ISSN 1027-5495. Functional Materials, 27, No.4 (2020), p. 767-773.
doi:https://doi.org/10.15407/fm27.04.767

Development of calcium phosphate-silicate glass ceramic materials resistant to biochemical and mechanical destruction

***O.V.Savvova*[1], *V.M.Shimon*[2], *O.V.Babich*[3], *O.I.Fesenko*[1]**

[1]O.Beketov National University of Urban Economy in Kharkiv,
17 Marshal Bazhanov Str., 61002 Kharkiv, Ukraine
[2]State University "Uzhhorod National University", 3 Narodna Sq.,
88000 Uzhhorod, Ukraine
[3]Ukrainian Research Institute for Environmental Problems,
6 Bakulina Str., 61166 Kharkiv, Ukraine

Received April 25, 2020

The promising directions of the bioactive glass-materials development for bone endoprosthetics with high ability to bone regeneration are analyzed. The relevance of the development of bioactive glass-ceramic materials with reduced resorption periods has been established. Has been developed a methodological approach to establish the destruction of bioactive materials for bone endoprosthetics *in vitro*, which consists in assessing the generalizing effect of chemical, biological and mechanical factors on the endoprosthesis material *in vivo*. Were grounded the choice of the oxide system Na_2O–K_2O–Li_2O–CaO–MgO–ZnO– ZrO_2–TiO_2–Al_2O_3–B_2O_3– P_2O_5–SiO_2 and microadditives CaF_2, MnO_2, CeO_2, CoO, V_2O_5, SrO, Cu_2O, MoO_3, La_2O_3, for obtaining bioactive glass-ceramic materials; were synthesized model glasses with a CaO/P_2O_5 ratio = 1.66÷1.7, and based on which were obtained glass-ceramic materials under the conditions of a low-temperature single-stage heat treatment. The ability to destruction research glass-ceramic materials *in vitro* and their mechanical properties under load conditions in model body fluids have been determined.

Keywords: calcium phosphate glass-ceramic materials, bioactivity, single-stage heat treatment, mechano-destruction, endoprosthetics.

Розробка кальційфосфатосилікатних склокристалічних матеріалів, стійких до біохімічної та механічної деструкції. *О.В.Саввова, В.М.Шимон, О.В.Бабіч, О.І.Фесенко*

Проаналізовано перспективні напрямки розробок біоактивних скломатеріалів для кісткового ендопротезування з високою здатністю до регенерації кістки. Встановлено актуальність розробки біоактивних склокристалічних матеріалів зі скороченими строками резорбції. Розроблено методологічний підхід до встановлення деструкції біоактивних матеріалів для кісткового ендопротезування *in vitro*, який полягає в оцінці узагальнюючого впливу хімічних, біологічних та механічних факторів на матеріал ендопротезу *in vivo*. Обгрунтовано вибір кальційфосфатосилікатної оксидної системи та мікродомішок CaF_2, MnO_2, CeO_2, CoO, V_2O_5, SrO, Cu_2O, MoO_3, La_2O_3 для одержання біоактивних склокристалічних матеріалів. Розроблено зміцнені склокристалічні матеріали в умовах низькотемпературної термічної обробки. Визначено здатність до гідролітичної, клітинної, бактеріальної та механічної деструкції розроблених склокристалічних матеріалів *in vitro*.

Проанализированы перспективные направления разработок биоактивных стекломатериалов для костного эндопротезирования с высокой способностью к регенерации кости. Установлена актуальность разработки биоактивных стеклокристаллических материалов с сокращенными сроками резорбции. Разработан методологический подход к

установлению деструкции биоактивных материалов для костного эндопротезирования *in vitro*, который заключается в оценке обобщающего влияния химических, биологических и механических факторов на материал эндопротеза *in vivo*. Установлена перспективность создания биоактивных стеклокристаллических материалов для костного эндопротезирования с высокой способностью к регенерации кости, эксплуатируемых в условиях переменных динамических нагрузок. Обоснован выбор оксидной системы Na_2O–K_2O–Li_2O–CaO– MgO–ZnO–ZrO_2–TiO_2–Al_2O_3– B_2O_3–P_2O_5–SiO_2 и микродобавок CaF_2, MnO_2, CeO_2, CoO, V_2O_5, SrO, Cu_2O, MoO_3, La_2O_3 для получения биоактивных стеклокристаллических материалов; синтезированы модельные стекла с соотношением CaO/P_2O_5 = 1,66÷1,7, на их основе получены стеклокристаллические материалы в условиях низкотемпературной одностадийной термической обработки. Определена способность к деструкции исследуемых стеклокристаллических материалов *in vitro* и их механические свойства в условиях нагрузок в модельных жидкостях организма.

