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PCL/CHLORAMPHENICOL/HEXAFLUORO-2-PROPANOL SOLUTION FOR FABRICATION OF VARIOUS BIOACTIVE DRUG DELIVERY MATERIALS

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ПРИМЕНЕНИЕ РАСТВОРОВ НА ОСНОВЕ СМЕСИ ПКЛ/ХЛОРАМФЕНИКОЛ/ГЕКСАФТОРИЗОПРОПАНОЛ ДЛЯ СОЗДАНИЯ РАЗЛИЧНЫХ МАТЕРИАЛОВ ДЛЯ ДОСТАВКИ ЛЕКАРСТВ

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Аннотация. *В работе рассмотрен вопрос создания стабильного раствора поли - (ε-капролактона) (ПКЛ) в гексафторизопропаноле (ГФИП) с сорастворенным антибактериальным препаратом – хлорамфениколом и формирования, с его помощью, функциональных материалов. Получены растворы с соотношением ПКЛ:ГФИП – 2 масс.% и хлорамфеникол: ПКЛ 5, 15 и 25 масс.% соответственно. Растворы применены для пропитки кальций-фосфатных покрытий МДО-покрытий и для формирования скаффолдов методом электроспиннинга. Показано, что использование разработанных растворов позволяет успешно получить как однородные пленки на поверхности кальций-фосфатов, так и волокнистые скаффолды с нормальным распределением волокон по диаметрам. Произведен подбор оптимальных параметров электроспиннинга и продемонстрирована необходимость корректировки соотношения ПКЛ:ГФИП для повышения эффективности процесса накопления волокон.*

Introduction Polymers are promising materials for production of the local drug delivery and controlled release bioactive materials. Those polymer-based matrices can be obtained by various techniques, and production from a melt solution is one of the most popular one. In this work we present results of using different approaches to form a biodegradable antibacterial coating on the surface of metal implant: film formation and electrospinning. In our previous work [1], we have already demonstrated the effectiveness of plasma electrolytic oxidation (PEO) coatings impregnation with a polymeric solution based on poly (ε-caprolactone) in order to improve coating elasticity and realization of a sustained antibacterial effect for 7 days [2]. The aim of this work was to find the appropriate parameters of electrospinning the obtained PCL/Chloramphenicol/Hexafluoro-2-propanol solutions and compare the structures of obtained by impregnation films and electrospun scaffolds.

Research methods. Materials. PCL (Mw = 80,000) was purchased from Sigma–Aldrich (St. Louis, MO), Hexafluoroisopropanol (HFIP) (Ekos-1, Russia) was used as a solvent for preparation of the spinning solutions. Chloramphenicol powder (Pharmstandart, Russia) was used as purchased. Phosphate Buffer Saline (PBS, pH 7.4) used for drug release modelling was purchased from Biolot (Russia).

Methods. Preparation of PCL/Chloramphenicol/Hexafluoro-2-propanol solutions. The polymer solution with concentration of 2 wt.% was prepared by dissolving PCL and Chloramphenicol with a weight ratio of 5, 15, and 25 wt./wt.% in HFIP and left for 24 h at room temperature. Before processing, the solutions were stirred for 20 min at room temperature until total homogenization.

Preparation of PCL fibers by electrospinning. The solution was electrospun (NANON-01A, MECC CO., LTD., Japan) from 10 ml syringe with a G22 needle and a 1,5 ml/h flow rate. A 20 kV voltage was applied to the tip of the needle attached to the syringe when a fluid jet was ejected. The resulting fibers were collected on 200 mm diameter drum collectors with 200 rpm set rotation speed, 130 mm syringe-collector distance and 15 mm/min syringe linear speed.

Thin film formation on the surface of titanium disks with a calcium phosphate coating deposited by the PEO method is described in our previous publication [1].

Results. Results of morphological and chemical composition studies of obtained polymer-drug films on the PEO coatings are presented in Figure 1.

