veloped several synthetic approaches to achieve this (Figure 2).

We started with vanillin glycosylation (Figure 2-a) to obtain vanillinoside **3** which was further reducted to the alcohol **4** (Figure 2-b) by $NaBH_4$ in the presence of CTMAB (cetyltrimethylammoniumbromide) as phase-transfer catalyst. Then this glycoside **4** was treated in three different ways to obtain corresponding esters: with benzoyl and acetylated vanilloyl and caffeoyl chlorides and pyridine (Figure 2-c); with acetylated benzoic, caffeic and vanillic acids in DCC/DMAP system (Figure 2-d); with application of an Appel reaction to and further acylation pf the bromide with the same acids in the presence of K_2CO_3 (Figure 2-e). The final deacetylation was carried out in selective system of $HCl/EtOH/CHCl_3$ (1 : 3 : 1 vol.) [6] giving products **5a-c** (Figure 2-f).

The aldehyde **3** was also deacetylated with sodium methylate (Figure 2-g). Deprotected carbohydrate then was exposed to esterification with benzoyl chloride. As it could be expected, primary hydroxyl 6-OH showed the highest reactivity giving the ester **6** in yields of approximately 35 % though with several by-products whilst the conversion was not complete.

The reported study was funded by RFBR, project number 19-31-27001.

References

1. *Lindroth R.L., et al. // Oecologia, 1987. – №70. – P. 144.*
2. *Argyropoulou A., et. al. // Phyther. Res., 2012. – №26. – P. 1800–1806.*
3. *Wang Q.-H., et.al. // J. Mol. Struct., 2014. – №1074. – P. 284–288.*
4. *Rayavarapu S., et.al. // Sci. Rep., 2017. – №7. – P. 8309.*
5. *Itoh A., et. al. // Phytochemistry, 2008. – №69. – P. 1208–1214.*
6. *Stepanova E.V., et al. // Carbohydr. Res., 2014. – №388. – 3. – 105–111.*

FABRICATION OF BACTERICIDAL 3D GRADIENT MATERIALS BASED ON HYDROXYAPATITE

V.T. Badretdinova[1], T.A. Serykh[1]
Scientific supervisor – PhD, associate research professor S.A. Ulasevich[1];
PhD associate research professor A.P. Chernova[2]

[1]ITMO University
197101, Russia, St Petersburg, Lomonosova St. 9

[2]National Research Tomsk Polytechnic University
634050, Russia, Tomsk, 30 Lenin Avenue, badretdinova@infochemistry.ru

Reparation of bone tissue is a topical medical problem. It is so significant due to the spread of bone tissue pathological conditions, caused, in particular, as a result of trauma, tumor (primary and metastatic) lesions, age-related osteoporosis [1]. One of the rational ways to solve the problem is using the synthetic biocompatible materials. The most promising materials are based on calcium phosphates, which are close in composition to the mineral component of bone tissue [2]. The use of chemically synthesized calcium phosphate materials opens up more and more possibilities for eliminating bone defects. Biocompatible and bioactive hydroxyapatite (HA) can be easily integrated into bone tissue and adjacent tissue areas. In addition, HA is able to interact with young bone tissue cells – osteoblasts, positively affecting their growth and division. [3].

In medicine, there is a need for osteoplastic materials, including medicinal substances, which allow targeted action on the identified pathogens. Local delivery of antibacterial substances allows to reduce the toxic effect on the patient, to use antibiotics in smaller quantities than orally, and to deliver stable constant concentrations.

In this regard, the goal of this work is to create calcium phosphate materials that include medicinal substances that will inhibit the growth of bacteria. Such material will have antibacterial properties. First of all, we made gradient samples with calcium phosphate, varying the concentration of antibiotics. Tetracycline and gentamicin were used as model antibiotics. Samples were prepared in six-well plates. We also made a control sample consisting of calcium phosphate without antibiotics. Next, we investigated the biocompatible properties of structures using the C2C12 cell line. The medium was DMEM containing 1 g/L of glucose with the addition of penicillin 100 EU/mL and 10 % bovine serum. The sample medium was changed every day. The images of cells were made using an optical microscope "Leica DMi8", and the number of cells was counted by ImageJ program. The optical images below are taken in different parts of the Petri dishes and show cell growth on periodically-ordered calcium phosphate patterns (Figure 1).

