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Synthesis and structural-morphological study of composite materials based on mesoporous bioglass and cucurbit[n]urils

Rustam T. Sadykov[1], Arthur E. Ukhov[2], Alina A. Mikhailichenko[3], Daria N. Lytkina[4], Abdigali A. Bakibaev[5], Irina A. Kurzina[6]

[1, 2, 3, 4, 5, 6] *Tomsk State University, Tomsk, Russian Federation*
[1] *nate_river_2017@mail.ru*
[2] *artyryxov1@gmail.com*
[3] *nekochan2004@mail.ru*
[4] *darya-lytkina@yandex.ru*
[5] *bakibaev@mail.ru*
[6] *kurzina99@mail.ru*

Abstract. Mesoporous bioglass (MBG) is a promising biomedical material, but controlling its surface properties is challenging. This study modified MBG with cucurbit[n]uril macrocycles (CB[6], CB[7], CB[8]) to alter its surface. Modification was performed by evaporating macrocycle solutions onto MBG. Analysis showed this process significantly changed the MBG's morphology. Its characteristic spherical nanostructure disappeared, replaced by a heterogeneous organo-inorganic layer containing aggregates and crystalline formations. The extent of change depended on the specific cucurbituril used, due to differences in their solubility, geometry, and self-organization. Energy-dispersive X-ray spectroscopy confirmed successful modification, showing a large increase in carbon and nitrogen with a simultaneous decrease in silicon and oxygen. CB[8] created the densest and most massive organic coating. This work establishes that cucurbituril size and structure dictate the interaction with MBG and the degree of surface modification. It demonstrates the potential of supramolecular macrocycles to specifically tailor bioglass properties for creating advanced functional biomaterials.

Keywords: mesoporous bioglass, cucurbiturils, supramolecular modification, SEM/EDS analysis, organo-inorganic composites

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Синтез и структурно-морфологическое исследование композиционных материалов на основе мезопористого биостекла и [n]-урилов

Рустам Талгатович Садыков[1], Артур Эдуардович Ухов[2], Алина Андреевна Михайличенко[3], Дарья Николаевна Лыткина[4], Абдигали Абдиманапович Бакибаев[5], Ирина Александровна Курзина[6]

[1, 2, 3, 4, 5, 6] *Томский государственный университет, Томск, Россия*
[1] *nate_river_2017@mail.ru*
[2] *artyryxov1@gmail.com*
[3] *nekochan2004@mail.ru*
[4] *darya-lytkina@yandex.ru*
[5] *bakibaev@mail.ru*
[6] *kurzina99@mail.ru*

Аннотация. Мезопористое биостекло (МБГ) является перспективным биомедицинским материалом, но контролировать свойства его поверхности непросто. В этом исследовании MBG модифицировали макроциклами тыквенного [n]урила (CB[6], CB[7], CB[8]), чтобы изменить его поверхность. Модификация проводилась путем выпаривания растворов макроциклов на MBG. Анализ показал, что этот процесс значительно изменил морфологию MBG: его характерная сферическая наноструктура исчезла, сменившись гетерогенным органо-неорганическим слоем, содержащим агрегаты и кристаллические образования. Степень изменений зависела от конкретного используемого кукурбитурила из-за различий в их растворимости, геометрии и самоорганизации. Энергодисперсионная рентгеновская спектроскопия подтвердила успешность модификации, показав значительное увеличение содержания углерода и азота при одновременном снижении содержания кремния и кислорода. CB[8] создал самое плотное и массивное органическое покрытие. В настоящей работе установлено, что размер и структура кукурбитурила определяют взаимодействие с MBG и степень модификации поверхности. Это демонстрирует потенциал супрамолекулярных макроциклов, которые позволяют специально адаптировать свойства биостекла для создания передовых функциональных биоматериалов.