1. Introduction

A prospective way of solving the problem of bone tissue regeneration and replacement is creation of cellular matrices (scaffoldings) which allow to reproduce the architectonics of the bone tissue [1]. An important role in regeneration of the bone tissue functionality belongs to the scaffolding material itself, enabling the restoration of not only the shape of the bone tissue, but, most importantly, its function, i.e. the ability to create a uniform bioengineering structure. Among the prospective materials that have successfully passed implementation in the clinical practice are calcium phosphate glass ceramic materials with the gradient structure characterized by high biocompatibility and the ability to generate apatite-like layer in the short terms, which is an important social task that provides efficient short-term recovery of patients [2–4].

Nowadays, there exists a number of special highly efficient technological solutions for creating biocompatible glass-ceramic materials with controlled resorption terms that considers their *in vivo* mineralization ability [5]. The leading idea in the evolution of bioactive materials is the creation of compositions based on inorganic (e.g. glass ceramics) and organic components produced, for instance, using sol-gel technology [6]. However, even though creation of such compositions allows to solve the problem of osteogenesis (the process of bone tissue formation) during implantation, it does not provide the increase in the rate of bonding between the implant and the bone in conditions of significant variable dynamic loads.

Known bioactive glass-ceramic materials ("Cerabone", "Ceravital") having the terms of bonding with a bone in range of the second and fourth weeks after the implantation, attain high tensile strength between the bone and implant (1.5÷3.9 MPa) only after 25 weeks [7]. The latest achievements in the field of development of bioactive glass-ceramic materials include, in particular, creation of diopside-fluorapatite glass ceramics characterized by *in vitro* formation of hydroxyapatite (HAP) precursors already on the 28th day, and activity to alkaline phosphatase on the 14th day after contact with stem cells [8]. However, high level of destruction of developed materials due to release of ionic pairs $(Ca–F)^+$ or $(Mg–F)^+$ may lead to osteoporosis, and their accumulation may cause fluorosis.

The authors of this work have previously established [5] the possibility of accelerated generation of the apatite-like layer on the surface of bioactive glass-ceramic materials and coatings within 6 months due to the structural features. Formation of precipitated amorphous calcium phosphate (AFC) and non-stoichiometric HAP after 180-hour exposure of the specimens to the model liquid is the evidence of possible presence of apatite-like layer on the surface of developed bioactive materials. However, the resorption level of developed materials is not sufficient for accelerated bonding of the implant with the bone, since there is not enough tissue regeneration around these biomaterials soon after the implantation.

The aim of the present work is development of biocompatible strengthened glass-ceramic materials and determining the features of *in vitro* destruction processes of the calcium phosphate glass-ceramic materials in correlation with their *in vivo* ability to form bone tissue.

2. Experimental

The first and foremost task during the first stage of developing novel biomaterials is establishing the mechanisms of *in vitro* biological degradation of vitreous materials [9].

The following processes and environments used as the models for the processes occurring during the implantation into a living organism can be listed according to

the mechanism of destruction of a biomaterial by biological media: 1) hydrolytic destruction: non-enzymatic hydrolysis (physiological saline, phosphate buffer); enzymatic hydrolysis (papain, urease, esterase etc.); oxidative destruction, catalysis by metallic ions; 2) cellular destruction (osteoclasts, macrophages); 3) bacterial destruction (*E. Coli*, streptococci, staphylococci); 4) mechanodestruction [10].

The assessment of hydrolytic destruction of the developed meterials has been carried out in non-enzymatic media (distilled water (DW), physiological saline (PS) (0.9 wt.% NaCl) and by extreme (ES) and model solution (MS) techniques by weight loss in respective solutions L_{DW}, L_{PS}, L_{ES} and B_{MS}. Weight loss (wt.%) was determined by weighing on analytical balance Radwag AS 220.R2 and calculated as a difference between the values of initial mass of the experimental specimens and the mass of the specimens after exposure to the model media.

