

# BIOMATERIALS

UDC 754.056:54.053:616.71:666.7

## BIOACTIVE CERAMICS BASED ON ZIRCONIUM, ALUMINUM, AND TITANIUM OXIDES

**M. A. Medkov,<sup>1,3</sup> D. N. Grishchenko,<sup>1,4</sup> P. M. Nedorozov,<sup>1</sup> V. G. Kuryavyi,<sup>1</sup> and V. S. Rudnev<sup>1,2</sup>**Translated from *Steklo i Keramika*, No. 9, pp. 38 – 42, September, 2017.

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A method for producing porous ceramic biocompatible with living tissues owing to the introduction of calcium phosphates in the interior of the ceramic was developed on the basis of zirconium, titanium, and aluminum oxides. A bioactive coating is formed directly during the fabrication of the sample. The resulting two-phase ceramic is characterized by developed microrelief. The samples meet the mechanical requirements of implants to be used as bone tissue replacements.

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**Key words:** bioactive ceramic, implants, oxides of zirconium, titanium, and aluminum, calcium phosphates.

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Research and development work on and the production of materials to be used to restore lost bone tissue are considered to be one of the most promising trends in modern medical material science. Ceramic materials for bone implants are of great interest because of growing demands in orthopedic surgery. Inertness to biological media and high strength make it possible to successfully use these materials for manufacturing porous structures to be implanted in humans. High chemical and corrosion resistance places them in a high-priority position in comparison with other materials for the development of such structures [1, 2].

The efforts of current research groups are aimed at expanding the list of materials addressing different problems of modern medicine and best satisfying the requirements of any particular clinical case. Ceramics based on  $\text{Al}_2\text{O}_3$ ,  $\text{ZrO}_2$ , and  $\text{TiO}_2$  are bioinert. One way to increase the bioactivity of ceramic materials is to develop a multiphase ceramic containing a resorbable phase. Calcium phosphate compounds can play the role of such a phase: tricalcium phosphate, calcium pyrophosphate, and hydroxyapatite, whose mineral composition is closest to that of bone [3, 4].

Dense ceramic can be obtained by pressing, slip casting, and hot uniaxial or isostatic pressing [5, 6]. Sinter-activating

additives can be used, for example, additives forming a liquid phase during sintering [7]. However, in order to replace bone tissue a developed porous structure must be present in the implant, since penetrative growth of biological tissue into the pores of an implant provides the best contact at the implant-biotissue boundary. The production of biocompatible ceramics with a developed porous structure and high strength opens new possibilities for the treatment of diseases requiring bone replacement.

The aim of the present work is to produce strong porous composite ceramic materials which are biocompatible with live tissues in the body due to the fact that calcium phosphates are formed in the interior of the ceramic directly in the process of its fabrication.

### EXPERIMENTAL PART

The initial batch was prepared using commercial samples of analytically pure grade zirconium oxides, ultrapure grade titanium and aluminum oxides, No. 29 KhS-2 laboratory glass, and chemically pure grade magnesium oxide (only to stabilize zirconium dioxide). The composition of laboratory glass was (weight content, %): 68.8  $\text{SiO}_2$ ; 3.7  $\text{Al}_2\text{O}_3$ ; 7.5  $\text{CaO}$ ; 3.5  $\text{BaO}$ ; 10.0  $\text{Na}_2\text{O}$ ; 3.0  $\text{K}_2\text{O}$ ; and, 3.5  $\text{MgO}$ . A foaming agent — mixture of di-substituted ammonium phosphate (pure grade) with calcium carbonate (chemically pure) — was added into each sample in amount 15 or 20 % of the sample weight. For the present studies different ratios of

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<sup>1</sup> Institute of Chemistry, Far-East Branch of the Russian Academy of Sciences, Vladivostok, Russia.

<sup>2</sup> Far-East Federal University, Vladivostok, Russia.

<sup>3</sup> E-mail: medkov@ich.dvo.ru.

<sup>4</sup> E-mail: grishchenko@ich.dvo.ru.