Ключевые слова: мезопористое биостекло, тыквенные семечки, супрамолекулярная модификация, СЭМ/ЭДС-анализ, органо-неорганические композиты

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Introduction

Osteoporosis, most prevalent in the elderly and postmenopausal women, leads to impaired bone homeostasis, reduced bone mass, and an increased risk of fractures [1]. Conventional systemic drug administration methods are often ineffective due to the rapid clearance of the drug from the body [2].

A promising alternative is drug-delivery implants, which provide localized and sustained release of active agents, thereby enhancing therapeutic efficacy [3–4]. Bioactive glasses (BGs) and mesoporous bioactive glasses (MBGs) are widely used as matrices for such implants. Their key properties include the ability to bond with bone tissue, stimulate its regeneration, and promote angiogenesis [5, 6]. A significant advantage of BGs is the possibility of deliberately tailoring their texture and surface properties to control the rate of hydroxyapatite deposition [7–9].

To endow the materials with therapeutic functions, such as an antibacterial effect, they are modified with biologically active compounds. Macrocyclic compounds, particularly cucurbit[n]urils (CB[n]), are of special interest due to their high stability and superior control over drug release compared to other delivery systems [10–13]. CB[n]s can selectively encapsulate various molecules via host-guest interactions, making them highly promising for targeted drug delivery [14–16].

Thus, the development of porous bone-substitute materials based on bioglass and modified with supramolecular systems is a relevant objective. The aim of this work is to fabricate composite biomaterials from mesoporous bioglass (MBGs) and cucurbit[6,7,8]urils and to characterize them using various physicochemical methods.

Materials and methods

The synthesis of cucurbit[n]urils (CB[n], where n = 6, 7, 8) was carried out according to a previously described procedure (Figure 1) [16]. Into a three-necked round-bottom flask equipped with a magnetic stirrer and a reflux condenser, 4.22 g (0.14 mol) of paraformaldehyde and 14 ml of 10 M sulfuric acid were loaded. The mixture was stirred until the paraformaldehyde was completely dissolved. Thereafter, 10 g (0.07 mol) of glycoluril was added in portions with constant stirring to prevent premature oligomerization. The reaction mixture was thermostated and maintained at a temperature of 95 °C for 24 hours, and sequentially separated according to the method [16].

The schematic diagram of the synthesis steps for mesoporous bioactive glass is shown in Figure 2. The synthesis process was carried out using a magnetic stirrer. After preparing a clear aqueous CTAB solution (2% by weight) by stirring CTAB in 26 mL of deionized water at 30°C, 8 mL of ethyl acetate were added dropwise to the reaction vessel. After stirring for another 30 minutes, a 25% ammonia solution was added to adjust the pH of the solution. The mixture was then stirred for another 15 minutes. At this stage, 2.88 mL of TEOS (the primary precursor for nanoparticle synthesis) and 0.53 g of $Ca(NO_3)_2 \cdot 4H_2O$ were added at 30-minute intervals. After a 4-hour reaction period, the colloidal particles were

collected by centrifugation at 7000 rpm for 20 minutes. The collected particles were washed three times with deionized water and acetone and then dried for 12 hours at 80°C. Next, the mesoporous bioactive glass nanoparticle powder was placed in an oven at 700°C for 4 hours with a temperature increase rate of 2°C/min.