Buffer solution of citric acid with pH = 3 has been used as the extreme solution, solution of tris(hydroxymethyl)aminomethane (TRIS) and HCl with pH = 7.25 was used as the model solution. The choice of citric acid was driven by the ability of osteoblasts to transfer it to the resorptive zone. Hydrochloric acid was chosen because of its ability to denaturize proteins and kill bacteria. Pencil test according to EN 14483/1:2007 was selected as an express method of assessing acid resistance class of vitreous materials.

We have selected pepsin, a hydrolase-class proteolytic enzyme active in pH = 1.5–2.0, as the enzymatic media. Pepsin is secreted by the main cells of gastric mucosa, it breaks up food proteins into peptides. Medical bile, which contains organic acids, inorganic salts, enzymes and vitamins, has been selected as a medium close to the interstitial fluid. The assessment of destruction during 120 h in 10 wt.% solutions of pepsin and medical bile was conducted by measuring the loss of mass (L_P, L_{MB}).

Cellular destruction of vitreous materials has been modelled with the consideration of activity of activated macrophages releasing metabolism products, in particular hydrogen peroxide. The study of material destruction in 3 wt.% hydrogen peroxide solution during (HP) 120 hours was conducted, the destruction was assessed by mass loss of the material, in wt.% (L_{HP}).

Consideration of bacterial destruction is important to prevent tissue inflammations during implanting. The increase in the rate of implant biodegradation occurs due to intensification of enzymatic and oxidative destruction. As an index of opportunistic pathogenic flora, *E. Coli* bacterium was selected, which generates lactate, succinate, ethanol, acetate and carbon dioxide as metabolic waste product in anaerobic conditions. Bactericidal effect of experimental materials has been assessed by the change in dehydrogenase activity (DHA) of the biotest culture. DHA method is based on measuring performance of enzymatic system of biotest *E. Coli B* with initial concentration of colony forming units (CFU) $C_{init} = 10^6$ cells/ml ($K_{culture}$) in contact with experimental specimens. Qualitative (diffusion) method for migrating compounds with $C_{init} = 10^6$ cells/ml according to ASTM E2149 has been selected for modelling infectious contamination of the materials and studying bactericidal effect.

With the purpose of increasing the rate of degradation processes and decreasing the time of exposure to the model media, experimental materials were subjected to mechanical stresses in MS (P = 140 MPa) prior to incubation, and their susceptibility to mechanodestruction has been determined by changes in mechanical properties.

In order to analyze the regeneration of bone tissues, activity of alkaline phosphatase has been determined by kinetic method in rat blood serum on the 7th, 14th and 30th day after introducing the implant into the distal metaphysis of murine hip bone.

2.1. Selection of composition and synthesis of vitreous materials

Adding microelements along with phase forming calcium and phosphorous oxides to the vitreous materials is essential for ensuring their durability against the destruction by biological media and for approximating their composition to that of a natural bone tissue. The choice of microadditives was made with the consideration of the role of microelements in remodeling of bone tissue [9–13].

Introduction of the modifying components into calcium phosphate-silicate glass matrix, along with a positive effect on bone formation processes, provides substantial improvement in physico-chemical properties of glasses and glass ceramics on their base: Al_2O_3, B_2O_3 increase chemical durability, SrO, La_2O_3 improve mechanical properties; V_2O_5 and MoO_3 decrease surface tension (to enable application of defect-free coatings); Cu_2O, CoO impart coloration (to facilitate visual control of the implants *in vivo*). Introduction of TiO_2, ZnO, CaF_2 allow cata-

lyzed crystallization of calcium phosphates as main structural units of inorganic bone component in the structure of glass ceramic materials.

