

Effect of the polymer component on biocompatibility and physicochemical properties of porous zirconium ceramics

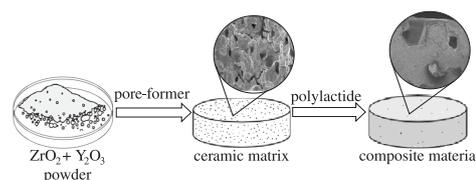
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The dependence of the porosity, mechanical and surface properties of the obtained zirconium ceramics on the content of polylactide as a pore-forming agent was explored. It was shown that modification of ceramics with the polymer material leads to the improvement of mechanical properties and to the decrease in the cytotoxicity of materials.



Keywords: biocomposites, polylactide, zirconium oxide ceramics, strength, porosity, cytotoxicity.

Ceramic materials for bone implants are of much interest to orthopedic surgery. Among the existing materials, ceramics exhibit major advantages as biocompatible, chemically inert, possessing great strength and good wear resistance.

Particular attention has been given to zirconium dioxide based ceramics as bioinert, corrosion-proof, possessing perfect wear resistance, good biocompatibility, and increased fracture toughness owing to the capability for transformational strengthening. However, the application of ceramics is limited by the fact that the implant must have a developed pore structure, since the best contact of the bone with the implant is achieved in case of the invasion of biological tissue in the pore.¹ It was reported earlier, that mechanical properties of partially stabilized zirconium ceramics strongly decrease with increasing porosity, which limits the use of highly porous ceramics.² The promising way to solve this problem might be the development of zirconium dioxide ceramics–biodegradable polymers composite materials. In particular, polylactide [poly(lactic acid)] represents a biodegradable polymer material, which does not induce an immune response in the body and has a lower modulus of elasticity in comparison with ceramics. These characteristics can help to prevent an unintended damage to healthy tissues and improve the mechanical properties of porous ceramic products. The aging of the polymer material in the composite causes its degradation and makes room for the (ingrowth) invasion of bone tissue.^{3–6}

The purpose of this work was to obtain composite materials based on ceramics from zirconium oxide and polylactide, which are suitable for designing osteo implants.

The first component of the composite material was ceramics from zirconium dioxide partially stabilized by 3 mol% of yttrium oxide (3Y-TZP, Tosoh Co., Tokyo, Japan), having increased fracture toughness owing to the capability for transformational strengthening.⁷ The particles of the 3Y-TZP powder had a spherical shape with an average diameter of 5 μm.

Ceramic matrix was molded by the method of uniaxial cold pressing at a pressure of 200 MPa into the samples of cylindrical and beam-type shape. The formed samples were sintered using two-stage sintering in air at 800 °C for 8 h and then at 1300 °C for

2 h. To obtain porous ceramic matrices, a pore former (granulated polypropylene with the granule size of 200–250 μm) was added to the initial powder. Five series of samples with various mass contents of the pore former (0, 20, 30, 40 and 50%) were produced.[†]

The obtained diffraction pattern of the ceramics containing 50 vol% of the pore-forming agent (Figure 1) shows that the ceramics contain a metastable tetragonal phase of zirconium oxide, as expected.

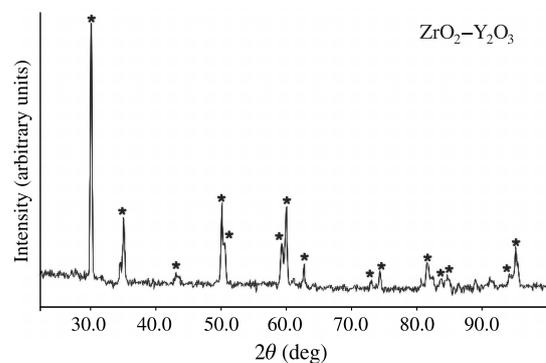


Figure 1 X-ray powder diffraction pattern of the obtained ceramics.

[†] The phase composition of the fabricated ceramics was determined by X-ray phase analysis on the diffractometer XRD-6000. The strength of ceramics and the composite material was measured by radial and axial compression of the cylinder and beam shape samples^{8,9} using the universal testing machine DVT Devotrans with a loading rate of 0.1 mm s⁻¹. The ultimate compression strength (for the samples of the cylindrical shape) and the ultimate bending strength (for the samples of the beam shape) were assessed. The modulus of elasticity of ceramics was determined as the slope of the initial section of the stress–strain curve within the limits of linear elastic deformation.

The total porosity was determined by the method of hydrostatic weighing. Surface roughness was characterized by measuring an arithmetic average profile deviation (Ra) on the contact profilometer Profilometer 296. The morphology of the surface and porosity of the produced ceramics was studied by scanning electron microscopy using the device Leo Supra 50VP.