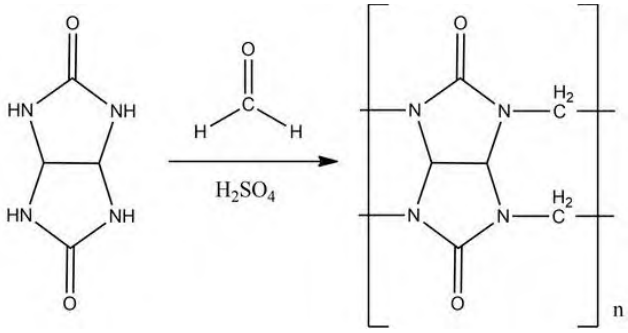

Fig. 1. Scheme of synthesis of cucurbitu[n]urils

Morphological analysis of the surface of the samples studied was carried out using a QUANTA 200 3D scanning electron microscope (SEM) equipped with a dual electron and ion beam (FIB) system. The instrument provides the capability to operate over a wide range of accelerating voltages — from 200 V to 30 kV with smooth adjustment. The microscope's resolution is 3.5 nm in ESEM (Environmental Scanning Electron Microscope) mode at an accelerating voltage of 30 kV. When operating in Low Vacuum Mode at 3 kV, the resolution is less than 15 nm. This functionality allows for detailed examination of the surface of non-conductive materials without the need to apply a conductive coating.

Results and Discussion

Mesoporous bioglass (MBGs) was modified by slow evaporation of cucurbit[n]urils (CB[n], where n = 6, 7, 8). Due to the limited solubility of CB[6] and CB[8] in deionized water, hydrochloric acid solutions were used for their deposition. CB[7], which has increased solubility, was dispersed in deionized water. This approach maximized the specific surface area. The resulting materials were dried to constant weight in an oven at 60°C and examined using SEM.

The unmodified MBG exhibits a uniform nanostructured surface composed of well-defined spherical particles, which is characteristic of sol–gel-derived mesoporous silicate materials. These spheres form a loose, highly textured structure, indicative of a high surface area and open porosity. All modified samples (MBG-CB[6], MBG-CB[7], and MBG-CB[8]) show pronounced morphological changes. The characteristic spherical MBG particles are no longer distinguishable, indicating their surface encapsulation and aggregation upon interaction with cucurbiturils. The composites exhibit a pronounced heterogeneous topography consisting of compact agglomerates, irregular particle domains, and dense organo-inorganic clusters.

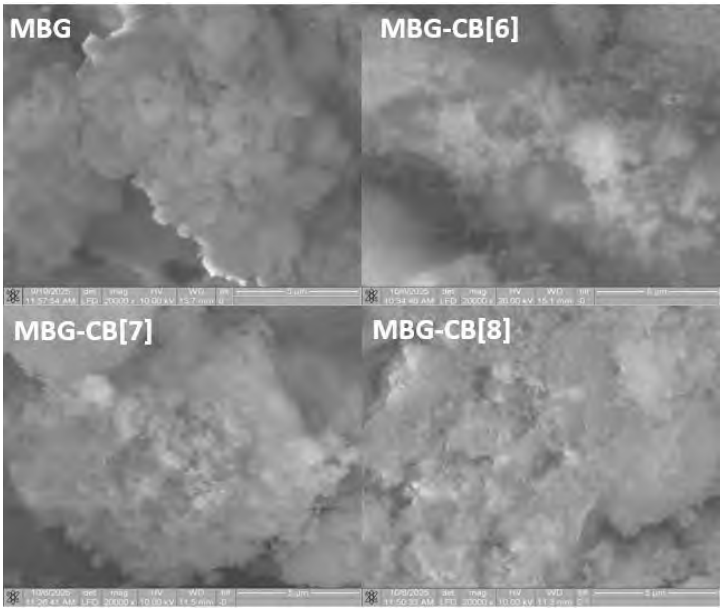

Fig. 2. Surface morphology of the initial MBG and MBG samples modified with cucurbiturils CB[6], CB[7], and CB[8]

To verify the successful modification of MBG with cucurbiturils, elemental analysis was performed using energy-dispersive X-ray spectroscopy (EDS). The atomic composition values are presented in the Table. Pristine MBG contains only Si, O, and Ca, with no detectable carbon or nitrogen. After modification, all MBG-CB[n] composites show substantial incorporation of C and N, which originate exclusively from the cucurbituril macrocycles. Their presence therefore serves as a direct marker of the efficiency of CB[n] deposition. The carbon content increases systematically from MBG-CB[6] (18.08 at%) to MBG-CB[7] (19.25 at%), reaching its highest value in MBG-CB[8] (43.61 at%). A similar trend is observed for nitrogen, which rises from 6.64 at% in the CB[6] composite to 9.85 at% in MBG-CB[7] and 17.78 at% in MBG-CB[8]. These results confirm that CB[8], the largest macrocycle, demonstrates the highest level of surface adsorption or retention on MBG, which may be attributed to its larger cavity size, increased number of carbonyl groups, and enhanced interaction with the silicate surface.

