Sol-gel synthesis of spherical biomaterials of TiO$_2$–SiO$_2$–P$_2$O$_5$/MgO composition and study of their properties

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Abstract. The authors obtained spherical biomaterials of TiO$_2$ – SiO$_2$ – P$_2$O$_5$/MgO composition by sol-gel method. TOKEM-200, a weakly acid porous cation exchanger based on acryl-divinylbenzene was used as organic matrices. The cation exchangers were saturated with Mg$^{2+}$ ions. Sol based on titanium butoxide, tetraethoxysilane and phosphoric acid was deposited on them. The temperature condition for producing spherical materials TiO$_2$–SiO$_2$–P$_2$O$_5$/ MgO were proposed. To obtain a spherical material, the treated cation exchangers were subjected to stepwise heat treatment in the temperature range from 60 to 600 °C. To study the biologically active properties of the material, the samples were immersed in simulation body fluid (SBF).

1. Introduction

The discovery and development of new technologies and innovations, as well as the development and synthesis of new biomaterials are necessary to meet the requirements in the fields of tissue engineering and bone regeneration [1–3]. The restoration and replacement of bone tissue lost as a result of trauma, osteoporosis and other diseases caused by aging or an accident are key factors in orthopedic tissue engineering [4, 5]. Metallic prostheses, materials based on metal alloys, polymers, calcium phosphate ceramics, glass ceramics and bone grafts are widely used as implants [6, 7]. Phosphate materials are used in various forms, which differ in the method of preparation and particle size [8]. There are many methods for producing phosphates. One of the common methods of synthesis is the sol-gel method, which replaces the traditional melt cooling, is carried out at room temperature and improves the homogeneity and purity of the synthesis products [9, 10].

One of the promising areas recently is the production of layered spherical materials with a hierarchical structure. Such materials are designed to fill the volume of complex forms, when restoring bone tissue. Material is proposed for the development of additive technologies, such as 3D printing of biomedical materials [11, 12]. To improve the functional characteristics of a promising material for implants, compositions based on calcium phosphate or magnesium modified with silicon and titanium can be considered [13, 14]. It is proved that the presence of silicon and titanium in the volume of phosphate-calcium or magnesium material and on its surface accelerates the connection of the implant with the bone (osteointegration) [5, 8, 13].

There are many studies describing the different effects of elements, such as strontium, zinc, copper, silver, lithium and magnesium in the composition of phosphate bioceramics to achieve certain characteristics, such as osteoconductiveness, angiogenicity, and antibacterial properties [5, 6]. Magnesium is the second most common intracellular cation and the fourth most common metal cation...
in humans [15]. About 50–60% of total amount of Mg in the body is contained in the bones [16, 17]. In addition, Mg plays an important role in the development of bones, increases the activity of osteoblasts and inhibition of osteoclasts [17]. Mg is an element that can be absorbed by the human body, it is vital for the assimilation and fixation of calcium in the bones [16, 17].

But still not resolved two issues. Firstly, it is the effect of the Mg$^{2+}$ content in the composite on the rate of hydroxyapatite (HA) formation on the surface of the biomaterial. Secondly, it is the optimal amount of substituted MgO in materials, which enhances cell proliferation.

2. Experimental part

It was obtained spherical biomaterials, the outer frame of which was TiO$_2$–SiO$_2$–P$_2$O$_5$ and the inner part was filled with MgO oxide (sample TiO$_2$ – SiO$_2$ – P$_2$O$_5$/MgO). TOKEM-200, a weakly acid porous cation exchanger based on acryl-divinylbenzene (PO "Tokem" LLC, Kemerovo, Russia), was used as organic matrices for the preparation of TiO$_2$ – SiO$_2$ – P$_2$O$_5$/MgO oxide composites. This cation exchanger had a spherical shape with a granule size from 0.315 to 1.600 mm and a high selectivity to Mg$^{2+}$.

