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SI-MODIFIED HIGHLY-POROUS CERAMICS BASED ON NANOSTRUCTURED BIOGENIC HYDROXYAPATITE FOR MEDICAL USE

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Abstract:

Highly-porous ceramics samples based on nanostructured biogenic hydroxyapatite and superfine fumed silica have been prepared using a foam replication method at a sintering temperature of 850°C. They were shown to possess a total porosity 86-89 % and a permeable open-porous (~ 90 % of the total porosity) structure with pore sizes in the range 500-1000 μm. The compression strength is equal to 0.3-0.4 MPa. According to the XRD analysis it was established that during sintering hydroxyapatite phase remains, which was also confirmed by IR spectroscopy data. The carried out studies in vitro (the dissolution rate in saline) of the obtained highly-porous bioceramics showed that the samples are resorbable and their dissolution rate increases with growing porosity and decreasing HA content. Evaluation of adsorption activity (by the example of antibiotic Ceftriaxon) demonstrated prospectivity of ceramics as carriers of drugs for acceleration of patients' post surgery rehabilitation in orthopedic, traumatic and dentistry surgery.

1. Introduction

Recovery of injured bone tissue is an important and urgent problem not only for orthopaedics, traumatology and dentistry, but also for the current biomedical material science. Today porous bioresorption materials have become preferable osteoplastic materials as they are capable to stimulate the growth and differentiation of mesenchymal stem cells, which provides a rapid recovery of patients. Over many recent years, hydroxyapatite materials have been keeping leading positions among the other osteoplastic materials thanks to their perfect bioactive properties and similarity to the inorganic component of bone tissue.

L. Hench, one of the founders of biomedicine material science, showed that knitting of bone tissue and an implant requires the presence of silicon, one of the important elements of human body, which actively participates in the formation of bone tissue [1]. A number of authors have revealed improvement in bioactive properties of hydroxyapatite ceramics and cements, in particular in the rate of apatite layer formation, after incorporation of silicon ions into their composition [2-5].

Many researchers pay much attention to the positive effect of silicon on bone tissue metabolism. Furthermore, strength and biocompatibility of silica itself promote its wide application in orthopaedics and tissue engineering [6-9]. Today there is observed a tendency to the use of Si-modified ceramics based on fumed silica introduced in to control delivery of bioactive substances and drugs for prevention of inflammatory reactions in post surgery time and for shortening of the recovery time. Thanks to high dispersion, a developed and accessible surface as well as to high chemical purity and physiological compatibility, fumed silica is widely used in the solution of various medical and biological problems [5, 8].

The authors' previous work [10] has established that modification of hydroxyapatite ceramics with silicon (using superfine silica) prolongs release of drug (Rifampicin) out of porous samples prepared by powder metallurgy methods for the first 24h, which is twice longer than without superfine silica. It was also shown that addition of nanosized silica, even 2 mass%, to ceramics based on nanostructured biogenic hydroxyapatite (BHA) markedly changes the structure of ceramic samples made by dry double-action pressing followed with heat treatment above 600°C, namely makes it finer and more porous [11].

In addition to the study of bioceramics composition, a possibility to produce highly-porous ceramics through duplication of the polymer matrix structure has been studied [12-15], and it was established that such highly-porous materials raise the efficiency of cloning and stimulate proliferation and differentiation of osteogene cells (precursors of marrow) [16].

The aim of the present work was to produce Si-modified highly-porous ceramics with a controlled structure and bioactive properties based on nanostructured biogenic hydroxyapatite by foam replication method.

Table 1. The initial composition for preparation of highly-porous ceramics

Type	Composition, mass%			
	BHA	**Aerosil®200**	**NaOH**	**Water-soluble SiO_2-Na_2O glass**
Type 1	95	5	–	–
Type 2	90	5	5	–
Type 3	75	4.2	4.2	16.6

2. Material and methods

Nanostructured BHA obtained through calcination of cattle bones at 900°C, superfine fumed silica Aerosil® 200 (Germany) and a foamed polyurethane matrix (ST 3542, Interfom, Ukraine) with a permeable porous structure were used as starting materials. Samples of three types were made (Table 1) using the foam replication method described in [17], which includes the following procedures:

i) preparation of slurry from BHA, Aerosil® 200 and water in a ball mill at a solid phase/liquid phase ratio of 3:2;

ii) application of slurry onto a polymer matrix blank;

iii) drying and sintering of samples at 850°C. Type 2 samples were fabricated according to the above described procedure for Type 1 samples plus addition of 5 mass % NaOH to slurry. Type 3 samples were added with water-soluble SiO_2-Na_2O glass (Table 1).

