Functional Materials 13, No.2 (2006)

Porosity and bioactivity of hydroxyapatite-glass composites

V.V.Skorokhod, L.A.Ivanchenko, N.D.Pinchuk, O.I.Getman, S.M.Solonyn, V.V.Panichkina, P.Ja.Radchenko

Department of Physical and Chemical Fundamentals of Powder Materials Technology, I.Frantsevich Institute for Materials Science Problems, National Academy of Sciences of Ukraine, 3 Krzhyzhanovsky St., 03142 Kyiv, Ukraine

Received November 22, 2005

Composition, manufacturing method, and some properties of composite ceramics for medical purposes on the basis of bone apatite has been described. The studies include determination of pycnometric density, porosity, and bioactivity degree of composites with various mass ratios of crystalline and amorphous phases depending on sintering conditions. Some results of tests *in vivo* are presented, the influence of the glassy phase presence in the implants on the bone regeneration rate and size of the implanted biomaterial granules is noted.

Описан состав, способ получения и ряд свойств композитной керамики медицинского назначения на основе костного апатита. Исследования включают определение пикнометрической плотности, пористости и степени биоактивности композитов с разным массовым соотношением кристаллической и аморфной фаз в зависимости от условий спекания. Представлены некоторые результаты испытаний *in vivo*, отмечено влияние присутствия стеклофазы в имплантатах на скорость регенерации кости и размеры имплантированных гранул биоматериала.

Biomaterials based on calcium hydroxyapatite (HAp) attract a serious attention of researchers all over the world due to high affinity to bone tissue and ability to be substituted by a new bone. These materials are used widely in general surgery, orthopaedics, traumatology and dentistry to cure bone defects. The materials differ in preparation technology, structure, and features of biological interaction and can be called "calcium phosphate ceramics" [1]. The biogenic hydroxyapatite (BHAp) is a bone mineral that we refer to as "osteoapatite". It can be used to produce the "hydroxyapatite-glass" composites in the form of particles differing in size and having intrinsic porosity and can be used as a native bone [1, 2]. We used its interaction with low-melting glass based on silicon, sodium, and boron oxides under liquid sintering to increase the hardness of implants [2]. The purpose of this work was to determine experimentally the pore size distribution in BHAp-glass specimens obtained under various sintering conditions and to establish a relationship between the bioactivity and the pore structure.

The composite preparation process consists of two stages: (i) the primary sintering at temperature T_1 being varied within 750–1300°C range; and (ii) the secondary sintering at a constant temperature T_2 not exceeding 800°C. The primary sintering duration is also varied from 0.25 to 2 h [1–4].

For the primary sintering, free-flowing powders were used. Then the sintered material was crushed down to granule size L_2, compacted and sintered again. The biomaterial initial composition (mole per cent) can be presented as:

Table 1. Apparent density of composite samples

Osteoapatite content (% mol.)	Density ρ, ±0.054 (g·cm^{-3})		Apparent density ρ_{ap}, ±0.05 (g·cm^{-3})	
	Calculated	Picnometric	T_1 = 1100°C	T_1 = 1300°C
3	2.724	2.750	2.257	2.301
4	2.750	2.757	2.193	2.292
5	2.772	2.770	2.163	–
6	2.790	2.790	2.026	2.238
8	2.819	2.809	1.968	2.185
12	2.858	2.871	–	1.848

$45SiO_2 \cdot 25Na_2O \cdot (18–27.5)B_2O_3 \cdot (12–2.5)Ca_{10–X}(PO_4)_6(OH)_2$

where $Ca_{10–X}(PO_4)6(OH)_2$≡Osteoapatite, (Ca/P = 1.63 – 1.65).

The experimental calcium and silicon content values coincide with the calculated ones within the determination accuracy. The total mass percentage of impurity elements in biomaterials reaches 2.0 %, which meets the requirements of ASTM F1185-88 "Standard Specification for Composition of Ceramic Hydroxyapatite for Surgical Implants". The elemental compositions of various structural parts of the samples were determined using the electronic microstructure analysis of the outer surface and the fracture surface. The sample phase composition was determined using X-ray and IR optical absorption spectra obtained in KBr. The picnometric density, porosity, pore size distribution, ultra-violet optical reflection spectra, and mechanical strength were chosen as main composite characteristics. The basic X-bands for the samples coincide with those for hydroxyapatite. The absence of X-bands for sodium, calcium,and other silicates testifies to amorphous structure of the glassy phase. The same conclusion can be drawn from the IR optical absorption spectra of the samples.