As a result, the biocompatibility of the calcium phosphate samples was evaluated. It was found that the highest concentration of cells is in the center of the Liesegang rings and on the rings. Cells density is higher in Gentamicin samples, while tetracycline is more toxic to growth. In addition, high concentrations of tetracycline and gentamicin do not inhibit cell growth. Hence, such materials can be used in medicine, to inhibit bacteria and local drug delivery, as this will facilitate the treatment of patients with bone defects.

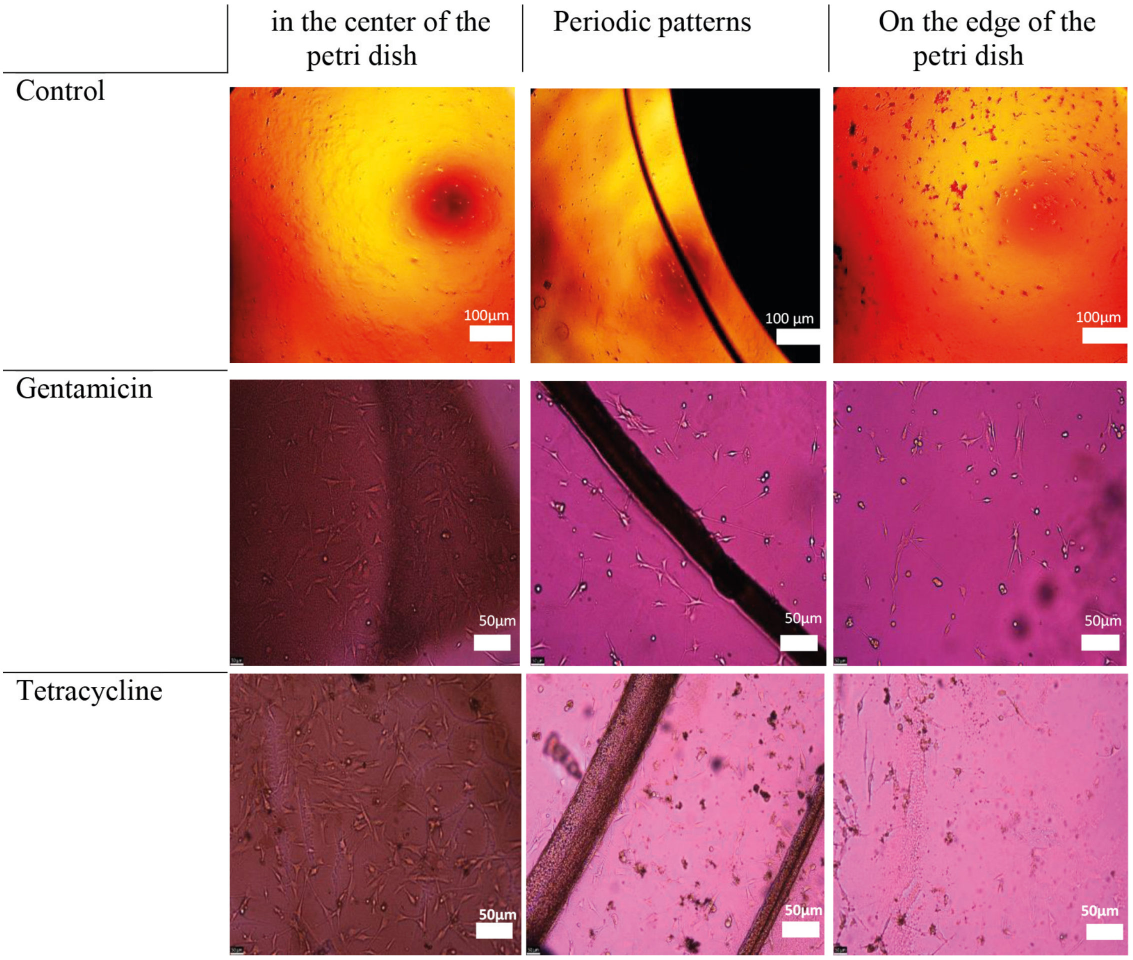

Fig. 1. *Optical images of the cells grown on periodically-ordered calcium phosphate patterns*

References

1. *Campbell A.A. Bioceramics for implant coatings. Materials Today, 6 (11), 26–30. (2003).*
2. *Lotsari A. Transformation of amorphous calcium phosphate to bone-like apatite. Nature Communication 9, 4170 (2018).*
3. *Dorozhkin S.V. Biological and medical significance of calcium phosphates. Angew. Chem. Int. Ed. 41, 3130–3146. (2002).*