© КОЛЛЕКТИВ АВТОРОВ, 2026

UDC 615.4- 678.067:678.742.3:620.22
DOI 10.59598/ME-2305-6053-2026-119-2-136-145

A. A. Khrustaleva[1], A. T. Yedrissov[1], D. P. Khrustalev[1], I. V. Chernykh[2], I. V. Losseva[1], A. F. Savelyev[1]*, V. V. Kazantsev[1], M. A. Kiikbayev[1], P. Yu. Rusyaeva[1], K. A. Perepelitsyna[1], S. V. Shapovalenko[1]

DEVELOPMENT AND CHARACTERIZATION OF A BIOACTIVE COMPOSITE BASED ON POLYLACTIC ACID

[1]School of Pharmacy, NC JSC «Karaganda Medical University» (100008, Republic of Kazakhstan, Karaganda c., Gogolya str., 40; e-mail: info@qmu.kz)
[2]Department of Pharmaceutical Chemistry and Pharmacognosy, Ryazan State Medical University named after Academician I. P. Pavlov (390026, Russian Federation, Ryazan c., Vysokovoltnaya str., 9; e-mail: rzgmu@rzgmu.ru)

***Artyom Fedorovich Savelyev** – School of Pharmacy, Karaganda Medical University NC JSC; 100008, Republic of Kazakhstan, Karaganda c., Gogolya str., 40; e-mail: savelevrtm@gmail.com

Aim. Development and experimental characterization of a bioactive composite based on polylactic acid, modified with hydroxyapatite and gentamicin, for implant applications.

Materials and methods. PLA-based composites were prepared by solution mixing followed by hot pressing, with variation of the hydroxyapatite content (0 – 40 wt. %). The microstructure and distribution of the inorganic filler were analyzed using scanning electron microscopy and energy-dispersive X-ray analysis. Mechanical properties were evaluated by three-point bending tests with determination of flexural strength and Young's modulus in accordance with ISO 178:2019. Antimicrobial activity was assessed in vitro by the agar diffusion method against standard test strains of *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa,* and *Candida albicans.*

Results and discussion. The developed composite fabrication approach was shown to provide a homogeneous microstructure with a dispersed distribution of hydroxyapatite within the polymer matrix without pronounced macro-agglomeration. An increase in hydroxyapatite content resulted in a systematic decrease in flexural strength accompanied by a moderate increase in Young's modulus, reflecting the trade-off between stiffness and resistance to bending deformations characteristic of particulate-filled polymer systems. Gentamicin-containing composites exhibited pronounced antimicrobial activity against Gram-positive and Gram-negative bacteria.

Conclusions. The obtained results confirm the potential of PLA-based composites modified with hydroxyapatite and gentamicin as functional biodegradable materials for implant applications in regions with moderate mechanical loading, combining mechanical support, bioactivity, and local antimicrobial protection.

Key words: polylactic acid; hydroxyapatite; gentamicin; biodegradable composites; antimicrobial activity; mechanical properties; bone implants

INTRODUCTION

Modern medicine is facing a steady increase in the number of traumatic injuries to the musculoskeletal system, caused by both age-related degenerative changes and the high frequency of road traffic accidents, sports and domestic injuries [1, 2]. The restoration of bone tissue in severe fractures, extensive bone defects after tumor resection, or infectious complications requires the use of bone scaffolds that promote targeted regeneration of bone structures. Materials for bone implant structures must meet requirements for providing temporary mechanical support and the ability to osseointegrate [3].

In clinical practice, metal, ceramic, and polymer non-biodegradable implants are widely used to replace bone defects. Metal structures, including titanium and cobalt-chromium alloys, are highly durable and long-lasting, but their use may be accompanied by stress shielding, corrosion processes, and the need for secondary surgical intervention [4]. Ceramic materials, including hydroxyapatite-containing systems, are characterized by high biocompatibility and bioactivity, but are fragile and have limited mechanical reliability. Polymer materials provide good biocompatibility, but their biological inertness limits osseointegration processes [5]. A significant disadvantage of non-biodegradable implants is the need for their removal, which increases the trauma of treatment and the risk of complications.

The WHO notes that surgical site infections (SSIs) are among the most common hospital-acquired infections and lead to repeat hospitalizations,

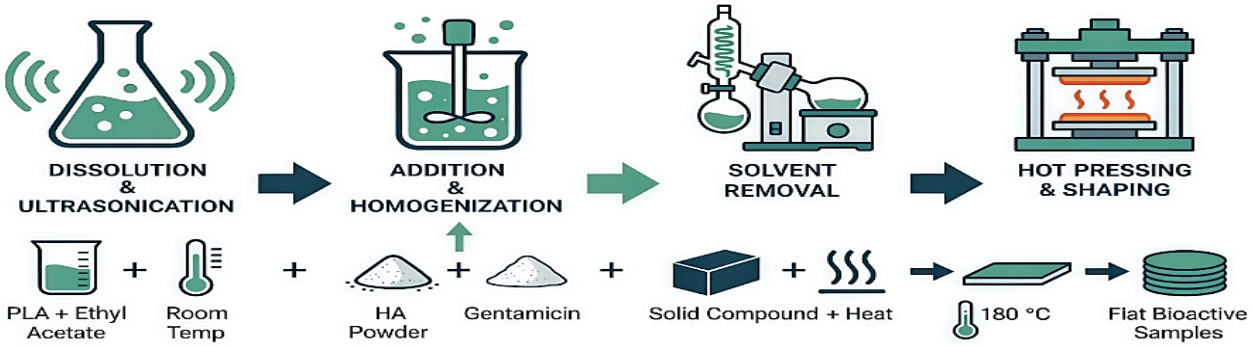


Figure 1 – Fabrication scheme of bioactive polylactic acid composite

prolonged antibiotic therapy, and increased burden on the healthcare system [6]. The incidence of SSI after orthopedic surgery averages 1–5%, and can reach 30% in cases of open fractures and revision surgery [7, 8]. In orthopedic traumatology, up to 10-15% of all surgical interventions are revision surgeries aimed at eliminating complications such as nonunion, mechanical instability, and infection; at the same time, it is after repeat interventions that the risk of infection increases 2-3 times compared to primary surgeries [9, 10]. The formation of bacterial biofilms on the surface of implanted materials plays a significant role in the development of implant-associated infections, which significantly reduces the effectiveness of systemic antibiotic therapy and contributes to the chronicity of the inflammatory process [17].