At T_1 = 1100°C, the experimentally obtained dependence of the composite picnometric density on the osteoapatite content proved to be very close to the calculated one while at higher temperatures T_1, the picnometric density values are lower than calculated ones (Table 1). For the composites sintered at T_1 = 1300°C, the apparent density exceeds that of composites of the same composition sintered at T_1 lower than 1100°C. The composite powders primarily sintered at T_1 are compacted better than initial powders, provided the compacting pressure does not exceed of 2 tons per·cm^{-2}. The porosity of all the composite component mixture increases after sintering depending on the particle sizes of the powders primary sintered and crushed before the secondary sintering. Some pore sizes are shown in Table 2. Pores of 1 to 4 μm size are fixed in all the samples and thus are not indicated. The pore volume does not exceed 8.7 % of the total porosity of composite specimens.

The microstructure of ОК 8 sample (typical of other samples) is shown in Fig. 1. The main elements of this structure are crystalline osteoapatite grains (white particles), included in the glass matrix (dark background). Both the crystalline grains and glassy matrix contain pores of various sizes. The elemental analysis specified the presence of calcium, phosphorus, and silicon ions in both crystalline grains and glassy interspace. The contents of calcium and phosphorus ions in crystalline grains exceed those in the glassy phase. To determine the smallest pores fraction, the computer processing of specimens microphotos obtained under three magnifications was performed.

Table 2. Pore sizes in composite samples with 5–6 mol. % osteoapatite

Particle size before secondary sintering L_2 (μm)	Conglomerate size (μm)	Pore size (μm)
<160	60–500	15–160
50–160	10–160	7–50
160–250	(130–330)±45	(65–145)±13
250–500	(195–510)±53	(120–240)±33

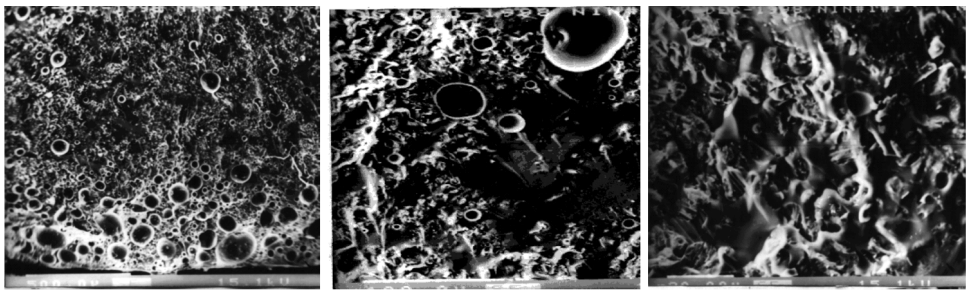

Fig. 1. Typical structure. Magnification: 62, 250, 1000.

The results are presented in Fig. 2. As seen, it is possible to distinguish three basic pore groups of maximum sizes close to 2, 10, and 40 μm. The dependences of the composite porosity on the temperature T_1 and the osteoapatite content are shown in Fig. 3.

The results of the optical visible and ultra-violet reflection spectra analysis give confirmation to surface interaction of osteoapatite particles with the glassy phase during sintering (Table 3). All the spectra contain a distinct reflection minimum within the spectral interval 37000–42000 cm^{-1} and almost linear change in $R(\nu)$ in the region of decreasing wave numbers (Fig. 4). The spectral position of the increase $R(\nu)$ onset usually defines the optical band gap width in semiconductor substances: $E_g = h\nu_g$ (Table 3) [5].

The results of X-ray and gystomorphologic studies of animal bone parts with implants from osteoapatite-glass composite confirm their high osteoconductivity. The studied dynamics of osteogen growing into implant granules and bloks with gradual formation of a dense network of osteal beams testifies to the adequate interaction of the biomaterials with adjacent tissues. The absence of any inflammatory responses of animal organisms and high adhesion of the newly created osteal tissue to the implant surface without development of a fibrous sheath also testifies to their osteoconductivity. The process of osteon growing

Table 3. Interband optical electron transitions in composites OK 6

Content of osteoapatite (mol. %)	T_1 (°C)	$E_g = h\nu_g$, ±0.04 (eV)
6, native bone in composite	780	4.59
6	900	4.46
6	1100	4.53
6	1300	4.96
6, with ready glass	1300	4.46

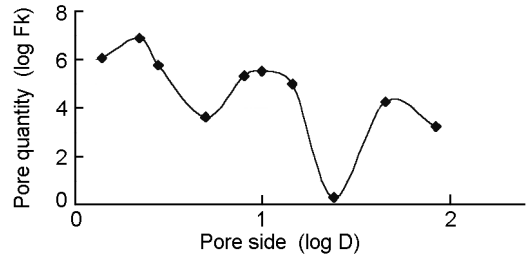

Fig. 2. Pore size distribution in OK 6 composite specimen.

