d = 10\text{ mm}$), which was then covered with plates on top and bottom to obtain a 1-mm-thick BOC sample. This sample was placed in the center of an X-ray film next to an aluminum wedge with a thickness range of 1 to 10 mm. Next, the BOC sample, the aluminum wedge, and the film were exposed to X-rays (voltage on the X-ray tube = 65 kV; distance = 300 mm) for a period of time during which the exposed part of the film had a blackening density of 1.5–2.5. After developing, fixing, and drying the exposed film, the blackening density of the X-ray image of the sample, each step of the aluminum wedge, and the uncovered area of the film was measured using a photographic densitometer (DNS-2, JSC SPA, Russia). By comparing with the image of the aluminum wedge, the thickness of the aluminum layer equivalent to the BOC sample was determined. The test was performed three times for each BOC sample, and the average value was calculated and recorded as the experimental radiopacity value.

To determine the solubility of BOC in distilled water, a ring mold ($h = 1.5\text{ mm}$; $d = 20\text{ mm}$) was placed on a glass plate with a known mass ($\pm 0.001\text{ g}$) and filled with a portion of BOC mixed with distilled water at a mass ratio

of 1:3. Then, another glass plate with a sheet of polyethylene film underneath was pressed against the surface of the material and then removed so that the surface of the BOC sample was smooth and flat. The filled mold was placed in a thermostat (37 ± 1 °C) for a time exceeding the experimental setting time by 50%. The mass of the material was recorded (± 0.001 g), after which two prepared BOC samples were placed in a Petri dish so that their surfaces did not touch, and the material in the mold remained intact. Then, 50 ± 1 mL of distilled water was added, the dish was sealed and kept at a temperature of 37 ± 1 °C for 24 h, after which the samples were removed and washed with a small amount of water over the Petri dish. Then, the water was evaporated without boiling, the dish dried to a constant mass at 150 °C, and was weighed after cooling in a desiccator at room temperature. Two tests were performed for each BOC sample. The average difference between the initial and final masses of the Petri dish (± 0.001 g) was recorded as the amount of material washed off the BOC samples. The difference in mass was determined as a percentage of the initial total mass of the two samples, accurate to 0.1%, as the experimental solubility value.

2.5. Assessment of biomimetic obturating composition bioactivity *in vitro*

Bioactivity of BOC samples of varying compositions was evaluated under neutral and acidic model conditions using SBF (pH 7.40) and acetate buffer (pH 5.50), together with assessment of apatite-forming ability of hydrated BOC samples in SBF.^{43,44}

The model SBF was prepared according to the method proposed by Kokubo and Takadama.⁴³ The composition of SBF is presented in Table 5. To simulate solubility, 0.2 g of BOC samples were placed in a series of chemical beakers, 50.0 mL of model media was added, and the samples were thermostated for 1–7 days at 37 °C. At specified intervals (1, 2, 3, 4, 5, 6, and 7 days), the concentration of Ca^{2+} in the model solution was determined by the ionometric method using an IPL-112 ionometer (NPP Semiko LLC, Russia) with a Ca-selective electrode HS-Ca-001 (Sensorniy Sistem, Russia) and a silver chloride reference electrode. Based on the obtained data, solubility curves for BOC samples were constructed as a function of $C(\text{Ca}^{2+})$ in the model solution and exposure time.

Table 5. Chemical composition of the simulated body fluid

Ion	Concentration (mmol/L)
Na^+	142.0
K^+	5.0
Mg^{2+}	1.5

(Cont'd...)

Table 5. (Continued)

Ion	Concentration (mmol/L)
Ca^{2+}	2.5
Cl^-	147.8
HCO_3^-	4.2
HPO_4^{2-}	1.0
SO_4^{2-}	0.5

Evaluation of the bioactivity of BOC samples was performed by measuring their apatite-forming ability, as described by Kokubo and Takadama.⁴³ Hydration of BOC was performed by mixing BOC powder with distilled water at a mass ratio of 1:3. The resulting BOC sample (3.00 g) was pressed at 20 MPa and then placed in a beaker containing 50.0 mL of model SBF for six days. At the end of the exposure period, pressed BOC samples were removed from SBF. The thickness of the apatite layer formed on the BOC pellet was evaluated from SEM micrographs.

2.6. Statistical analysis and data processing

Synthesis of MTA and BOC components, preparation of BOC samples, and subsequent analytical control using TEM, XRD, FTIR, and SEM were performed in at least five parallel experiments. The experimental data were processed using standard methods of mathematical statistics with a confidence level of 0.95. A *t*-test was used to assess the statistical significance of the differences between the samples.

Quantitative experimental values in this work are presented as mean $\pm$ standard deviation. Statistical analysis was performed using OriginPro 2024 SR1 (OriginLab, United States [US]) and Microsoft Excel (Microsoft, US). Qualitative analysis of the XRD diffractograms was performed using PDXL-2 Qualitative Analysis software (Rigaku Corporation, Japan) and the International Centre for Diffraction Data (ICDD)/powder diffraction file (PDF)-2 2008 database.

Crystallite size (*D*, nm) for powder samples was calculated based on the parameters of the diffraction peaks (Equation 1).⁴⁵

$$D = \frac{K\lambda}{\beta \cos\theta} \quad (1)$$

where *D* is the crystallite size (nm); *K* is a dimensionless coefficient (0.9); λ is the wavelength of the X-ray radiation used (0.154178 nm); β is the half-width of the diffraction peak (rad); and θ is the position of the diffraction peak (rad).

The degree of crystallinity (*X*, %) of the powder samples

was calculated according to Equation 2.⁴⁵

$$X = \frac{S_{cr}}{S_{cr} + S_{am}} \quad (2)$$

where X is the degree of crystallinity of the powder sample (%); S_{cr} is the area of crystalline peaks (a.u.); and S_{am} is the area of amorphous halos (a.u.).

Construction of plots (diffractograms obtained from XRD and FTIR spectra), baseline correction, and calculation of the integral areas of peaks were performed using OriginPro 2024 SR1. Instrumental peak broadening correction was performed using standard lanthanum hexaboride (LaB_6) samples. TEM and SEM micrographs were processed using Paint. NET 5.1.5 software (dotPDN LLC, US). Determination of crystallite size and calculation

of objects' dimensions on TEM and SEM micrographs was performed using Microsoft Excel.

3. Results and discussion

3.1. Analysis of synthesized CaCO_3 and mineral trioxide aggregate components

As mentioned in Section 2.2.1, CaCO_3 was used as a precursor for the production of dental cement. According to XRD data (Figure 4, Table 6), the synthesized powder corresponding to the formula CaCO_3 was represented by the phases of vaterite and calcite.