In this regard, biodegradable polymer materials capable of providing temporary mechanical support to bone tissue, followed by replacement with newly formed bone matrix, are of considerable interest. Among them, special attention is paid to polyester biopolymers, in particular polylactic acid (PLA), due to its biocompatibility, controlled degradation rate, and technological suitability for producing scaffolds of various architectures [11, 12]. At the same time, pure PLA is characterized by low bioactivity and limited osteointegration capacity, which limits its use as a standalone material for bone implant structures [13, 14].

One effective approach to improving the biological functionality of PLA is the introduction of inorganic bioactive fillers, in particular hydroxyapatite (HA). The chemical composition of hydroxyapatite is similar to that of the mineral phase of bone tissue, which determines its osteoconductive properties and ability to stimulate the adhesion and proliferation of osteogenic cells. In addition, the dispersed introduction of HA particles allows the physical and mechanical characteristics of the polymer matrix to be regulated, which is an important factor in the design of implant materials for bone tissue [15, 16].

A promising direction in the prevention of implant-associated infections is the creation of materials with local antimicrobial activity by incorporating antibiotics directly into the implant structure. Gentamicin, a broad-spectrum aminoglycoside antibiotic, is widely used in orthopedic practice and can effectively reduce the risk of bacterial colonization of the surface of implanted materials when released locally [18, 19].

Therefore, the development of biodegradable composites based on PLA modified with hydroxyapatite and gentamicin represents a promising direction in the creation of implant materials with combined osteoconductive and antimicrobial properties.

The aim of the work was to develop and experimentally characterize a bioactive composite based on polylactic acid, modified with hydroxyapatite and gentamicin, for implant applications.

MATERIALS AND METHODS

In the study, polylactic acid (PLA, NatureWorks, Ingeo 4032D, USA) was used as the polymer matrix. Bioactive additives, including hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) (Sigma-Aldrich, USA) and gentamicin sulfate (Sigma-Aldrich, USA), were used to modify the polymer matrix. Ethyl acetate (Sigma-Aldrich, USA) was used to dissolve the components.

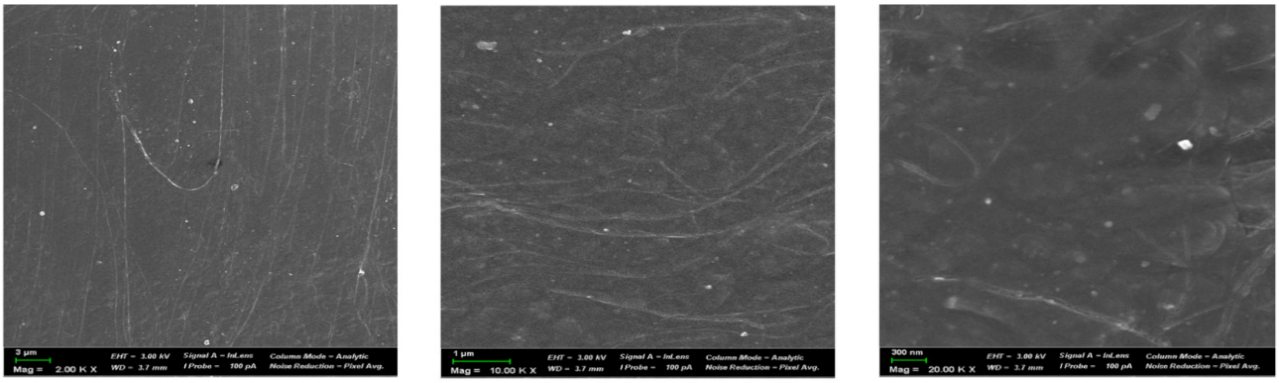
The production of a bioactive composite based on polylactic acid, hydroxyapatite, and gentamicin was carried out in several consecutive stages using solution and thermal processing methods.

In the first stage, polylactic acid was dissolved in ethyl acetate at room temperature using an ultrasonic bath until a homogeneous solution was obtained. Ultrasonic treatment was used to accelerate the dissolution of the polymer and prevent the formation of agglomerates.

In the second stage, hydroxyapatite and gentamicin were sequentially added to the resulting solution. The mixture was subjected to intensive homogenization in order to evenly distribute the inorganic filler and antibiotic in the poly-lactic acid solution.

In the third stage, the organic solvent was removed by distillation until a solid compound was obtained. The process was carried out under controlled conditions to minimize the residual solvent content.

The resulting compound was molded by hot pressing using a thermopress. Pressing was carried



(a) ×2 000 (b) ×10 000 (c) ×20 000

Figure 2 – Images of the surface of PLA-HA-Gen composite obtained using a scanning electron microscope

out at a temperature of 180 °C to obtain flat samples suitable for subsequent studies of structural, mechanical, and antimicrobial properties.

The mechanical properties of the composites were evaluated by bending tests followed by calculation of the Young's modulus. Composite samples with different hydroxyapatite contents (0%, 10%, 20%, 30%, 40%) were used for the tests.

The tests were performed at a temperature of 23°C and a relative humidity of 50% in a three-point loading mode in accordance with ISO 178:2019. The geometric parameters of the samples and the distance between the supports were selected in accordance with the requirements of the standard. The results of the tests were used to determine the flexural strength and flexural modulus of elasticity.

For each composite composition, mechanical tests were performed on at least five samples. The results obtained were used to evaluate the effect of hydroxyapatite content on the mechanical properties of composite materials.

The surface morphology of composite materials was studied using scanning electron microscopy with the Helios 5 CX SEM/FIB system (Thermo Fisher Scientific, USA). Microstructural analysis was performed at low accelerating voltages in the range of 3-5 kV, which allowed obtaining high-contrast images of the polymer sample surfaces. The working distance during imaging was maintained within 3-4 mm, and the electron probe current was approximately 100 pA. Images were recorded in secondary electron (SE) mode.

An integrated energy-dispersive X-ray analysis (EDS) system was used to evaluate the elemental composition and spatial distribution of the inorganic filler. Elemental mapping was performed on areas corresponding to the SEM observation areas. The distribution of the main elements, including carbon, oxygen, and calcium, was recorded at standard detection parameters. The maps obtained were used to analyze the uniformity of hydroxyapatite distribution in the polymer matrix volume.

The antimicrobial properties of composite materials were evaluated *in vitro* using the agar diffusion method. Standard test strains were used as model microorganisms: *Staphylococcus aureus* (ATCC 6538), *Bacillus subtilis* (ATCC 6633), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), and *Candida albicans* (ATCC 10231) were used as model microorganisms.