**TABLE 1.** Composition of the Experimental Ceramic Samples

Sample No.	Composition, weight content, %
1	ZrO <sub>2</sub> – 71%, MgO – 4%, glass – 10%, mixture I – 15%
2	ZrO <sub>2</sub> – 71%, MgO – 4%, glass – 10%, mixture II – 15%
3	ZrO <sub>2</sub> – 71%, MgO – 4%, glass – 10%, mixture III – 15%
4	ZrO <sub>2</sub> – 62%, MgO – 3%, glass – 15%, mixture I – 20%
5	ZrO <sub>2</sub> – 62%, MgO – 3%, glass – 15%, mixture II – 20%
6	ZrO <sub>2</sub> – 62%, MgO – 3%, glass – 15%, mixture III – 20%
7	Al <sub>2</sub> O <sub>3</sub> – 75%, glass – 10%, mixture I – 15%
8	Al <sub>2</sub> O <sub>3</sub> – 75%, glass – 10%, mixture II – 15%
9	Al <sub>2</sub> O <sub>3</sub> – 75%, glass – 10%, mixture III – 15%
10	Al <sub>2</sub> O <sub>3</sub> – 65%, glass – 15%, mixture I – 20%
11	Al <sub>2</sub> O <sub>3</sub> – 65%, glass – 15%, mixture II – 20%
12	Al <sub>2</sub> O <sub>3</sub> – 65%, glass – 15%, mixture III – 20%
13	TiO <sub>2</sub> – 75%, glass – 10%, mixture II – 15%
14	TiO <sub>2</sub> – 65%, glass – 15%, mixture II – 20%

these components were used: mixture I — Ca/P = 1; mixture II — Ca/P = 1.33; and, mixture III — Ca/P = 1.66. Each composition was ground in a vibratory mill, after which 90% of the particles were smaller than 50 μm. The compositions of the experimental ceramic samples are shown in Table 1.

The samples were pressed into pellets under pressure 180 or 200 kPa/cm<sup>2</sup>. The resulting pellets were calcined in a muffle furnace to temperature 1300°C at heating rate 15 K/min.

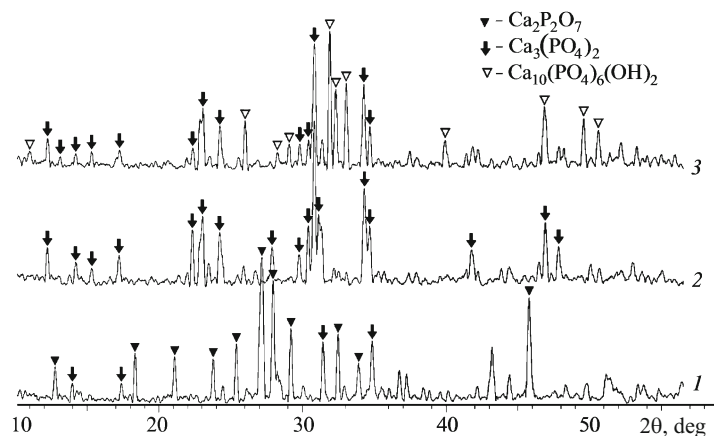
A D8 ADVANCE diffractometer (CuK<sub>α</sub> radiation) with a graphite monochromator was used to record the diffraction patterns. The composition of the obtained powders was monitored by means of x-ray phase analysis using the EVA search program with the PDF-2 powder data bank. Scanning electron microscopy was used to determine the size and morphology of the ceramic particles. A Hitachi S5500 scanning electron microscope was used to obtain SEM images of the powders. The sample was deposited on conductive carbon tape. A SHIMADZU AUTOGRAPU AG-X plus 50 kN ma-

chine was used to investigate the strength of the samples in compression. An JXA-8100 Electron Probe Microanalyzer (Japan) with an INCA (England) attachment with accelerating voltage of 20 kV was used to obtain the average elemental composition of a sample. The content of the elements was determined as the average of five measurements, obtained in different locations during scanning of 300 × 200 μm areas of the samples. Carbon was pre-deposited on the samples in order to prevent charging.