The phase composition of dental cement included belite (C2S) and an admixture of gehlenite ($\text{Ca}_2\text{Al}_2\text{SiO}_7$) (Table 6). No precursors were detected in the experimental samples. The average value of the degree of crystallinity

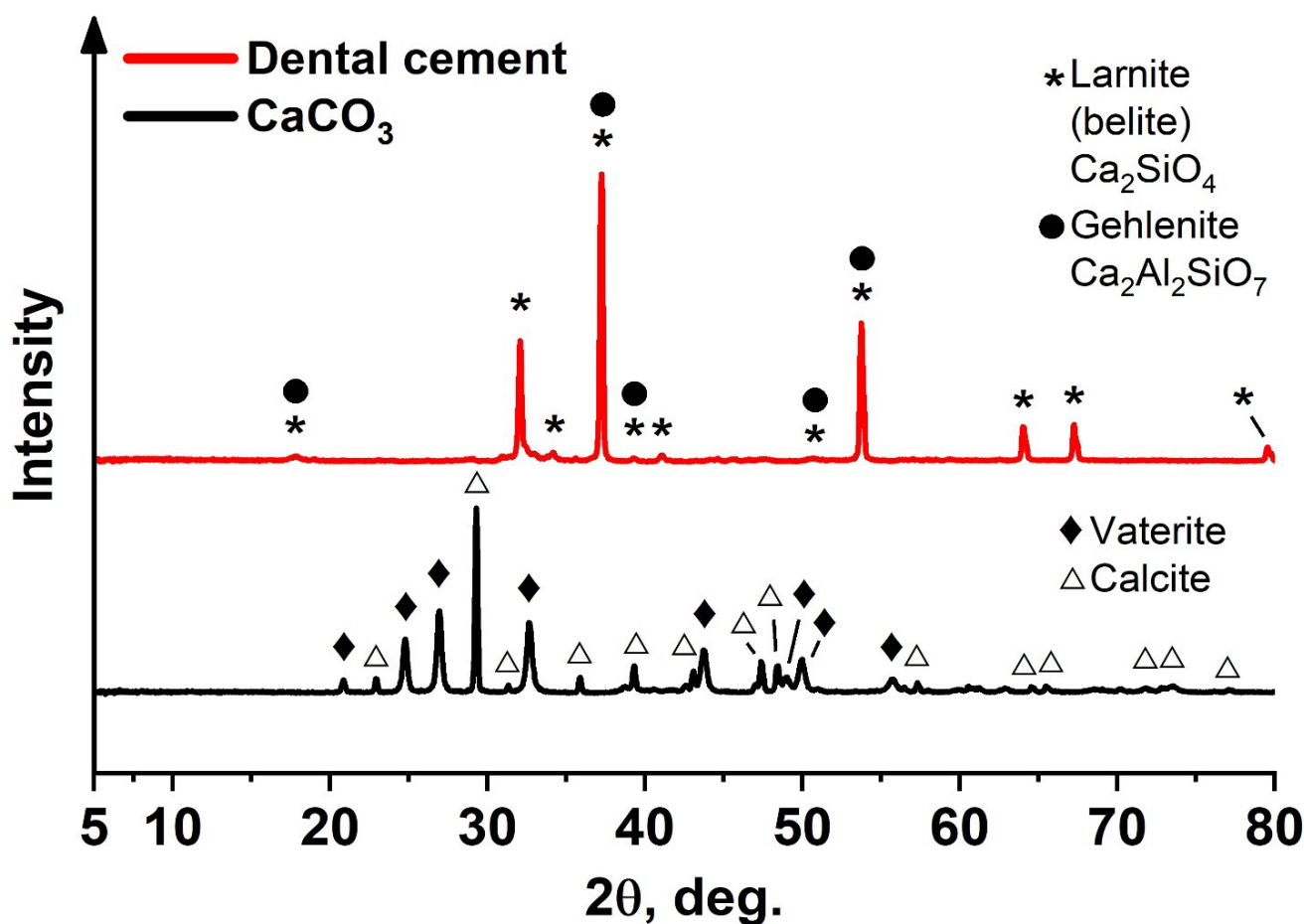


Figure 4. Powder diffractograms of synthesized CaCO_3 and dental cement samples

Table 6. Phase composition of the synthesized CaCO_3 and dental cement samples

Sample	Phase	Content (wt.%)	D (nm)	X (%)
CaCO_3	Vaterite (CaCO_3 , PDF card No. 01-072-0506)	76.4 ± 1.6	22.85 ± 0.85^a	95.63 ± 0.89
	Calcite (CaCO_3 , PDF card No. 01-072-1937)	23.6 ± 1.1	46.29 ± 1.22^b	
Dental cement	Larnite (Ca_2SiO_4 , PDF card No. 01-077-0409)	97.0 ± 0.9	42.88 ± 2.08^c	91.46 ± 2.33
	Gehlenite ($\text{Ca}_2\text{Al}_2\text{SiO}_7$, PDF card No. 01-089-6887)	3.0 ± 1.0		

Notes: ^a According to the peak parameters corresponding to (101) reflection of the vaterite phase; ^b According to the peak parameters corresponding to (104) reflection of the calcite phase; ^c Average for all identified peaks; D indicates crystallite size, and X indicates the degree of crystallinity.

for these phases was 91.46%. This indicates the presence of an amorphous phase, either SiO_2 formed during TEOS hydrolysis or clinker mineral phase nuclei formed during thermal treatment. The FTIR data are consistent with the phase-composition data (Figure 5).

The SEM micrographs (Figure 6) of the synthesized dental cement powder showed isolated agglomerates with diameters ranging from 5 to 30 μm formed by nanoscale (100–600 nm) spherical particles and larger (1–6 μm) irregularly shaped particles. The commercial Bi_2O_3 powder consisted of large agglomerates (5–60 μm) composed of crystals ranging from 500 nm to 2 μm in length (Figure 6).

3.2. Analysis of nanostructured calcium phosphate biomimetic filler

The study of calcium phosphate biomimetic filler hydrodispersions after aging was carried out using TEM. The TEM micrographs showed spherical crystalline particles aggregated into mesh structures, with predominant sizes ranging from 13 to 20 nm (Figure 7).

An additional structural-morphological study of the calcium phosphate biomimetic filler in powder form after drying the hydrodispersions was carried out using SEM. SEM micrographs of the powder showed isolated prismatic particles measuring 8–30 μm (Figure 8).