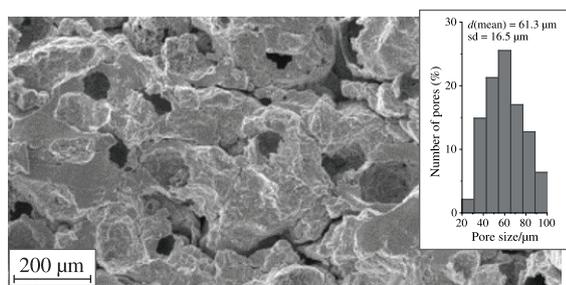


Figure 2 SEM images and pore–size distribution of the obtained ceramics.

The porosity of the obtained ceramics turned out to be lower than the volume content of the pore forming agent, and the porosity increases evenly when the pore former content is raised, *viz.* the porosity increases from 2% (without the pore former) to 21% (at 50 vol% of pore former). Thus, one can assume that this discrepancy is related to the sintering process itself, where shrinkage of ceramics owing to the viscous flow and volume and surface diffusion, occurring in the material,¹⁰ takes place. In this way, the shrinkage and flow of the polymer material during sintering result in the decrease of the porosity.

When the porosity increases, roughness increases accordingly, which was characterized by the value of the arithmetic average deviation profile Ra. Ra increases from 1 μm (without the pore former) to 10 μm (at 50 vol% of pore former). This increase in the roughness is related to the creation of more pores on the surface. For this reason, the polymer material burns out through them during sintering. The pore–size distribution for ceramics, containing 50 vol% of the pore-forming agent in the initial mixture, calculated from SEM images, is presented in Figure 2.

When the porosity increases, elasticity modulus decreases evenly and varies from 12400 ± 1620 to 3020 ± 580 MPa. According to the reported data,¹¹ the elasticity modulus of the bone tissue is in the range from 500 to 20000 MPa, and the compression ultimate strength varies from 2 to 170 MPa. This allows us to conclude that mechanical properties of the obtained materials are similar to those of human bone tissues. Therefore, in case of the implantation it may lead to the destruction of the bone tissue or the implant in the contact zone.

When studying the effect of porosity on the mechanical properties of ceramics, it was found (Figure 3) that during the initial increase in the porosity up to 9%, a sharp decrease in the bending strength (from 180 to 70 MPa) and in the diametral compression (from 138 to 24 MPa) takes place. Further on, when the amount of the pore former increases, the strength continues to decrease, though more gradually. Since the pores formed in the sample entail the reducing of the cross-sectional area of the

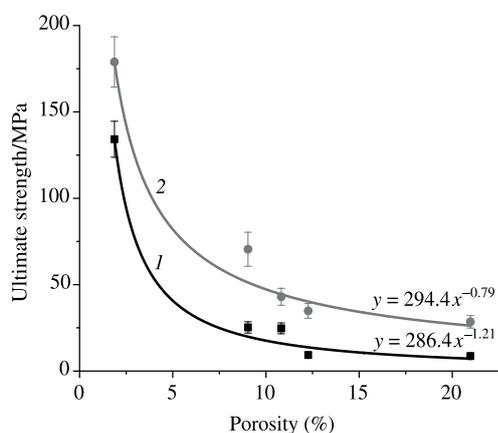


Figure 3 (1) Ultimate diametral compression strength and (2) ultimate bending strength dependence on the ceramics porosity.

Table 1 Dependence of the porosity, arithmetic average deviation profile (Ra), and the elastic modulus on the volumetric content of the pore former.

Pore former content (vol%)	Porosity (%)	Ra/μm	Elasticity modulus/MPa
0	1.87 ± 0.15	0.99 ± 0.04	12440 ± 1627
20	9.04 ± 0.72	1.79 ± 0.09	8394 ± 1115
30	10.82 ± 1.44	2.94 ± 0.14	8162 ± 1197
40	12.27 ± 1.80	7.91 ± 0.44	6094 ± 725
50	20.97 ± 2.43	10.03 ± 0.51	4019 ± 583

material to which the load is applied, they act as stress concentrators.¹²

The second component of the composite was a biocompatible, biodegradable polymer – polylactide – with mass-average molecular mass of 26000 g mol⁻¹ and polydispersity index of 2.29. Polylactide was synthesized by polymerization, accompanied by ring opening.¹³ Composites were prepared by the impregnation of the ceramic sample with the polylactide solution in chloroform and subsequent ultrasonic treatment for 20 min. To find out the effect of the polymer solution concentration on the mass of the precipitated polymer, the impregnation was carried out with the solutions of various concentrations (0.001, 0.05, 0.1 and 0.2 g ml⁻¹). It was determined that the mass of polylactide deposited on ceramics depends linearly on the concentration of the polylactide solution used for impregnation, and this dependency can be described by the equation:

$$y = 0.1469x + 0.0012. \quad (1)$$

Mass of the polylactide, deposited on the ceramics, increases from 0.0019 g (at polylactide concentration of 0.01 g mol⁻¹) to 0.03 g (at polylactide concentration of 0.2 g mol⁻¹). At the polymer concentration exceeding 0.2 g mol⁻¹ the solution became too viscous, and it was impossible to obtain a homogeneous coating. Further experiments were conducted using the materials, impregnated with the polylactide solution with the concentration of 0.2 g mol⁻¹. Ceramics with the porosity of 35% were prepared and used to develop the composite material. Mechanical properties of ceramics were determined before and after the impregnation with the polymer solution. The increase in ultimate diametral compression strength from 3.11 to 4.13 MPa was observed; the strength increment was about 30%.