## RESULTS AND DISCUSSION

The method of obtaining a bioactive coating of hydroxyapatite on porous ceramic based on ZrO<sub>2</sub> is described in [8]. The method provides for permeation of a slurry obtained by a special technology and containing hydroxyapatite and borosilicate glass, followed by firing at 1300°C. Previously [9], we showed that the process of obtaining porous zirconium dioxide based ceramic can be combined with the process of forming a bioactive layer. For this, the components which in the course of firing led to the formation of calcium phosphates in the entire volume of the ceramic and kind of lined the pores with a bioactive coating from within were used as foaming agents. A mixture of calcium carbonate with ammonium hydrophosphate was used as foaming agent. It was of interest to obtain by the same method a ceramic based on aluminum and titanium oxides and to compare them with the zirconium ceramic in terms of their strength.

As indicated in the experimental part a mixture of calcium carbonate and ammonium hydrophosphate taken in different proportions was used as an additive forming a bioresorbable phase during the firing process: (I) Ca/P = 1; (II) Ca/P = 1.33; (III) Ca/P = 1.66. As a result of the burnout of these mixtures, calcium phosphates with different compositions can form depending on the ratio of the components. According to x-ray analysis, calcium phosphates with the composition Ca<sub>2</sub>P<sub>2</sub>O<sub>7</sub> and Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> are formed during burning of mixture I, Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> in the case of mixture II, and Ca<sub>3</sub>(PO<sub>4</sub>)<sub>2</sub> and Ca<sub>10</sub>(PO<sub>4</sub>)<sub>6</sub>(OH)<sub>2</sub> in the case of mixture III (Fig. 1).



**Fig. 1.** Diffraction patterns of a mixture after firing at 1300°C: 1) mixture I; 2) mixture II; 3) mixture III.

The presence of not one but simultaneously several calcium phosphates in the products of calcination is not a disadvantage but rather an advantage, because different calcium phosphates have different rates of resorption in the body and, consequently, can provide prolonged delivery of calcium and phosphorous ions. Since the used mixtures are foaming agents, the calcium phosphates must be formed inside pores in the process of obtaining ceramic.

The obtained samples have the form of porous ceramic sintered from two types of particles differing in terms of morphology and composition. Ceramic samples with  $ZrO_2$  are characterized by round particles with transverse dimensions  $0.6 - 3.0 \mu m$  as well as particles shaped like rectangular prisms with visible faces  $5 - 10 \mu m$  long and  $1 - 2 \mu m$  wide (Fig. 2a). According to EMF data the round particles contain zirconium and virtually no phosphorus with calcium. Conversely, prismatic particles contain large amounts of calcium and phosphorus and practically no zirconium (Table 2). In addition, protuberances in the form of  $0.2 - 0.5 \mu m$  wide and up to  $3 \mu m$  long whiskers are observed on many of the rounded particles (Fig. 2b). Presumably, the whiskers have the same composition as the prismatic particles. Zirconium may occur in the spectrum of a whisker as a result of scattering from neighboring regions containing rounded particles, which consist of zirconium oxide, and could be a result of the process of the formation of whiskers on the surface of these particles. According to x-ray phase analysis, zirconium oxide is present in the samples as a mixture of two modifications — monoclinic and cubic.

Ceramic samples with  $Al_2O_3$  are represented by rounded particles with transverse dimensions of  $0.5 - 1.0 \mu m$  as well as particles in form of a polyhedron and distinguished by larger sizes  $2 - 5 \mu m$  (Fig. 3). The round particles consist mainly of aluminum oxide and the polyhedral particles consist of calcium phosphate (Table 2). According to x-ray phase analysis, aluminum oxide is present in the form of corundum in the samples. Table 2 shows the compositions of ceramic samples obtained as the average of five measurements during scanning of the fracture surfaces of the samples.