Elemental atomic composition of MBG and MBG samples modified with CB[n] cucurbiturils

	C (At. %)	N (At. %)	O (At. %)	Si (At. %)	Ca (At. %)
MBG	–	–	63.35	33.63	03.02
MBG-CB[6]	18.08	06.64	45.80	28.87	00.61
MBG-CB[7]	19.25	09.85	43.78	25.18	01.94
MBG-CB[8]	43.61	17.78	29.22	07.46	01.90

Conclusion

In this work, composites based on mesoporous bioglass modified with cucurbiturils CB[6], CB[7], and CB[8] were obtained. It has been shown that the process of applying macrocycles leads to significant changes in the morphology of the MBG surface: the characteristic spherical structure of the initial material disappears, forming a heterogeneous layer that includes agglomerates, dense organo-inorganic coatings, and, in some cases, crystalline structures of CB[n]. The EDS analysis confirms the successful fixation of cucurbiturils on the surface, which is manifested in a significant increase in the atomic fractions of carbon and nitrogen with a simultaneous decrease in the fractions of silicon and oxygen. The most pronounced modification effect is observed for CB[8], which is consistent with its higher molecular weight and ability to form denser surface layers.

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***Information about the authors*:**
Sadykov Rustam T. – Junior Researcher, Tomsk State University (Tomsk, Russian Federation). E-mail: nate_river_2017@mail.ru
Ukhov Arthur E. – Junior Researcher, Tomsk State University (Tomsk, Russian Federation). E-mail: artyryxov1@gmail.com
Mikhailichenko Alina A. – Laboratory Assistant, Tomsk State University (Tomsk, Russian Federation). E-mail: nekochan2004@mail.ru
Lytkina Daria N. – Ph.D., Senior Researcher, Tomsk State University (Tomsk, Russian Federation). E-mail: darya-lytkina@yandex.ru
Bakibaev Abdigali A. – Professor, Doctor of Chemical Sciences, Leading Researcher, Tomsk State University (Tomsk, Russian Federation). E-mail: bakibaev@mail.ru
Kurzina Irina A. – Doctor of Physical and Mathematical Sciences, Associate Professor, Head of the Department of Natural Compounds, Pharmaceutical and Medicinal Chemistry, Tomsk State University (Tomsk, Russia). E-mail: kurzina99@mail.ru

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***Сведения об авторах*:**
Садыков Рустам Талгатович – младший научный сотрудник, Томский государственный университет (Томск, Россия). E-mail: nate_river_2017@mail.ru
Ухов Артур Эдуардович – младший научный сотрудник, Томский государственный университет (Томск, Россия). E-mail: artyryxov1@gmail.com
Михайличенко Алина Андреевна – лаборант, Томский государственный университет (Томск, Россия). E-mail: nekochan2004@mail.ru
Лыткина Дарья Николаевна – кандидат технических наук, старший научный сотрудник, Томский государственный университет (Томск, Россия). E-mail: darya-lytkina@yandex.ru
Бакибаев Абдигали Абдиманапович – профессор, доктор химических наук, ведущий научный сотрудник, Томский государственный университет (Томск, Россия). E-mail: bakibaev@mail.ru
Курзина Ирина Александровна – доктор физико-математических наук, доцент, заведующая кафедрой природных соединений, фармацевтической и медицинской химии Томского государственного университета (Томск, Россия). E-mail: kurzina99@mail.ru

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