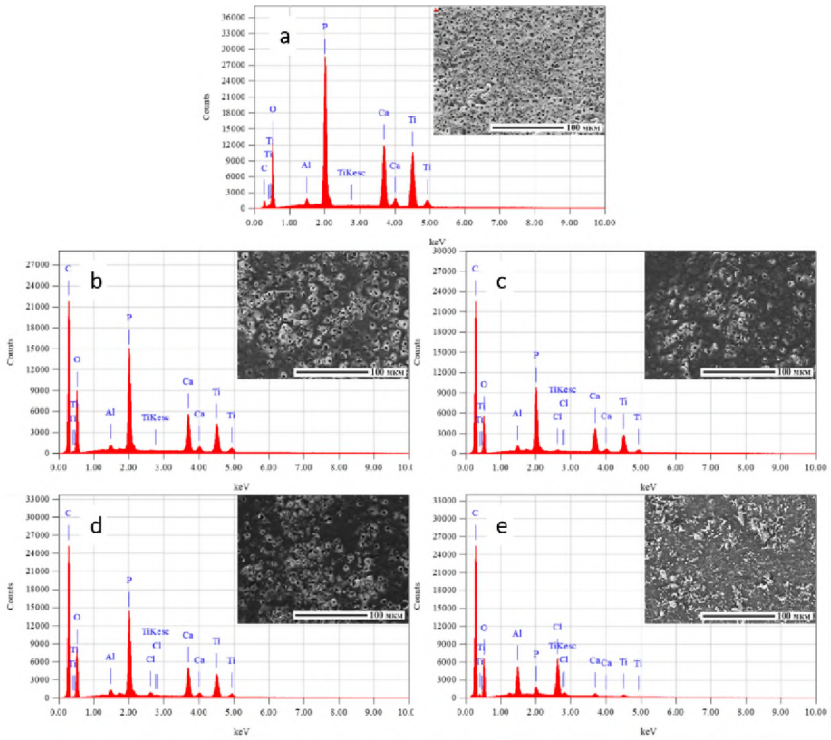

Fig. 1. SEM-images and the results of EDAX-analysis of PEO coatings: a- untreated, b - impregnated with pure PCL/HFIP solution, c,d,e - impregnated with pure PCL/HFIP/ Chloramphenicol solution with a weight ratio of 5, 15, and 25 wt./wt.%, respectively

It can be clearly concluded form the Fig. 1 that high drug loading (up to 25 wt./wt.%) leads to the Chloramphenicol crystal formation on the surface of samples.

Meanwhile, all the obtained solutions performed good spinnability forming fibers with a normal diameter distribution and no defects (Fig. 2). There are no visible crystals on the surface of scaffolds electrospun from 25 wt./wt.% Chloramphenicol solution.

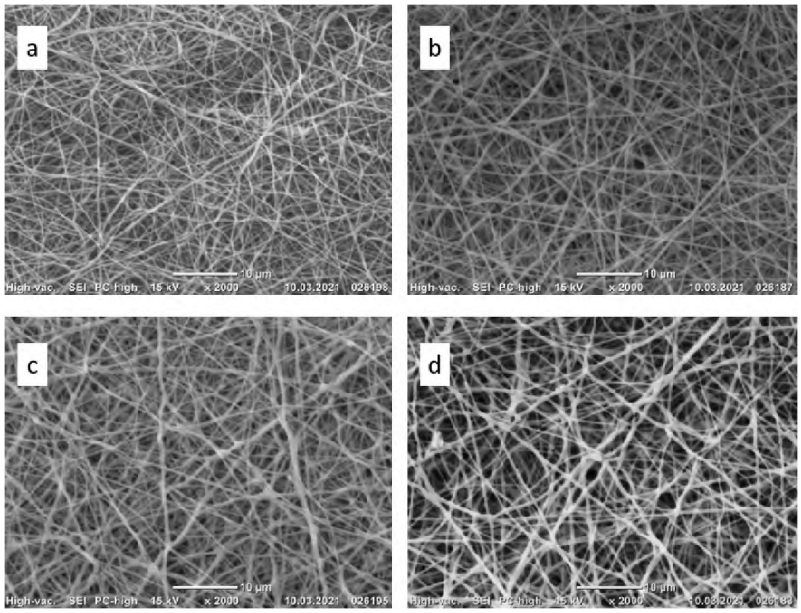

Fig. 2. SEM-images of the electrospun scaffolds: PCL/HFIP/ Chloramphenicol solution with a weight ratio of 0 (a), 5 (b), 15 (c), and 25 (d) wt./wt.%, respectively

It is important to mention that stable electrospinning process can only be achieved at flow rates up to 1,5 ml/h due to low viscosity of obtained solutions what leads to lower process productivity compared to those with higher PCL/HFIP ratios.

Conclusion. Thus, it was shown that the biodegradable polymeric antibacterial coatings on the metal-based implants surface antibacterial could be fabricated by two different techniques using one type of precursor solution. Electrospinning is favorable if non-crystal form of drug deposition is required.

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