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LOWERING THE TEMPERATURE OF BIOGLASS SYNTHESIS IS A PRIORITY AREA OF MODERN BIOMEDICAL ENGINEERING

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Abstract: *The development and synthesis of biomedical materials is one of the key areas of biomedical engineering. Today, bioglass is one of the most popular bioactive materials from the moment of its discovery to its fourth generation. Among the various methods of bioglass synthesis, classical cooking with fritting in cold water remains the most widely used. The biggest problem in the implementation of this method is the high temperature melting of glasses, which requires high energy consumption and specialized high-temperature equipment. The conducted studies showed the possibility of reducing the cooking temperature of bioglasses from 1350 to 1280°C due to the rational selection of raw materials and their initial preparation. The resulting bioglasses have a high ability to form hydroxyapatite when in contact with biological media and can be used in bone tissue regeneration.*

Keywords: *Bioglass, Regeneration of Bone Tissue, Melting Temperature, Raw Materials, Biocompatibility*

INTRODUCTION

Materials involved in bone regeneration have many potential clinical applications: from the treatment of poorly healing fractures to the fixation of endoprostheses by ingrowing the patient's own bone tissue into the porous surface of the implant (Hulsen, D.J., van Gestel, N.A., Geurts, J.A.P. & Arts, J.J., 2017). In recent decades, the development, fabrication, and modification of biomaterials with specified properties have been in the spotlight.

Bioglass occupies a special place among these materials (Baudín, C. & Pena, P., 2023). It was discovered in 1969 by Larry Hench and had a simple composition of $Na_2O–CaO–SiO_2$ with a percentage ratio of 24:24:45 (Hench, L.L., 1970). The basic unit is a SiO_2 tetrahedron with 4 Si–O–Si atoms connected by sodium and calcium, forming non-bridging bonds with oxygen atoms. Later, in 1971, the University of Florida marketed the popular name ‘bio-glass’ or bioactive glass as 45S glass.

Subsequently, a variety of in vivo experimental studies were conducted, which showed that the human body accepted the bio-glass material with little immunological reaction (Clark, A.E., Hench, L.L. & Paschall, H.A., 1976). They have demonstrated the ability to deposit calcium-phosphate bridges at the node interface, thereby enhancing hard tissue regeneration. In addition, bioglass also demonstrates various unique properties such as cytocompatibility, the ability to induce apatite formation and angiogenesis (Kohrs, N.J., Liyanage, T., Venkatesan, N., Najarzadeh, A.,

Puleo & D. A., 2019). These properties have led to numerous studies of bio-glass-mediated tissue regeneration, particularly in the fields of orthopaedics and dentistry. Further, in vivo and animal model studies have been conducted that have endorsed the use of bioglass, making it a reliable and biologically safe material for biomedical applications.

Today, there are dozens of glass compositions that have distinct properties, are modified at the nanoscale with various ions to improve their efficiency, and new production methods are being introduced. In addition to the classical melt boiling and quenching, bio-glass can be synthesised using the sol-gel method, spray pyrolysis, microwave irradiation, flame synthesis, and microemulsion (Krishnan L., Chakrabarty, P., Govarthanan, K., Rao, S. & Santra, T. S., 2024).

Despite the fact that more than five decades have passed since the discovery of this biomaterial, there are still many challenges to be addressed in the future. The creation of bone grafts with good mechanical properties and huge bone marrow spaces is still an obstacle in the field of regenerative medicine. The development of pore-controlled skeletons as well as the modification of reactive calcium phosphate layers for cell differentiation and proliferation is still a major challenge (Farooq, S., Mehmood, Z., Qais, F.A., Khan, M.S. & Ahmad, I., 2018). In addition, the replacement tissue must have good mechanical properties and porosity to allow cellular infiltration and angiogenesis.

Despite the emergence of new methods of manufacturing bioglasses, their production by the classical method of melting the charge and quenching in cold water remains the most commonly used (Ibrahim, N. F., Mohamad, H., Noor, S. N. F. M. & Ahmad, N., 2018). This method makes it possible to introduce various modifying elements into the glass, to obtain sufficient microporosity for better hydrolysis and the formation of hydroxyapatite in contact with physiological fluids. However, the disadvantage of this method is the high energy consumption for the cooking process.