Considering the above, a glass matrix based on Na_2O–K_2O–Li_2O–CaO–ZrO_2– TiO_2–MgO–ZnO–Al_2O_3–B_2O_3– P_2O_5–SiO_2 system has been developed, in which we have selected: composition s of AS series glasses (wt. %): SiO_2 47.0–50.0; Al_2O_3 2.0–3.0; Li_2O 2.0–4.5; Na_2O 3.5–6.0; K_2O 4; ZrO_2 0.5–1.0; P_2O_5 9.0–10.0; CaO 15.0–17.0; ZnO 1.0–3.0; B_2O_3 4.0–5.0; TiO_2 0.3–1.0; CaF_2 0.5–2.4; MnO_2 1.0–2.0; MgO 0.1–1.0; CeO_2 0.4–0.5; CoO 0.01–0.03; V_2O_5 0.02–0.03; SrO 0.01–0.04; Cu_2O 0.01; MoO_3 0.01–0.02; La_2O_3 0.01–0.02 with the ratio of CaO/P_2O_5 = 1.66÷1.7 to obtain glass-ceramic materials performing under varying dynamic loads.

Experimental glasses of the AS series marked as AS 1, AS 2, AS 3, AS 4, AS 5 were melted in the identical conditions at the temperatures of 1250÷1350°C in corundum crucibles with subsequent cooling on a metal sheet.

In order to obtain glass ceramic materials, powders of experimental glasses ground to 008 sieve residue not greater than 5 % have been used. Specimens have been prepared using semi-dry isostatic pressing method (P = 35÷40 MPa), they were shaped to cylinders with the diameter of 4 mm and height of 10 mm, with carboxymethyl cellulose solution as a temporary binder. 5 wt.% of yttrium-stabilized zirconium dioxide filler has been added to the glass compositions to improve mechanical properties.

Heat treatment of the experimental glass ceramic materials on the base of AS glasses has been performed in conditions of a low-temperature (750÷800°C) short-term (≈15 min) single-stage regimen. Developed calcium phosphate-silicate materials have been marked as ASZ-1, ASZ-2, ASZ-3, ASZ-4 and ASZ-5.

3. *Results and discussion*

A distinctive feature of the structure of experimental glasses after melting is their intensive crystallization, determined by the high content of HAP crystalline phase in the amount of 20÷30 vol. %. After the single-stage heat treatment of the glasses, an increase in the amount of HAP crystalline phase to up to 50÷60 vol. % is observed. Providing a ceramized structure that contains resistive phase of HAP is a determining factor in assuring destruction resistance under conditions of chemical and biological effects and mechanical loads.

Substantial increase of water and acid resistance of the glass matrix has been achieved due to polycationic effect by introducing mixed alkali metal cations in the ratio of (1÷3)Na_2O:(1÷2)K_2O:1Li_2O and alkaline earth oxides, CaO, MgO, ZnO and SrO, as well as TiO_2 and ZrO_2, which significantly increase chemical durability of the materials.

The addition of aluminum and boron, apart from providing the polyalkaline effect, allows to significantly increase chemical durability of experimental calcium phosphate-silicate glass materials. Presence of ions with the close values of ionic radii in the structure: P^{5+} — 0.34 nm and B^{3+} — 0.2 nm, helps to form glasses with stable structure; while substantial Dietzel field potential, [14] P^{5+} — 43.2 $Å^{-2}$ and B^{3+} — 75,0 $Å^{-2}$, leads to the increase in acidic properties of the cations. The role of Al^{3+} in the increase of chemical durability of experimental glasses is due to its ability to promote $BO_3 \rightarrow BO_4$ transition at high CaO content (15–17 wt.%), whereas Si^{4+} forms structural groups that lead to the weakening of the vitreous phosphate lattice.

Results of conducted investigations allowed to conclude that experimental materials of ASZ series have high chemical durability and can be classified as surface-active glass ceramics. Weight loss in distilled water and physiological salines is insignificant for experimental ASZ materials, reaching 0.32 to 0.60 wt.% due to the presence of resistive HAP crystalline phase. The loss is limited by water resistant high-silica vitreous matrix, exhibiting the processes of hydrolysis, condensation and formation of protective silica layer.

The lowest weight losses are observed for ASZ-3 and ASZ-5 materials, considering their placement in low silica area and low connectivity index of silicon-oxygen framework f_{Si} = 0,28. For these glasses, which have the lowest content of sodium oxide, there exists a re-allocation of sodium cations in the structure from silicon-oxygen groups of $(SiO_3)O^-$ type to phosphorus-oxygen $(P_2O_4)O_2^-$ and $(P_nO_{4+n})O_n^-$ types to compensate for their negative charge. Silicon-oxygen groups $(SiO_3)O^-Na^+$ are transformed into $[SiO_4]^-$, increasing connectivity index of glass structure [15].