The sample structure was examined by optic microscopy using a binocular stereomicroscope MTRZ (MEIJI Techno, Japan).

The material composition was determined by the following methods:

i) X-ray diffraction (XRD) analysis using diffractometer DRON-3 ("Burevestnik", Russia) equipped with an X-ray tube with a copper anode, graphite monochromator and computer-based system of scanning;

ii) infrared (IR) spectroscopy using a Fourrier-spectrometer FCM 1202 (Infraspectr Ltd., Russia) in the frequency range 4000–400 cm^{-1};

iii) energy-dispersive X-ray fluorescent element analysis using an apparatus Expert 3L (INAM, Ukraine).

Total and open porosity of samples as well as compression strength were determined with the aid of a multipurpose machine Ceram Test System (Ukraine).

Bioresorption of materials, in particular the rate of dissolution in isotonic saline (0.9% NaCl demonized water solution) at 36.5±0.5 °C, was studied *in vitro*.

Estimation of adsorption activity of the prepared materials was performed using drug *Ceftriaxon* («Arterium», Ukraine), a multipurpose antibiotic of the third generation used for parenteral administration in treatment of various diseases, including infection of bones (osteomyelitis) and joints, as well as for prophylaxis of post surgery complications. Adsorption activity was determined through saturation of material for 0.5, 1.0, 2.0, 3.0, and 4.0 h with *Ceftriaxon* solution in an isotonic saline at an antibiotic concentration of 40000 mg/ml on the basis of the solution optical density measured by the photocalorimetric method (FEK-56M, Russia).

3. Results and Discussion

Figure 1 demonstrates XRD patterns from initial BHA powders and superfine powder of silica Aerosil® 200 as well as highly-porous ceramics of three types. Silica exhibits an amorphous structure whereas the initial BHA is presented by the crystalline HA phase $Ca_5(PO_4)_3(OH)$, corresponding to the standard data in JCPDS Card No. 09-0432. All of the samples preserves their phase composition, which confirms the literature information and our previous investigations of BHA thermal stability [18-21], but sometimes, under sintering, secondary phases can be formed [12, 13, 15, 22].