A method of producing S53P4 bio-glass frits is known (Forero-Sossa, P.A., Salazar-Martinez, J.D., Barajas-Aguilar, V.J. at ell., 2023), which includes the preparation of a charge from a mixture of oxides and two-stage heat treatment of the charge in a platinum crucible - at 950 °C with holding for 5 hours to promote the dissociation of Na_2CO_3, followed by an increase in temperature to 1450 °C and holding for 4 hours and obtaining frits from the molten glass by abrupt cooling in water at room temperature. Another method (Sinitsyna, P., Engblom, M. & Hupa, L., 2023) involves mixing high-purity raw materials Na_2CO_3, $CaCO_3$, $CaHPO_4 \cdot 2(H_2O)$ and quartz sand as SiO_2 starting material, melting the charge in a platinum crucible at 1360 °C for 3 hours, casting, annealing at 520°C for 1 hour, and grinding to a particle size of 300-500 μm. Another method for producing S53P4 bio-glass frits (Shams, M., Karimi, M., Ghollasi, M., Nezafati, N. & Salimi A., 2018) involves preparing a glass melting charge from SiO_2, Na_2CO_3, $CaCO_3$ and P_2O_5 of p.d.a, thorough mixing using a ball mill for 3 hours, pressing discs with a diameter of 10 mm using a hydraulic press, melting the discs in an alumina crucible with holding at a maximum temperature of 1400 °C for 3 hours, and obtaining frits from the melt by abrupt cooling in distilled water at room temperature. Thus, the disadvantages of the classical method are high temperatures (1360–1450°C) and the duration (up to 3 hours) of holding the glass mass at the maximum temperature, and in some cases, the use of toxic components (P_2O_5 is classified as a hazard class 3 according to NFPA 704).

Therefore, from the point of view of improving the technology of manufacturing bio-glasses, it is important to reduce their melting temperatures without adversely affecting their biocompatible and resorption properties.

EXPOSITION

The aim of the study was to investigate the effect of modifying additives on reducing the firing temperature of glasses and their active properties in contact with saline.

S53P4 glass was chosen as the base glass, wt.%: SiO_2 – 53; Na_2O – 23; CaO – 21, P_2O_5 – 3 (Hulsen, D.J., van Gestel, N.A., Geurts, J.A.P. & Arts, J.J., 2017). SrO, ZnO, and B_2O_3 (more than 100 wt.%) were added to the glasses both jointly and separately.

The experimental results were planned and processed using the simplex method. The raw material blends containing SiO_2 (marshalite), Na_2CO_3, $CaCO_3$, $NH_4H_2PO_4$ and test oxides were crushed to a particle size of less than 100 μm, carefully averaged and poured into a hot corundum

crucible at 1000 °C with a subsequent increase in temperature until a melt was obtained. The melting points of the compositions were recorded to plot the isolines in the experimental triangles (Fig.1).

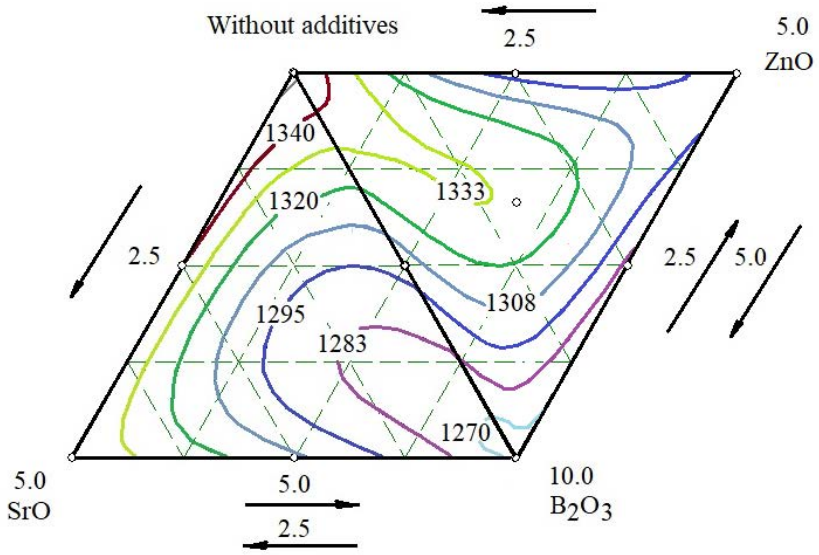

Fig. 1 Dependence of bio-glass melting points on the content of modifying additives

The data presented here indicate that without additives, the experimental base charge, despite a well-chosen raw material composition, melts at a temperature of over 1340 °C. As the temperature increases, ammonium dihydrogen phosphate begins to melt at 190 °C, calcium carbonate at 825 °C, and sodium carbonate at 854 °C. An increasing amount of liquid phase, which is formed during the melting of these components with increasing temperature, actively dissolves the highly dispersed marshalite grains. Due to the release of ammonia during heat treatment and decomposition of ammonium dihydrogen orthophosphate, the process of clarification and homogenisation of the melt is accelerated, which improves the quality of the fritters during melting at low temperatures. The introduction of SrO up to 5 wt.% reduced the glass melting temperature to only 1320°C, and manifestations of segregation processes were observed (Fig. 2). The most effective was the addition of B_2O_3 up to 10 wt.% – the melting temperature decreased to 1270 °C, and after cooling, visual analysis showed that a homogeneous, transparent glass was formed. The addition of up to 5 wt.% ZnO reduced the temperature to 1295 °C; the glass was also homogeneous and transparent.

