# Biocompatible scaffolds based on glass-ceramic materials for bone tissue engineering

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***Abstract – The aim of the work is to develop scaffolds based on biocompatible glass-ceramic materials for tissue engineering. Porous bioactive glass-ceramic materials based on hydroxyapatite and lithium dissilicate have been developed, which are characterized by high biocompatibility and crack resistance and can be effectively used for bone engineering.***

Keywords – glass-ceramic materials, scaffolds, tissue engineering, hydroxyapatite, lithium disilicate.

## Introduction

The development of tissue engineering over the past decade is the result of various factors: the deepening of the theoretical foundations for the use and increase in the availability of stem cells, the development of genomics and proteomics, the emergence of new biomaterials as potential templates for tissue growth, the improvement of bioreactor designs for growing cells *in vitro* and increasing understanding of tissue repair processes [1]. However, despite the fact that research in the field of tissue engineering is developing very rapidly, it should be noted that in the field of commercialization of tissue engineering products and in the field of their clinical application, progress is less impressive. The development of new types of biocompatible materials and the creation of specialized biomedical products based on them is becoming the leading direction of research and commercialization at present.

A special and significant problem is the need to create biodegradable materials that can imitate the properties and functions of biological structures. This is due to the revolutionary changes currently taking place in medicine in connection with the emergence and development of new works in the field of transplantology and artificial organs, based on a fundamentally new approach to restoring the functions of vital organs. This is the use of genetic, cellular and tissue engineering technologies for the development of artificial (hybrid) organs and tissues, cloning of organs and tissues from the patient's stem cells *in vitro*. So-called scaffolds (scaffolds - matrices, carriers, linings, scaffolds) are needed to control the processes of formation, ensure growth, proliferation and differentiation of cells in the process of reconstruction of damaged tissue. This direction is called «bioimitation», and the corresponding materials are called «self-monitoring», «smart» or «intelligent». A feature of spacesuits is their porous structure, which increases the contact area of the biomaterial with body fluids and allows vessels and capillaries to grow through them. It is the space suits that make it possible to simultaneously ensure the possibility of germination of living tissues through their voids and the mechanical strength of the implant.

To date, various types of materials have been successfully used to create matrices (Table 1), but all of them have both advantages and disadvantages, which does not allow to fully reproduce the organocellular structure [2].

Thus, the search, study and introduction of new materials and products from them into biomedical practice is an urgent and highly demanded direction, the success of which will contribute to the progress of many areas of medicine and ultimately improve the quality of treatment and human life.

*Table 1*

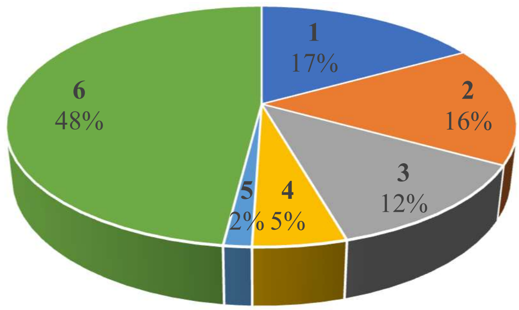
Comparative characteristics of materials for the manufacture of scaffolds

| Material | Advantages | Potential limitations |
|---|---|---|
| Hydrogels | The high water content and inclusion of the growth medium allows the cells to be encapsulated.<br>Mechanical properties can be changed by varying the cross-linking level of the structure.<br>Controlled release of the drug or growth factor is possible.<br>Ease of patterning with 3D printing to mimic tissue microarchitecture. | Mechanical properties limit their use in load-bearing structures.<br>The need to optimize printing conditions for individual hydrogels.<br>The possibility of breaking the structure of the product during physical manipulation of the structures.<br>Uneven loading of the cells of the product during operation. |
| Polymers | Natural polymers can be obtained from the extracellular matrix, which ensures their high biocompatibility, low toxicity and biodegradation.<br>Presence of biofunctional molecules on the surface.<br>Synthetic polymers are characterized by high control of physical properties. | Natural and synthetic polymers usually have insufficient mechanical properties for use on loaded areas.<br>The presence of pathological impurities in natural polymers.<br>Synthetic polymers are often hydrophobic and not recognized by cells. |
| Ceramic materials | Osteoconductive and osteoinductive properties ensure strong integration with tissues.<br>The composition is similar to the content of minerals in bones. | Hard and brittle when used alone.<br>May exhibit an inappropriate rate of degradation or resorption with reduced mechanical properties as a result. |
| Bioactive glasses | Osteoconductive, osteoinductive properties.<br>Adapted to clinical applications. | Low crack resistance.<br>High speed of resorption. |
| Metals | High mechanical properties can be useful when slow bone formation is required.<br>Changes of structures into three-dimensional forms for the treatment of specific defects. | The potential for release of toxic metal ions may cause local and distal toxicity.<br>A high modulus of elasticity will result in voltage shielding.<br>Low biodegradability. |

**Experimental part**

The aim of the work is to develop scaffolds based on biocompatible glass-ceramic materials for tissue engineering.

To solve the problems of tissue engineering, it is important to choose the right materials for obtaining matrices. Today, research and development of polymeric medical materials is a priority due to their multifunctionality and competitiveness. Metals are gradually losing their leading position, while bioactive ceramic materials and glasses have already confidently conquered the market of biocompatible materials for prosthetics and are increasing the pace of their segment (Fig. 1).