The initial microbial suspensions were prepared at a concentration corresponding to 0.5 on the McFarland scale and evenly applied to the surface of a dense nutrient medium. Composite samples were molded into 6 mm diameter discs and placed on the surface of the seeded agar.

Standard discs containing gentamicin (for bacterial strains) and nystatin (for *C. albicans*) were used as positive controls. Composite samples without antibiotic addition served as negative controls.

Bacterial cultures were incubated at 37 °C for 24 hours, while *C. albicans* cultures were incubated at 28 °C. At the end of the incubation period, antimicrobial activity was assessed by measuring the diameters of the zones of microorganism growth inhibition around the samples using a standard measuring template.

The following activity gradation was used to interpret the results: no antimicrobial effect – zone diameter less than 10 mm; weak activity – 10-15 mm; moderate activity – 15-20 mm; pronounced antimicrobial activity – more than 20 mm. All measurements were performed at least three times independently, and the results were presented as the mean ± standard deviation.

RESULTS AND DISCUSSION

The microstructure of the surface of composite samples based on polylactic acid modified with hydroxyapatite and gentamicin was studied using scanning electron microscopy (Fig. 2a, 2b).

SEM images of the initial surface of the composites, obtained at magnifications of ×2,000 and ×10,000, demonstrate a relatively smooth and morphologically homogeneous structure without pro-

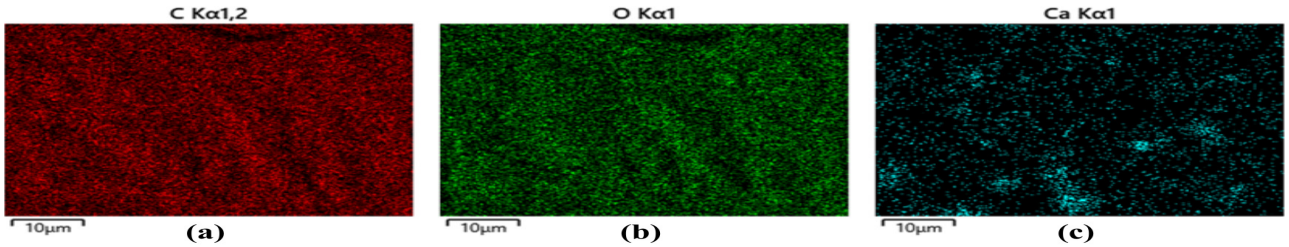


Figure 3 – EDS analysis of PLA-HA-Gen composite. (a) C Kα mapping (b) O Kα mapping, (c) Ca Kα mapping, (d) Sum EDS spectrum

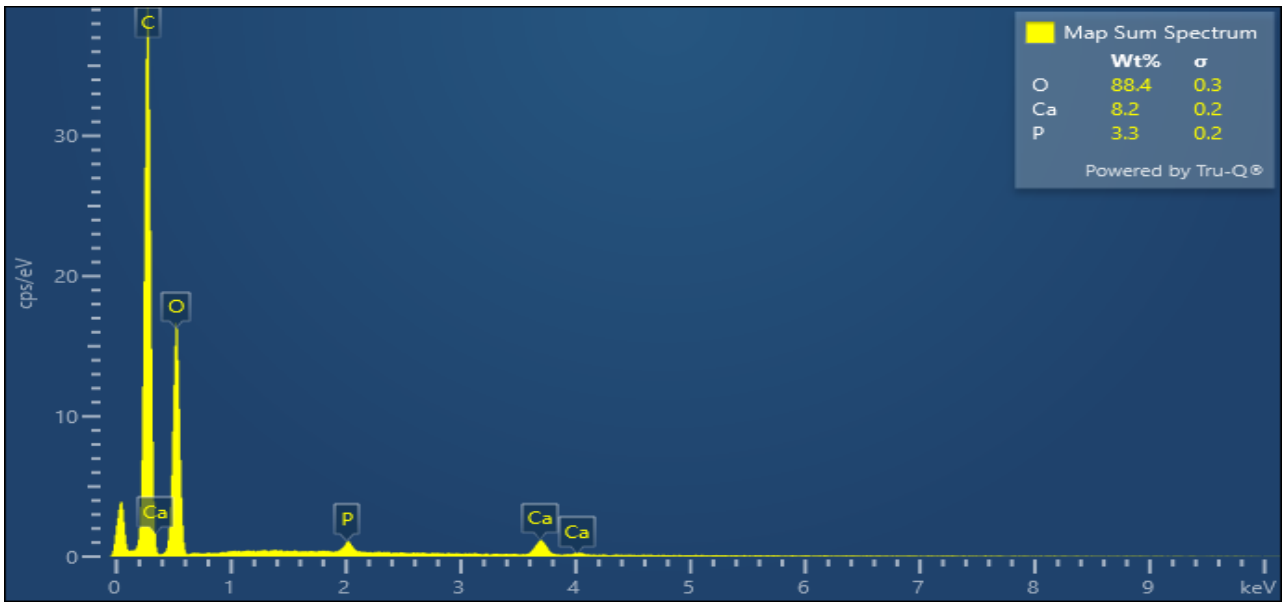


Figure 4. Total EDS spectrum of PLA-HA-Gen composite

nounced porosity and macrodefects (Fig. 2a, 2b). The observed elongated linear elements are oriented and are likely due to the processing characteristics of the material (hot pressing) rather than the formation of microcracks or disruption of the polymer matrix integrity.

Analysis of SEM images at medium magnification did not reveal any large agglomerates of micron-scale inorganic filler (Fig. 2b). The matrix contains dispersedly distributed light inclusions of submicron size, corresponding to hydroxyapatite particles. The absence of pronounced aggregation zones indicates effective dispersion of the filler during the composite production process and the formation of a structurally homogeneous material.

SEM analysis at high magnification (up to ×20,000, Fig. 2c) showed that no characteristic signs of interphase delamination, such as voids, radial microcracks, or local defects, were found at the phase boundary, indicating a sufficient level of adhesive interaction between PLA and the inorganic filler. The absence of sharp boundaries and defective areas around the particles reduces the likelihood of stress concentration and premature failure of the material under mechanical loading.

Energy dispersive X-ray analysis was performed to confirm the presence and spatial distribution of the inorganic filler. Carbon and oxygen distribution maps showed a continuous and uniform surface structure corresponding to the polymer matrix (Fig. 3a, 3b).

The distribution of calcium was finely dispersed and was not accompanied by the formation of local areas with increased concentration of the element (Fig. 2c), which confirmed the uniform dispersion of hydroxyapatite in the composite volume.