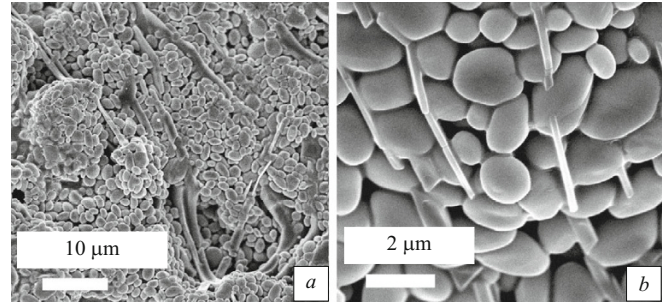


Fig. 2. SEM image of ceramic samples with  $ZrO_2$ .

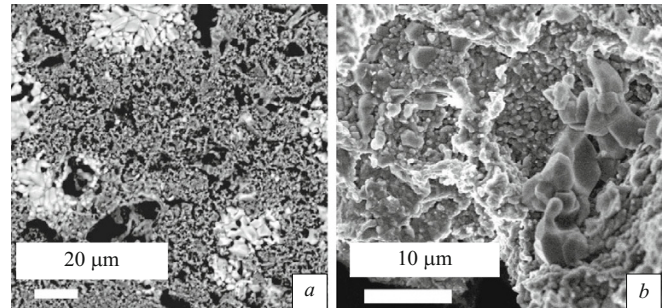


Fig. 3. SEM images of ceramic samples with  $Al_2O_3$ .

The particles of the ceramic samples with  $TiO_2$  are nearly cubic with edge length from  $1$  to  $10 \mu m$ . Protuberances in the form of  $0.5 - 1.0 \mu m$  wide and  $5 - 10 \mu m$  long whiskers are observed between the grains in the sample (Fig. 4a). Swollen shapeless formations in the form of corals occur in many sections of whisker accumulation (Fig. 4b). The cubic grains consist of tin oxide. The shapeless sections and whiskers are close in terms of composition and consist mainly of calcium phosphates. X-ray diffraction analysis shows titanium oxide to be present in the form of rutile in the samples.

Table 3 shows the strength for the samples as a function of composition and pellet pressing conditions. As one can see in Figs. 1 – 3, all ceramic samples have pores, which are

TABLE 2. Average Elemental Composition of Ceramic Samples

Sample including	Particle shape	Elemental composition, weight content, %								
		O	Na	Mg	Si	P	Ca	Zr	Al	Ti
$ZrO_2$	Round	69.09	0.70	0.82	1.92	0	0.17	27.31	–	–
	Prism	46.66	1.71	1.86	1.63	17.41	28.92	1.81	–	–
	Whisker	68.30	1.12	0.96	0.91	4.93	7.68	16.10	–	–
$Al_2O_3$	Round	65.95	0.91	0	1.43	1.75	2.71	–	27.25	–
	Polyhedron	63.08	1.96	0.91	0.39	14.26	18.44	–	0.96	–
$TiO_2$	Cubic	67.56	0	0	0.72	0	0.15	–	–	31.72
	Shapeless sections	64.41	1.89	1.66	0.27	13.61	17.10	–	–	0.74
	Whisker	61.94	1.25	1.00	0.96	9.08	23.09	–	–	2.68

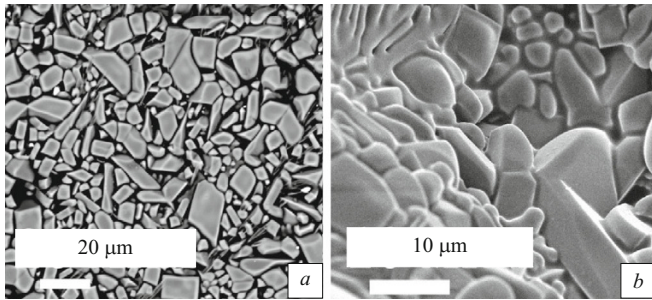


Fig. 4. SEM images of ceramic samples with  $\text{TiO}_2$ .

seemingly lined with calcium phosphates on the inside. Unfortunately, the similarity ends here, since the strength characteristics (see Table 3) of ceramic based on the oxides of aluminum and titanium are greatly inferior to zirconium ceramic.