According to powder diffractograms of the calcium phosphate biomimetic filler sample, the only crystalline phase was hydroxyapatite (Figure 9). The change in the lattice parameters a and c is characteristic of silicon- and fluorine-substituted hydroxyapatite (Table 7), indicating the success of doping with F^- and SiO_4^{4-} during synthesis.

The degree of crystallinity of the calcium phosphate biomimetic filler was 94.85%. The average crystallite size was 6.04 ± 0.93 nm. FTIR data are consistent with the XRD method and confirm the presence of O–H, P–O, Si–O, and Ca–F bonds (Figure 10).^{46,47}

3.3. Structural-morphological and functional characteristics of biomimetic obturating composition

The initial and hydrated powders of the experimental BOC samples were studied using SEM (Figures 11 and 12). According to SEM micrographs, the initial BOC powders were a mechanical mixture of dental cement and bismuth oxide, with or without (the BOC-0 sample) a nanostructured calcium phosphate biomimetic filler. Hydrated BOC samples were composed of agglomerates with a diameter of 5 to 200 μm , the structure of which includes particles of bismuth oxide and nanostructured calcium phosphate biomimetic filler. Thus, during BOC hydration, a structure forms with a practically uniform distribution of bismuth oxide particles and a nanostructured calcium phosphate biomimetic filler.

The flowability of the experimental BOC compositions was at least 20 mm for all samples, meeting the requirements of ISO 6876:1986 (Table 8). It was noted that the flowability of BOC grew with increasing nanostructured calcium phosphate biomimetic filler content. This may be due to a decrease in the content of hydrate-forming substances.

The working time and setting time of all compositions were less than 30 min, classifying, according to ISO 6876:1986, all BOC samples as type I root canal filling materials. The setting time of BOC-10 and BOC-20