The total EDS spectrum (Fig. 4) was characterized by the dominance of carbon, which corresponded to the predominance of the polymer matrix, with the simultaneous presence of calcium and phosphorus associated with the calcium phosphate phase.

It should be noted that EDS analysis data were qualitative and semi-quantitative in nature and were used to confirm the elemental composition and distribution of the filler, rather than to evaluate its stoichiometric ratio.

In general, the results of SEM and EDS analysis indicated the formation of a homogeneous microstructure of the composite material with a uniform distribution of hydroxyapatite and the absence of pronounced interphase defects. Such microstructural organization is an important prerequisite for the formation of reproducible mechanical characteristics

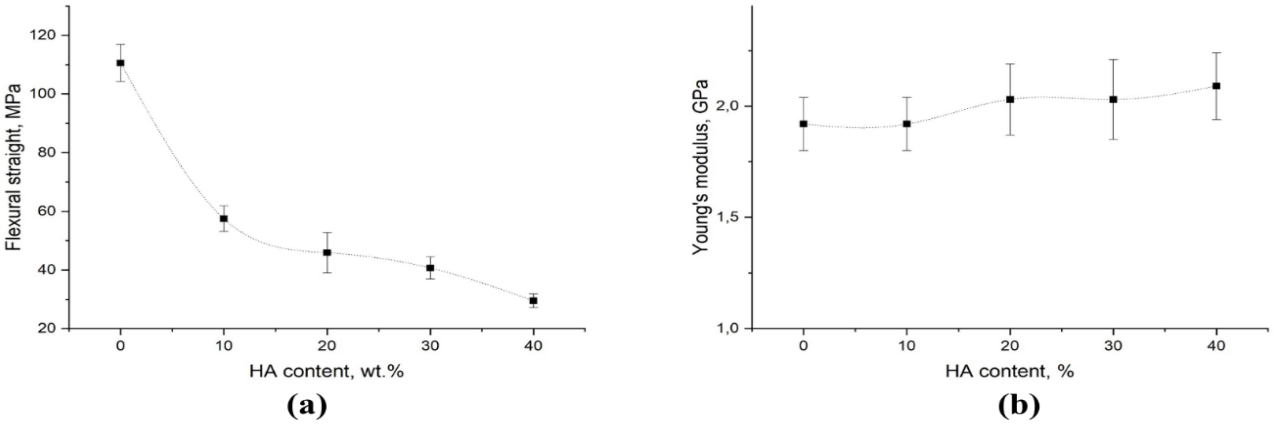


Figure 5 – Dependence of the mechanical properties of PLA composites on hydroxyapatite content: (a) flexural strength; (b) Young's modulus

and is consistent with the results of mechanical tests, as well as creating conditions for the realization of the bioactive and antimicrobial properties of the material.

The dependence of the Young's modulus and flexural strength of PLA composites on the hydroxyapatite (HA) content is shown in Fig. 5 a, b.

With an increase in HA content, there is a marked decrease in ultimate flexural strength. For unmodified PLA, the strength is 110.6±6.3 MPa. When 10% HA is added, the strength decreases to 57.5±4.4 MPa, which corresponds to a decrease of more than 40%. A further increase in HA content to 20% leads to a decrease in strength to 45.9±6.9 MPa, and at 30% and 40% HA, the values are 40.7±3.8 MPa and 29.5±2.3 MPa, respectively (Fig. 5a).

At the same time, there is a moderate increase in Young's modulus: from 1.92±0.12 GPa for PLA and PLA-HA-Gen 10% to 2.09±0.15 GPa for the composite with 40% HA, which reflects an increase in the stiffness of the material due to the introduction of a solid inorganic phase (Fig. 5b).

The observed combination of a decrease in flexural strength and an increase in elastic modulus reflects the compromise between stiffness and the ability to deform without breaking that is characteristic of dispersion-filled polymer composites. As the hydroxyapatite content increases, the proportion of the continuous polymer phase capable of plastic deformation decreases, and the probability of local stress concentration in the interphase contact areas increases. At the same time, the results of microstructural analysis indicate a dispersed distribution of hydroxyapatite particles in the polymer matrix without pronounced macroagglomeration, which reduces the likelihood of premature crack initiation by structural defects and causes a smooth change in mechanical characteristics with an increase in filler content. The uniform distribution of the rigid phase also contributes to the reproducible growth of the Young's modulus due to the more efficient involvement of hydroxyapatite particles in load transfer.

Comparison of the obtained bending strength values (29 – 58 MPa for composites with 10 – 40 wt. % HA) with the mechanical properties of cancellous (trabecular) bone tissue determined by the three-point bending method shows that the developed composites demonstrate higher strength values compared to natural cancellous bone. In particular, according to F. Mohd Ghazali et al., the average values of cancellous bone strength in three-point bending are about 17.0 MPa (with a wide range depending on the anatomical site and tissue morphology) [20]. At the same time, the values obtained are significantly lower than those of cortical bone, which indicates the potential applicability of the developed composites as biodegradable structures for temporary mechanical support and filling of bone defects in areas with limited operational load.

The antimicrobial properties of composite materials were evaluated by the agar diffusion method using standard test strains of Gram-positive and Gram-negative bacteria, as well as yeast-like fungi. Quantitative results are presented in Table 1, and

Table 1 – Growth inhibition diameters of test strains

Title	Growth inhibition diameters of test strains, mm				
	S. aureus (ATCC 6538)	*B. subtilis* (ATCC 6633)	*E. coli* (ATCC 25922)	*P. aeruginosa* (ATCC 9027)	*C. albicans* (ATCC 10231)
PLA-HA-Gen	20,0±1,0	33,0±1,4	19,3±1,4	29,7±1,0	–
PLA	8,3±1,0	6,7±0,8	6,0±1,0	7,0±1,2	–
Gentamicin sulfate	15,0±0,3	29,0±0,3	15,0±1,0	26,0±0,3	–
Nystatin	–	–	–	–	20,3±0,1