The study of the total exchange and sorption capacity of ion exchangers was performed using sorption methods [18], the moisture content was investigated by gravimetry. The content of Mg$^{2+}$ ions in solutions with a concentration of ~ 0.001 M and above was determined by the method of complexometric titration with the indicator murexide [18].

Spherical materials with the composition TiO$_2$ – SiO$_2$ – P$_2$O$_5$/MgO were obtained by thermal treatment of a cation exchanger (TOKEM-200) with a supported sol based on butanol, titanium butoxide (Acros, USA) and tetraethoxysilane (Russia). For this, cation exchangers were placed in a saturated aqueous solution of magnesium nitrate (pure 99%, Yugreaktiv, Russia) and kept for 1 day at room temperature. The cation exchangers were washed with a small amount of water, filtered and dried at a temperature of 60 °C to constant weight after ion exchange. Then, dried cation exchangers saturated with Mg$^{2+}$ ions were placed in a sol. For the formation of a framework of a bioactive material of spherical shape, an aggregally stable sol was prepared. Butanol (99.9%, Russia) was used as a solvent, and phosphoric acid (5 mol.%, Russia) was used as a polycondensation catalyst. After the onset of chemical equilibrium in a solution of C$_6$H$_{12}$OH – H$_3$PO$_4$, a mixture of titanium butoxide (35 mol.%, Russia) and tetraethoxysilane (60 mol.%, Russia) was added. The ripening of sols was carried out at room temperature for 3 days. The method of preparation of the sol is presented in [18]. After applying the sol to cation exchangers, the samples were dried at 60°C to constant weight. To obtain a spherical material, the treated cation exchangers were subjected to stepwise heat treatment in the temperature range from 200 to 600 °C. The heating rate of the muffle furnace was 14 °/min.

The kinematic viscosity of the solutions was determined in a HPLC-2 capillary viscometer. The thermo-gravimetric analysis was performed on a NETSCH Jupiter STA 449 F1 thermal analyzer in the temperature range from 25 to 1000°C with a heating rate 30°/min in air atmosphere. IR spectra of dried solutions were reordered on an Agilent Cary 630 FTIR IR spectrometer in the frequency range from 400 to 4000 cm$^{-1}$. Phase composition of the dispersed materials was determined by X-ray diffraction on Rigaku MiniFlex 600 diffractometer (CuKα radiation). Surface morphology of the obtained materials was studied using a scanning electron microscope (SEM) HITACHI TM-3000. Elemental composition was determined by X-ray microanalysis by using a Quantax-70 instrument. Evaluation of the bioactivity of the obtained materials was studied in vitro by keeping the samples in a cell-free simulation of SBF for 14 days. Samples were placed in SBF at a temperature 37 ± 0.5°C. Value of pH was 7.4. The solution was changed every day for 14 days. The composition of the SBF solution is described in [19].

3. Results and discussion

The results of studies of the physicochemical properties and selectivity of sorbents to the Mg$^{2+}$ ion were used as the basis for the choice of cation exchanger for the production of spherical materials. During the study, quantitative characteristics of the physicochemical properties of the TOKEM-200...
cation exchanger were obtained. It was established that the total exchange value was 10.25 ± 0.27 mmol/g, and the sorption capacity was 6.95 ± 0.13 mmol-eq/g, which was 63% of the total exchange capacity. The moisture content of the cation exchanger was 54.0 ± 0.5%. It follows the most of the functional groups are involved in the sorption process.

The aggregatively stable sol was prepared to form a frame of a bioactive material of spherical shape. As a criterion of the film-forming ability of solutions, their viscosity was measured (Figure 1). It was found that the viscosity of the solutions after their preparation, increases sharply during two days. Films were obtained after the viscosity reached a value of 3.2 mm2/s. Solutions were stable for 12 days.

