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PULSED E-BEAM IRRADIATION TO MODULATE DRUG RELEASE FROM POLYMERIC FIBERS

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ИСПОЛЬЗОВАНИЕ ИМПУЛЬСНОГО ЭЛЕКТРОННОГО ПУЧКА ДЛЯ МОДУЛИРОВАНИЯ ВЫСВОБОЖДЕНИЯ ЛЕКАРСТВЕННЫХ СРЕДСТВ ИЗ ПОЛИМЕРНЫХ СКАФФОЛДОВ

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Аннотация. *В работе рассмотрен вопрос влияния обработки импульсным электронным пучком на параметры высвобождения инкорпорированных в полимерные волокна лекарственных средств. В качестве экспериментальной модели использованы синтетические полимерные нетканые скаффолды, полученные методом электроспиннинга. Полимер – поли (ε-капролактон), лекарственное средство — хлорамфеникол 5, 15 и 25 масс.%. Образцы скаффолдов были облучены на импульсном электронном ускорителе, причем поглощенная доза составила 25, 50 и 75 кГр (один импульс – 25 кГр). Было показано, что обработка электронным пучком влияет на профиль высвобождения лекарственного средства, однако эффекты зависят как изначального содержания лекарства в полимерной матрице, так и от количества импульсов.*

Introduction Polymeric electrospun scaffolds are widely considered as suitable candidates as for drug delivery and controlled release [1]. However, most polymers used as matrices are synthetic ones. They are hydrophobic, what affects the process of matt swelling and followed drug release. In our previous works, we have already demonstrated that pulsed e-beam irradiation can increase the rate of paracetamol [2] and ibuprofen [3] release from highly hydrophobic poly (ε-caprolactone) (PCL) electrospun fibers. The aim of this work was to access the influence of increasing the number of impulses on the chloramphenicol (CHL) release from PCL electrospun scaffolds.

Research methods. Materials. PCL (Mw = 80,000) was purchased from Sigma–Aldrich (St. Louis, MO, USA), Chloramphenicol powder (Pharmstandart, Moscow, Russia) was used as purchased. Phosphate Buffer Saline (PBS, pH 7.4) used for drug release modelling was purchased from Biolot (Moscow, Russia).

Methods. Preparation of PCL-CHL fibers by electrospinning is described in our previous publication [4]. Electron beam irradiation of PCL-CHL scaffolds was conducted using pulsed e-beam accelerator TEA–500

within 25–75 kGy range of absorbed dose in the air under atmospheric pressure. The electron beam diameter — 5 cm, beam kinetic energy – 350–400 keV, current – 6–9 kA, duration of 1 pulse at half-maximum – 60 ns, and the electron beam energy – 90 J. The 50 μm thick titanium foil was used in the accelerator exit window.

Drug release was studied by drug dissolution testing according to standard protocol. Probes were analyzed by HPLC (Agilent 1100, Agilent technologies, HP, CA, USA) on C18 column (5 μm). Parameters set: 45/55 ACN/water, elution time – 3 min, volume – 3 μL.

Results. Immediately after the e-beam irradiation scaffolds were cut into samples at the drug dissolution test were performed. Drug concentration observed in probes was recalculated to "drug released"/" drug loaded" ratio. Results of drug release – time dependance calculation are presented in Figure 1.