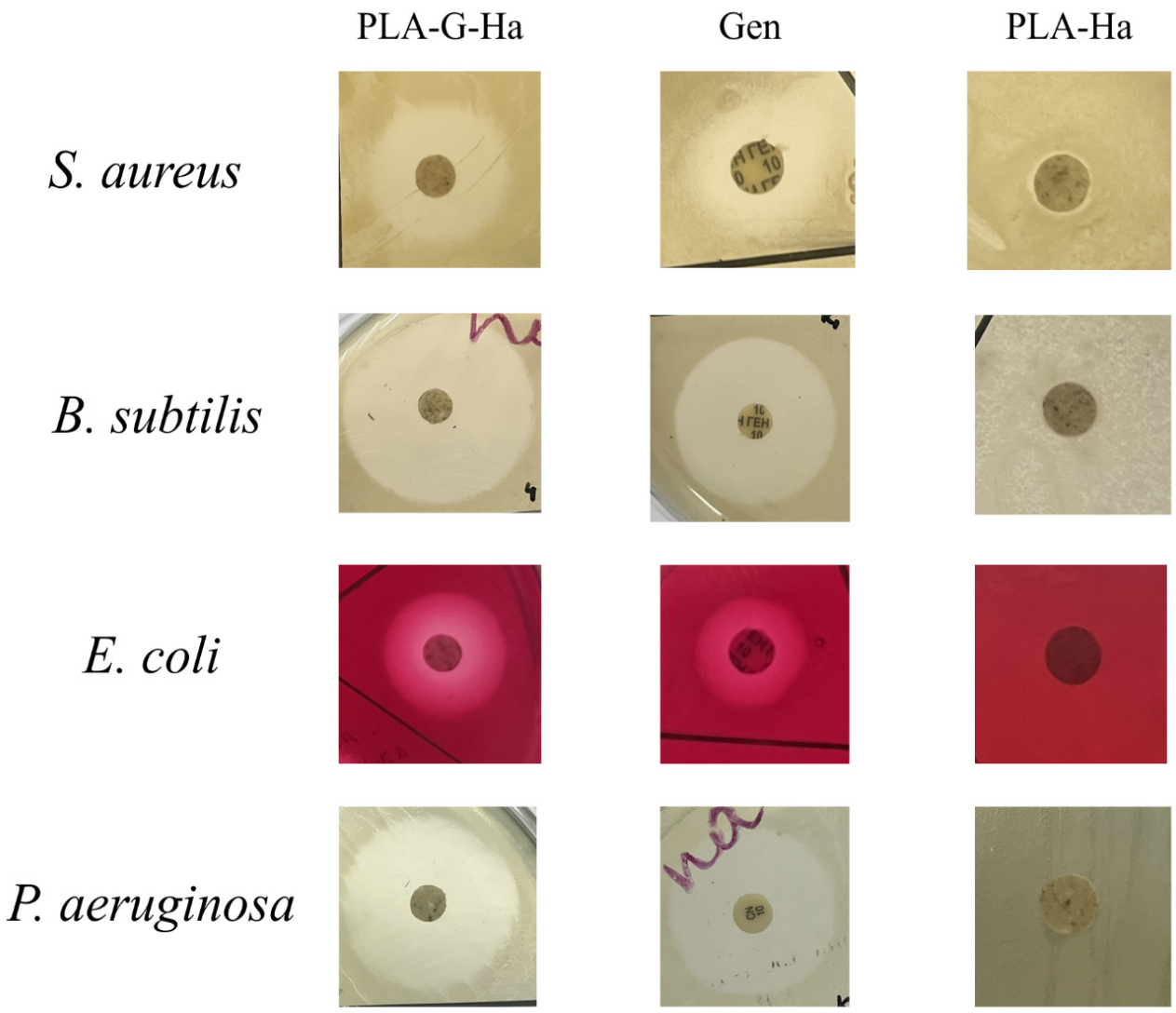


Figure 6 – Growth inhibition zones of test strains

characteristic examples of zones of inhibition of microbial growth are shown in Fig. 6.

Samples of unmodified polylactic acid did not exhibit pronounced antimicrobial activity against the test strains studied, as confirmed by the small diameters of the growth inhibition zones, which did not exceed 6-8 mm. This result indicates the biological inertness of the polymer matrix and excludes the contribution of PLA to the suppression of microbial growth.

PLA composites containing gentamicin formed pronounced growth inhibition zones for all bacterial strains studied, including *S. aureus*, *B. subtilis*, *E. coli*, and *P. aeruginosa*. For *S. aureus* and *E. coli*, the diameters of the growth inhibition zones were 20.0±1.0 mm and 19.3±1.4 mm, respectively, while for *B. subtilis* and *P. aeruginosa*, the most pronounced antimicrobial effect was observed (33.0±1.4 mm and 29.7±1.0 mm, respectively) (Table 1). The values obtained correspond to moderate and pronounced antimicrobial activity and indicate the preservation of the biological activity of gentamicin after its introduction into the polymer matrix.

A comparison of the antimicrobial effect of composite samples with that of standard gentamicin discs showed that the inhibition zones formed by the PLA composite with gentamicin are comparable and, in some cases, exceed the values for gentamicin sulfate discs (Table 1). It should be emphasized that under the conditions of the agar diffusion test, the composite material is a solid matrix from which the antibiotic diffuses into the environment, while standard discs provide a rapid initial release of the active substance. The observed comparable efficacy indicates the availability of gentamicin for diffusion from the polymer matrix volume and the functional viability of the composite system as a carrier of the antimicrobial agent.

The composite samples showed no antimicrobial activity against *C. albicans*, which is consistent with the known spectrum of action of gentamicin sulfate. The formation of pronounced growth inhibition zones exclusively for the standard antimycotic drug nystatin confirms the correctness of the methodology and the validity of the experimental conditions.

Taken together, the data obtained demonstrate that the developed PLA composite provides effective local antimicrobial activity against clinically significant bacterial strains, including P. aeruginosa, which is often associated with implant-related infections. At the same time, the polymer matrix acts as a structural carrier of the antibiotic, ensuring its availability for diffusion into the environment without loss of biological activity. Quantitative assessment of gentamicin release kinetics requires further research and is planned for subsequent stages of the work.

CONCLUSIONS

This work demonstrates the possibility of obtaining biodegradable PLA composites modified with hydroxyapatite and gentamicin, intended for use in implant structures with simultaneous support for bone regeneration and reduction of the risk of infectious complications. The developed approach ensures the formation of a homogeneous microstructure with a dispersed distribution of the calcium phosphate phase in the polymer matrix without pronounced macroagglomeration and interphase defects.

Mechanical tests revealed a regular decrease in flexural strength with an increase in hydroxyapatite content, accompanied by a moderate increase in Young's modulus. This combination reflects the compromise between stiffness and resistance to bending deformation characteristic of dispersively filled polymer systems. The obtained flexural strength values exceed those of cancellous bone tissue, which determines the prospects for their use in areas with moderate loads.