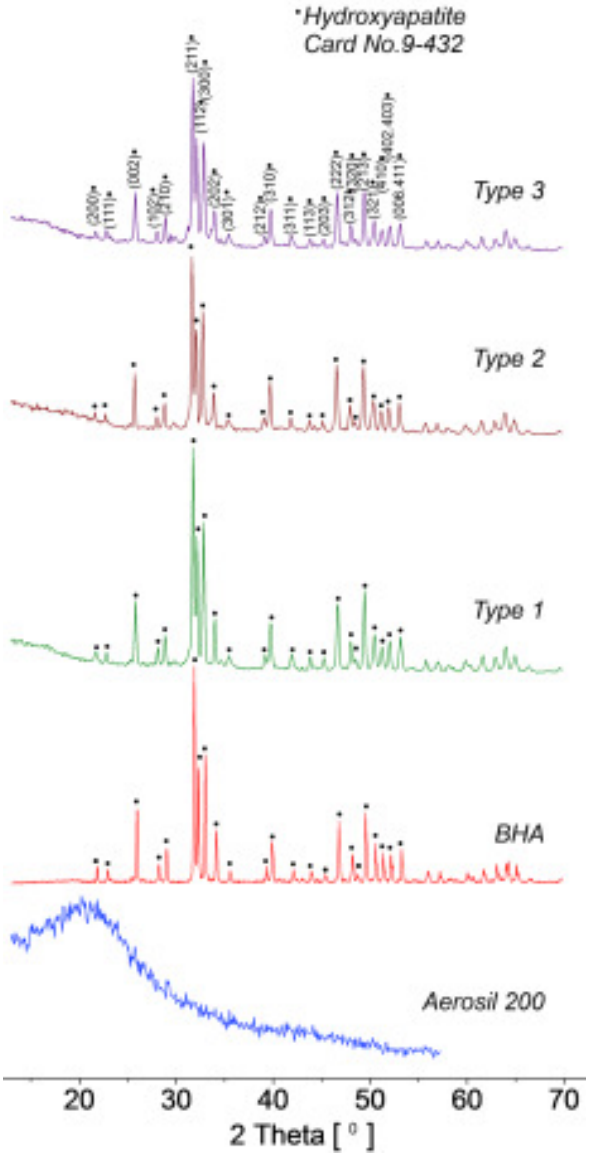

Figure 1. Fragments of XRD patterns from highly-porous ceramic samples and initial Aerosil® 200 and BHA with indices for the main peaks

These results are confirmed by IR spectroscopy data (Figure 2). The IR spectra of Aerosil® 200 are characterized by wide adsorption bands, typical for

amorphous materials. The bands within v ~ 1400-1000cm^{-1} are characteristic for valence Si-O-Si vibrations, the band v ~ 806 cm^{-1} is associated with asymmetric Si-O-Si vibrations, and the band with a frequency of ~470cm^{-1} can be related to the deformation Si-O-Si vibrations. Also, the spectra reveal adsorption bands inherent for OH^- groups at the frequencies 3425cm^{-1} and 1632cm^{-1}, characteristic for valence and deformation vibrations, respectively. The band v ~ 967 cm^{-1} is interpreted as librational OH- vibrations [23].

IR spectra of the initial BHA and of all types of highly-porous ceramics reveal characteristic adsorption bands for crystalline HA related to the vibrations of the basic structure components such as PO_4^{3-} (~ 1090, 1050, 960, 604, 570, 473 cm^{-1}) and OH^- (~ 3570, 3425, 1630-1640, 634 cm^{-1}). In addition, the spectra show up vibrations of the CO_3^{2-} group, characterized by the adsorption bands ~ 1550, 1457, 1415, 880cm^{-1}; herein carbonate-ions are located at both A-positions (replacing OH group) and B-positions (replacing group PO_4^{3-}). Unlike the initial BHA, there is observed broadening of the main bands within the frequency range ~ 1100-800cm^{-1}, related to vibration of phosphate ions along with a shift of characteristic bands at v ~1092 and 1056 cm^{-1} towards long waves as well as a decrease in the intensity of all bands. In our opinion, such changes may be prescribed to the formation of different (mixed acid-base) surface-active centers due to the interaction between the silanol –SiOH groups of amorphous Aerosil® 200 and the OH^- groups of BHA and possible formation of hydrogen. Moreover, as a result of sintering, the intensity of adsorption bands characteristic for the CO_3^{2-} and OH^- groups decreases.