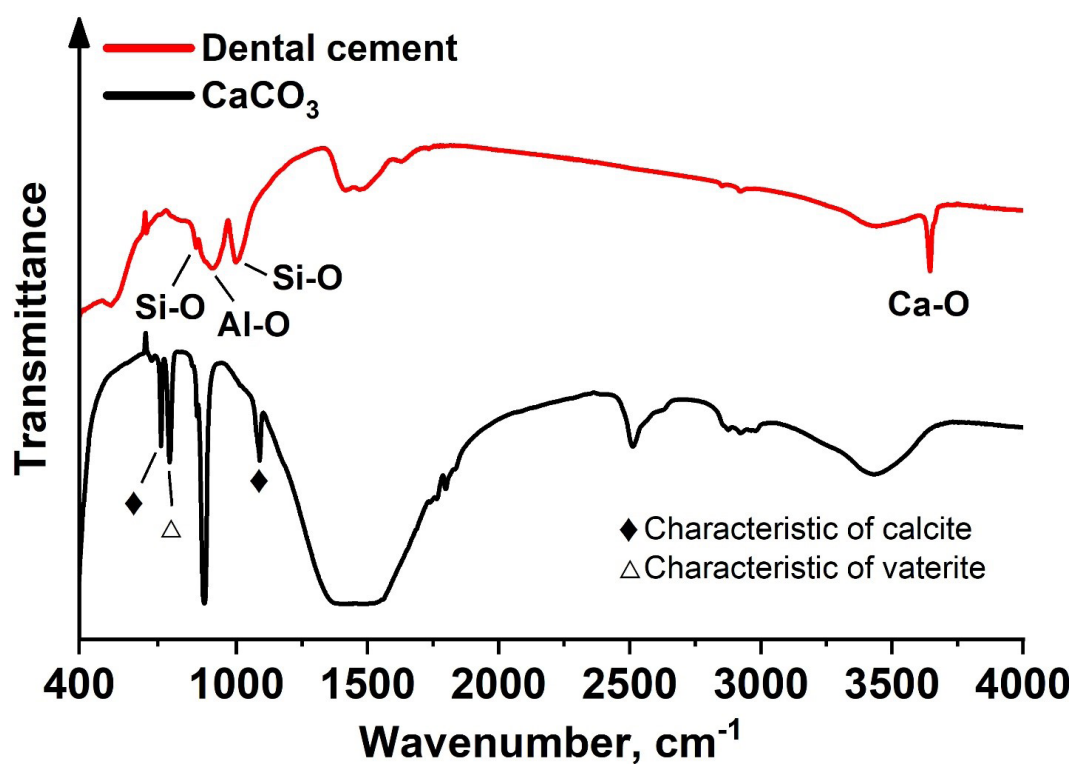


Figure 5. Infrared spectra of synthesized CaCO₃ and dental cement samples

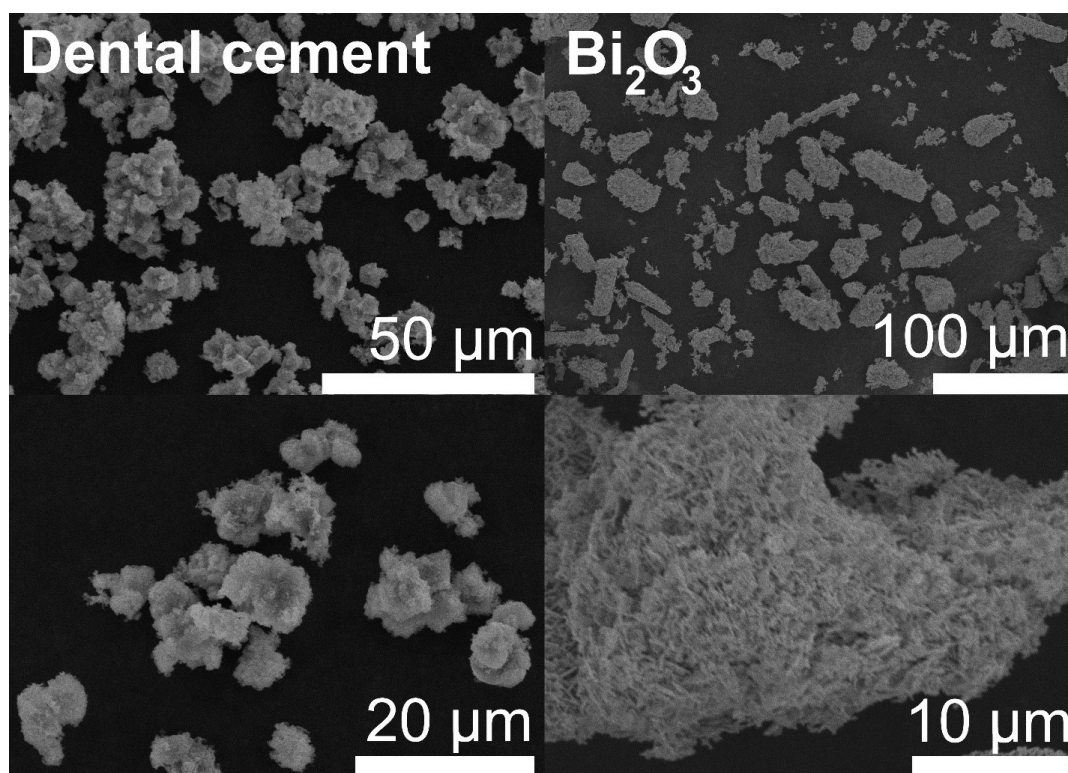


Figure 6. Scanning electron microscopic images of base mineral trioxide aggregate components. Scale bars: 10 μm, 20 μm, 50 μm, 100 μm; magnification: 1000X (top left), 300X (top right), 2000X (bottom left), and 4000X (bottom right).

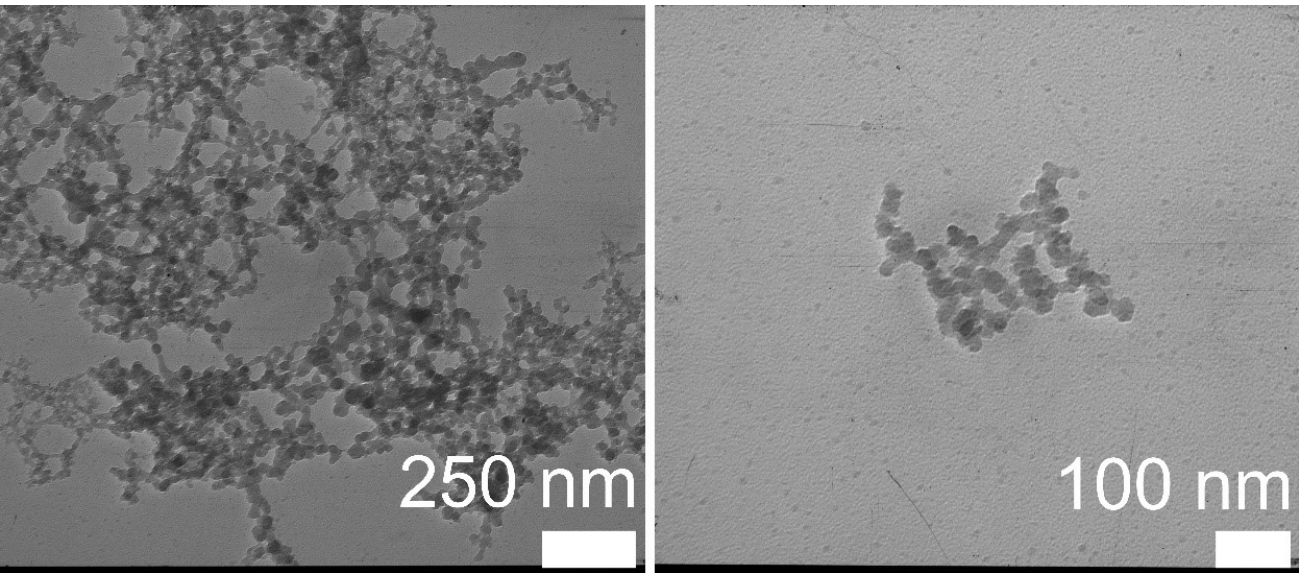


Figure 7. Transmission electron microscopic images of calcium phosphate biomimetic filler hydrosuspension. Scale bars: 100 nm, 250 nm; magnification: 50000× (left), and 100000× (right).

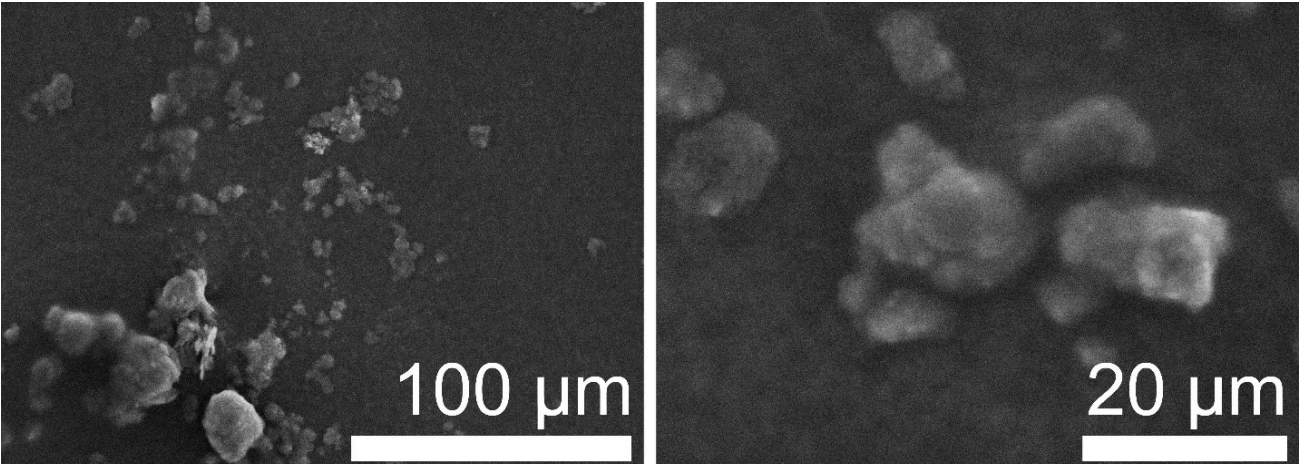


Figure 8. Scanning electron microscopic images of calcium phosphate biomimetic filler. Scale bars: 20 µm, 100 µm; magnification: 500× (left), and 2000× (right).

Table 7. Phase composition of the calcium phosphate biomimetic filler sample

Phase	Lattice parameters (Å)		D (nm)	X (%)
	a = b	c		
100% $\text{Ca}_{9.04}(\text{PO}_4)_6(\text{OH})_{1.68}$ (PDF card No. 01-086-1203)	9.4403	6.8580	6.04 ± 0.93^a	94.85 ± 2.89
$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ hexagonal ³³	9.4320	6.8810	-	-

Notes: ^a According to the peak parameters corresponding to (211) reflection of the hydroxyapatite phase; D indicates crystallite size, and X indicates the degree of crystallinity.
Abbreviation: PDF: Powder diffraction file.