In vitro antimicrobial studies confirmed the preservation of the biological activity of gentamicin and the formation of pronounced local antimicrobial activity against clinically significant bacterial strains. Taken together, the results confirm the potential of PLA-HA-Gen composites as functional biodegradable materials for regenerative medicine and orthopedics.

Authors' contribution:

A. A. Khrustaleva, A. T. Yedrissov – concept and design of the study.

V. V. Kazantsev, S. V. Shapovalenko – collection and processing of material.

M. A. Kiikbaev, P. Yu. Rusyaeva – experimental part.

K. A. Perepelitsyna – statistical processing.

A. F. Savelyev, A. A. Khrustaleva – text writing.

D. P. Khrustalev, I. V. Losseva, I. V. Chernykh – editing.

Conflict of interest:

No conflict of interest declared.

Funding:

The study was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (Grant No. AP 26197781).

REFERENCES

1. *World Health Organization. Musculoskeletal conditions.* https://www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions

2. Gu D., Ou S., Liu G. Global burden of road injuries and their attributable risk factors from 1990 to 2021: A systematic analysis for the global burden of disease study 2021. *Prev. Med. Rep.* 2025; 53: 103051. https://doi.org/10.1016/j.pmedr.2025.103051

3. Lee S. S., Du X., Kim I., Ferguson S. J. Scaffolds for bone-tissue engineering. *Matter*. 2022; 5 (9): 2722-2759. https://doi.org/10.1016/j.matt.2022.06.003

4. Davis R., Singh A., Jackson M..J, Coelho R.T., Prakash D., Charalambous C.P., Ahmed W., da Silva L.R.R., Lawrence A.A. A comprehensive review on metallic implant biomaterials and their subtractive manufacturing. *Int. J. Adv. Manuf. Technol.* 2022; 120 (3-4): 1473-1530. https://doi.org/10.1007/s00170-022-08770-8

5. Amirtharaj Mosas K.K., Chandrasekar A.R., Dasan A., Pakseresht A., Galusek D. Recent Advancements in Materials and Coatings for Biomedical Implants. *Gels*. 2022; 8 (5): 323. https://doi.org/10.3390/gels8050323

6. *World Health Organization. Surgical site infection.* https://www.who.int/teams/integrated-health-services/infection-prevention-control/surgical-site-infection

7. Durand F., Berthelot P., Cazorla C., Farizon F., Lucht F. Smoking is a risk factor of organ/space surgical site infection in orthopaedic surgery with implant materials. *Int. Orthop.* 2013; 37 (4): 723-727. https://doi.org/10.1007/s00264-013-1814-8

8. Magalhães J.M., Zambelli R., Oliveira-Júnior O., Avelar N.C.P., Polese J.C., Leopoldino A.A.O. Incidence and associated factors of surgical site infection in patients undergoing foot and ankle surgery: a 7-year cohort study. *Foot (Edinb)*. 2024; 59: 102092. https://doi.org/10.1016/j.foot.2024.102092

9. Heinz N.R., Clement N.D., Young R.N., Duckworth A.D., White T.O., Molyneux S.G. Rate and factors associated with surgical site infection following aseptic revision fixation of orthopaedic trauma injuries. *Eur. J. Orthop. Surg. Traumatol.* 2023; 33 (8): 3511-3517. https://doi.org/10.1007/s00590-023-03573-3

10. Liu H., Wang Y., Xing H., Chang Z., Pan J. Risk factors for deep surgical site infections following orthopedic trauma surgery: a meta-analysis and systematic review. *J. Orthop. Surg. Res.* 2024; 19 (1): 811. https://doi.org/10.1186/s13018-024-05299-2

11. da Silva D., Kaduri M., Poley M., Adir O., Krinsky N., Shainsky-Roitman J., Schroeder A. Bio-

compatibility, biodegradation and excretion of polylactic acid (PLA) in medical implants and theranostic systems. *Chemical Engineering Journal*. 2018; 340: 9-14. https://doi.org/10.1016/j.cej.2018.01.010

12. Hussain M., Khan S. M., Shafiq M., Abbas N. A review on PLA-based biodegradable materials for biomedical applications. *Giant*. 2024; 18: 100261. https://doi.org/10.1016/j.giant.2024.100261

13. Yang Z., Yin G., Sun S., Xu P. Medical applications and prospects of polylactic acid materials. *iScience*. 2024; 27 (12): 111512. https://doi.org/10.1016/j.isci.2024.111512

14. Khrustaleva A., Khrustalev D., Yedrissov A., Rusyaeva P., Savelyev A., Kiikbayev M., Perepelitsyna K., Kazantsev V. Bioactive Polymer Composites for 3D-Printed Bone Implants: A Systematic Review. *Polymers (Basel)*. 2026; 18 (3): 397. https://doi.org/10.3390/polym18030397

15. Liu W., Cheong N., He Z., Zhang T. Application of Hydroxyapatite Composites in Bone Tissue Engineering: A Review. *J. Funct. Biomater.* 2025; 16 (4): 127. https://doi.org/10.3390/jfb16040127

16. Subramaniyan M., Karuppan S., Helaili S., Ahmad I. Structural, mechanical, and in-vitro characterization of hydroxyapatite-loaded PLA composites. *Journal of Molecular Structure*. 2024; 1306: 137862. https://doi.org/10.1016/j.molstruc.2024.137862

17. Rozis M., Evangelopoulos D.S., Pneumaticos S.G. Orthopedic Implant-Related Biofilm Pathophysiology: A Review of the Literature. *Cureus*. 2021; 13 (6): e15634. https://doi.org/10.7759/cureus.15634

18. Rozis M., Evangelopoulos D.S., Pneumaticos S.G. Orthopedic Implant-Related Biofilm Pathophysiology: A Review of the Literature. *Cureus*. 2021; 13 (6): e15634. https://doi.org/10.7759/cureus.15634

19. Kennedy D.G., O'Mahony A.M., Culligan E.P., O'Driscoll C.M., Ryan K.B. Strategies to Mitigate and Treat Orthopaedic Device-Associated Infections. *Antibiotics (Basel)*. 2022; 11 (12): 1822. https://doi.org/10.3390/antibiotics11121822

20 Mohd Ghazali F., Syahrom A. Mechanical behaviour of cancellous bone: compression and three-point bending test. *Malaysian Journal of Fundamental and Applied Sciences*. 2022; 18: 295-303. https://doi.org/10.11113/mjfas.v18n3.2274