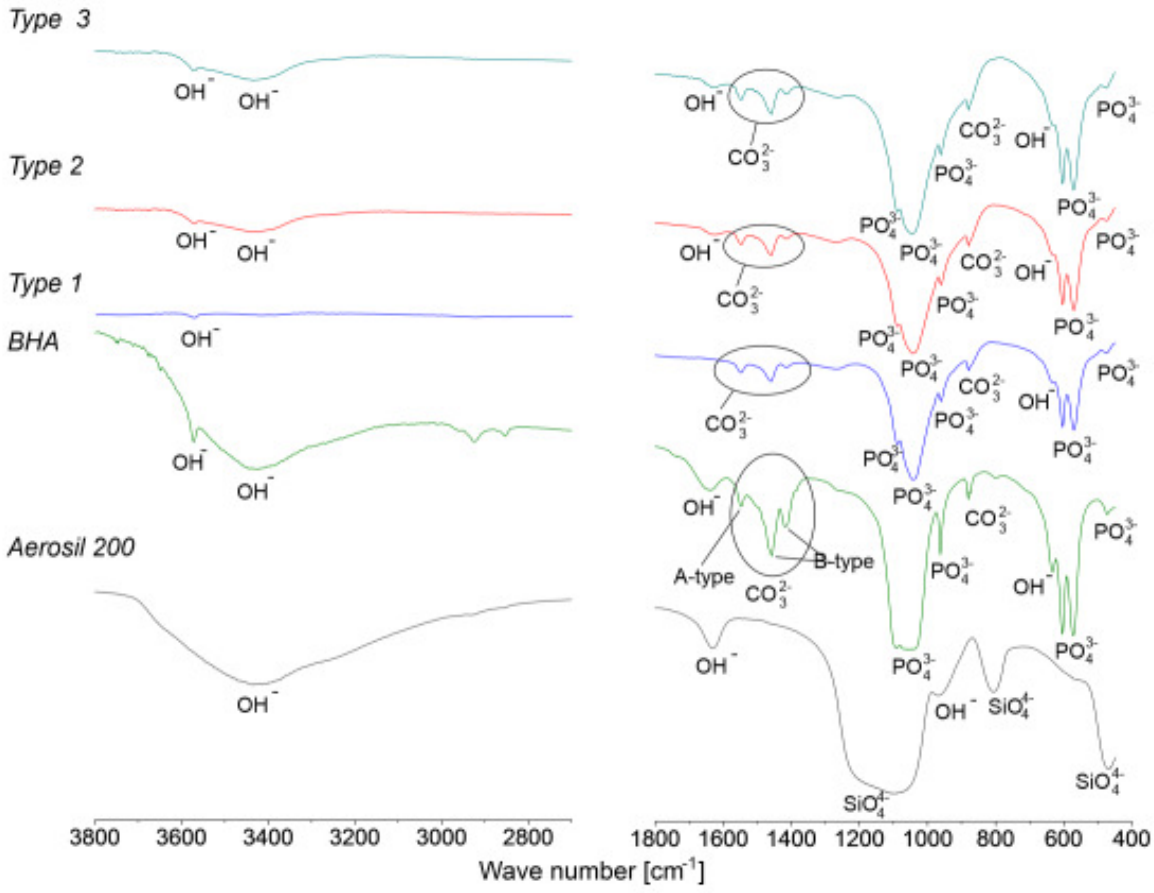

Figure 2. IR spectra of highly-porous ceramic samples and initial Aerosil® 200 and BHA