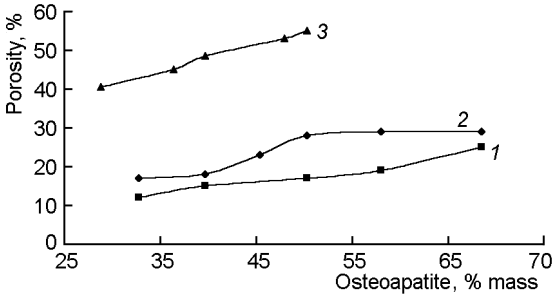

Fig. 3. Dependence of the composite porosity on the osteoapatite content: T_1 (°C): 1300 (*1*); 1100 (*2*); 1100 (using native bones) (*3*).

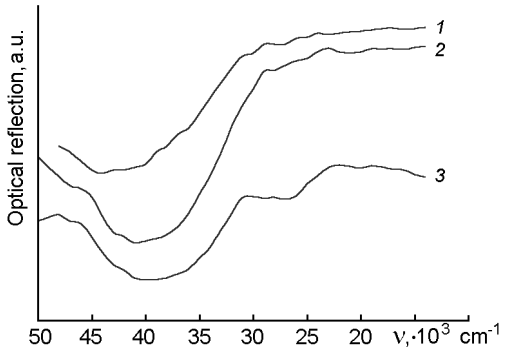

Fig. 4. Optical diffusive reflection from surfaces of OK 6 biomaterial samples: T_1 (°C): 1300 (*1*); 1100 (*2*); 780 (*3*).

Table 4. Pore size distribution in OK 6 composites

T_1 (C)	Heating rate $\Delta T_1/\Delta t_1$, deg·min−1	Size pore range (μm)	Porosity (%)	Mean pore size D (μm)
1100	100	20–135	10.6	41.0
		4–20	13.6	10.0
		1–4	7.3	2.6
780	6–7	18–100	24.4	46.0
		3–18	7.6	10.2
		1–3	8.7	2.3
780	6–7, with using ready glass	20–260	21.1	35.2

into porous implant granules is accompanied by their fragmentation and gradual dissolution of the outer and inner surfaces of separate granules with subsequent replacement with a new bone [6]. Using X-ray study of the implants 3 weeks after the implantation, we observed inhomogeneous thickening of osteal tissue with indistinct contours. The blood vessels had grown into the biomaterials with formation of bone islands close to granule surfaces. The depth of bone growth into the implant volume was 1.5–2.0 mm after 26 weeks. The density and sizes of separate granules decreased significantly.

The presence of small sodium and silicon amounts in crystalline grains and of calcium and phosphorus in the glass phase testifies to the interdiffusion of these elements during sintering. The outer sample surface is enriched in the glass phase as compared to the bulk. The presence of pores in composites is due to the following causes: the intrinsic porous structure of the osteoapatite particles sizing from 50 to 160 μm before sintering and the formation of pores in the glassy matrix during sintering due to intense release of gases such as water vapors, carbon oxides and in part boron oxide, from the glass phase. It should be noted that in the compacted composite samples before the sintering, the pores are predominantly open, but after compacting and sintering, a partial transformation of the open pores into closed ones occurs. The ratio between quantities of open and closed pores depends on the amount of glassy phase in the sample composition and on the sintering conditions. The mechanism of the porosity transformation is now under study. The nature of pores of under 40 μm size is mainly connected with the polyporous osteoapatite structure. The osteoapatite pore sizes are within the range of 1 to 650 μm and can be subdivided into small, medium, and large groups corresponding to 1–3, 4–19, and >20 μm, respectively. The pore size distribution is more distinct for OK 6 sample obtained at T_1 = 1100°C than that in the samples obtained at T_1 = 780°C (Table 4).

The composite samples obtained at T_1 over 1100°C exhibit the lowest porosity (<17 %) and the highest mechanical hardness (270 MPa). It is evident that the penetration of the liquid phase between the solid phase particles under high-temperature primary sintering is more intensive than at $T_1 < 1100$°C, which results in a greater sample strengthening at the final sintering stage. An increase in the composite porosity with increasing crystalline phase amount is caused by the intrinsic porosity of osteoapatite particles. A significant decrease in the composite porosity with increasing T_1 may be due to two causes: 1) with increasing sintering temperature, the glassy phase viscosity decreases, which results in easier removal of releasing gases and thus in better densification of the glassy phase; 2) an intensified interaction between amorphous and crystal phases at $T_1 > 1000$°C results in increased penetration of the glassy phase into osteoapatite particle volume and so in decreased initial porosity.