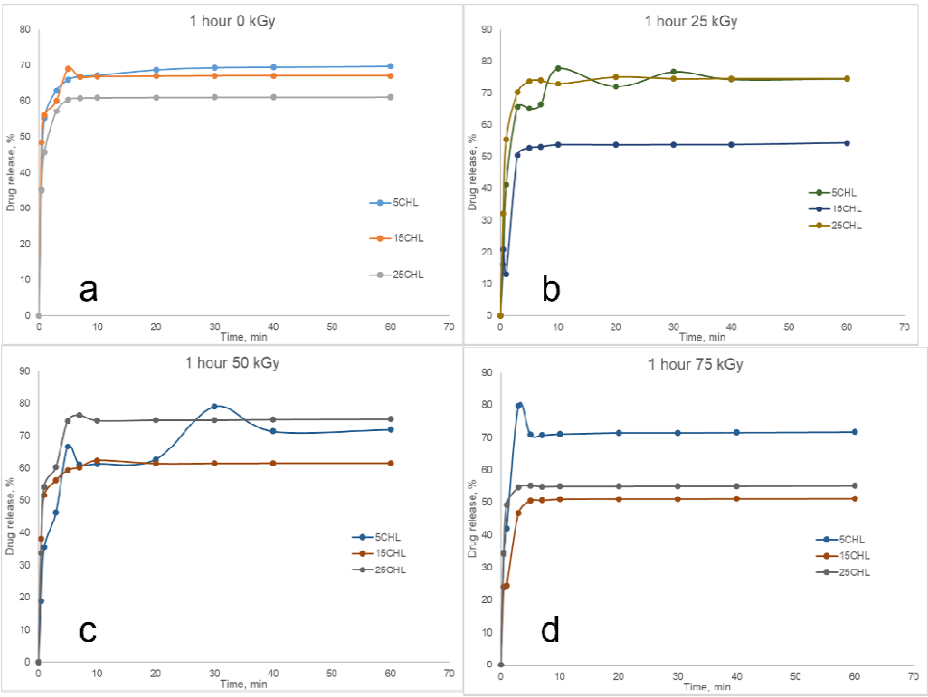

Fig. 1. Chloramphenicol release profiles: a – untreated, b, c, d, e – irradiated with 1, 2 and 3 impulses, respectively

It cannot be clearly concluded form the Fig. 1 how drug loading and number of pulses effect drug release. For 20 wt.% CHL there is a tendency for increase in the release rate after one and two impulses, the third impulse leads to a decrease even compared to the non-irradiated sample. Scaffolds loaded with 15 wt.% of CHL show a major decrease after one pulse and 5 wt.% loaded ones are the least affected.

As we investigated before, main effects of e-beam irradiation of scaffolds are changes in the molecular weight and crystallinity of the polymer. The crystallinity of the obtained samples was calculated from the XRD-data (Fig. 2).

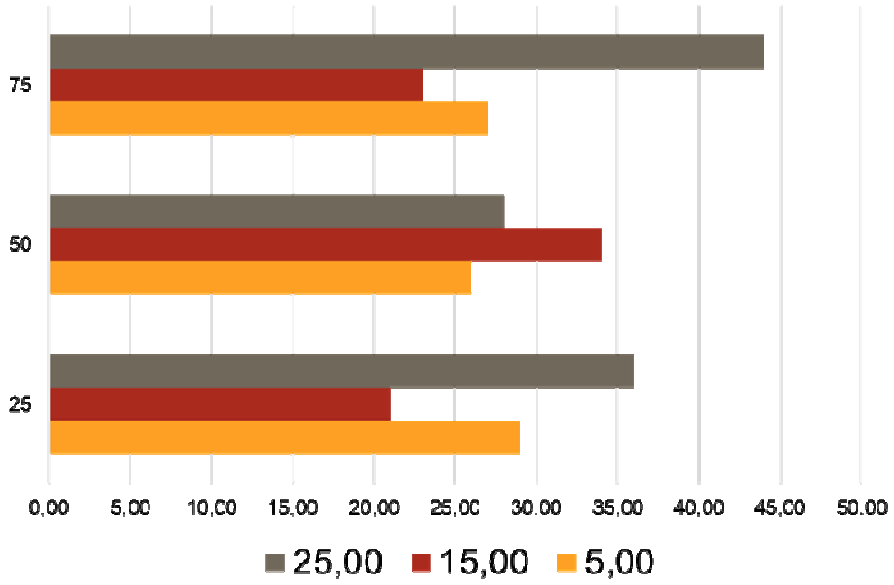

Fig. 2. Crystallinity of the electrospun scaffolds after e-beam irradiation: PCL–CHL 5 wt.% – yellow bars, 15 wt.% – red bars, 25 wt.% – grey bars

Results of the crystallinity evaluation correspond well with drug release profiles shown above. The higher crystallinity is – the harder it is for drug molecules to leave the matrix. Samples with the lowest drug concentration are shown not to change in crystallinity; loaded with 15 wt.% has a maximum after two impulses and for 24 wt.% the crystallinity decreases after two impulses and then reaches maximum after the dose of 75 kGy is absorbed.

Conclusion. Thus, it was shown that the absorbed dose is not the only crucial parameter in the process of the e-beam irradiation. Changes in the polymer molecules orientation and the ability of the drug to diffuse from the matrix is dependent on the drug dose and the absorbed irradiation dose.

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