For the ASZ-1, ASZ-2 and ASZ-4 materials, the decrease in weight loss in DW

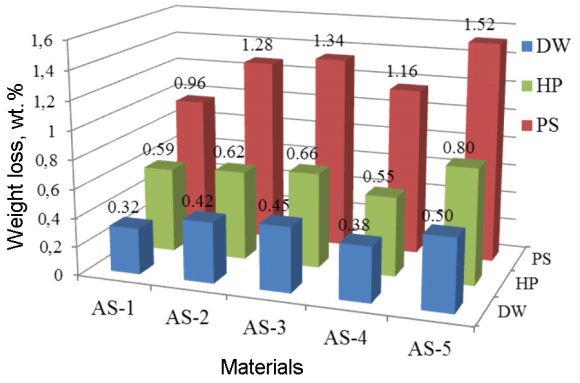

Fig. 1. Destruction of the experimental materials in distilled water (DW), hydrogen peroxide (HP), physiological saline (PS).

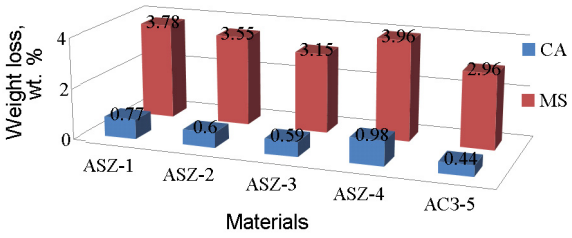

Fig. 2. Destruction of the experimental materials in citric acid buffer solution (CA), model solution (MS).

(Fig. 1) may indicate the decrease of leaching intensity of alkaline ions from the structure of vitreous materials, including that due to the increase of f_{Si} to 0.3. For the ASZ-3 and ASZ-5 materials, the increased leaching intensity in DW will create favorable conditions for the short-term in vivo apatite formation process on the surface of experimental material.

Investigation of chemical durability of the experimental materials by "pencil test" has shown that they have A class resistance, which demonstrates their durability in citric acid solution. This is confirmed by the results of determining chemical resistance of glass ceramic materials after exposure to buffer solutions by extreme (citric acid buffer solution) and model solution models (L_{ES} = 0.44÷0.98 wt.% and L_{MS} = 2.96–3.96 wt.% (Fig. 2)). All of the above allows to make a conclusion that the materials have low destruction rate and can be used in medical devices.

Significant acid resistance of ASZ-5 material is explained by the high total content of zinc, titanium, zirconium and lithium oxides in it (to 7 wt.%). For the materials ASZ-1, ASZ-2, ASZ-3 and ASZ-4, the increase in L_{ES}, L_{MS} can both negatively affect leaching mechanism of metal cations and phosphate groups *in vivo*, and lead to a decrease in strength of the surface layer of developed materials. As a result, structural strength will deteriorate during *in vivo* use. Provision of acid resistance to ASZ-5 material will allow preventing the destruction of the material as a result of osteoclasts and phagocytes action at the initial stages of bone formation.

Comparative assessment of hydrolytic and cellular destruction of experimental materials allows to conclude that weight loss trend in HP and PS solutions are analogous to that in DW. However, due to the increased aggressiveness of the medium, material loss is higher for PS (L_{PSD} = 0.96÷1.52), since chlorine ions it contains are substantially more active than oxygen free radicals formed in the body tissues during plasma and erythrocytes catalysis reaction with hydrogen peroxide, which demonstrates weak acidic properties. It should be noted that cations of transitional metals contained in experimental materials allow to increase the rate of hydrogen peroxide decomposition. Upon oxidation of a number of ions, hydroxyl radicals or perhydroxyl are formed, which promotes hydrogen peroxide decomposition on release of microphages. At the same time, resistance to PW solution and increasing the rate of its decomposition are contributing to tissue decontamination after implantation and conserve the integrity of the implant material.