1 – calcium phosphates; 2 – metals; 3 – biosensors; 4 – bioglass; 5 – carbon; 6 – polymers
Fig. 1 Distribution of the main directions of development biocompatible materials (2022).

However, the known bioactive materials for replacement surgery are characterized by long periods of fusion with the bone and can be used to create scaffolds operated only under minor loads. The solution to this problem is the creation of scaffolds for bone arthroplasty based on biocompatible glass-ceramic materials with high mechanical properties and a significant level of bioactivity. Such materials based on calcium silicophosphate glasses are distinguished by shortened periods of fusion with the bone. However, their low crack resistance does not allow their use in areas of bone tissue with high but variable dynamic loads [3, 4].

For this purpose, compositions of model glasses of the system $Na_2O – K_2O – Li_2O – CaO – ZrO_2 – TiO_2 – MgO – ZnO – Al_2O_3 – B_2O_3 – P_2O_5 – Nb_2O_5 – SiO_2$ in the region of metastable liquation were designed, which are characterized by the ratio $CaO / P_2O_5 = 1.67$ and $SiO_2 / Li_2O = 4$.

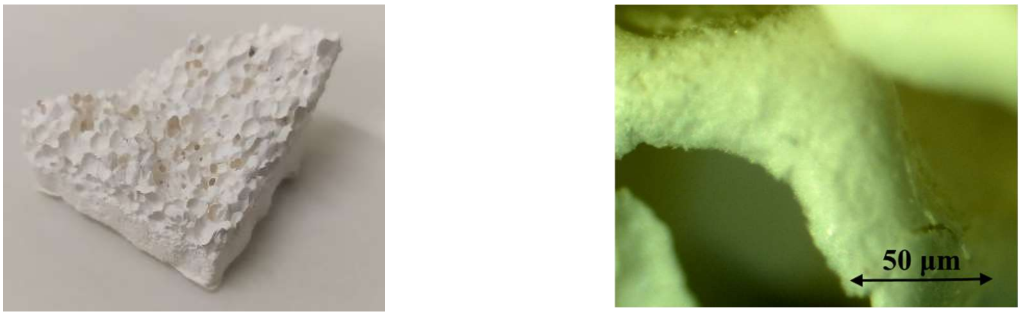
An important factor in the approximation of the structure of scaffolds to the structure of natural bone is the possibility of providing a gradient porous structure of the material [5]. Based on the analysis of methods for obtaining porous silicate materials, as the most optimal for industrial applications, the technology of duplication of the polymer matrix was chosen. It will provide a regular (given) change in the pore size of the material and their connection to each other. This technology provides:

- tempering of alcohol-based slip on the base of the original glass;
- obtaining a polymer matrix (the negative of the future scaffold);
- impregnation of the polymer matrix with a slip;
- heat treatment of the product (drying, firing) during which the polymer matrix burns out;
- mechanical processing of the scaffold.

To prepare the slip, the original glass powder was mixed with ethyl alcohol in a ratio of 1 to 2, and 0.2 wt. % xanthan gum was added to each sample to improve the rheological properties. Samples of polypropylene sponge with different pore sizes, made in the form of cubes with an edge of 1 cm, were impregnated with a freshly prepared slip. After excess slip drained off, the samples were dried and fired in a muffle oven ($T = 750–760$ °C, $\tau = 10–15$ minutes).

By the method of a complete three-factor experiment (input parameters: the ratio of the masses of glass powder and alcohol, firing temperature, firing time; output parameters: the degree of sintering of the product, the constancy of the geometric shape) it was determined that the use of slip with a ratio of components of 1.5 and firing of products at a temperature of 750 °C during 15 minutes is optimal (Fig. 2).

With the application of the method of duplicating the polymer matrix, scaffolds were obtained, which differ in porosity values of 45–65 % with the presence of connected pores with a size of 150–200 μm. Studies of the structure of the developed scaffolds using a scanning electron microscope made it possible to establish the presence of hydroxyapatite and dissilicatulithium crystals (55 vol. %) with sizes of about 1 μm in the structure of the fired materials. A characteristic feature of the samples is an increase in the size of crystals on the inner surface of the pores up to 3–5 μm, which is explained by a decrease in the activation energy of crystal growth at the phase boundary. These crystals provide the structural strength of the product during firing, and small crystals evenly distributed in the volume of the material provide high mechanical properties of materials – compressive strength of 107 MPa and crack resistance $K_{1c}$ = 3.8 $MPa^{1/2}$.




*a* *b*

Fig. 2 The appearance of the obtained samples (*a*) and the nature of the connection of the pores (*b*)

The biocompatibility of the samples was assessed by the toxic effect of the sample against opportunistic pathogens *E. coli*. The toxicity of the experimental materials was assessed by the change in the dehydrogenase activity of the biotest cultures (the initial concentration of the culture was $10^6$ cells/$cm^3$). After 24 hours of contact of the sample with the medium, the concentration of formazan approaches the values of the control variant, which is evidence of the absence of the toxic effect of the samples.

## Conclusions

Glass-ceramic porous scaffolds with the presence of hydroxyapatite and lithium disilicate crystals in a total amount of 55 vol % have been developed. They are characterized by a pore content of 45–65 vol % which is compatible with a pore size of 150–200 μm. The developed materials are characterized by the possibility of creating a structure with a given pore size distribution, high mechanical properties and non-toxicity, which makes them a promising matrix for the use of composite bioactive scaffolds.

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