To assess the cytotoxic properties of the obtained materials, the analysis with the AlamarBlue indicator was conducted.¹⁴ The cell cytotoxicity test (Figure 4) showed that the viabilities of human macrophages incubated on the samples of ceramics and composite are comparable to the values for the control sample

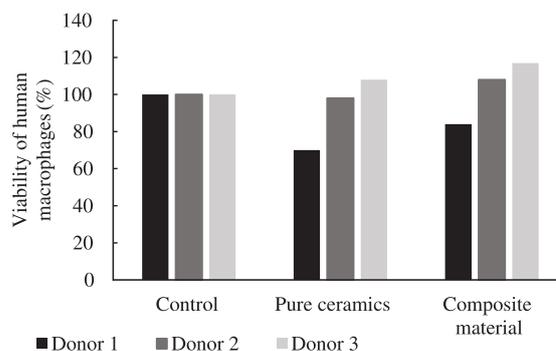


Figure 4 Cytotoxicity data of the pure ceramics and the composite material.

(incubated cell culture), and the materials do not have a toxic effect on the human macrophages.

The viability of cells on the composite material is slightly higher than on the pure ceramics. Therefore, the impregnation of ceramics with the polymer material leads to the decrease in the material toxicity. Since the resulting composite material is characterized by low cytotoxicity, it may be of interest for use in the field of regenerative medicine.

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References

- 1 C. Hadjicharalambous, O. Prymak, K. Loza, A. Buyakov, S. Kulkov and M. Chatzinikolaidou, *Front. Bioeng. Biotechnol.*, 2015, **3**, 175.
- 2 S. N. Kulkov, S. P. Buyakova, M. Chatzinikolaidou and I. Kocserha, *Építőanyag: JSBCM*, 2015, **4**, 155.
- 3 S. P. Buyakova, I. A. Khlusov and S. N. Kulkov, *Fizicheskaya Mezomekhanika*, 2004, **S2**, 127 (in Russian).
- 4 C. A. Maziero Volpato, L. G. D'Altoé Garbelotto, M. C. Fredel and F. Bondioli, in *Advances in Ceramics – Electric and Magnetic Ceramics, Bioceramics, Ceramics and Environment*, ed. C. Sikalidis, IntechOpen, London, 2011, pp. 397–420.
- 5 A. Marti, *Injury*, 2016, **S4**, 33.
- 6 S. Farah, D. G. Anderson and R. Langer, *Adv. Drug Delivery Rev.*, 2016, **107**, 367.
- 7 J. Chevalier, L. Gremillard, A. V. Virkar and D. R. Clarke, *J. Am. Ceram. Soc.*, 2009, **9**, 1901.
- 8 I. Deniz Akin and W. Likos, *Geotech. Test. J.*, 2017, **4**, 608.
- 9 *ASTM C1424-15(2019), Standard Test Method for Monotonic Compressive Strength of Advanced Ceramics at Ambient Temperature*, ASTM International, West Conshohocken, 2019.
- 10 A. S. Tolkacheva and I. A. Pavlova, *Obshchie voprosy tekhnologii tonkoi keramiki (General Questions of Technology of Fine Ceramics)*, UrFU, Ekaterinburg, 2018 (in Russian).
- 11 I. A. Khlusov, V. F. Pichugin and M. A. Ryabtseva, *Osnovy biomekhaniki biosovmestimyykh materialov i biologicheskikh tkanei (Fundamentals of Biomechanics of Biocompatible Materials and Biological Tissues)*, TSU, Tomsk, 2007 (in Russian).
- 12 E. M. Nikiforova, R. G. Eromasov and A. F. Shimansky, *Fizikokhimiya keramicheskikh, kompozitsionnykh i nanomaterialov (Physicochemistry of Ceramic, Composite and Nanomaterials)*, SFU, Krasnoyarsk, 2016 (in Russian).
- 13 V. V. Botvin and O. S. Gordeeva, *Sbornik tesisov uchastnikov foruma 'Nauka budushchego – nauka molodykh' (Science of Future – Science of Youth: Collection of Abstracts of Participants)*, Moscow, 2015, p. 390 (in Russian).
- 14 S. N. Rampersad, *Sensors*, 2012, **9**, 12347.

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