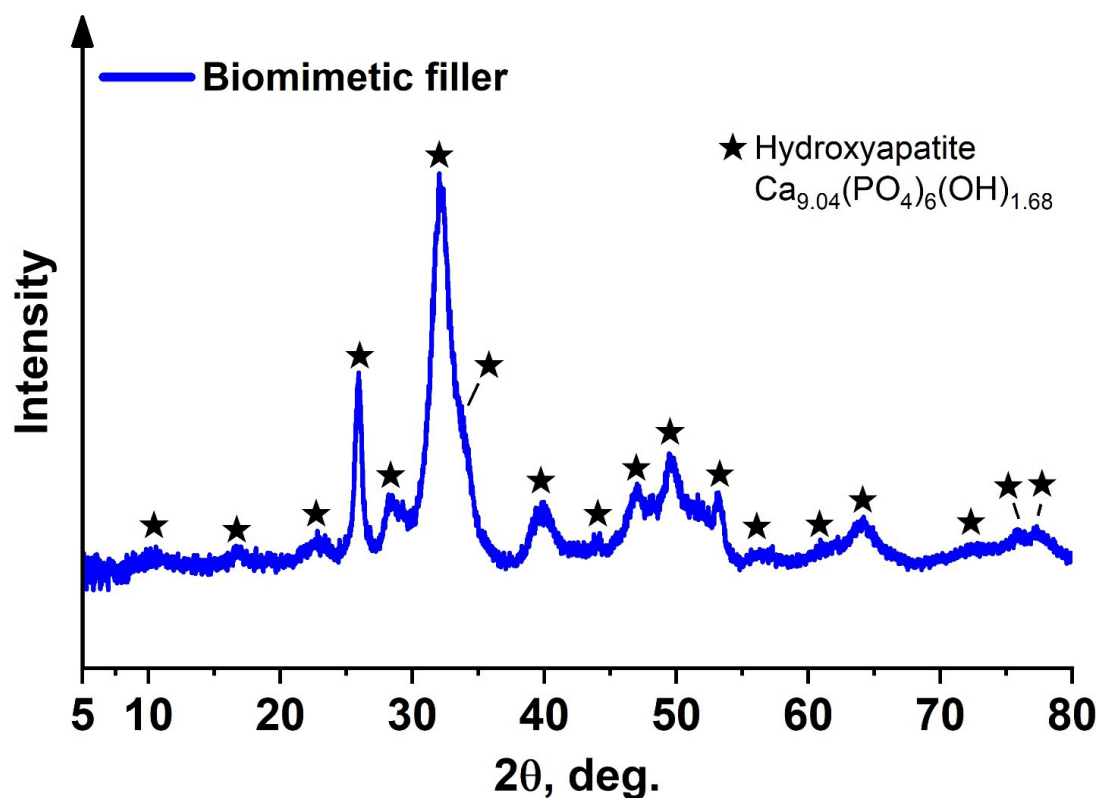


Figure 9. Powder diffractogram of calcium phosphate biomimetic filler sample

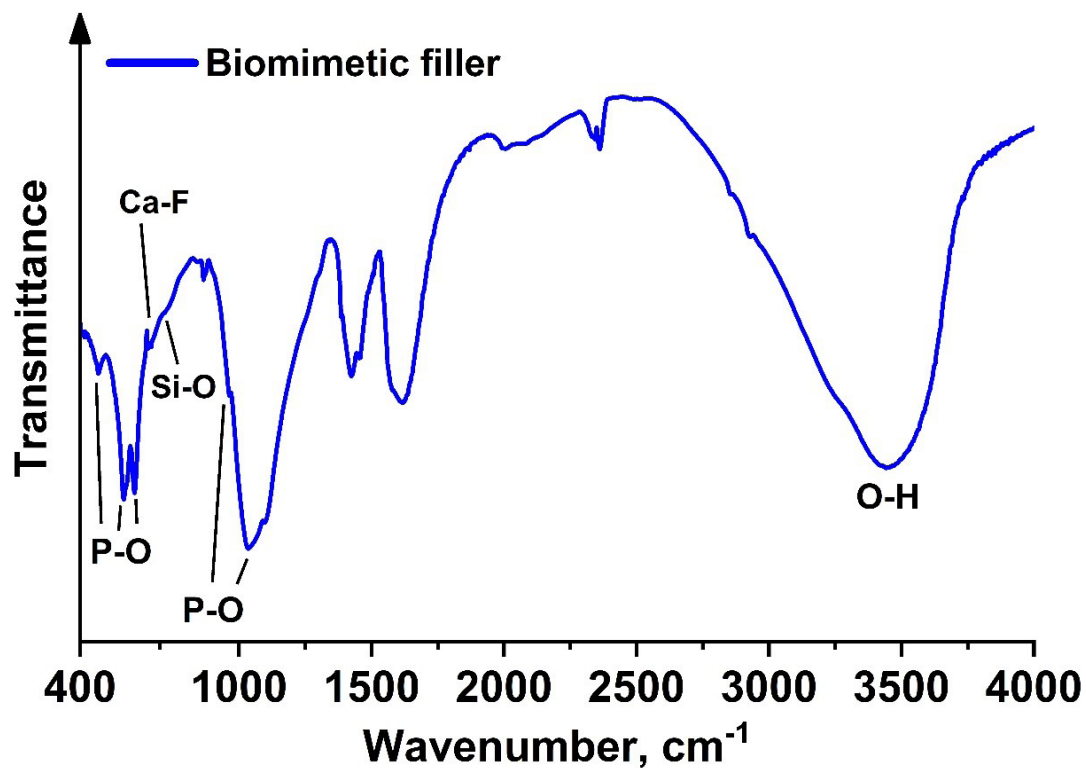


Figure 10. Infrared spectrum of calcium phosphate biomimetic filler sample

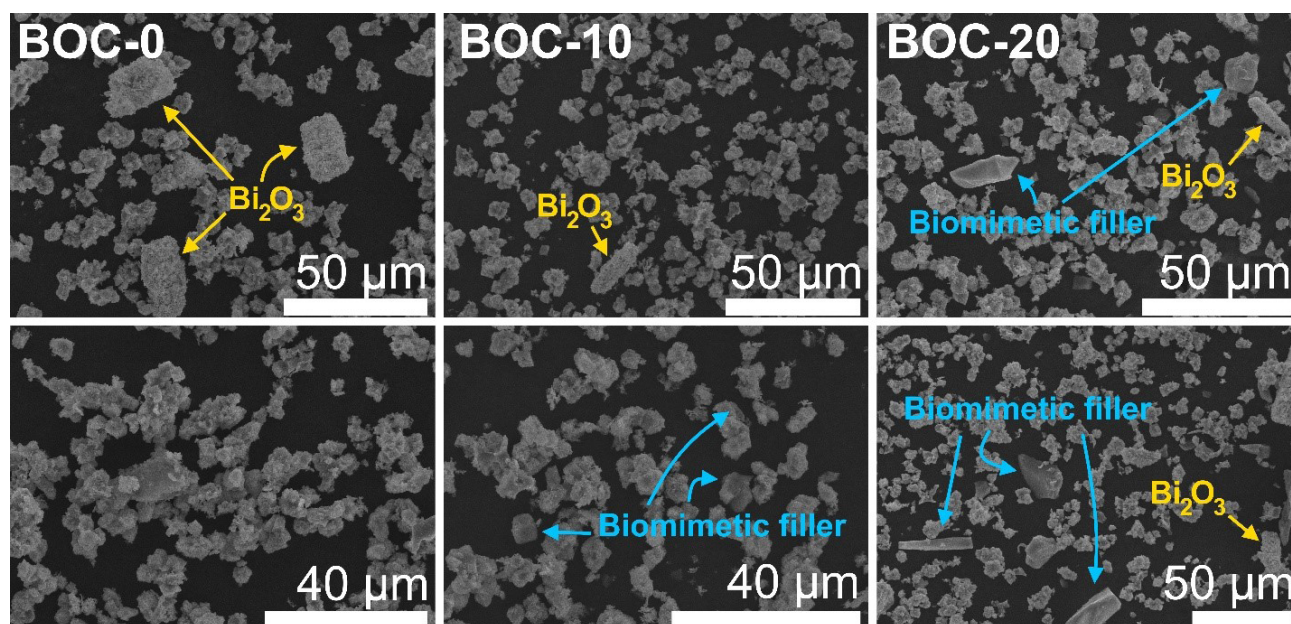


Figure 11. Scanning electron microscopic images of initial biomimetic obturating composition (BOC) powders. Scale bars: 40 µm and 50 µm; magnification: 800× (top left), 800× (top middle), 900× (top right), 1200× (bottom left), 1400× (bottom middle), and 600× (bottom right).

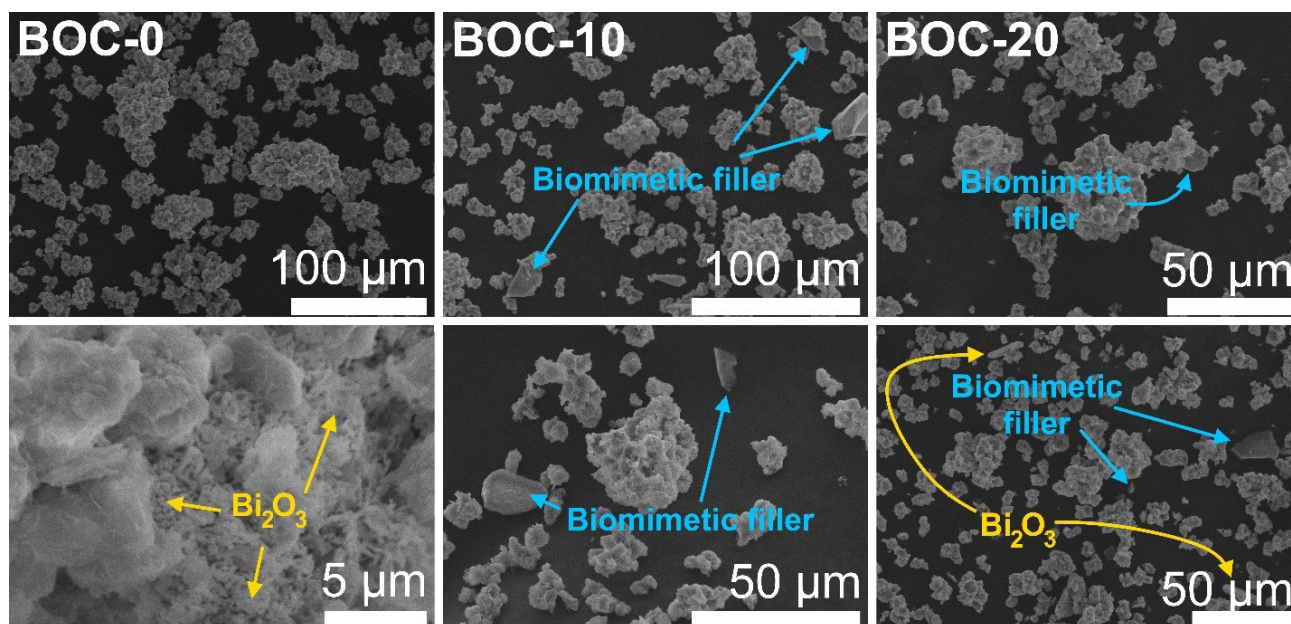


Figure 12. Scanning electron microscopic images of hydrated biomimetic obturating composition (BOC) powders. Scale bars: 5 µm, 50 µm, 100 µm; magnification: 400× (top left), 500× (top middle), 700× (top right), 6000× (bottom left), 1000× (bottom middle), and 600× (bottom right).

increased from 420 s to 510 s and 680 s (1.21 and 1.62 times, respectively). The working time of BOC also increased with the content of nanostructured calcium phosphate biomimetic filler.

The radiopacity of all samples was at least 3 mmAl (Table 8), meeting the requirements of ISO 6876:1986. Meanwhile, the solubility of the experimental samples in distilled water decreased with increasing biomimetic filler content and did not exceed 3% of the BOC mass, meeting the requirements of ISO 6876:1986 (Table 8). This may be due to a decrease in the cement activity of BOC, which explains the slowdown in setting processes.

3.4. Bioactivity of biomimetic obturating composition *in vitro*

Solubility curves for the experimental BOC samples, along with the equilibrium and maximum release of Ca^{2+} in the model solutions, are shown in Figures 13 and 14 and Table 9. BOC-0 exhibited the lowest solubility in all model media. BOC-20 exhibited the highest maximum Ca^{2+} release, while BOC-10 exhibited the highest equilibrium Ca^{2+} release.