TRANSLITERATION

1. *World Health Organization. Musculoskeletal conditions*. https://www.who.int/news-room/fact-sheets/detail/musculoskeletal-conditions

2. Gu D., Ou S., Liu G. Global burden of road injuries and their attributable risk factors from 1990 to 2021: A systematic analysis for the global burden of disease study 2021. *Prev. Med. Rep.* 2025; 53: 103051. https://doi.org/10.1016/j.pmedr.2025.103051

3. Lee S. S., Du X., Kim I., Ferguson S. J. Scaffolds for bone-tissue engineering. *Matter*. 2022; 5 (9): 2722-2759. https://doi.org/10.1016/j.matt.2022.06.003

4. Davis R., Singh A., Jackson M..J, Coelho R.T., Prakash D., Charalambous C.P., Ahmed W., da Silva L.R.R., Lawrence A.A. A comprehensive review on metallic implant biomaterials and their subtractive manufacturing. *Int. J. Adv. Manuf. Technol.* 2022; 120 (3-4): 1473-1530. https://doi.org/10.1007/s00170-022-08770-8

5. Amirtharaj Mosas K.K., Chandrasekar A.R., Dasan A., Pakseresht A., Galusek D. Recent Advancements in Materials and Coatings for Biomedical Implants. *Gels*. 2022; 8 (5): 323. https://doi.org/10.3390/gels8050323

6 *World Health Organization. Surgical site infection.* https://www.who.int/teams/integrated-health-services/infection-prevention-control/surgical-site-infection

7. Durand F., Berthelot P., Cazorla C., Farizon F., Lucht F. Smoking is a risk factor of organ/space surgical site infection in orthopaedic surgery with implant materials. *Int. Orthop.* 2013; 37 (4): 723-727. https://doi.org/10.1007/s00264-013-1814-8

8. Magalhães J.M., Zambelli R., Oliveira-Júnior O., Avelar N.C.P., Polese J.C., Leopoldino A.A.O. Incidence and associated factors of surgical site infection in patients undergoing foot and ankle surgery: a 7-year cohort study. *Foot (Edinb).* 2024; 59: 102092. https://doi.org/10.1016/j.foot.2024.102092

9. Heinz N.R., Clement N.D., Young R.N., Duckworth A.D., White T.O., Molyneux S.G. Rate and factors associated with surgical site infection following aseptic revision fixation of orthopaedic trauma injuries. *Eur. J. Orthop. Surg. Traumatol.* 2023; 33 (8): 3511-3517. https://doi.org/10.1007/s00590-023-03573-3

10. Liu H., Wang Y., Xing H., Chang Z., Pan J. Risk factors for deep surgical site infections following orthopedic trauma surgery: a meta-analysis and systematic review. *J. Orthop. Surg. Res.* 2024; 19 (1): 811. https://doi.org/10.1186/s13018-024-05299-2

11. da Silva D., Kaduri M., Poley M., Adir O., Krinsky N., Shainsky-Roitman J., Schroeder A. Biocompatibility, biodegradation and excretion of polylactic acid (PLA) in medical implants and theranostic systems. *Chemical Engineering Journal*. 2018; 340: 9-14. https://doi.org/10.1016/j.cej.2018.01.010

12. Hussain M., Khan S. M., Shafiq M., Abbas N. A review on PLA-based biodegradable materials for biomedical applications. *Giant*. 2024; 18: 100261. https://doi.org/10.1016/j.giant.2024.100261

13. Yang Z., Yin G., Sun S., Xu P. Medical applications and prospects of polylactic acid materials. *iScience*. 2024; 27 (12): 111512. https://doi.org/10.1016/j.isci.2024.111512

14. Khrustaleva A., Khrustalev D., Yedrissov A., Rusyaeva P., Savelyev A., Kiikbayev M., Pere-

pelitsyna K., Kazantsev V. Bioactive Polymer Composites for 3D-Printed Bone Implants: A Systematic Review. *Polymers (Basel).* 2026; 18 (3): 397. https://doi.org/10.3390/polym18030397

15. Liu W., Cheong N., He Z., Zhang T. Application of Hydroxyapatite Composites in Bone Tissue Engineering: A Review. *J. Funct. Biomater.* 2025; 16 (4): 127. https://doi.org/10.3390/jfb16040127

16. Subramaniyan M., Karuppan S., Helaili S., Ahmad I. Structural, mechanical, and in-vitro characterization of hydroxyapatite-loaded PLA composites. *Journal of Molecular Structure*. 2024; 1306: 137862. https://doi.org/10.1016/j.molstruc.2024.137862

17. Rozis M., Evangelopoulos D.S., Pneumaticos S.G. Orthopedic Implant-Related Biofilm Pathophysiology: A Review of the Literature. *Cureus*. 2021; 13 (6): e15634. https://doi.org/10.7759/cureus.15634

18. Rozis M., Evangelopoulos D.S., Pneumaticos S.G. Orthopedic Implant-Related Biofilm Pathophysiology: A Review of the Literature. *Cureus*. 2021; 13 (6): e15634. https://doi.org/10.7759/cureus.15634

19. Kennedy D.G., O'Mahony A.M., Culligan E.P., O'Driscoll C.M., Ryan K.B. Strategies to Mitigate and Treat Orthopaedic Device-Associated Infections. *Antibiotics (Basel)*. 2022; 11 (12): 1822. https://doi.org/10.3390/antibiotics11121822

20 Mohd Ghazali F., Syahrom A. Mechanical behaviour of cancellous bone: compression and three-point bending test. *Malaysian Journal of Fundamental and Applied Sciences*. 2022; 18: 295-303. https://doi.org/10.11113/mjfas.v18n3.2274

Received 08.10.2025
Sent for revision 14.11.2025
Accepted 29.12.2025
Published online 30.06.2026

А. А. Хрусталева[1], А. Т. Едрисов[1], Д. П. Хрусталев[1], И. В. Черных[2], И. В. Лосева[1], А. Ф. Савельев[1], В. В. Казанцев[1], М. А. Киикбаев[1], П. Ю. Русяева[1], К. А. Перепелицына[1], С. В. Шаповаленко[1]*

РАЗРАБОТКА И ХАРАКТЕРИСТИКА БИОАКТИВНОГО КОМПОЗИТА НА ОСНОВЕ ПОЛИМОЛОЧНОЙ КИСЛОТЫ

[1]Школа фармации, НАО «Карагандинский медицинский университет» (100008, Республика Казахстан, г. Караганда, ул. Гоголя, 40; e-mail: info@qmu.kz)
[2]Кафедра фармацевтической химии и фармакогнозии, Федеральное Государственное Бюджетное Образовательное учреждение Высшего Образования «Рязанский государственный медицинский университет имени академика И. П. Павлова» Министерства здравоохранения Российской Федерации (390026, Российская Федерация, г. Рязань, ул. Высоковольтная, д. 9; e-mail: rzgmu@rzgmu.ru)

***Артём Федорович Савельев** – Школа фармации, НАО «Медицинский университет Караганды»; 100008, Республика Казахстан, г. Караганда, ул. Гоголя, 40; e-mail: savelevrtm@gmail.com

Цель исследования. Разработка и экспериментальная характеристика биоактивного композита на основе полимолочной кислоты, модифицированного гидроксиапатитом и гентамицином, для имплантационных применений.