![Figure 1. Viscosity values for prepared solutions in dependence on time.](image)

The film-forming ability of solutions was achieved due to hydrolysis and polycondensation processes. They are accompanied by an increase in the viscosity of the solutions. Electrostatic interactions between dissolved ions and solvent molecules also lead to an increase in viscosity. Phosphoric acid increases the acidity of the medium and leads to acceleration of the processes of hydrolysis and polycondensation.

The results of thermal analysis showed that the decomposition of cation exchangers had two exothermic effects (Figure 2).

Exothermic effects with a maximum at a temperature of 285°C correspond to the removal of physically adsorbed H2O. The complete combustion of hydrocarbon fragments to CO2 occurred above 450°C, the product yield was 37.6%.

Despite the fact that the decomposition of the sample was completed at about 500°C, an annealing temperature of 600°C was chosen. This is related to the literature data [38], according to which the crystalline phase of silicon oxide (IV) is formed at a temperature of 600°C.

For a more complete removal of the organic component of the cation exchanger, the dried samples were subjected to stepwise heat treatment at 200°C, 300°C, 350°C, and 450°C. The heat treatment time at each temperature was 60 minutes. After that, the samples were annealed at 600°C for 4 hours.
According to the results of scanning electron microscopy (Figure 3), the sample has a spherical structure and the TiO$_2$–SiO$_2$–P$_2$O$_5$ framework is uniformly fixed on the cation exchanger.

Heat treatment of hybrid mesostructures leads to the formation of mesoporous materials with a specific regular structure and a highly developed surface. It is necessary for the fixation of biological cells when the sample is introduced into the biological medium. Elemental analysis (Figure 4) showed a uniform distribution of elements throughout the sample.

The evaluation of the bioactivity of the obtained materials was studied in vitro by keeping the samples in cell-free imitation of SBF blood plasma for 14 days.
When studying the morphology of the coatings obtained after immersion in the SBF solution, there are large, loose and porous particles on the surface. Their presence is favorable for the formation of a strong connection of the implant with the bone. (Figure 4).

![Micrographs of the samples and the distribution of elements along the line after immersion in SBF.](image)

Figure 4. Micrographs of the samples and the distribution of elements along the line after immersion in SBF.

After the samples were kept in the SBF solution, the mineralization and precipitation of calcium phosphate compounds on the active centers of the coating surface was occurred. It was evidenced by the presence of Ca and P ions on the data X-ray microanalysis (Figure 4). After immersion in the SBF solution, sodium ions were fixed on the sample surface. It indicates the precipitation of the solution components. Ion Na⁺ helps to accelerate the process of bone tissue recovery [12-20]. Silicon ions improve the process of bone recovery, because silicon-oxygen bridges help to build in ions from the surface of materials into the intercellular fluid, promoting adhesion to bone tissue [18].

4. Conclusions
Thus, biomaterials of spherical shape based on Tokem-200 were synthesized by sol-gel method from FFS. The framework of the material was TiO₂–SiO₂–P₂O₅, and the inner part was filled with MgO. It was established that the total exchange value was 10.25 ± 0.27 mmol/g, and the sorption capacity was 6.95 ± 0.13 mmol-eq/g, which was 63% of the total exchange capacity. The moisture content of the cation exchanger was 54.0 ± 0.5%. It follows that most of the functional groups are involved in the sorption process.

It was established that the solutions were suitable for obtaining materials up to 12 days. For a more complete removal of the organic component of the cation exchanger, the dried samples were subjected to stepwise heat treatment at 200°C, 300°C, 350°C, and 450°C. The heat treatment time at each temperature was 60 minutes. After that, the samples were annealed at 600 °C for 4 hours. Heat treatment of hybrid mesostructures leads to the formation of mesoporous materials with a specific regular structure and a highly developed surface. It is necessary for the fixation of biological cells when the sample is introduced into the biological medium. After the samples were kept in the SBF solution, the mineralization and precipitation of calcium phosphate compounds on the active centers of the coating surface was occurred. It proves biologically active properties of the material.

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