It is noteworthy that the strength of the obtained samples depends strongly on their pressing conditions in the manufacturing process. The strength of zirconium samples compacted at  $180 \text{ kPa/cm}^2$  with the content of calcium phosphates 15% and glass 10% in the mixture equals 123 – 167 MPa (see Table 3). With increasing ratio Ca/P in a mixture of di-substituted ammonium phosphate with calcium carbonate the strength of the samples increases, which corresponds to the data of [10]. Increasing the amounts of glass and the mixture of calcium phosphates in the batch significantly reduces the strength of the samples. Thus, the strength of samples with 20% foaming agent (mixtures I, II, III) and glass 15% for  $\text{ZrO}_2$  equals on average to about around 90 MPa (see Table 3), which is 30 – 40% lower than the

strength of samples with foaming agent and glass contents in the amounts 15 and 10%, respectively. The samples with  $\text{Al}_2\text{O}_3$  and  $\text{TiO}_2$  behave similarly: increasing the amounts of glass and mixture of calcium phosphates in the batch reduces the strength of the samples on average by 20 – 25%. Increasing the pressing pressure by  $20 \text{ kPa/cm}^2$  on the sample increases the strength of the final product on average by 10% for the samples with  $\text{Al}_2\text{O}_3$  and  $\text{TiO}_2$  and 20% with  $\text{ZrO}_2$ .

As is well known [11], the main characteristics ensuring stable fixation of endoprostheses in bone tissue and therefore their durability and functionality are the texture and surface properties of implants. Implants with developed microrelief give better clinical results than smooth implants. Experimental studies show that surface microgeometry with 1 – 10  $\mu\text{m}$  irregularities gives the maximum bonding between newly formed bone tissue and the implant surface. The morphology of the fracture surface of our samples is characterized by the presence of pores with average size 10 – 30  $\mu\text{m}$ . The number and size of pores can be controlled by adjusting the percentage ratio of the additives and the quality of grinding of the components of the sample.

Samples with  $\text{Al}_2\text{O}_3$  and  $\text{TiO}_2$  will require higher pressing pressure or a different method of obtaining ceramic based on these oxides. In our investigations the mechanical properties of the samples based on  $\text{Al}_2\text{O}_3$  and  $\text{TiO}_2$  are greatly inferior to the mechanical properties of bone tissue. This makes it impossible to consider them as materials for joint replacement. A defect in bone must be replaced by an implant with suitable mechanical characteristics, and according to medical studies the strength of cortical bone in compression is of the order of 100 – 230 MPa [12]. The zirconium ceramic samples meet this requirement.

TABLE 3. Sample Strength versus Composition and Pellet Pressing Conditions (See Table 1 for Compositions)

Sample no.	Sample pressing, $\text{kPa/cm}^2$	Strength in compression, MPa
1	180	123
2	180	141
	200	182
3	180	167
4	180	86
5	180	88
	200	97
6	180	93
7	180	20
8	180	22
	200	24
9	180	24
10	180	15
11	180	17
12	180	19
13	180	12
14	180	9

## CONCLUSIONS

Owing to their unique combination of properties required for use in medicine — chemical inertness, biocompatibility, durability, and strength — zirconia ceramic materials can be used as biological structures for bone replacement therapy.

We have developed a method of producing a porous, zirconium oxide based ceramic that is biocompatible with living tissues by introducing calcium phosphates into the interior of the ceramic. A distinguishing feature of this study is that a bioactive coating is formed not on a prepared porous ceramic but rather it is formed directly during the manufacturing process of the ceramic itself. Samples of zirconium ceramic, pressed at  $180 - 200 \text{ kPa/cm}^2$ , with calcium phosphate mixture content 15% and glass content 10% and heat-treatment at  $1300^\circ\text{C}$  satisfy the mechanical requirements of implants for replacement of bone tissue. This ceramic is characterized by a developed microrelief and the presence of pores in which bioactive particles of calcium phosphate are present.

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