Материалы и методы. Композиты на основе PLA получали методом растворного смешения с последующим горячим прессованием с варьированием содержания гидроксиапатита (0 – 40 мас. %). Микроструктуру и распределение неорганического наполнителя анализировали методами сканирующей электронной микроскопии и энергодисперсионного рентгеновского анализа. Механические свойства оценивали в испытаниях на изгиб в режиме трёхточечного нагружения с расчетом прочности при изгибе и модуля Юнга в соответствии со стандартом ISO 178:2019. Антимикробную активность оценивали *in vitro* методом диффузии в агар в отношении стандартных тест-штаммов *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa* и *Candida albicans*.

Результаты и обсуждение. Показано, что разработанный подход к получению композитов обеспечивает формирование однородной микроструктуры с дисперсным распределением гидроксиапатита в полимерной матрице без выраженной макроагломерации. Увеличение содержания гидроксиапатита приводит к закономерному снижению прочности при изгибе при одновременном умеренном росте модуля Юнга, что отражает компромисс между жесткостью и сопротивлением изгибным деформациям, характерный для дисперсно-наполненных полимерных систем. Композиты, содержащие гентамицин, демонстрируют выраженную антимикробную активность в отношении грамположительных и грамотрицательных бактерий.

Выводы. Результаты исследования подтверждают потенциал PLA-композитов, модифицированных гидроксиапатитом и гентамицином, в качестве функциональных биоразлагаемых материалов

для имплантационных применений в зонах с умеренной эксплуатационной нагрузкой, сочетающих механическую поддержку, биоактивность и локальную антимикробную защиту.

Ключевые слова: полимолочная кислота; гидроксиапатит; гентамицин; биоразлагаемые композиты; антимикробная активность; механические свойства; костные импланты

А. А. Хрусталева[1], А. Т. Едрисов[1], Д. П. Хрусталев[1], И. В. Черных[2], И. В. Лосева[1], А. Ф. Савельев[1], В. В. Казанцев[1], М. А. Киикбаев[1], П. Ю. Русяева[1], К. А. Перепелицына[1], С. В. Шаповаленко[1]*

ПОЛИЛАКТИКАЛЫҚ ҚЫШҚЫЛ НЕГІЗІНДЕГІ БИОАКТИВТІ КОМПОЗИТТІҢ ДАМУЫ ЖӘНЕ СИПАТТАМАСЫ

[1]Фармация мектебі, «Қарағанды медицина университеті» КеАҚ (100008, Қазақстан Республикасы, Қарағанды қ., Гоголь к-сі, 40; e-mail: info@qmu.kz)
[2]Фармацевтік химия және фармакогнозия кафедрасы, Федералдық Мемлекеттік Бюджеттік Жоғары Білім беру мекемесі «академик И. П. Павлов атындағы Рязань мемлекеттік медицина университеті» Ресей Федерациясы денсаулық сақтау министрлігі (390026, Ресей Федерациясы, Рязань қ., Высоковольтная к-сі, 9; e-mail: rzgmu@rzgmu.ru)

***Артём Федорович Савельев** – Фармация мектебі, «Қарағанды медицина университеті» КеАҚ; 100008, Қазақстан Республикасы, Қарағанды қ., Гоголь к-сі, 40; e-mail: savelevrtm@gmail.com

Зерттеудің мақсаты. Имплантациялық қолдануға арналған гидроксиапатитпен және гентамицинмен модификацияланған полилактикалық қышқыл негізіндегі биоактивті композитті әзірлеу және эксперименттік сипаттау.

Материалдар және әдістер. PLA негізіндегі композиттер ерітінділік араластыру әдісімен, кейіннен гидроксиапатит мөлшерін (0 – 40 мас. %) өзгерте отырып, ыстық престеу арқылы алынды. Микроқұрылым мен бейорганикалық толтырғыштың таралуы сканерлеуші электрондық микроскопия және энергодисперсиялық рентгендік талдау әдістерімен зерттелді. Механикалық қасиеттері ISO 178:2019 стандартына сәйкес үш нүктелі жүктеу режиміндегі иілу сынақтарында иілу беріктігі мен Юнг модулін есептеу арқылы бағаланды. Антимикробтық белсенділік in vitro жағдайда агарға диффузия әдісімен *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa* және *Candida albicans* стандартты тест-штамдарына қатысты бағаланды.

Нәтижелер және талқылау. Композиттерді алудың әзірленген тәсілі полимерлік матрицада гидроксиапатиттің айқын макроагломерациясыз дисперсті таралуымен біртекті микроқұрылымның қалыптасуын қамтамасыз ететіні көрсетілді. Гидроксиапатит мөлшерінің артуы иілу беріктігінің заңды түрде төмендеуіне және Юнг модулінің бірқалыпты өсуіне алып келеді, бұл дисперсті толтырылған полимерлік жүйелерге тән қаттылық пен иілу деформацияларына төзімділік арасындағы компромисті көрсетеді. Құрамында гентамицин бар композиттер грамоң және грамтеріс бактерияларға қатысты айқын антимикробтық белсенділік көрсетті.

Қорытындылар. Алынған нәтижелер гидроксиапатитпен және гентамицинмен модификацияланған PLA-композиттердің механикалық қолдауды, биоактивтілікті және жергілікті антимикробтық қорғанысты үйлестіретін, пайдалану жүктемесі орташа аймақтардағы имплантациялық қолдануға арналған функционалдық биоыдырайтын материалдар ретіндегі әлеуетін растайды.

Кілт сөздер: полилактикалық қышқыл; гидроксиапатит; гентамицин; биоыдырайтын композиттер; антимикробтық белсенділік; механикалық қасиеттер; сүйек имплanттары