It was found that the concentration of Ca^{2+} rapidly increased for up to two days of exposure and stabilized, with a slight decrease in SBF or a sharp decrease in acetate buffer to an equilibrium value starting from the fourth day of exposure; this effect was most noticeable for BOC-20. This observation can be explained by the fact that when BOC components are dissolved in the model media, SiO_4^{4-} , PO_4^{3-} , OH^- , F^- , and pH-dependent forms of Al^{3+} are released.⁴⁸ When the model environment is saturated

with these ions, precipitation occurs, mainly of various calcium hydrosilicates, calcium fluoride, and brushite ($\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$).⁴⁹

It is worth noting that the most pronounced change in Ca^{2+} concentration occurred for BOC-20. This is explained by the more intense formation of sediment in the presence of a larger amount of soluble calcium, the content of which, when converted to elemental mass, is approximately 14.3 wt.% in MTA and 34.9 wt.% in the biomimetic filler. When sediment appears on the experimental sample, the area that may contain easily soluble calcium compounds is mechanically blocked. As a result, the amount of precipitated calcium is not replenished, and a sharp drop is observed on the solubility curve. Considering the “blocking” effect, sample BOC-10 reported the best bioresorbability, since no sharp drop in Ca^{2+} concentration was observed on the solubility curve of this sample. The composition of this formulation has the highest equilibrium Ca^{2+} release.

The SEM micrographs of pressed BOC samples before and after exposure to SBF are shown in Figure 15. According to the data, all BOC compositions formed a thin apatite layer on the surface when exposed to SBF. The thickness of this layer increased in proportion to the amount of nanostructured calcium phosphate biomimetic filler in the BOC samples (Table 10). It should be noted that the method used to assess bioactivity does not take into account the ability of the material to bind directly to body tissues (without the formation of a detectable apatite layer).⁴³ In this regard, due to the excellent osteoconductivity of hydroxyapatite²², BOC samples may exhibit higher bioactivity *in vivo*.

Table 8. Experimental functional characteristics of biomimetic obturating composition (BOC) samples

Composition code	Flowability, mm	Working time, s	Setting time, s	Radiopacity, mmAl	Solubility, wt. %
BOC-0	20 ± 1	630 ± 30	420 ± 30	>3	2.1 ± 0.2
BOC-10	21 ± 1	630 ± 30	510 ± 30	>3	1.8 ± 0.1
BOC-20	23 ± 1	660 ± 30	680 ± 30	>3	1.6 ± 0.2

Table 9. Equilibrium and maximum Ca^{2+} release from biomimetic obturating composition (BOC) samples in different model media

Composition code	Model media			
	SBF solution		Acetate buffer	
	Equilibrium Ca^{2+} release, mmol/L	Maximum Ca^{2+} release, mmol/L	Equilibrium Ca^{2+} release, mmol/L	Maximum Ca^{2+} release, mmol/L
BOC-0	9.54 ± 0.81	10.22 ± 1.01	6.99 ± 0.62	16.33 ± 1.98
BOC-10	10.51 ± 1.22	13.18 ± 1.05	10.55 ± 1.76	25.22 ± 2.71
BOC-20	9.54 ± 0.64	14.68 ± 1.12	7.03 ± 0.55	21.30 ± 2.44

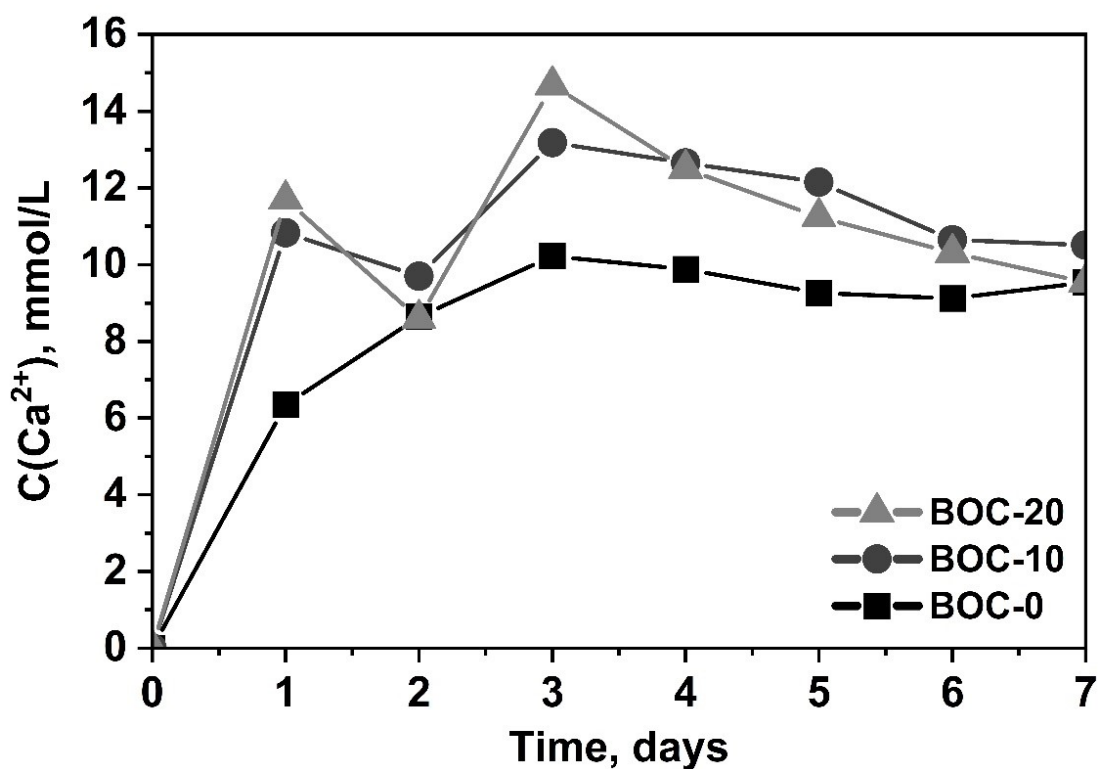


Figure 13. Solubility curves of biomimetic obturating composition (BOC) samples in simulated body fluid solution