Chemical activity of the developed materials towards enzymatic medium of pepsin proteolytic enzyme (enzyme of acidic phosphatase class, cathepsin D, which are bone tissue resorption indicators) is quite low, which is indicated by insignificant weight loss ($L_P \approx 0.01$ %). This is explained by high chemical durability of the material, including that to amino acids and phosphoric acid, both being components of pepsin. The effect of medical bile is also related to the activity of organic acids and inorganic salts, which are group I reagents. As a result of leaching, dissolution and transfer of the components into the solution, alkaline silicates on the surface layer of developed materials hydrolyze, or silicic acid is formed. On the surface of vitreous material which have L_{MB} = 0.01–0.06 %, a dense protective layer with high silica concentration is formed. This indicates that the materials have high chemical resistance to enzy-

Table. Mechanical properties of ASZ series materials

Properties	Material				
	ASZ-1	ASZ-2	ASZ-3	ASZ-4	ASZ-5
Index of silicon-oxygen framework f_{Si}	0.30	0.30	0.28	0.30	0.28
Properties of the initial materials					
HV, MPa	4950	5550	4000	4780	3800
K_{1C}, MPa·m$^{1/2}$	1.5	1.8	1.7	1.5	2.8
$\delta_{bending}$, MPa	120	140	130	120	160
$\delta_{compression}$, MPa	250	350	250	250	400
Properties of the materials after exposure to MS					
HV, MPa	3800	4550	3800	4000	3700
K_{1C}, MPa·m$^{1/2}$	1.2	1.5	1.6	1.2	2.6
$\delta_{bending}$, MPa	100	120	120	100	150
$\delta_{compression}$, MPa	200	300	220	200	380

matic media and concurrent likelihood of ≡Si–OH bonds formation on their surface, the adhesive islets to which osteoblast cells are attached during bone remodeling.

As a result of the contact of biotest cultures with ASZ-5 material, formazane concentration, being hydrogenase activity indicator for *E. Coli* with experimental specimen, and $K_{culture}$ are close. This fact is the evidence of the absence of toxicity of experimental material to bacterial cultures. Investigation results also allowed to conclude that developed material is not a nutritious media that enables growth of the experimental biotests. This, together with non-toxicity, demonstrates feasibility of their application in bone implants.

Investigation of the bactericidal properties of the material allowed to establish that in extreme conditions (under C_{init} *E. Coli* up to 10^6 cell/ml and 24 h exposure) bactericidal activity of ASZ-5 measured with bacterial growth stunt zone is approximately 10 mm. This is the evidence of its biostatic properties due to elevated structural strength of the material and presence of Zn^{2+}, La^{3+}, metal cations that have bactericidal properties in its composition.

Investigation of mechanical properties of developed glass-ceramic materials has demonstrated that modifying agents and structural features of the materials have significant influence on these characteristics. The highest Vickers hardness values (*HV*) are attributable to ASZ-1, ASZ-2 and ASZ-4 specimens due to high content of zinc, magnesium and lanthanum oxides in the initial composition (Table). For A ASZ-5 specimen, hardness is slightly lower and approximates to the hardness of a bone, allowing to use it as a biocompatible material in human locomotor system without added stress on bone tissue. Fracture resistance coefficient (K_{1C}) is highest for ASZ-5 material due to the formation of oriented interpenetrated fine crystalline structure. Compressive and bending strength of experimental materials are correlated to their K_{1C} and have the highest values for ASZ-5 material, allowing its use it under variable load *in vivo*.

Mechanical properties of developed materials after exposure to MS have decreased in a similar manner to their durability to MS. The lowest changes in mechanical properties have been observed for ASZ-5 material, which possesses high structural strength due to formation of ceramized structure by phase separation mechanism [15], the highest — for ASZ-4 material. Generally, the decrease in mechanical properties is related to damaging of glass material surface by the group I reagents and formation of dense silica-gel layer for chemically durable materials: ASZ-5, ASZ-3, and developed structure of silica-gel layer for more soluble materials: ASZ-1, ASZ-2, ASZ-4. This allows to conclude that ASZ-5 material is capable to withstand mechanical stresses under conditions of hydrolytic destruction.

Results of biochemical analysis of murine blood serum after implantation of ASZ-5 specimen have shown the dynamics of alkaline phosphatase activity according to regeneration stages of implant bone tissue: (411.80±27.60) *U/L* on day 7, (952.50–63.30) *U/L* on day 14, (828.00±98.60) *U/L* on day

30. It has been established that on the days 7 and 14, the activity of alkaline phosphatase increases, which is the evidence of its release by osteoblasts in the process of bone formation. On the 30th day, the deceleration of this process indicates gradual completion of bone tissue remodeling process.