a b c d e

Fig. 2 Visual assessment of some formed bio-glasses: a – without additives (1360ºC), b – 5 wt.% SrO (1320ºC), c – 10 wt.% B_2O_3 (1270ºC), d – 2.5 wt.% SrO and 5 wt.% B_2O_3 (1308ºC), e – 5 wt.% ZnO (1295ºC)

The choice of modifying additives for the redusing glass melting temperature was based on numerous studies of the role of these oxides in the regeneration of tissues in living organisms.

Strontium, together with calcium, phosphate and other elements, forms hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$), a mineral component of bone (Ali, A., Singh, S.P. & Pyare, R. 2020). Strontium is one of the most important elements that plays a key role in the formation of healthy bone tissue, bone metabolism, increased bone mineral density, active osteoblast formation and prevents osteoclast-mediated bone resorption, thereby regulating the overall condition of bones. In terms of

physical and mechanical properties, SrO-modified bioglasses demonstrate high biological compatibility, bioactivity and mechanical properties.

Zinc is one of the most abundant components present in bones and demonstrates a stimulatory effect on the mineral deposition phase of bone both in vitro and in vivo. It is crucial for the normal functioning of human cells and for regulating the genetic control of cell proliferation by binding to specific regions of deoxyribonucleic acid (DNA). The addition of ZnO to bioactive glass further stimulates cell proliferation and differentiation and promotes the development of a strong bond with bone (Mohan Babu, M., Rao, P. V., Singh, R. K., Kim, H.-W., Veeraiah, N., Özcan, M., & Prasad, P. S., 2021). The presence of zinc oxide in bioactive glass increases its mechanical strength and chemical durability (reduces its decomposition in aqueous solutions such as SBF). In addition, it also promotes bone mass, has anti-inflammatory, antibacterial and bone healing properties by increasing osteoblast DNA. However, the release of excessive amounts of zinc during the dissolution of bio-glass is undesirable as it can cause adverse toxic effects. To overcome this problem, the rate of zinc release from implants must be optimised, for example by incorporating divalent cations with appropriate ionic radii.

Borate glasses are also attracting the attention of researchers and physicians due to their increased chemical reactivity (Wen, C., Xie, M., Yan, S. in press, 2024). Borate bio-glasses can form hydroxyapatite faster than silicate glass. For example, due to the complete replacement of SiO_2 with B_2O_3, glass 1393-B3 shows a fivefold increase in reactivity to simulated body fluids, expanding its potential applications, including soft tissue regeneration.

To compare the solubility of some of the experimental bioglasses, they were ground to a particle size of 100–200 μm and kept in Ringer's physiological solution for 14 days at 37°C. The solubility was determined by the mass loss index (Table 1), and the presence of hydroxyapatite (Ha) was determined by X-ray diffraction analysis.

Table 1 – Activity characteristics of some experimental bioglasses

№ glass	Temperature melting, °C	Content of modifying oxides (over 100%), wt.%.			Activity characteristics after 14 days in Ringer's solution	
		SrO	B_2O_3	ZnO	Mass loss, %	Presence of Ha
basic	1360	–	–	–	2.9	+
3	1320	5.0	–	–	3.2	++
4	1308	2.5	5.0	–	5.2	+
5	1270	–	10.0	–	10.4	+
8	1283	–	5.0	2.5	4.1	+
9	1308	–	–	5.0	3.0	++

Thus, the data shows that the nature of the modifying oxide, in addition to the technological factor of lowering the temperature, has a direct impact on the biological activity of the experimental glasses. Thus, the introduction of modifying oxides SrO and ZnO slightly or not at all accelerates the solubility of bio-glasses, while more intense manifestations of the crystalline phase, hydroxyapatite, are recorded in the X-ray diffraction patterns. At the same time, the addition of 10 wt.% of B_2O_3 accelerated the solubility of the basic bio-glass by more than three times.

CONCLUSION

Thus, the research made it possible to combine the technological and medical aspects of the development of bioglasses. A model of the dependence of the bio-glasses melting temperature on the content of modifying oxides SrO, ZnO and B_2O_3 was developed, which will allow us to select a rational mode of their synthesis, minimising unnecessary energy consumption. On the other hand, the biological activity indicators will allow us to adjust the purpose and scope of the experimental materials.

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