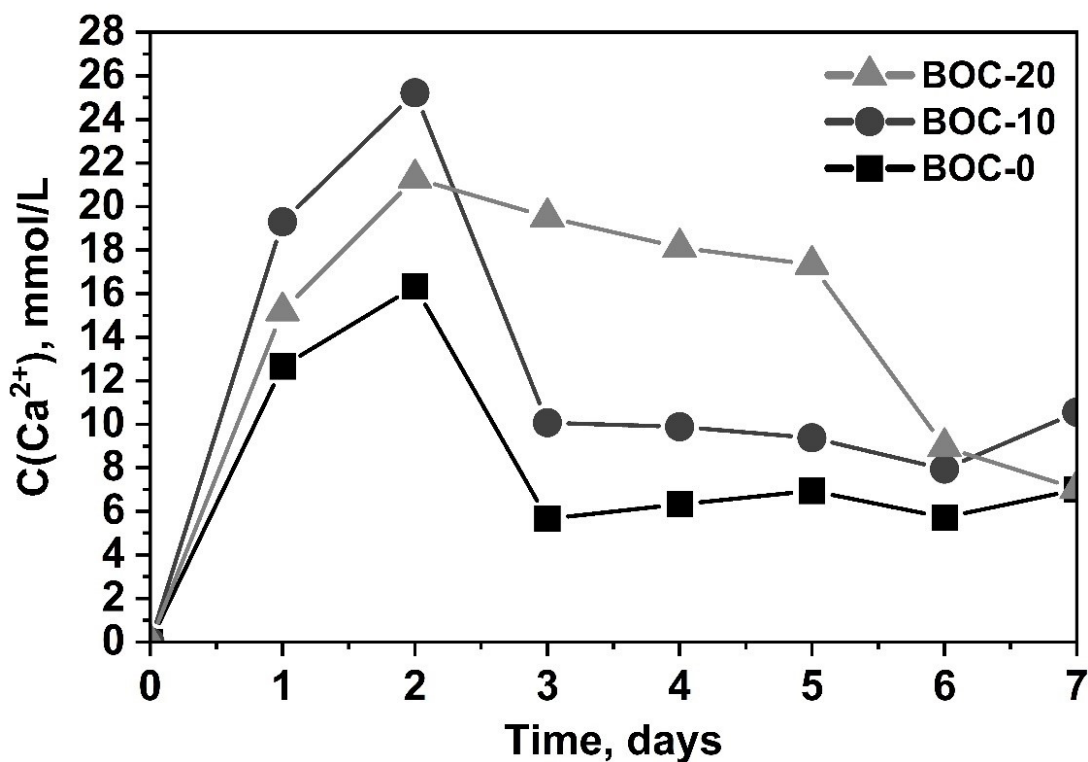


Figure 14. Solubility curves of biomimetic obturating composition (BOC) samples in acetate buffer solution

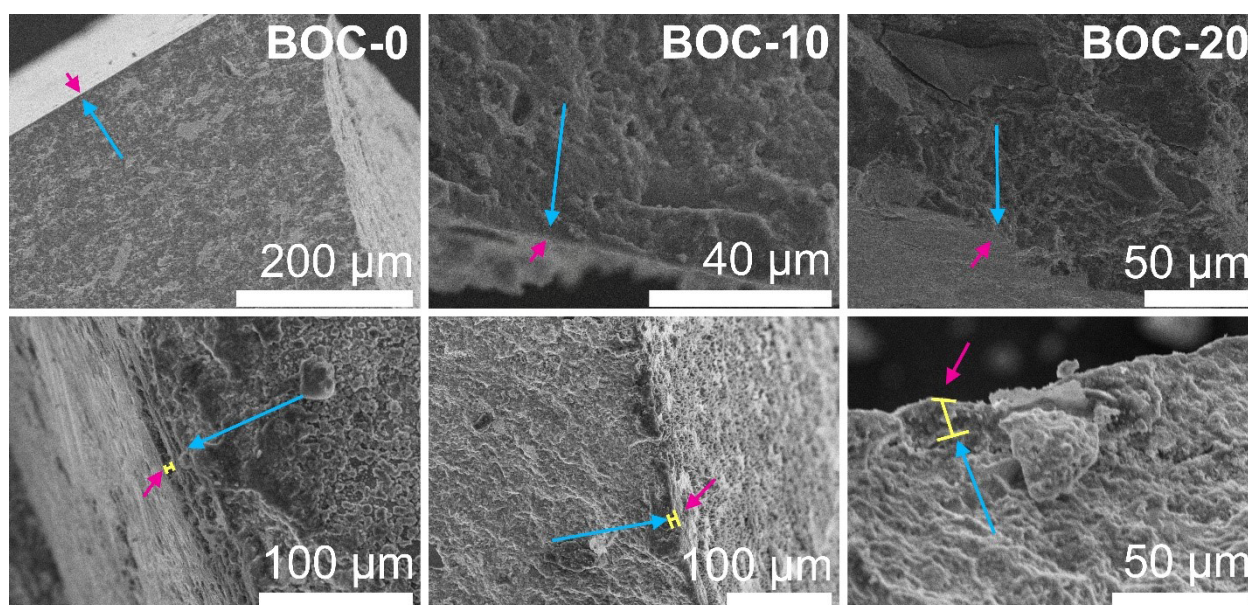


Figure 15. Scanning electron microscopic images of pelletized biomimetic obturating composition (BOC) samples before and after exposure to simulated body fluid solution (blue and pink arrows indicate the phase boundary in orthogonal directions; yellow lines indicate the thickness of the apatite layer). Scale bars: 40 μm , 50 μm , 100 μm , 200 μm ; magnification: 300 $\times$ (top left), 1400 $\times$ (top middle), 650 $\times$ (top right), 500 $\times$ (bottom left), 300 $\times$ (bottom middle), and 850 $\times$ (bottom right).

Table 10. Thickness of apatite layer formed on pelletized biomimetic obturating composition (BOC) samples

Composition code	Thickness of apatite layer, μm
BOC-0	5.86 ± 0.25
BOC-10	11.03 ± 1.42
BOC-20	18.32 ± 1.99

4. Conclusion

In this work, experimental compositions of a BOC—a new MTA-type dental material based on a nanostructured calcium phosphate biomimetic filler—were obtained and studied for the first time. A nanostructured calcium-deficient Si–F-substituted biomimetic hydroxyapatite synthesized using our methodology was used as a filler.

The results demonstrate that all BOC compositions meet the requirements of ISO 6876:1986 and can be classified as type I dental materials. The bioactivity of experimental BOC samples was evaluated *in vitro* using SBF (pH 7.40) and acetate buffer (pH 5.50). It was found that the apatite-forming ability of the BOC increases with increasing nanostructured calcium phosphate biomimetic filler content. Furthermore, as a result of the introduction of the nanostructured calcium phosphate biomimetic filler, the composition has the following advantages: improved

apatite-forming ability, excellent solubility (up to a 54% increase in Ca^{2+} release into model media), and potentially enhanced osteoinductivity and bactericidal properties (due to the presence of SiO_4^{4-} and F in the biomimetic filler).

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Conflict of interest

The authors declare they have no competing interests.

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Writing–review & editing: Mikhail Aleksandrovich Trubitsyn, Lyubov Vladimirovna Furda

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data

The data are available from the corresponding author upon reasonable request.

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