Therefore, high durability of developed glass-ceramic material ASZ-5 to hydrolytic, cellular, bacterial and mechanical destruction *in vitro*, along with its ability to accelerated process of bone remodeling *in vivo*, allow to consider it as a prospective material for creation of defect-free biocompatible bone implants performing under dynamic and static stresses.

5. Conclusions

Feasibility of creation of bioactive glass-ceramic materials for bone implants with high bone regeneration ability used in conditions of variable dynamic loads has been analyzed.

Methodological approach for determining the destruction of bioactive materials for bone implants has been developed. It includes assessment of a bioactive material's susceptibility to chemical, mechanical and biologic destruction considering their structural features under varying conditions *in vitro*.

The choice of the oxide system Na_2O–K_2O–Li_2O–CaO–MgO–ZnO–ZrO_2–TiO_2–Al_2O_3–B_2O_3–P_2O_5–SiO_2 with micro additives of CaF_2, MnO_2, CeO_2, CoO, V_2O_5, SrO, Cu_2O, MoO_3, La_2O_3 has been substantiated for the purpose of obtaining bioactive glass-ceramic materials; model glasses with the ratio of $CaO/P_2O_5 = 1.66 \div 1.7$ have been synthesized. Glass ceramic materials have been obtained on their base after low temperature single-stage heat treatment.

It has been established that the resistance to chemical, biologic and mechanical destruction of the experimental glass-ceramic materials *in vitro*, being the principal factor of maintaining integrity of the implant *in vivo*, is determined by their structural strength and the ability to form protective silica-gel layer on their surface, including in conditions of variable dynamic and static loads. It is an important condition of their efficient and long-term performance as bone implants.

Developed calcium silicophosphate glass-ceramic materials are characterized by chemical durability, non-toxicity, bacteriostatic properties, ability to retain initial mechanical properties under the effect of mechanical destruction *in vitro* and the ability for short-term bone formation *in vivo*. This allows to view them as perspective materials for creation of biocompatible bone implants of the new generation.

References

1. Huawei Qu, Hongya Fu, Zhenyu Han, Yang Sun, *RSC Adv.*, **9**, 26252 (2019).
2. O.Savvova, O.Babich, O.Fesenko, Biocompatible Glass-ceramic Coatings. Calcium-phosphate-silicate Coatings on Titanium for Dental Implants, SIA OmniScriptum Publishing, Mauritius (2018).
3. L.L.Hench, *J. Mater. Sci. Mater. Med.*, **26**, 86 (2015).
4. D.Shi, Biomaterials and Tissue Engineering, Ser.: Biological and Medical Physics, Biomedical Engineering, Springer-Verlag, Berlin Meidelberg (2004).
5. O.V.Savvova, L.L.Bragina, G.N.Shadrina et al., *Glass and Ceramics*, **74**, 1 (2017).
6. M.Catauro, F.Bollino, *J. Bone Rep. Recomm.*, **3**, 1 (2017).
7. P.D.Sarkisov, N.Yu.Michailenko, E.E.Stroganova et al., .Proc. XIX Int. Congr. on Glass, Edinburg (2001), p.23.
8. I.Kansal, Diopside-Fluorapatite-Wollastonite Based Bioactive Glasses and Glass-ceramics, Universidade de Aveiro, Departamento de Engenharia de Materiais e Ceramica (2015).
9. L.Floroian, *Med. Sci.*, **3**, VI (2010).
10. W.Elshahawy, Biocompatibility. Electric and Magnetic Ceramics, Bioceramics, Ceramics and Environment, INTEX (2011).
11. M.Caicedo, J.J.Jacobs, A.Reddy, N.J.Hallab, *J. Biomed Mater. Res. A.*, **86**, ??? (2008).
12. A.H.Wang, Y.Han, K.W.Xu, *Acta Biomater.*, 5 (2009).
13. A.M.Pietak, J.W.Reid, M.J.Stott, *Biomater.*, 28 (2007).
14. A.A.Appen, Glass Chemistry, Chemistry, Leningrad (1974) [in Russian].
15. O.V.Savvova, O.V.Babich, G.N.Shadrina, *Functional Materials*, **21**, 4 (2014).