The E_g values range from 4.3 to 5.0 eV for all the composites investigated. These exceed the osteoapatite band gap width (from 3.9 to 4.2 eV) [5]. That may be connected with the presence of a thin glass layer on the surfaces of separate crystalline grains (or agglomerates thereof). The band gap width of the thin layer glass is an addition of the E_g eigenvalues of both phases and is situated therefore within the interval 4.2–5.5 eV. The E_g value increases with increasing T_1 (Table 3) because of the best phase interaction at maximum sintering temperatures. If a ready glass is introduced

in the composite initial phase, the interaction on osteoapatite grain surfaces is less intense than in case of using glass components, and the energy E_g decreases. The high bioactivity of the composites developed is connected advantageously with their porous structure corresponding to the intrinsic porous structure of osteoapatite, also with its high bioactivity and with additional activating effect of the glassy phase on the osteogenesis [6–9].

The thickness of the osteal tissue layer on granule surfaces depends on the granule size. In the case of implantation of both osteoapatite and composite with granules sizing in the range of 160 to 500 μm, the layer of newly created osteal tissue was thicker than that at using 1000–3000 μm granules. An additional activating influence of the glassy phase promotes the growth of a new tissue. This is especially evident in early terms after implantation [6]. The amount of newly created tissue around cylindrical implants was established to depend on their composition and porosity [8]. 25 weeks after implantation, the greatest changes were observed in biomaterials like ОК 12, containing the maximal osteoapatite amount and having a porosity of 48 %. Such materials have successfully passed the clinical approbation at the Department of osteo-purulent surgery, Institute of Traumatology and Orthopaedics of the Academy of Medical Sciences, which confirmed the successful use thereof as plastic materials for curing from osteal defects of various origins. So experiments *in vivo* testify to high biocompatibility and osteoconductivity of our biomaterials.

Thus, the formation of required porosity of osteoapatite-glass composites has been attained due to using the liquid phase sintering and osteoapatite particles with intrinsic polysize porous structure. The total porosity of composites is maximal if native bones are used as component of their raw material. The high bioactivity of the composites is connected advantageously with their porous structure also its high bioactivity and additional activating effect of the glass phase on osteogenesis.

References

1. N.D.Pinchuk, L.A.Ivanchenko, *Powder Metallurgy and Metal Ceramics*, **7**, 36 (2003).
2. L.A.Ivanchenko, T.I.Falkovska, N.D.Pinchuk et al., *Powder Metallurgy and Metal Ceramics*, **9–10**, 448 (1999).
3. L.A.Ivanchenko, T.I.Falkovskaya, N.D.Pinchuk et al., *Powder Metallurgy and Metal Ceramics*, **1–2**, 54 (2003).
4. L.A.Ivanchenko, N.D.Pinchuk, A.A.Krupa et al., *Steklo i Keramika*, **6**, 30 (2003).
5. V.A.Dubok, E.A.Zhurakivsky, L.A.Ivanchenko et al., *Met.Phys.Adv.Tech.*, **17**, 313 (1998).
6. Ye.P.Podrushnyak, L.A.Ivanchenko, A.T.Brusko et al., *Problemy Osteologii*, **3**, 89 (2000).
7. N.D.Pinchuk, V.S.Sylima, *Problemy Osteologii*, **3**, 37 (2000).
8. V.S.Sulyma, L.A.Ivanchenko, N.D.Pinchuk et al., *Problemy Osteologii*, **4**, 21 (2001).
9. L.A.Ivanchenko, V.S.Sulima, N.D.Pinchuk, Nanostructured Materials and Coatings for Biomedical and Sensor Applications, NATO Science Series, Kluwer Academic Publishers, Netherlands, 77 (2003).

Пористість і біоактивність композитів гідроксиапатит-скло

В.В.Скороход, Л.А.Іванченко, Н.Д.Пінчук, О.І.Гетман, С.М.Солонин, В.В.Панічкіна, П.Я.Радченко

Описано склад, спосіб одержання і ряд властивостей композитної кераміки медичного призначення на основі кісткового апатиту. Дослідження містять визначення пікнометричної густини, пористості і ступеню біоактивності композитів з різним масовим співвідношенням кристалічної і аморфної фаз в залежності від умов спікання. Представлено деякі результати випробувань *in vivo*, відзначено вплив присутності склофази в імплантатах на швидкість регенерації кістки та розміри імплантованих гранул біоматеріалу.