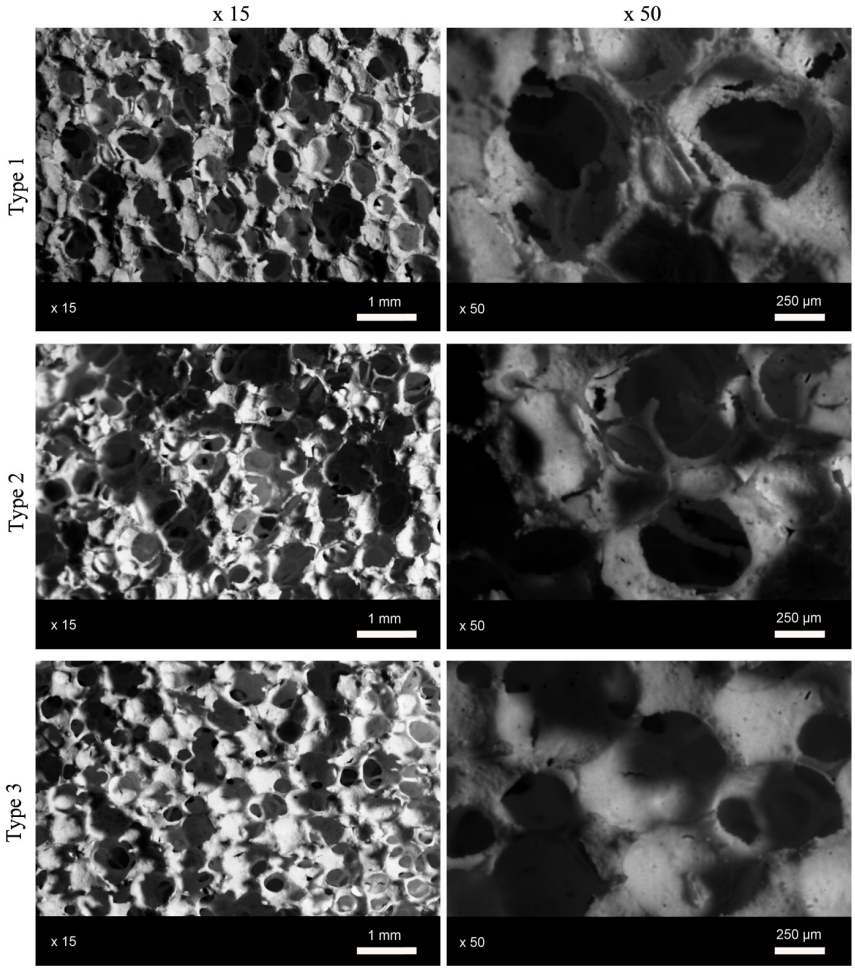

Figure 3. Structure of highly-porous ceramic samples

Table 2. Properties of highly-porous ceramics

Type	Density (g/cm^3)	Porosity (%)		Compression strength (MPa)	Dissolution rate (mass% /day)
		total	open		
Type 1	0.39	86	79	0.3	0.087
Type 2	0.34	88	78	0.3	0.091
Type 3	0.29	89	81	0.4	0.110

Figure 3 shows the structure of highly-porous ceramic samples prepared by foam replication method. All types of ceramics are characterized by a permeable porous structure with a pore size of 500-1000µm and porosity of 86-89 % (Table 2). Samples of Type 3 possess a more uniform structure of pores and isthmuses (narrow strip of material between pores) owing to the presence of a glass phase in the material composition during sintering, which provides formation of a stronger structure. In addition, an open porosity prevails in all types and equals ~ 90 % of the total porosity.

Despite the fact that the total and open porosity of Type 3 samples are the highest (Table 2), they exhibit some increase in compression strength,

which may be due to the presence of glass, strengthening the material.

On the basis of the data on the solubility of samples in physiologic saline (Table 2), it was established that the samples are resorbable and their dissolution rate increases with growing porosity and decreasing HA content (that is, increasing content of glass phase).

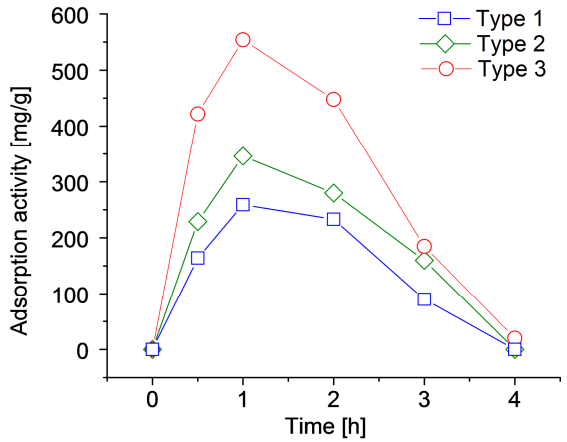

Figure 4. Adsorption activity of highly-porous ceramics towards Ceftriaxon against time

The adsorption activity of the materials towards *Ceftriaxon* is similar (Figure 4). The composition of Type 1 exhibits the lowest adsorption of the antibiotic whereas that of Type 3 does the highest one. Furthermore, the greatest saturation with the drug occurs for the first 60 min and decreases for the following 3 h in all of the materials. Herein after 4 h, the compositions of Type 1 and Type 2 stop adsorbing, whereas the adsorption activity of Type 3 samples is still 20 mg/g. Such peculiarities of adsorption activity are related to the fact that the three types of highly-porous ceramics differ in porosity and nature of surface-active centers.

4. Conclusions

Highly-porous samples (porosity 86-89 %) of bioceramics based on nanostructured biogenic hydroxyapatite and superfine fumed silica Aerosil® 200 have been prepared. The XRD analysis revealed that during sintering at 850 °C the hydroxyapatyte phase remains, which was also confirmed by IR spectroscopy data. Also, it was shown that the obtained samples were characterized by a permeable open-porosity (~ 90 % of the total porosity) structure with a pore size of 500-1000 μm and compression stress 0.3-0.4 MPa. The carried out studies of the dissolution rate and adsorption activity (by the example of antibiotic Ceftriaxon) demonstrated prospectivity of the obtained highly-porous bioceramics as implant materials for filling bone tissue defects and as carriers of drugs for acceleration of patients' post surgery rehabilitation in orthopedic, traumatic and dentistry surgery. Implant materials could be mixed with antibiotics just before a surgeon operation. Unlike traditional administration of drugs this method allows obtaining the aimed delivery permits and minimizes side effects.

Hence, the produced bioceramic materials are promising for complex treatment of bone tissue defects in reconstructive surgery.

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