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FABRICATION OF BACTERICIDAL 3D GRADIENT MATERIALS BASED ON HYDROXYAPATITE

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The development of biocompatible materials with an antibacterial effect has been going on for a long time.. This problem is relevant, since it will affect the healing process. The developed material will contain antibiotics or other anti-inflammatory substances.

Introduction. Bone infections remain a serious problem in orthopedics, traumatology, and surgery. They usually cause the long-term, expensive antimicrobial therapy and sometimes even surgical treatment.

Application of antibacterial agents via new technologies has improved the treatment of patients with various bone diseases. It became possible to create high local concentrations of antibacterial drugs without systemic toxic effects when drugs are taken orally. This material, besides biocompatibility and porosity, should not be rejected by the patient's immune system, simply established, modified, and removed from the tissues and gives stable concentrations of the drug.

In this regard, the hydroxyapatite (HA), a biologically active material, is of interest due to its surface-active properties, and a bone-like crystal structure. Currently, biocompatible chemically synthesized HA is widely used in bone treatment and controlled drug release. The addition of antibiotics to HA is used to inhibit the growth of bacteria, so the fabrication of composite materials based on HA with antibacterial properties could be a solution to existing bone defects.

Main part. The aim of the research is to fabricate the antibacterial material possessing enhanced biocompatible properties. For these experiments, we decided to obtain the gradient structure of calcium-phosphates and study the biocompatible properties using C2C12 cell line. Deposition of calcium phosphate in a form of periodic patterns allows to create the gradient structure. The center and rings close to the center are made of HA whereas the distant rings formed with lower amount of Ca^{2+} are made of tricalcium phosphate and acidic phosphates. Using this system, we can estimate the biocompatibility of the different calcium phosphate phases with loaded antibiotic via the one sample. We also may design not only the material gradient but also the antibiotic gradient.

The gentamicin and tetracycline were used as model antibiotics. The experiments were carried out in 6-well plates with different antibiotic concentrations. The samples with calcium-phosphate rings without antibiotics were taken as a control ones. A DMEM medium containing 1 g / L of glucose with the addition of 1% antibiotics (penicillin 100 EU / mL and 100 mg/mL streptomycin), 10% fetal bovine serum was used as a medium. The cells were seeded at a density of $5 \cdot 10^5$ cells/mL The medium was changed every other day. The cells were calculated using ImageJ program.

Conclusions. As a result, the highest cell concentration was observed on the calcium phosphate rings in the center of the Petri dish and on the rings. The high concentration of the antibiotic (ca. 10^{-4} mol/mL) does not inhibit the cell growth drastically. The antibacterial activity will be further studied. These materials could find its application in bone regenerative medicine. significantly improve the effectiveness and quality of treatment.

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