

**OBTAINING SYNTHETIC HYDROXYAPATITE FOR THE
FORMATION OF BIO-COATINGS WITH LOCAL DRUG
DELIVERY**

Biocompatible materials solve many problems in medicine such as materials for endoprostheses in traumatology and orthopedics, filling materials in dentistry, implants in maxillofacial surgery, medical and cosmetic products in cosmetology and pharmacology [1]. An important area is the design of biomaterials based on hydroxyapatite (HA) to replace damaged bone tissue, since HA is the main inorganic component of human and animal bone and dental tissue. The use of chemically synthesized HA provides wide possibilities in the presence of various bone tissue defects, as it promotes rapid reparative regeneration of the surrounding tissue. Now, it is known from the literature that HA is successfully used as a composite biomaterial, and calcium-phosphate ceramics in pure form in the treatment of patients [2].

Hydroxyapatite has all the necessary properties for using it as a bio-coating, which must be biologically compatible with body tissues, corrosion-resistant in the biological environment and have high adhesive strength with the base material. In addition, local drug delivery will allow to effectively use smaller dosages of the administered drug, reducing the load on the liver and kidneys of the body, while the patient does not need to worry about dosages and schedules of medication. In addition, it is much easier to prevent inflammation at an early stage [3].

In this regard, the aim of the work is to obtain biocompatible materials with loaded active substances on titanium medical implants from calcium phosphate systems and to study the structure of the obtained coatings. A water solution of agar was prepared with the addition of sodium phosphate and active substances, this solution was heated to 65-75°C. The mixture was continuously stirred and after complete dissolution of the agar, the solution was poured into plastic tubes with a length of 20 cm and Petri dishes with a diameter of 100 mm. Gentamicin, tetracycline and brilliant green were used as active substances. Then, calcium chloride solution was added to the solidified substance and the growth of Liesegang rings was observed.

Figure 1 shows the Liesegang rings when brilliant green is added to the system and the concentration of the active substance is varied 0.01

nmol/L (test tube №1), 0.01 mmol/L (test tube №2), 1 mmol/L (test tube №3).

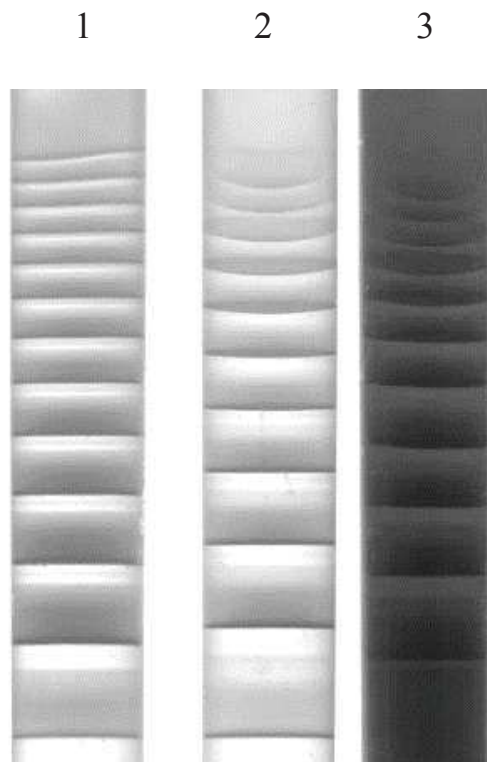


Fig. 1 - Photo of periodically ordered Liesegang rings obtained by precipitation of calcium phosphates in an agar matrix loaded with sodium phosphate at a concentration of 0.02 mol /L and brilliant green at a concentration of 0.01 nmol/L (test tube №1), 0.01 mmol / L (test tube №2), 1 mmol / L (test tube №3)

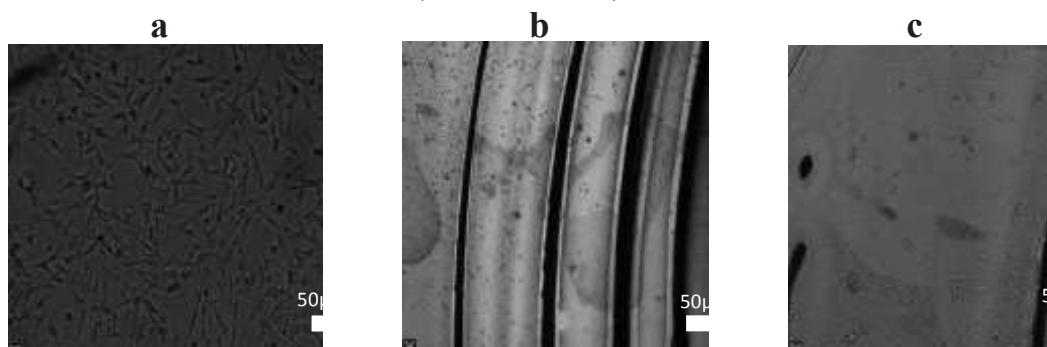


Fig. 2 - Cell growth on the periodic patterns of calcium phosphates with loaded brilliant green at a concentration of 1 mmol/L in a Petri dish in the different parts of the sample: a) in the center of the petri dish, b) Liesegang rings, c) On the edge of the Petri dish

The distribution of calcium ions along the diffusion path in Liesegang rings with active substances has been studied using Alizarin Red staining. The biocompatibility of substances at the cellular level was investigated using C2C12 cells. The cells were counted in the center of the

Liesegang rings, on the Liesegang rings, on the edge of the sample. The addition of antibiotics in the system does not interfere with cell growth. The spacing coefficient (p) of the systems was calculated by varying the concentrations of active substances and agar. It was found that an increase of the active substance's concentration leads to the increase of the p -value. The p -value decreases with an increase in the concentration of agar.

In the future, the physical and chemical properties such as porosity, specific surface area, phase composition and biosorption rate of the obtained samples will be investigated.

Authors acknowledge RSF grant no. 19-79-10244 for the financial support. ITMO Fellowship and Professorship Program 08-08 is acknowledged for infrastructural support.

REFERENCES

1. Dorozhkin S. V. Biological and medical significance of calcium phosphates / Dorozhkin S. V., Epple M. *Angew. Chem. Int. Ed.* 41, 3130–3146, 2002.

2. Lotsari A., Rajasekharan A. K., Halvarsson M., Andersson M. Transformation of amorphous calcium phosphate to bone-like apatite / Lotsari A., Rajasekharan A. K., Halvarsson M., Andersson, M. *Nat. Comm.* 9, 4170, 2018.

3. Habraken W. Calcium phosphates in biomedical applications: materials for the future? / Habraken W., Habibovic P., Epple M., Bohner M. *Mater. Today* 19, 69–87, 2016.